Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Mehra MR, Goldstein DJ, Uriel N, et al. Two-year outcomes with a magnetically levitated cardiac pump in heart failure. N Engl J Med 2018;378:1386-95. DOI: 10.1056/NEJMoa1800866

TABLE OF CONTENTS

STUDY ORGANIZATION 4

Study Oversight Committee 4

Clinical Events Committee (CEC) 4

Data Safety Monitoring Board (DSMB) 4

Investigator List 5

Role of Study Sponsor 7

INCLUSION/EXCLUSION CRITERIA[1] 8

Inclusion Criteria 8

Exclusion Criteria 9

MAJOR ADVERSE EVENT DEFINITIONS[1] 10

PUMP CHARACTERISTICS[1] 13

SAMPLE SIZE CALCULATION 14

SUSPECTED PUMP THROMBOSIS NARRATIVES 15

SUPPLEMENTARY FIGURES 22

Figure S1. CONSORT Diagram for the MOMENTUM 3 Two-Year Cohort 22

Figure S2. Subjects Failing the Primary End Point 23

Figure S3. Actuarial All Cause Survival (Per Protocol Population) 24

Figure S4. Freedom from Disabling Stroke (Per Protocol Population) 25

Figure S5. Freedom from Reoperation to Replace or Remove Pump (Per Protocol Population) 26

Figure S6. Freedom from Suspected or Confirmed Pump Thrombosis (Per Protocol Population) 27

Figure S7. Stroke Events and Severity (Per Protocol Population) 28

Figure S8. Mean Arterial Pressure (MAP) over Time (Per Protocol Population) 29

Figure S9. Lactate Dehydrogenase (LDH) Levels over Time 30

Figure S10. INR Levels over Time 31

Figure S11. Competing Risk Analyses (Per Protocol Population) 32

Figure S12. Subgroup Analyses of the Primary Endpoint for Age, Gender, Race, Implant Strategy and INTERMACS Profile between Treatment Groups (Intent to Treat Population) 33

Figure S13. Functional Status and Quality of Life (Per Protocol Population) 34

SUPPLEMENTARY TABLES 36
Table S1. Severity of Illness and Concomitant Medications and Interventions 36
Table S2. INTERMACS Profile/Classification 37
Table S3. Urgent Heart Transplant for Device Malfunction 38
Table S4. Sensitivity Analysis of Primary Endpoint (Intention to Treat) 38
Table S5. Summary of Suspected Pump Thrombosis Events 39
Table S6. Stroke Risk-Factor Analysis (Per Protocol Population) 40
Table S7. Gastrointestinal (GI) Bleeding Analysis (Per Protocol Population) 40
Table S8. Subjects with Aspirin and Other Antiplatelet Therapy (Per Protocol Population) 41
Table S9. Subjects with Normal, Sub, and Supratherapeutic INR Values over Time (Per Protocol Population) 42
Table S10. Renal and Hepatic Function over Time 43
Table S11. Adjudicated Causes of Death (Per Protocol Population) 44
REFERENCES 45

STUDY ORGANIZATION

Study Oversight Committee

Mandeep R. Mehra, MD (chair)	Brigham and Women's Hospital, Boston, MA
Daniel Goldstein, MD	Montefiore Medical Center, NY, NY
Joseph Cleveland, MD	University of Colorado, Denver, CO
Nir Uriel, MD	University of Chicago, Chicago, IL

Clinical Events Committee (CEC)

Valluvan Jeevanandam, MD (chair)	University of Chicago, Chicago, IL
Steve Gordon, MD	Cleveland Clinic Foundation, Cleveland, OH
Jeffrey Teuteberg, MD	Stanford University Medical Center, Palo Alto, CA
Carole Thomas, MD	Advocare Neurology of South Jersey, Lumberton, NJ

Data Safety Monitoring Board (DSMB)

William Holman, MD (chair)	University of Alabama at Birmingham, Birmingham, AL
Daniel Heitjan, PhD	Southern Methodist University, Houston, TX
Sharon Hunt, MD	Stanford University Medical Center, Palo Alto, CA
Stuart Russell, MD	Duke University Medical Center, Raleigh-Durham, NC
Benjamin Sun, MD	Abbott Northwestern Medical Center, Minneapolis, MN

Investigator List

Below is a list of investigators that contributed subjects to the Long Term cohort analysis

Investigators that contributed subjects to the 24-month cohort		
Principal Investigators	**Site Name**	**Location**
Yoshifumi Naka	Columbia University Medical Center	New York, NY
Mary Walsh	St. Vincent Medical Group	Indianapolis, IN
Carmelo Milano	Duke University Medical Center	Durham, NC
Akinobu Itoh	Barnes-Jewish Hospital	St. Louis, MO
David Dean	Piedmont Heart Institute	Atlanta, GA
Antone Tatooles	Advocate Christ Medical Center	Oak Lawn, IL
Ulrich Jorde	Montefiore Medical Center	Bronx, NY
Douglas Horstmanshof James Long	Integris Baptist Medical Center	Oklahoma City, OK
Brian Bruckner	Houston Methodist Hospital	Houston, TX
Sirtaz Adatya Gabriel Sayer (current PI)	University of Chicago Medical Center	Chicago, IL
Sanjeev Gulati Eric Skipper	Carolinas Medical Center	Charlotte, NC
Francis Pagani	University of Michigan	Ann Arbor, MI
Ranjit John	University of Minnesota	Minneapolis, MN
Robert Adamson	Sharp Memorial Hospital	San Diego, CA
Hari Mallidi Steven Singh Masahiro Ono (current PI)	Texas Heart Institute	Houston, TX
Christiano Caldeira	Tampa General Hospital	Tampa, FL
Scott Silvestry	Florida Hospital	Orlando, FL
Francis Downey	St. Luke's Medical Center	Milwaukee, WI
Michael McGrath Christopher Barreiro (current PI)	Sentara Norfolk General Hospital	Norfolk, VA
Aditya Bansal	Ochsner Medical Center	New Orleans, LA
Michael Givertz	Brigham and Women's Hospital	Boston, MA
Claudius Mahr Nahush Mokadam	University of Washington Medical Center	Seattle, WA
John Um	University of Nebraska Medical Center	Omaha, NE
Anelechi Anyanwu	Mount Sinai Hospital	New York, NY
Ahmet Kilic Bassam Shukrallah (current PI)	Ohio State University	Columbus, OH
John Ransom	Baptist Health Medical Center	Little Rock, AR
Stephen Bailey	Allegheny Singer Research Institute	Pittsburgh, PA
Brett Sheridan Jason Katz (current PI)	University of North Carolina	Chapel Hill, NC

Investigators that contributed subjects to the 24-month cohort		
Principal Investigators	**Site Name**	**Location**
Jeffrey Morgan Hassan Nemeh (current PI)	Henry Ford Hospital	Detroit, MI
Walter Pae	Penn State Milton S. Hershey Medical Center	Hershey, PA
Margarita Camacho	Newark Beth Israel Medical Center	Newark, NJ
Pavan Atluri	Hospital of the University of Pennsylvania	Philadelphia, PA
Leway Chen	University of Rochester Medical Center	Rochester, NY
David Majure Farooq Sheikh (current PI)	Washington Hospital Center	Washington, DC
Marc Katz Steven Fiser (current PI)	Bon Secours Heart & Vascular Institute	Richmond, VA
Mary Keebler	Vanderbilt Heart and Vascular Institute	Nashville, TN
John Kern Leora Yarboro (current PI)	University of Virginia Medical Center	Charlottesville, VA
Abeel Mangi	Yale School of Medicine	New Haven, CT
Allen Anderson	Northwestern Memorial Hospital	Chicago, IL
Charles Klodell Thomas Beaver (current PI)	Shands at the University of Florida	Gainesville, FL
John Entwistle III	Thomas Jefferson University Hospital	Philadelphia, PA
Marin Strueber Asghar Khagani Marzia Leacche (current PI)	Spectrum Health Butterworth Hospital	Grand Rapids, MI
Shashank Desai Ramesh Singh	Inova Fairfax Hospital	Falls Church, VA
Shahab Akhter Takushi Kohmoto (current PI)	University of Wisconsin Hospital and Clinics	Madison, WI
Don Chomsky	St. Thomas Hospital	Nashville, TN
Igor Gregoric	Memorial Hermann Hospital	Houston, TX
Vigneshwar Kasirajan Daniel Tang (current PI)	Virginia Commonwealth University Medical Center	Richmond, VA
John Stulak	Mayo Clinic	Rochester, MN
Meredith Brisco Adrian Van Bakel (current PI)	Medical University of South Carolina	Charleston, SC
Nader Moazami Edward Soltesz (current PI)	The Cleveland Clinic Foundation	Cleveland, OH
Andreas Brieke	University of Colorado Hospital	Aurora, CO
Jay Bhama	University of Iowa Hospitals and Clinics	Iowa City, IA

*Sites with two names have co-principal investigators (PIs). Current PIs are noted in cases where the previous PI has left, and previous PIs are also listed.

Below is a list of additional Investigators that also contributed subjects to the full cohort.

Principal Investigator(s)*	Site Name	Location
Brian Lima Shelley Hall (current PI)	Baylor University Hospital	Dallas, TX
Eric Adler	University of California San Diego Medical Center	San Diego, CA
Frederick Tibayan	Oregon Health & Science University	Portland, OR
Mark Slaughter	Jewish Hospital	Louisville, KY
Robert Kormos	University of Pittsburgh Medical Center	Pittsburgh, PA
Francisco Arabia	Cedars-Sinai Medical Center	Los Angeles, CA
David D'Alessandro	Massachusetts General Hospital	Boston, MA
Maya Guglin	University of Kentucky - Saha Cardiovascular Research Center	Lexington, KY
I-Wen Wang	IU Health Methodist Hospital	Indianapolis, IN
Richard Ha William Hiesinger (current PI)	Stanford University Medical Center	Stanford, CA
Karol Mudy	Abbott Northwestern Hospital	Minneapolis, MN
J. David Vega	Emory University Hospital	Atlanta, GA
Guilherme Oliveira Benjamin Medalion	University Hospitals of Cleveland	Cleveland, OH
Craig Selzman	University of Utah Hospital and Clinics (VA Medical Center)	Salt Lake City, UT
Robert Kincade	Sutter Memorial Hospital	Sacramento, CA
Brett Sheridan	California Pacific Medical - Ctr. Pacific Campus	San Francisco, CA
Ryan Tedford Glenn Whitman (current PI)	Johns Hopkins University Hospital	Baltimore, MD

*Sites with two names have co-principal investigators (PIs). Current PIs are noted in cases where the previous PI has left, and previous PIs are also listed.

Role of Study Sponsor

(a) Trial Design: The Sponsor designed the MOMENTUM 3 trial in collaboration with clinical advisors and the trial oversight committee with feedback from the FDA.

(b) Site Selection: The Sponsor selected experienced centers per established site qualification procedures. Qualification visits were conducted to ensure that investigators were qualified by training, education and experience and had adequate resources, staffing and facilities to conduct the trial.

(c) Patient Assessment, Enrollment, Site Supervision & Data Collection: The Sponsor was responsible for training the clinical sites on patient eligibility assessment, enrollment procedures, and data collection requirements; once trained, site personnel were responsible for conducting these activities under supervision of the principal investigator.

(d) Data Analysis: The Sponsor was responsible for analyzing the study data per the pre-specified Statistical Analysis Plan (SAP) and an independent statistician was responsible for verifying all the results.

(e) Manuscript Writing, Revision and Publication Decisions: The manuscript writing, revision and decision to submit the paper for publication were driven by the National PI's, the chair of the MOMENTUM 3 Publication and Presentation (P&P) Committee and its members along with the authors in compliance with the P&P Charter; the manuscript was written by the first author, all versions fully controlled by him in collaboration with the other authors; the Sponsor assisted with data requests under the direction of the corresponding author. The decision to submit the paper rested with the P and P committee and principally its chair.

INCLUSION/EXCLUSION CRITERIA[1]

Inclusion Criteria

1) Patient or legal representative has signed Informed Consent Form (ICF)
2) Age ≥ 18 years
3) Body Surface Area (BSA) ≥ 1.2 m2
4) NYHA Class III with dyspnea upon mild physical activity or NYHA Class IV
5) Left Ventricular Ejection Fraction (LVEF) ≤ 25%
6) a) Inotrope dependent

   OR

   b) Cardiac Index (CI) < 2.2 L/min/m^2, while <u>not</u> on inotropes and patient must also meet <u>one</u> of the following:

   - On optimal medical management (OMM), based on current heart failure practice guidelines for at least 45 out of the last 60 days and are failing to respond
   - Advanced heart failure for at least 14 days AND dependent on intra-aortic balloon pump (IABP) for at least 7 days,
7) Females of child-bearing age must agree to use adequate contraception

Exclusion Criteria

1) Etiology of heart failure due to or associated with uncorrected thyroid disease, obstructive cardiomyopathy, pericardial disease, amyloidosis, or restrictive cardiomyopathy
2) Technical obstacles which pose an inordinately high surgical risk, in the judgment of the investigator
3) Existence of ongoing mechanical circulatory support (MCS) other than IABP
4) Positive pregnancy test if of childbearing potential
5) Presence of mechanical aortic cardiac valve that will not be either converted to a bioprosthesis or oversewn at the time of LVAD implant
6) History of any organ transplant
7) Platelet count < 100,000 x 10^3/L (< 100,000/ml)
8) Psychiatric disease/disorder, irreversible cognitive dysfunction or psychosocial issues that are likely to impair compliance with the study protocol and LVAS management
9) History of confirmed, untreated abdominal aortic aneurysm (AAA) > 5 cm in diameter within six (6) months of enrollment
10) Presence of an active, uncontrolled infection
11) Intolerance to anticoagulant or antiplatelet therapies or any other peri/post-operative therapy that the investigator will require based upon the patient's health status
12) Presence of any one of the following risk factors for indications of severe end organ dysfunction or failure:
    a) An international normalized ratio (INR) ≥ 2.0 not due to anticoagulation therapy
    b) Total bilirubin > 43 µmol/L (2.5 mg/dl), shock liver, or biopsy proven liver cirrhosis
    c) History of severe chronic obstructive pulmonary disease (COPD) defined as the ratio of forced expiratory volume in one second to forced vital capacity (FEV_1/FVC) < 0.7, and FEV_1 < 50% predicted
    d) Fixed pulmonary hypertension with a most recent pulmonary vascular resistance (PVR) ≥ 8 Wood units that is unresponsive to pharmacologic intervention
    e) History of stroke within 90 days prior to enrollment, or a history of cerebrovascular disease with significant (> 80%) uncorrected carotid artery stenosis
    f) Serum Creatinine ≥ 221 µmol/L (2.5 mg/dl) or the need for chronic renal replacement therapy
    g) Significant peripheral vascular disease (PVD) accompanied by rest pain or extremity ulceration
13) Patient has moderate to severe aortic insufficiency without plans for correction during pump implant
14) Pre albumin < 150 mg/L (15mg/dL) or Albumin < 30g/L (3 g/dL) (if only one available); pre albumin < 150 mg/L (15mg/dL) and Albumin < 30g/L (3 g/dL) (if both available)

15) Planned Bi-VAD support prior to enrollment
16) Patient has known hypo- or hyper coagulable state such as disseminated intravascular coagulation and heparin induced thrombocytopenia (HIT)
17) Participation in any other clinical investigation that is likely to confound study results or affect the study
18) Any condition other than heart failure that could limit survival to less than 24 months

MAJOR ADVERSE EVENT DEFINITIONS[1]

Bleeding

An episode of SUSPECTED INTERNAL OR EXTERNAL BLEEDING that results in one or more of the following:

a. Death,
b. Reoperation,
c. Hospitalization,
d. Transfusion of red blood cells as follows:
   - If transfusion is selected, then apply the following rules:

     During first 7 days Post-implant
     - ≥ 50 kg: ≥ 4U packed red blood cells (PRBC) within any 24 hour period during first 7 days post- implant.
     - <50 kg: ≥20 cc/kg packed red blood cells (PRBC) within any 24 hour period during the first 7 days post-implant

     After 7 days Post-implant*
     - Any transfusion of packed red blood cells (PRBC) after 7 days following implant with the investigator recording the number of units given. (Record number of units given per 24 hour period).

Note: Hemorrhagic stroke is considered a neurological event and not as a separate bleeding event.

*Any transfusion of ≥ 2U packed red blood cells (PRBC) after 7 days following implant will be considered a serious bleed

Cardiac Arrhythmias

Any documented arrhythmia that results in clinical compromise (e.g., diminished VAD flow, oliguria, pre-syncope or syncope) that requires hospitalization or occurs during a hospital stay. Cardiac arrhythmias are classified as 1 of 2 types:

1) Sustained ventricular arrhythmia requiring defibrillation or cardioversion.
2) Sustained supraventricular arrhythmia requiring drug treatment or cardioversion.

Device Thrombosis

Device thrombosis is an event in which the pump or its conduits contain a thrombus that results in or could potentially induce circulatory failure. Suspected device thrombus is an

event in which clinical or MCSD parameters suggest thrombus on the blood contacting components of the pump, cannulae, or grafts. Signs and symptoms should include at least 2 of the 3 following criteria:

a. Presence of hemolysis
b. Worsening heart failure or inability to decompress the left ventricle
c. Abnormal pump parameters

Suspected pump thrombus should be accompanied by 1 or more of the following events or interventions:

i. Treatment with intravenous anticoagulation (e.g., heparin), intravenous thrombolytics (e.g., tPA), or intravenous antiplatelet therapy (e.g., eptifibatide, tirofiban)
ii. Pump replacement
iii. Pump explantation
iv. Urgent transplantation (UNOS status 1A)
v. Stroke
vi. Arterial non-CNS thromboembolism
vii. Death

Confirmed device thrombus is an event in which thrombus is confirmed by Sponsor returned product analysis to be found within the blood contacting surfaces of device inflow cannula or outflow conduit or grafts. This can also be reported via direct visual inspection or by incontrovertible contrast radiographic evidence or by the absence of an appropriate Doppler flow signal that results in or could potentially induce circulatory failure or result in thromboembolism.

Hemolysis*

A plasma-free hemoglobin value that is greater than 40 mg/dl, concomitant with a rise in serum LDH above three times the upper limit of normal, in association with clinical signs associated with hemolysis (e.g., anemia, low hematocrit, hyperbilirubinemia) occurring after the first 72 hours post-implant.

*Hemolysis in the presence of worsening heart failure or inability to decompress the left ventricle or abnormal pump parameters is reported as suspected device thrombosis, not as hemolysis

Hepatic Dysfunction

An increase in any two of the following hepatic laboratory values (total bilirubin, aspartate aminotransferase/AST and alanine aminotransferase/ALT) to a level greater than three times the upper limit of normal for the hospital, beyond 14 days post-implant (or if hepatic dysfunction is the primary cause of death).

Major Infection

A clinical infection accompanied by pain, fever, drainage and/or leukocytosis that is treated

by anti-microbial agents (non-prophylactic). A positive culture from the infected site or organ should be present unless strong clinical evidence indicates the need for treatment despite negative cultures. The general categories of infection are listed below:

Localized Non-Device Infection
Infection localized to any organ system or region (e.g. mediastinitis) without evidence of systemic involvement (see sepsis definition), ascertained by standard clinical methods and either associated with evidence of bacterial, viral, fungal or protozoal infection, and/or requiring empirical treatment.

Percutaneous Site and/or Pocket Infection
A positive culture from the skin and/or tissue surrounding the drive line or from the tissue surrounding the external housing of a pump implanted within the body, coupled with the need to treat with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis.

Internal Pump Component, Inflow or Outflow Tract Infection
Infection of blood-contacting surfaces of the LVAD documented by positive site culture.

Sepsis
Evidence of systemic involvement by infection, manifested by positive blood cultures and/or hypotension.

Neurologic Dysfunction
Any new, temporary or permanent, focal or global neurological deficit, ascertained by a standard neurological history and examination administered by a neurologist or other qualified physician and documented with appropriate diagnostic tests and consultation note; or an abnormality identified by surveillance neuroimaging. The examining physician will classify the event as defined below:

a. Transient ischemic attack*, defined as an acute transient neurological deficit conforming anatomically to arterial distribution cerebral ischemia, which resolves in < 24 hours and is associated with no infarction on brain imaging (head CT performed >24 hours after symptom onset; or MRI)
b. Ischemic Stroke*: a new acute neurologic deficit of any duration associated with acute infarction on imaging corresponding anatomically to the clinical deficit, or a clinically covert ischemic stroke seen by surveillance imaging, without clinical findings of stroke or at the time of event recognition.
c. Hemorrhagic Stroke*: a new acute neurologic deficit attributable to intracranial hemorrhage (ICH), or a clinically covert ICH seen by surveillance imaging, without clinical findings of ICH at the time of event recognition.
d. Encephalopathy: Acute new encephalopathy** due to hypoxic-ischemic injury (HIE), or other causes, manifest as clinically evident signs or symptoms, or subclinical electrographic seizures found by complete neurological diagnostic evaluation to be attributable to acute global or focal hypoxic, or ischemic brain injury not meeting one

of ischemic stroke or ICH events as defined above.

e. Seizure of any kind
f. Other neurological event (non-CNS event): examples include neuro muscular dysfunction or critical care neuropathy

*Modified Rankin Score will be used to classify the severity of all strokes
**Acute encephalopathy is a sign or symptom of some underlying cerebral disorder, and is manifest as depressed consciousness with or without any associated new global or multifocal neurologic deficits in cranial nerve, motor, sensory, reflexes and cerebellar function.

Renal Dysfunction
Two categories of renal dysfunction will be identified:

Acute Renal Dysfunction
Abnormal kidney function requiring dialysis (including hemofiltration) in Subjects who did not require this procedure prior to implant, or a rise in serum creatinine of greater than 3 times baseline or greater than 5 mg/dL sustained for over 48 hours.

Chronic Renal Dysfunction
An increase in serum creatinine of 2 mg/dl or greater above baseline, or requirement for hemodialysis sustained for at least 90 days.

Respiratory Failure
Impairment of respiratory function requiring reintubation, tracheostomy or (the inability to discontinue ventilatory support within six days (144 hours) post-VAD implant. This excludes intubation for reoperation or temporary intubation for diagnostic or therapeutic procedures.

Right Heart Failure
Symptoms and signs of persistent right ventricular dysfunction requiring RVAD implantation, or requiring inhaled nitric oxide or inotropic therapy for a duration of more than 1 week at any time after LVAD implantation.

PUMP CHARACTERISTICS[1]

The investigational Centrifugal Flow Pump being studied in the MOMENTUM 3 trial has been described previously.[1,2] The pump is characterized by optimized fluid dynamics, with large blood-flow passages designed to prevent stasis and avert thrombogenesis. The Pump leverages aspects of the commercially available control device[3] (an Axial Flow Pump with mechanical bearings) that provide high reliability and small size. The investigational pump includes a fully magnetically levitated rotor and a fixed artificial pulse every two (2) seconds.

The Centrifugal Flow Pump has a capacity to pump blood up to 10 L/min. As described previously, left ventricular blood is drawn into the inflow cannula along a central axis and is expelled at right angles by and between the impeller blades of a rotor rotating about the central axis.[1] Blood is angularly accelerated and travels around a volute before it is diffused to a desired pressure and flow rate by being directed tangentially into the outflow graft. The pump rotor is fully supported by magnetic levitation, obviating the need for mechanical or fluid bearings and essentially eliminating mechanical wear as a reliability factor. Both rotation and levitation of the rotor are accomplished using a single stator comprising iron pole pieces, a back-iron, copper coils, and position sensors. Measuring the position of a permanent magnet in the rotor and controlling the current in the drive and levitation coils enable active control of the radial position and rotational speed of the rotor. Because the permanent magnet is attracted to the iron pole pieces, the rotor passively resists excursion in the axial direction, whether translating or tilting. The electronics and software necessary to control motor drive and levitation are integrated into the lower housing with the stator; these components plus the rotor comprise the motor. The operating speed of the Centrifugal Flow Pump is in the range of 3,000 to 9,000 rpm. The artificial pulse mode is always enabled, which varies the rotor speed from the user set speed by 2000 rpm every two (2) seconds to produce changes in blood flow and arterial blood pressure.

SAMPLE SIZE CALCULATION

The objective was to demonstrate non-inferiority of the centrifugal-flow pump to the axial-flow pump for the primary outcome measure at 2-years. Enrollment first included 294 patients followed for 6-months which constituted the pre-specified short-term analysis and has been reported[1]. Enrollment continued to 366 patients, to provide sufficient power for the long-term analysis at 2-years for this report. We estimated that to achieve 80% power, 174 patients in each group were required (lower 95% confidence bound for the difference in primary endpoint success between treatment arms (centrifugal-flow pump minus axial-flow pump) greater than -10% would prove non-inferiority with a one-sided $\alpha = 0.025$ or 2 tailed p of <0.05) using the Farrington-Manning risk difference approach. To account for transplant or explant for recovery, 9 additional patients were included per arm. Thus, a total of 366 patients were required for the analysis, which included the 294 patients from the 6-month cohort (therefore 72 additional patients were further randomized and followed for 2-years). We have pre-specified a subsequent analysis powered for the secondary outcome measure of pump replacement at 2-years in 1028 patients[4]. These additional patients are not included in the present report.

SUSPECTED PUMP THROMBOSIS NARRATIVES

Two subjects in the Centrifugal Pump group experienced 2 suspected pump thrombosis events, and 27 subjects implanted with an Axial Flow Pump experienced 33 suspected or confirmed pump thrombosis events. Individual narratives for these patients appear below.

Centrifugal Flow Pump

Subject #1
Outcome/Status: Death due to heart failure
Subject implanted with Centrifugal Flow Pump developed evidence of hemolysis at day 191 post-VAD implantation with LDH rising to 727 U/L. There were also signs of worsening heart failure and abnormal pump parameters. The subject was hospitalized and managed medically. After discharge, the Subject experienced worsening heart failure. The subject was transferred to hospice and eventually expired on day 383. The cause of death was adjudicated as heart failure. No autopsy was performed per the subject's wishes and the device was not recovered for analysis.

Subject #2
Outcome/Status: Death due to cardiac arrhythmia causing cardiac arrest
Subject implanted with Centrifugal Flow Pump developed evidence of worsening heart failure at day 241 post-VAD implantation, with LDH rising from 120 to 166 U/L. There was also evidence of abnormal pump parameters. Log files revealed evidence of complete inflow or outflow obstruction. The subject was unable to be anticoagulated due to recent hemorrhagic stroke, and Coumadin had been discontinued for 4 days at time of suspected pump thrombosis. The pump was deactivated on day 244. The subject expired on day 270, and the cause of death was adjudicated as cardiac arrhythmia causing cardiac arrest. No autopsy was performed per the subject's wishes and the device was not recovered for analysis.

Axial Flow Pump

Subject #1
Outcome/Status: Urgent transplant
Subject implanted with an Axial Flow Pump admitted for system controller alarms at day 68 post-VAD implantation with suspicion of pump thrombosis, developed evidence of hemolysis with LDH baseline 225 rising to 1054 and evidence of worsening heart failure. Subject was continued on Aspirin, Warfarin and Persantine. On day 75, subject was started on IV Heparin and transplant evaluation was initiated. Subject continued to have multiple power spikes and driveline fault alarms. On day 81, subject was started on IV Dobutamine to treat decompensated heart failure and placed on transplant wait list with status 1A (LVAS malfunction). Subject remained

hospitalized and clinically stable. On day 92, urgent heart transplant was performed. The device was not recovered for analysis.

Subject #2
Outcome/Status: Urgent transplant
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 152 post-VAD implantation, with LDH baseline 298 rising to 1521 and evidence of worsening heart failure. The subject's status on the transplant waiting list was changed to 1A. On day 202, urgent heart transplant was performed. Pump thrombosis was confirmed by returned product analysis.

Subject #3
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed chest pain and dark urine at day 45 post-VAD implantation, evidence of hemolysis with LDH baseline 120 rising to 1286 on day 46 and evidence of worsening heart failure. On day 51, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #3; Event 2
Outcome/Status: Pump exchange followed by elective transplant
Subject with prior with Axial Flow Pump exchange was hospitalized on day 433 post-VAD implantation due to LDH rising to 718. On day 461, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis. On day 622, subject underwent elective transplant.

Subject #4
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed hematuria and low PI events at day 108 post-VAD implantation. On day 110, subject was admitted, developed evidence of hemolysis with LDH baseline 365 rising to 2102 and evidence of abnormal pump parameters. On day 111, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #5; Event 1
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 90 post-VAD implantation, with LDH baseline 329 rising to 2399 and evidence of worsening heart failure. On day 92, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #5; Event 2
Outcome/Status: Death due to stroke
Subject with prior Axial Flow Pump exchange was admitted for stroke at day 169 post initial VAD implantation (77 days after the pump exchange) and found to have evidence of hemolysis with LDH baseline 329 rising to 929 and evidence of worsening heart failure. Pump thrombosis was

suspected and hospitalization was prolonged due to stroke. On day 231, subject expired and the cause of death was adjudicated as hemorrhagic stroke. The device was not recovered for analysis.

Subject #6; Event 1
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 35 post-VAD implantation, with LDH rising to 1116 and evidence of worsening heart failure. On day 37, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #6; Event 2
Outcome/Status: Pump exchange (to non-study device)
Subject with prior Axial Flow Pump exchange developed evidence of hemolysis at day 54 post initial VAD implantation (17 days after the pump exchange), with LDH rising to 1209 and evidence of abnormal pump parameters. On Day 57 (20 days after the pump exchange), device was explanted and replaced with a non-study device. Pump thrombosis was confirmed by returned product analysis.

Subject #7
Outcome/Status: Urgent transplant
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 93 post-VAD implantation, with LDH baseline 177 rising to 684. On day 99, the subject was admitted for suspected pump thrombosis with evidence of PI events on LVAD interrogation and LDH rising to 868. Subject was continued on Aspirin and Warfarin and intravenous heparin was initiated. LDH remained stable to 600 and subject was discharged on day 101 with plans to change the subject's status on the transplant waiting list from 1B to 1A. Subject was readmitted on day 117 and urgent heart transplant was performed on day 118. The device was not recovered for analysis.

Subject #8; Event 1
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 80 post-VAD implantation, with LDH baseline 185 rising to 889 and evidence of worsening heart failure. On day 83, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #8; Event 2
Outcome/Status: Death due to pump thrombosis
Subject with prior Axial Flow Pump exchange developed evidence of hemolysis at day 93 post initial VAD implantation (10 days after the pump exchange), with LDH baseline 185 rising to 816, evidence of worsening heart failure and evidence of increased PI events. Subject declined a second pump exchange and was managed medically for suspected pump thrombosis. Subject expired on day 114 (31 days after the pump exchange); cause of death was adjudicated as pump thrombosis. The device was not recovered for analysis.

Subject #9; Event 1
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 17 post-VAD implantation, with LDH baseline 251 rising to 345 (day 20) and evidence of abnormal pump parameters indicating device malfunction. On day 22, pump was exchanged with another Axial Flow Pump for suspected pump thrombosis. Returned product analysis was inconclusive for pump thrombosis.

Subject #9; Event 2
Outcome/Status: Pump exchange (to non-study device)
Subject with prior Axial Flow Pump exchange developed evidence of hemolysis at day 70 post initial VAD implantation (48 days after the pump exchange), with LDH baseline 251 rising to 710 and evidence of abnormal pump parameters. On day 77 (55 days after the pump exchange), device was explanted and replaced with a non-study device. Pump thrombosis was confirmed by returned product analysis.

Subject #10
Outcome/Status: Medical management (patient ongoing at 2 years)
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 121 post-VAD implantation, with LDH baseline 208 rising to 259 and with evidence of abnormal pump parameters. Pump thrombosis was suspected, managed medically, and the subject was discharged on day 124.

Subject #11
Outcome/Status: Pump exchange followed by death due to infection
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 10 post-VAD implantation, with LDH baseline 236 rising to 1592, evidence of worsening heart failure and evidence of abnormal pump parameters. On day 22, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis. On day 382, subject expired and the cause of death was adjudicated as infection, pneumonia and aspiration.

Subject #12
Outcome/Status: Pump exchange (to non-study device)
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 28 post-VAD implantation, with LDH rising to 358 and evidence of worsening heart failure. On day 38, device was explanted and replaced with a non-study device. Pump thrombosis was confirmed by returned product analysis.

Subject #13
Outcome/Status: Elective transplant
Subject implanted with Axial Flow Pump developed, evidence of worsening heart failure and evidence of abnormal pump parameters at day 68 post-VAD implantation, with LDH rising from 245 to 1073. Pump thrombosis was suspected and was treated medically. On day 214, subject underwent elective heart transplant. The device was not recovered for analysis.

Subject #14
Outcome/Status: Elective transplant
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 17 post-VAD implantation, with LDH rising to 376 and evidence of abnormal pump parameters. Pump thrombosis was suspected and was treated medically. On day 155, elective heart transplant was performed.

Subject #15
Outcome/Status: Pump-exchange followed by elective heart transplant
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 323 post-VAD implantation with LDH rising from baseline 261 to 1300 U/L. There was also evidence of abnormal pump parameters. On day 323, subject also reported signs of ischemic stroke. Post-operatively, the subject's LV inflow cannula was misaligned causing concern for higher risk of device thrombosis. On day 359, subject pump was exchanged to Centrifugal Flow Pump (Compassionate Use). Returned product analysis was inconclusive for pump thrombosis. On day 524, subject underwent elective heart transplant.

Subject #16
Outcome/Status: Pump-exchange
Subject implanted with Axial Flow pump and was hospitalized 433 days post-VAD implantation for hemolysis with LDH rising from baseline 200 to 1000 U/L. On day 448, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #17
Outcome/Status: Urgent transplant
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 219 post-VAD implantation with LDH rising to 1913 U/L. There were also signs of worsening heart failure and abnormal pump parameters. On day 328, subject underwent urgent heart transplant. Pump thrombosis was not confirmed by returned product analysis.

Subject #18
Outcome/Status: Death due to pump thrombosis
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 385 post-VAD implantation with LDH rising from 248 at baseline to 1402 U/L. There was also evidence of worsening heart failure. On day 411, subject expired and the cause of death was adjudicated as pump thrombosis. The device was not recovered for analysis.

Subject #19
Outcome/Status: Death due to pump thrombosis
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 362 post-VAD implantation, with LDH rising to 2500 U/L. There was also evidence of abnormal pump parameters. On day 367, subject expired and the cause of death was adjudicated as pump thrombosis. Pump thrombosis was confirmed by returned product analysis.

Subject #20
Outcome/Status: Pump-exchange followed by death due to stroke
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 236 post-VAD implantation. There was also evidence of worsening heart failure. On day 245, the pump was exchanged with another Axial Flow Pump. Returned product analysis was inconclusive for pump thrombosis. On day 297, subject had hemorrhagic stroke. On day 298, subject expired and the cause of death was adjudicated as hemorrhagic stroke

Subject #21
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 285 post-VAD implantation after experiencing an Ischemic Stroke on day 266. LDH rose from 386 to 1053 U/L. There was also evidence of worsening heart failure. On day 296, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #22
Outcome/Status: Pump exchange followed by elective heart transplant
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 264 post-VAD implantation, with baseline LDH rising from 242 to 569 U/L. There was also evidence of abnormal pump parameters. On day 305, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis. On day 379, subject underwent an elective heart transplant.

Subject #23
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 728 post-VAD implantation, with LDH rising from 241 to 2067 U/L. There was also evidence of abnormal pump parameters. On day 729, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #24
Outcome/Status: Death due to device thrombosis
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 231 post-VAD implantation. There were also signs of worsening heart failure and abnormal pump parameters. On day 278, subject expired and the cause of death was adjudicated as device thrombosis. The device was not recovered for analysis.

Subject #25
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 270 post-VAD implantation, with LDH rising from 256 to 1100 U/L. There were also signs of worsening heart failure. On day 277, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

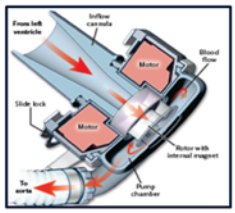
Subject #26
Outcome/Status: Pump exchange followed by death due to unknown cause
Subject implanted with Axial Flow Pump developed evidence of worsening heart failure at day 155 post-VAD implantation, with LDH rising from 385 to 3373 U/L. There was also evidence of abnormal pump parameters. On day 166, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis. On day 265, subject expired and the cause of death was unknown.

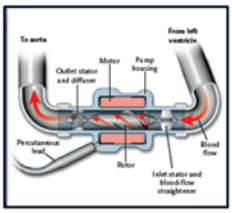
Subject #27; Event 1
Outcome/Status: Pump exchange
Subject implanted with Axial Flow Pump developed evidence of hemolysis at day 433 post-VAD implantation, with LDH rising from 206 to 983 U/L. There was also evidence of worsening heart failure. On day 459, pump was exchanged with another Axial Flow Pump. Pump thrombosis was confirmed by returned product analysis.

Subject #27; Event 2
Outcome/Status: Pump exchange to centrifugal flow pump
Subject with previous pump exchange for device thrombosis developed evidence of hemolysis at day 615 post-VAD implantation, with LDH rising to 1067 U/L. There was also evidence of worsening heart failure. On day 634, underwent placement of Centrifugal flow pump for emergency use. Pump thrombosis was confirmed by returned product analysis.

SUPPLEMENTARY FIGURES

Figure S1. CONSORT Diagram for the MOMENTUM 3 Two-Year Cohort





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
24-month follow-up

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

Centrifugal-Flow Pump
N=190

Axial-Flow Pump
N=176

Withdrawn before implant
N = 1
Death: 1

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

Per Protocol Population
N=361

Implanted with Centrifugal-Flow Pump
N=189

Implanted with Axial-Flow Pump
N=172

Status at 2 Years
Ongoing on support: 117
Death: 30
Transplant: 40
Explant to total artificial heart: 1
Withdrawal for non-compliance: 1

Median follow-up time: 706 days
Range: 9-802 days

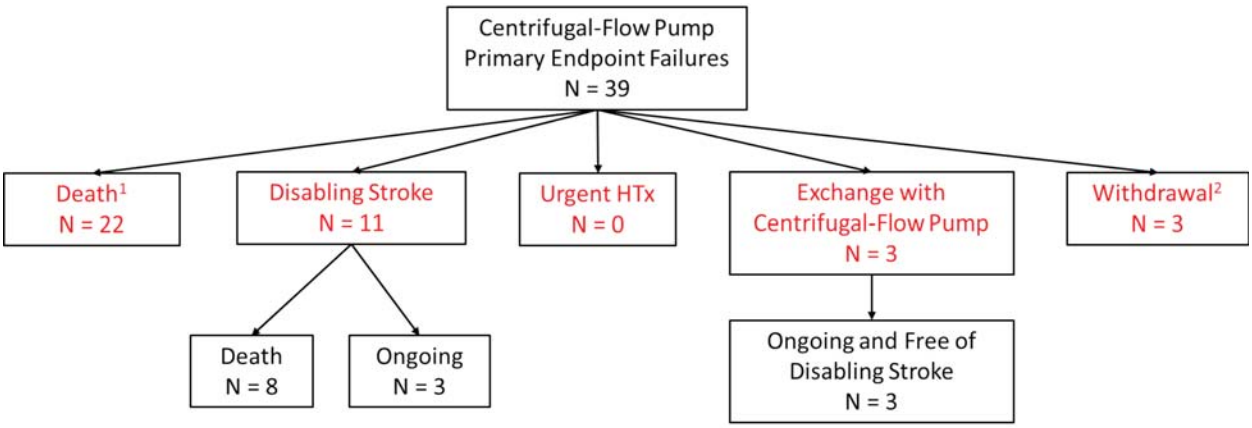
Status at 2 Years
Ongoing on support: 86
Death: 36
Transplant: 42
Explant for myocardial recovery: 1
Explant for infection: 1
Exchange to non-study or unassigned LVAD: 5
Withdrew consent: 1

Median follow-up time: 692 days
Range: 1-881 days

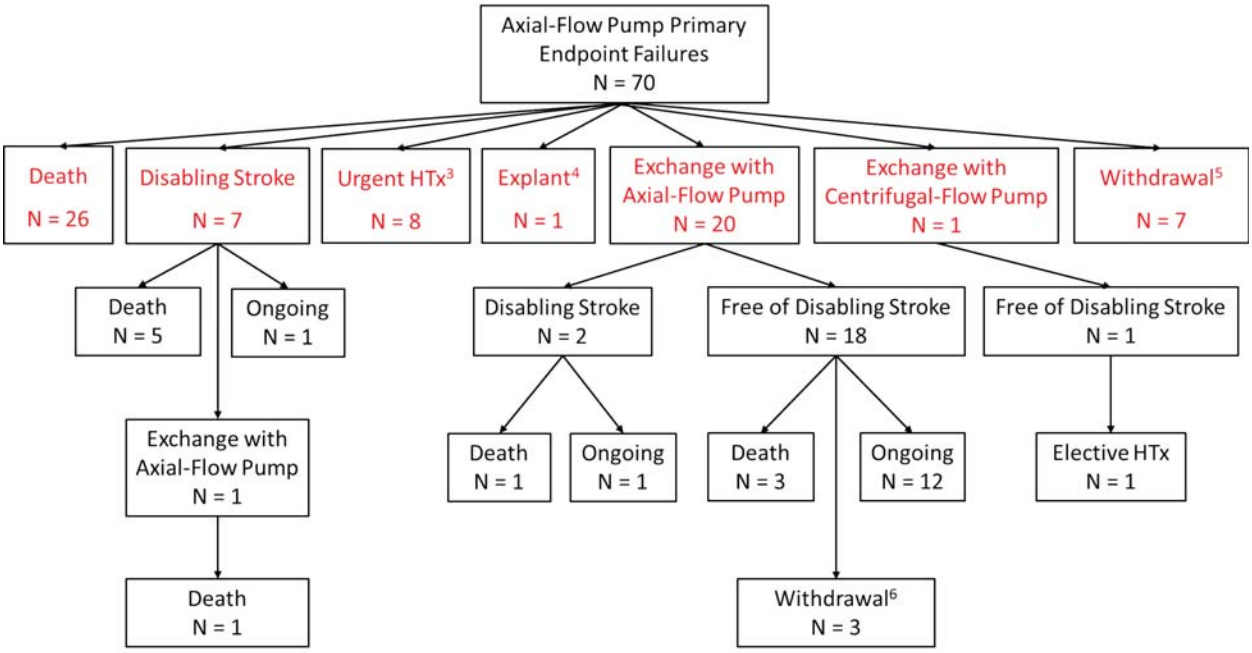
[1]Mehra MR, Naka Y, Uriel N, et al. A Fully magnetically Levitated Circulatory Pump for Advanced Heart Failure. N Engl J Med 2017;376(5):440-50.

Figure S2. Subjects Failing the Primary End Point

Events in red are the first event causing failure of the primary endpoint. The flow chart shows subsequent failure events if they were different from the first and the final outcome.

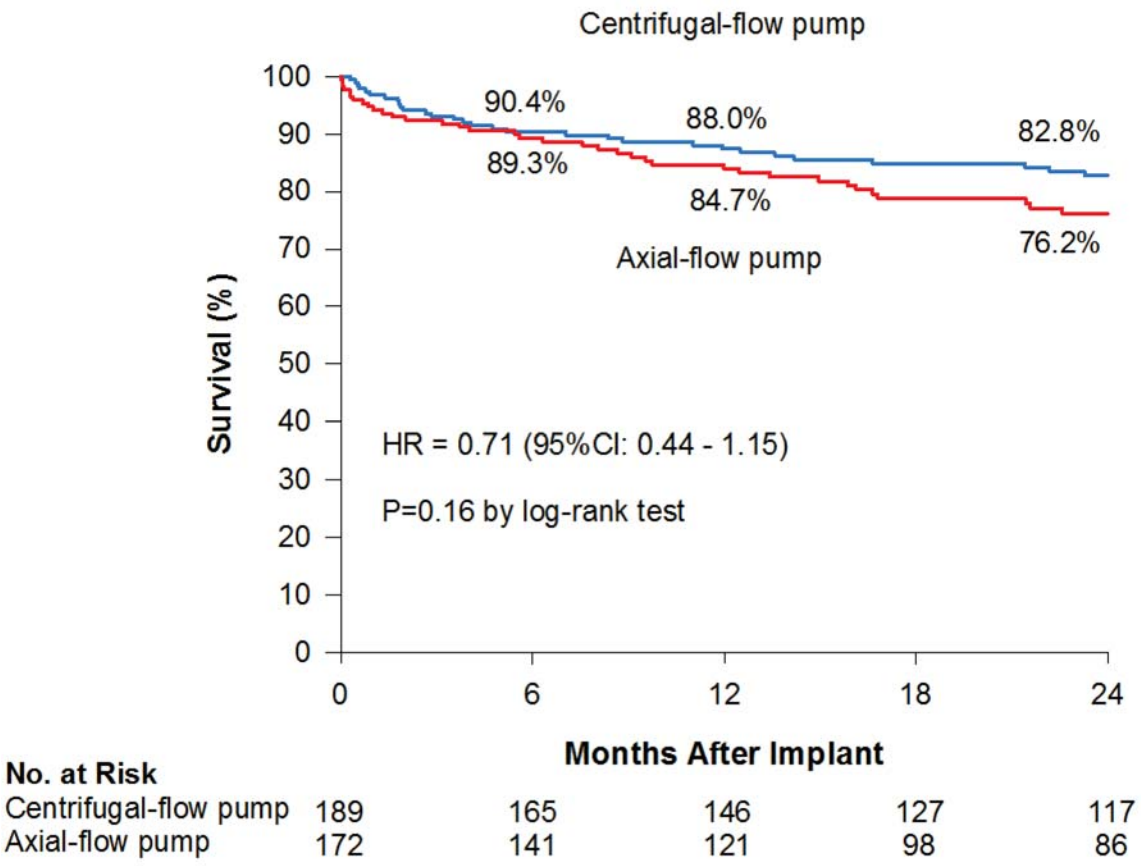


[1]Two subjects experienced disabling stroke but did not survive to 60 days post stroke for modified Rankin Score evaluation. [2]Includes withdrawal prior to implant (1), for noncompliance (1), and explant to total artificial heart (1).



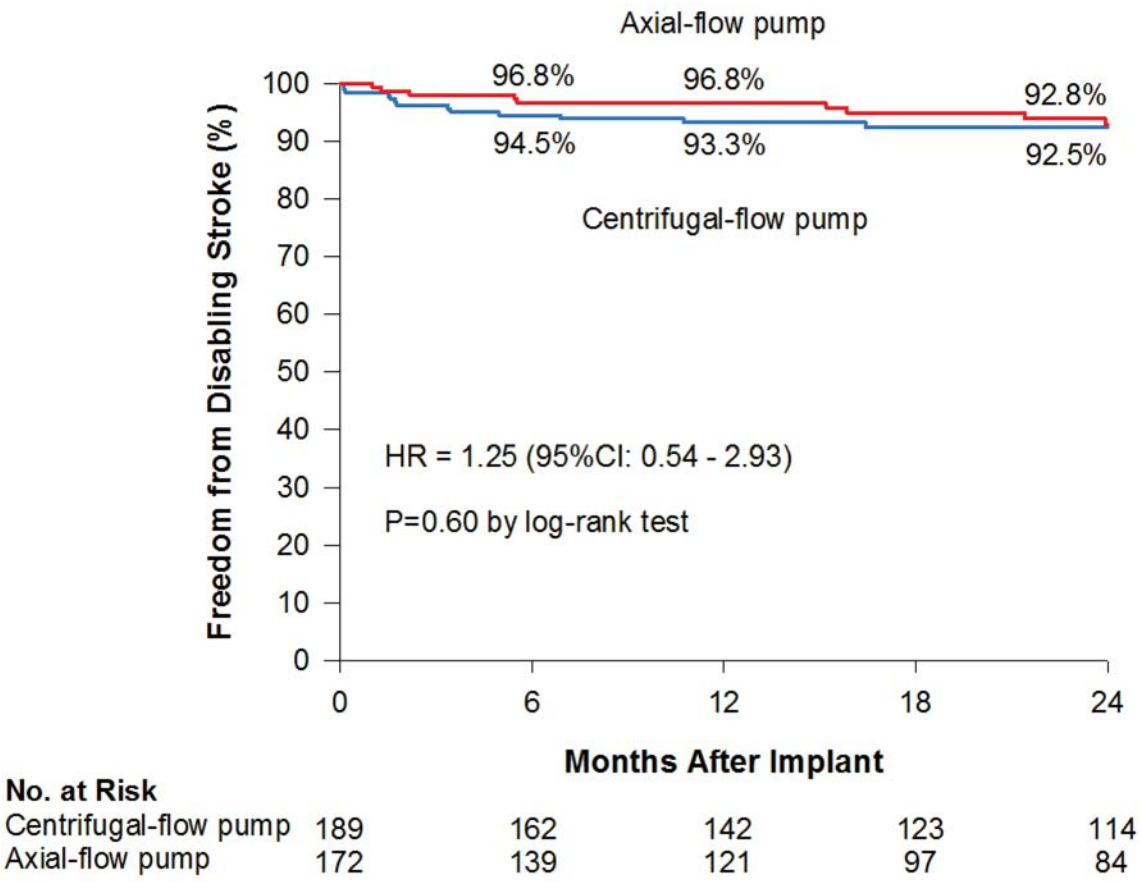
[3]Urgent heart transplant for pump thrombosis (4), severe hemolysis (1), and driveline fault/electrical failure (3). [4]Device explanted due to infection (1). [5]Includes withdrawals prior to implant (4), for exchange with non-study device (2), and withdrawal of consent (1). [6]Includes withdrawals for exchange with non-study device (2) and centrifugal-flow pump (1).

Figure S3. Actuarial All Cause Survival (Per Protocol Population)



No. at Risk					
Centrifugal-flow pump	189	165	146	127	117
Axial-flow pump	172	141	121	98	86

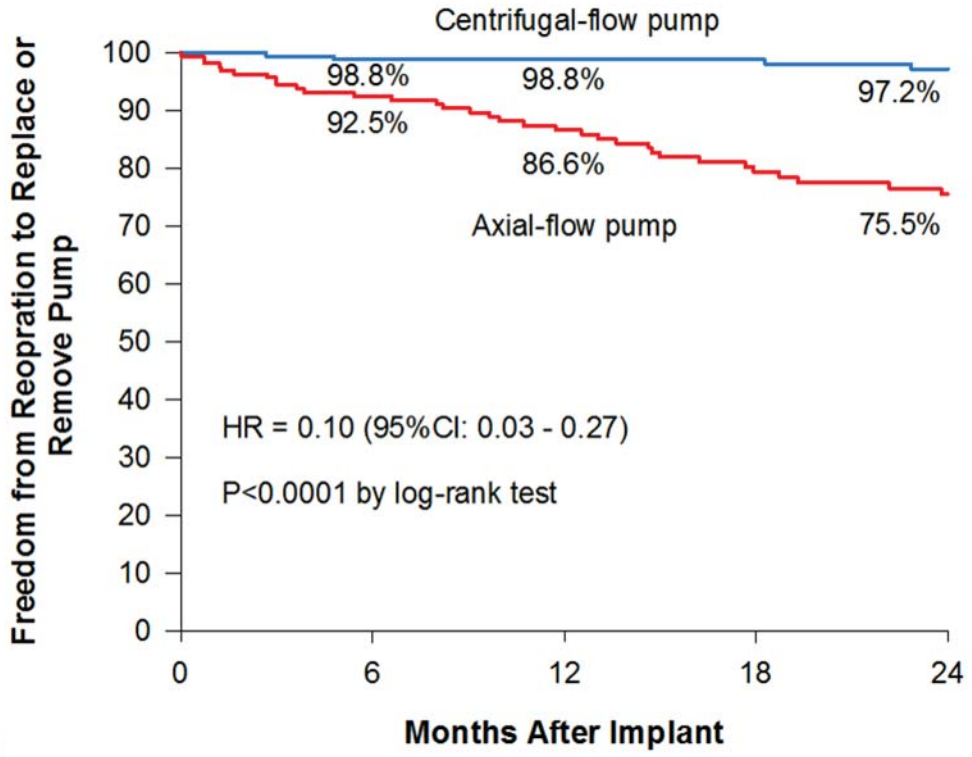
Figure S4. Freedom from Disabling Stroke (Per Protocol Population)



No. at Risk

Centrifugal-flow pump	189	162	142	123	114
Axial-flow pump	172	139	121	97	84

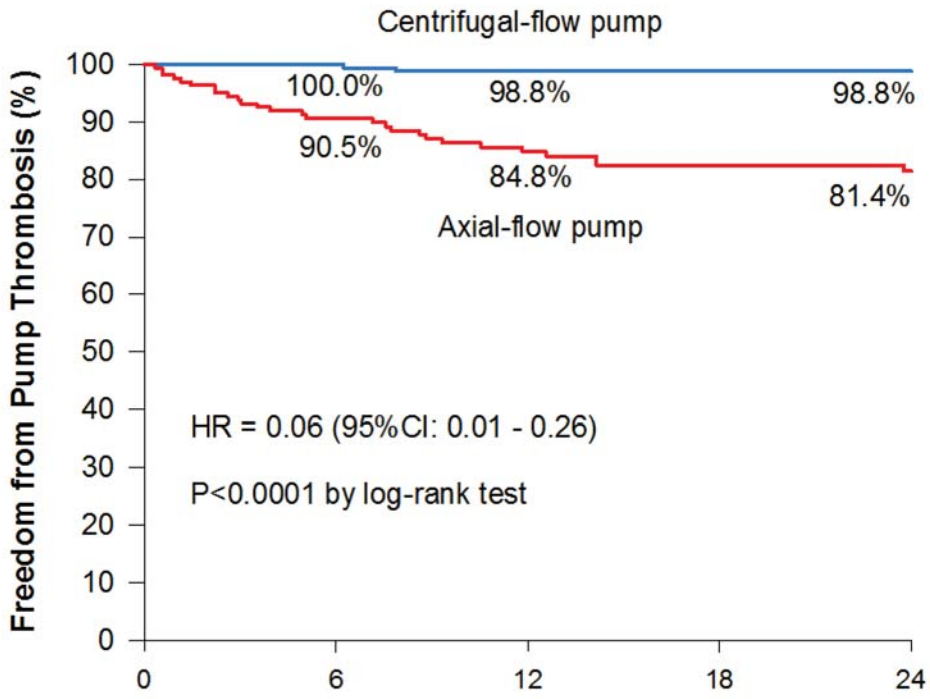
Figure S5. Freedom from Reoperation to Replace or Remove Pump (Per Protocol Population)



No. at Risk

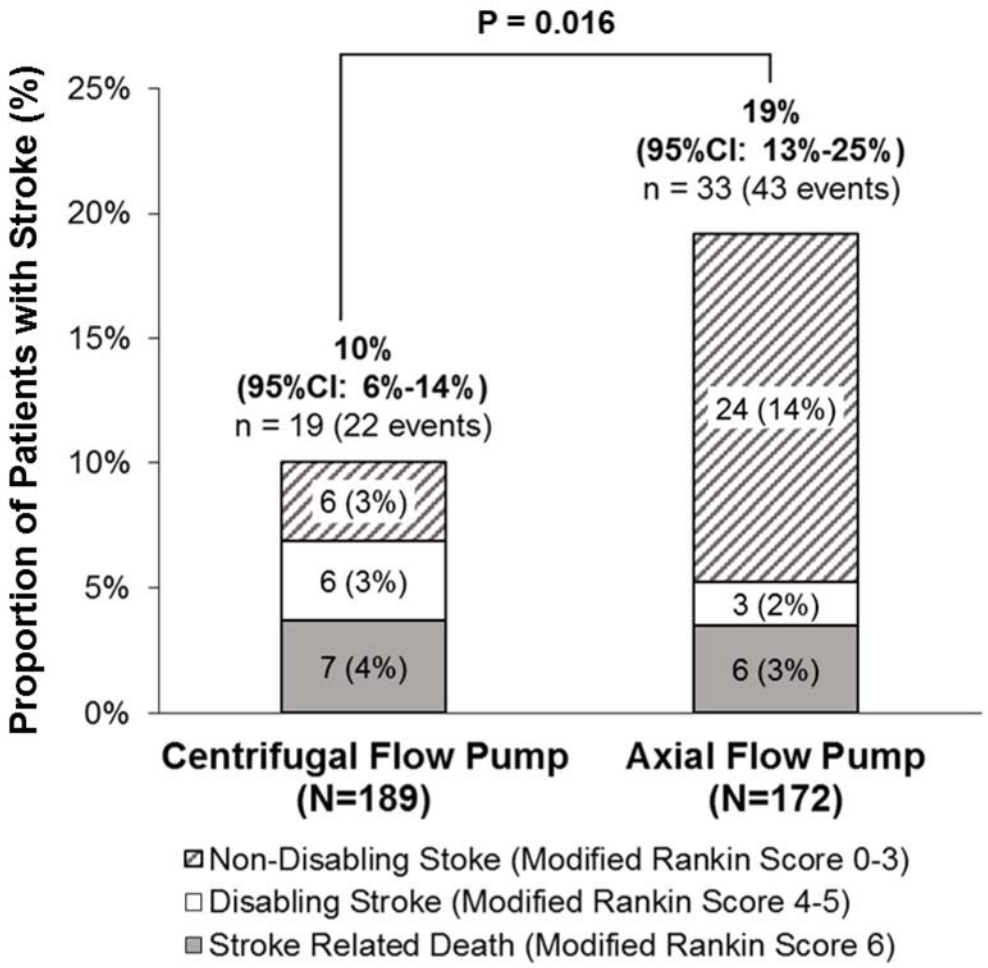
Centrifugal-flow pump	189	164	145	126	114
Axial-flow pump	172	135	114	90	76

Figure S6. Freedom from Suspected or Confirmed Pump Thrombosis (Per Protocol Population)



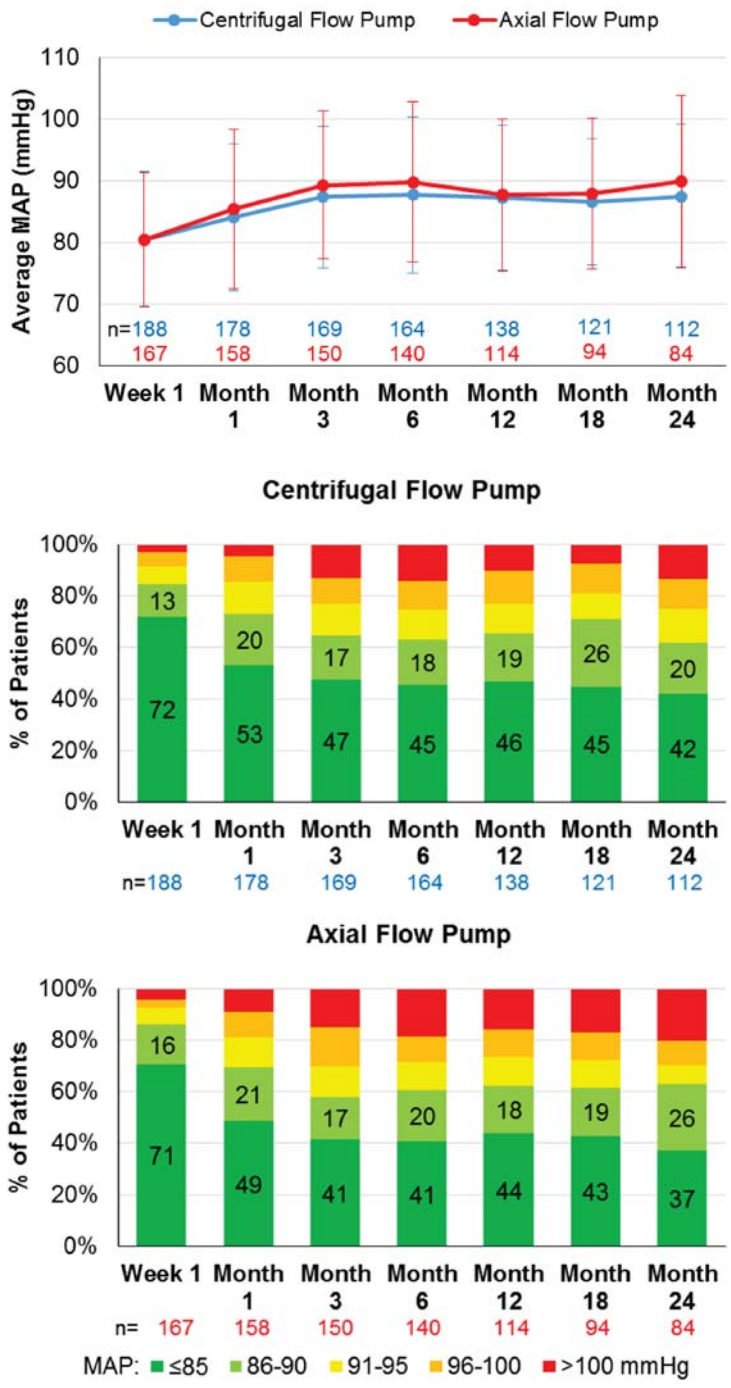
No. at Risk					
Centrifugal-flow pump	189	165	145	127	117
Axial-flow pump	172	133	112	91	80

Figure S7. Stroke Events and Severity (Per Protocol Population)



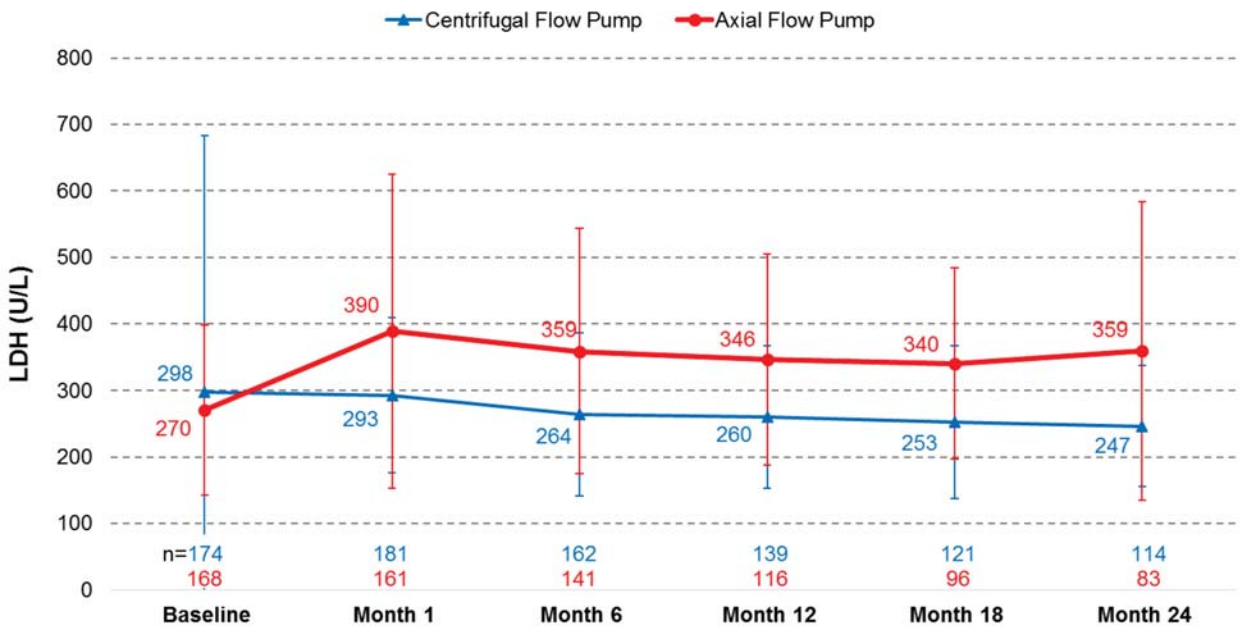
Two centrifugal flow pump subjects and 9 axial flow pump subjects had >1 stroke. The score for the most severe stoke is shown. 1.6% of centrifugal flow pump subjects (n = 3) and 5.2% of axial-flow pump subjects (n = 9) had a modified Rankin score of 0 at 60 days post-stroke.

Figure S8. Mean Arterial Pressure (MAP) over Time (Per Protocol Population)



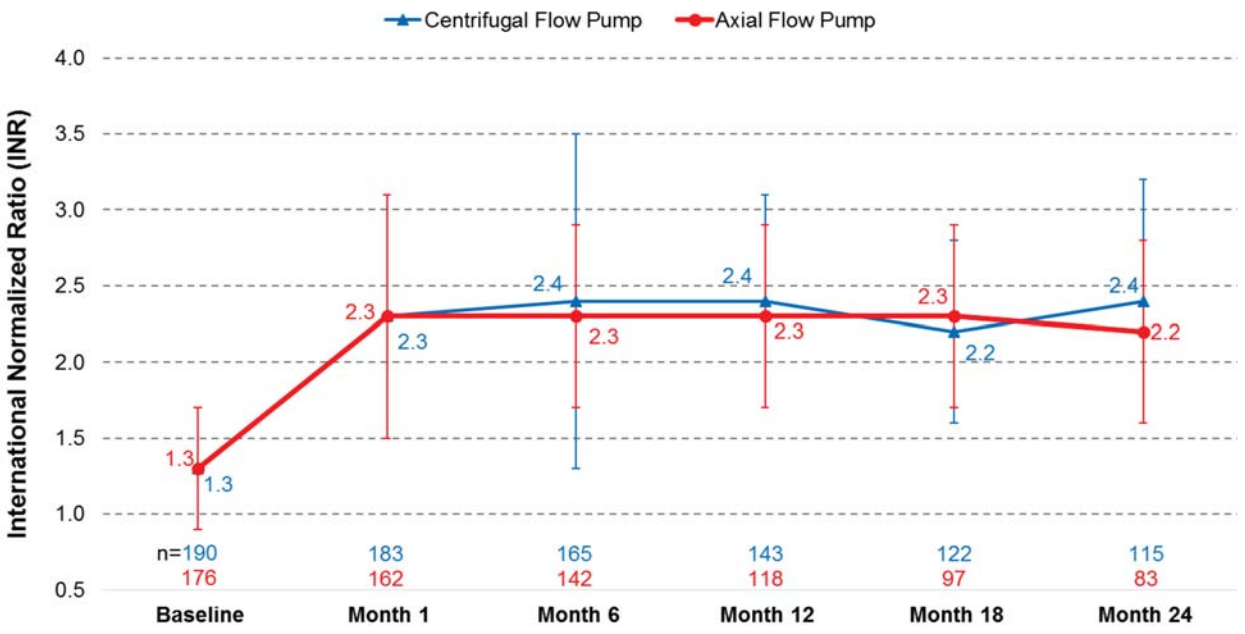
There were no significant differences in MAP between treatment groups at each follow-up visit.

Figure S9. Lactate Dehydrogenase (LDH) Levels over Time



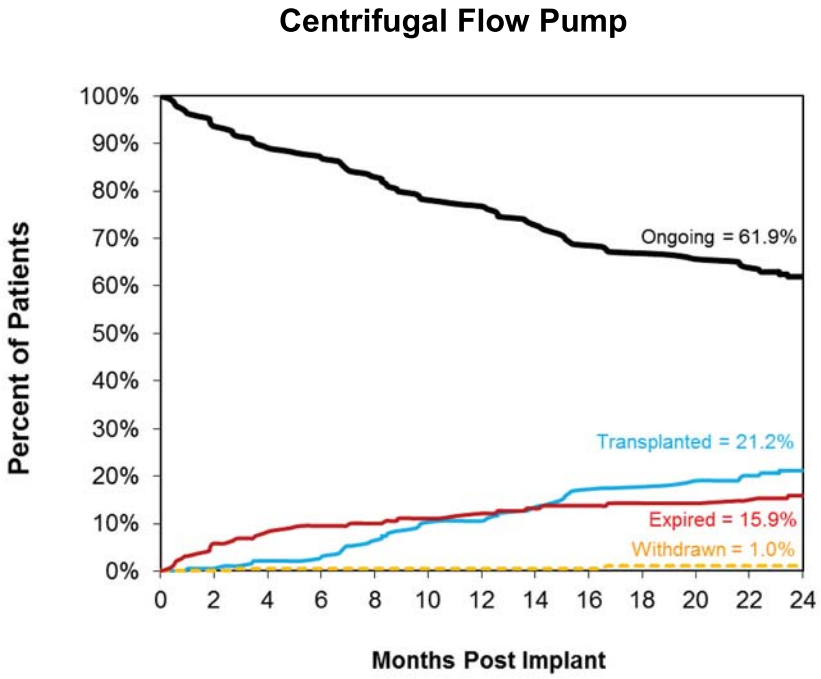
After implant, LDH levels were significantly lower in the centrifugal-flow pump group compared to the axial-flow pump group at each follow-up visit (P<0.0001). At month 24, LDH levels decreased from baseline in the centrifugal-flow pump group (P=0.01) and increased from baseline in the axial-flow pump group (P<0.0001).

Figure S10. INR Levels over Time



There were no significant differences in INR between treatment groups at each follow-up visit.

Figure S11. Competing Risk Analyses (Per Protocol Population)



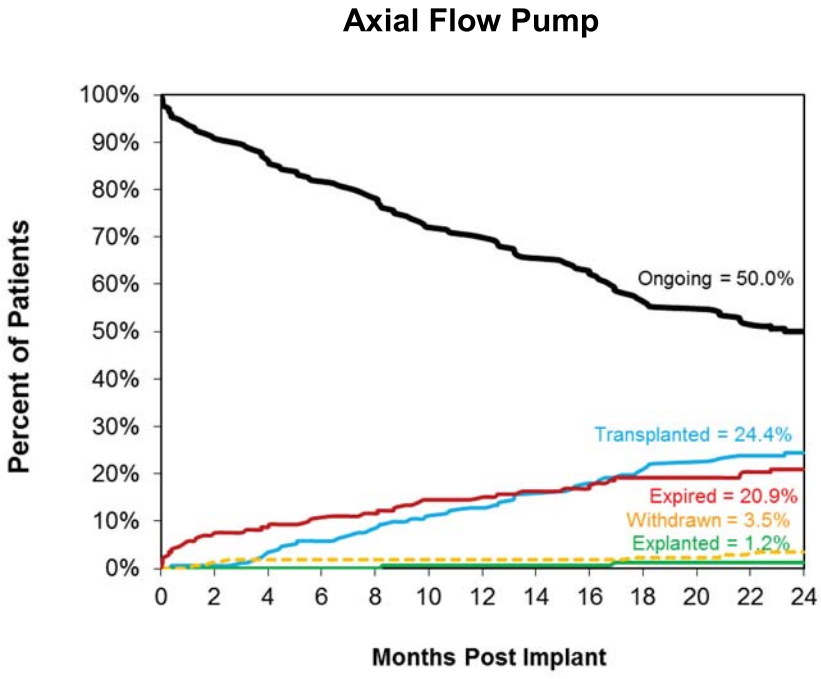
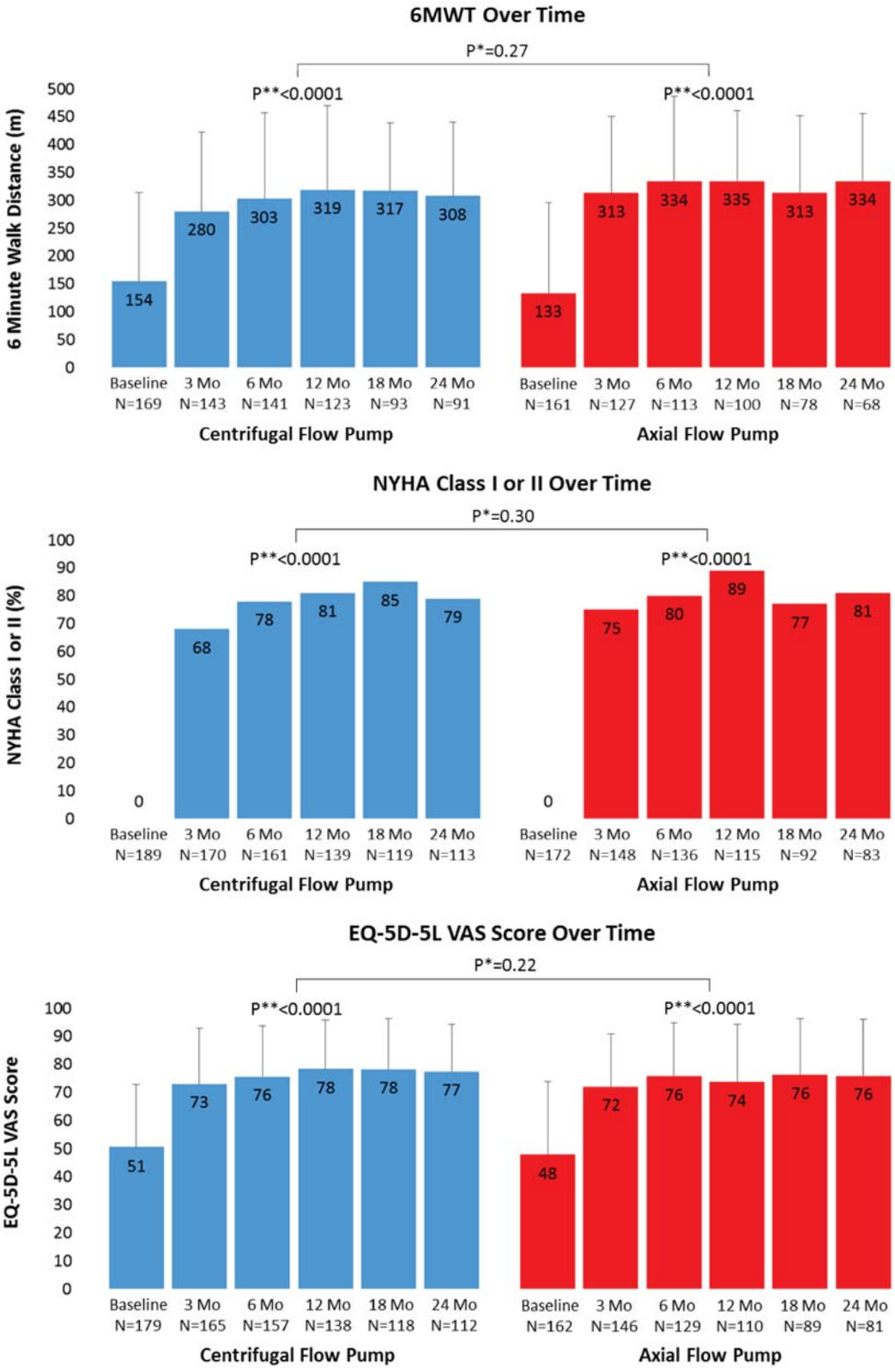


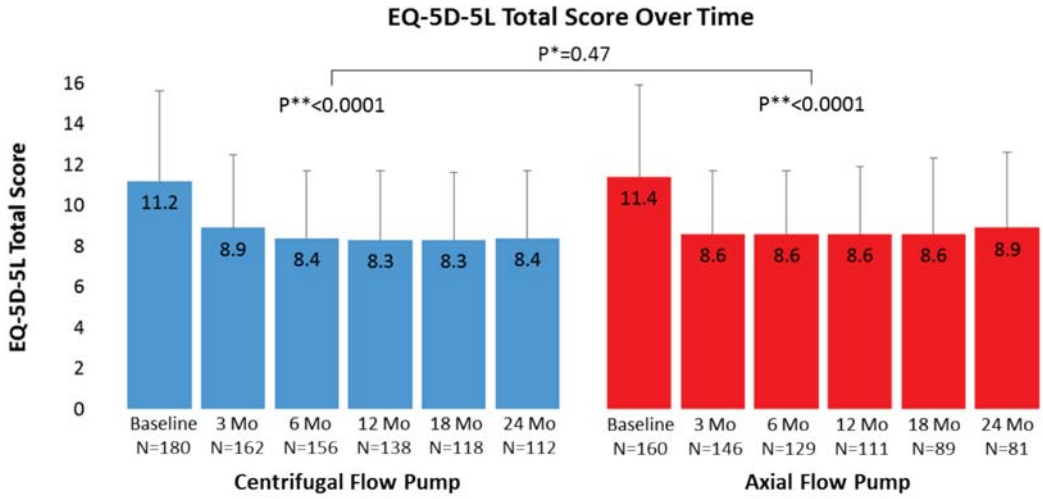
Figure S12. Subgroup Analyses of the Primary Endpoint for Age, Gender, Race, Implant Strategy and INTERMACS Profile between Treatment Groups (Intent to Treat Population)

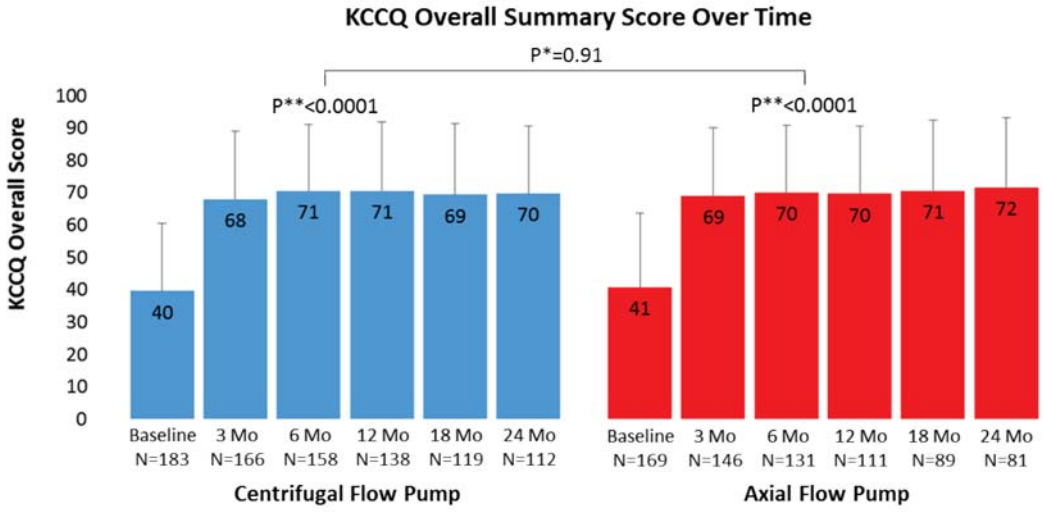
Variable	Groups	HR (95% CI)	Interaction p-value
Age (years)	18 - 59 (n = 154)	0.37 (0.19-0.73)	0.65
	60 - 69 (n = 128)	0.43 (0.21-0.87)	
	70+ (n = 84)	0.61 (0.31-1.21)	
Gender	Men (n = 293)	0.49 (0.31-0.76)	0.42
	Women (n = 73)	0.39 (0.16-0.90)	
Race	Caucasian (n = 258)	0.59 (0.38-0.93)	0.06
	Non-Caucasian (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)	

BTT = Bridge to Transplant. BTC = Bridge to Candidacy, DT = Destination Therapy, INTERMACS=Interagency Registry for Mechanical Circulatory Support

Figure S13. Functional Status and Quality of Life (Per Protocol Population)







*p value between treatment arms over time; **p value for treatment over time

On the European Quality of Life–5 Dimensions (EQ-5D) questionnaire (EQ-5D-5L), scores range from 1 to 5, with higher scores indicating more problems across five categories of quality of life. On the EQ-5D visual-analogue scale (EQ-5D VAS), scores range from 0 to 100, with higher scores indicating better health status. On the Kansas City Cardiomyopathy Questionnaire (KCCQ), scores range from 0 to 100, with higher scores indicating better quality of life and fewer symptoms. Patients who did not complete a six-minute walk test (6MWT) due to heart failure were assigned a score of zero meters. Additionally, there were patients who did not complete the 6MWT due to reasons other than heart failure (e.g., other illnesses, refusal to perform the test, site scheduling issues). Some patients who did not complete the 6MWT at a particular visit were able to complete quality of life questionnaires. Thus, the total number of patients at each time interval may not be the same across these tests. *A sensitivity analysis was performed in which all missing data for both treatment arms were assigned the worst possible score for the test. The data continue to show that functional status and quality of life improve over baseline in both treatment arms. There were no significant differences between arms in the NYHA class, 6MWT and KCCQ measures. However, patients assigned to the centrifugal-flow pump arm had significantly better EQ-5D-5L total scores (P=0.03) and VAS scores (P=0.01) than the axial-flow pump group.*

SUPPLEMENTARY TABLES

Table S1. Severity of Illness and Concomitant Medications and Interventions

Characteristic*	Centrifugal-Flow Pump Group (N=190)	Axial-Flow Pump Group (N=176)
Concomitant medication or intervention – no. (%)		
Intravenous inotropic agents	167 (87.9)	152 (86.4)
Diuretic	166 (87.4)	165 (93.8)
Angiotensin-converting-enzyme inhibitor or Angiotensin II-receptor antagonist	58 (30.5)	66 (37.5)
Beta-blocker	111 (58.4)	98 (55.7)
Cardiac resynchronization therapy with or without defibrillator	75 (39.5)	62 (35.2)
Implantable cardioverter-defibrillator with or without cardiac resynchronization therapy	122 (64.2)	123 (69.9)
Intraaortic balloon pump	25 (13.2)	26 (14.8)
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)

*There were no significant differences between the groups except for diuretic use (P = 0.05). [+]Interagency Registry for Mechanical Circulatory Support (INTERMACS) profiles range from 1 to 7; a profile of 1 represents the most severe illness and a profile of 7 the least severe illness. For more details, see Table S2. ‡One patient died before the INTERMACS assessment was performed.

Table S2. INTERMACS Profile/Classification

INTERMACS Profile[5]	Definition
1	Critical cardiogenic shock describes a patient who is “crashing and burning”, in which a patient has life- threatening hypotension and rapidly escalating inotropic pressor support, with critical organ hypoperfusion often confirmed by worsening acidosis and lactate levels.
2	Progressive decline describes a patient who has been demonstrated “dependent” on inotropic support but nonetheless shows signs of continuing deterioration in nutrition, renal function, fluid retention, or other major status indicator. Patient profile 2 can also describe a patient with refractory volume overload, perhaps with evidence of impaired perfusion, in whom inotropic infusions *cannot be maintained* due to tachyarrhythmias, clinical ischemia, or other intolerance.
3	Stable but inotrope dependent describes a patient who is clinically stable on mild-moderate doses of intravenous inotropes (or has a temporary circulatory support device) after repeated documentation of failure to wean without symptomatic hypotension, worsening symptoms, or progressive organ dysfunction (usually renal). It is critical to monitor nutrition, renal function, fluid balance, and overall status carefully in order to distinguish between a patient who is truly stable at Patient Profile 3 and a patient who has unappreciated decline rendering this person a Patient Profile 2. This patient may be either at home or in the hospital.
4	Resting symptoms describes a patient who is at home on oral therapy but frequently has symptoms of congestion at rest or with ADL. He or she may have orthopnea, shortness of breath during ADL such as dressing or bathing, gastrointestinal symptoms (abdominal discomfort, nausea, poor appetite), disabling ascites or severe lower extremity edema. This patient should be carefully considered for more intensive management and surveillance programs, by which some may be recognized to have poor compliance that would compromise outcomes with any therapy.
5	Exertion Intolerant describes a patient who is comfortable at rest but unable to engage in any activity, living predominantly within the house or housebound. This patient has no congestive symptoms, but may have chronically elevated volume status, frequently with renal dysfunction, and may be characterized as exercise intolerant.
6	Exertion Limited also describes a patient who is comfortable at rest without evidence of fluid overload, but who is able to do some mild activity. Activities of daily living are comfortable and minor activities outside the home such as visiting friends or going to a restaurant can be performed, but fatigue results within a few minutes of any meaningful physical exertion. This patient has occasional episodes of worsening symptoms and is likely to have had a hospitalization for heart failure within the past year.
7	Advanced NYHA Class 3 describes a patient who is clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent. This patient is usually able to walk more than a block. Any decompensation requiring intravenous diuretics or hospitalization within the previous month should make this person a Patient Profile 6 or lower.

Table S3. Urgent Heart Transplant for Device Malfunction

Axial Flow Pump Patient	Reason for Urgent Heart Transplant
1	Device thrombosis
2	Device thrombosis
3	Device thrombosis
4	Device thrombosis
5	Severe hemolysis
6	Driveline fault with persistent alarms
7	Low speed alarms with pump stops
8	External driveline fracture with possible internal fracture

Table S4. Sensitivity Analysis of Primary Endpoint (Intention to Treat)

	Percent Success	95% Confidence Limit	
Axial Flow Pump (n=176)	62.5%	54.9%	69.7%
Centrifugal Flow Pump (n=190)	79.5%	73.0%	85.0%
Noninferiority Analysis: absolute difference = 17.0 % (95% LCB: 6.7%), P<0.0001 Superiority Analysis: HR = 0.51 (0.34-0.75), P = 0.0003			

For subjects not implanted, those that were randomized to the axial flow pump (n = 4) are considered Success and those randomized to Centrifugal Flow Pump are considered a Failure (n = 1). LCB denotes lower confidence boundary; HR, hazard ratio.

Table S5. Summary of Suspected Pump Thrombosis Events

	Centrifugal Flow Pump	Axial Flow Pump
Total Patients	2/189 (1%)	27/172 (16%)
Total Events	2	33*
Mean time to first event (days)	216	195
Signs and Symptoms		
Hemolysis	1/2 (50%)	28/33 (85%)
Worsening heart failure	2/2 (100%)	20/33 (61%)
Abnormal pump parameters	2/2 (100%)	18/33 (55%)
Action Taken/Outcome		
Device exchange to assigned study device	0/2 (0%)	16/33 (48%)
Device exchange to non-assigned study device[+]	0/2 (0%)	2/33 (6%)
Device exchange to non-study device	0/2 (0%)	3/33 (9%)
Urgent transplant	0/2 (0%)	4/33 (12%)
Death	0/2 (0%)	4/33 (12%)
RPA Result		
Confirmed	0/2 (0%)	20/33 (61%)
Not confirmed	0/2 (0%)	1/33 (3%)
Inconclusive	0/2 (0%)	3/33 (9%)
Device not returned	2/2 (100%)	9/33 (27%)

*Six subjects had two suspected pump thrombosis events. [+]Subject in axial-flow pump group received device exchange with centrifugal-flow pump. RPA denotes returned product analysis.

Table S6. Stroke Risk-Factor Analysis (Per Protocol Population)

	Centrifugal Flow Pump (N=189)	Axial Flow Pump (N=172)	P-Value
Average INR*	2.23±0.46	2.23±0.50	0.92
Average INR<2.0 – n/N (%)	48/189 (25%)	48/168 (29%)	0.55
Antiplatelet use at 30 days - n/N (%)[+]	163/183 (89%)	145/162 (90%)	1.00
New onset atrial fibrillation during support – n/N (%)	17/189 (9%)	15/172 (9%)	1.00

*Average value of available measurements collected at week 1 to month 24 follow-up visits.
[+]Includes aspirin, clopidogrel, and persantine/dipyridamole. Baseline history of stroke and atrial fibrillation are in Table 1. There are no significant difference between arms in these two variables.

Table S7. Gastrointestinal (GI) Bleeding Analysis (Per Protocol Population)

	Centrifugal Flow Pump (N=189)	Axial Flow Pump (N=172)	P-Value*
Subjects with no GI Bleed	138 (73%)	125 (73%)	0.09
Subjects with 1 GI Bleed	34 (18%)	21 (12%)	
Subjects with more than 1 GI Bleed	17 (9%)	26 (15%)	

*Chi-square test

Table S8. Subjects with Aspirin and Other Antiplatelet Therapy (Per Protocol Population)

	Centrifugal Flow Pump (N=189)	Axial Flow Pump (N=172)	P-Value*
Baseline			
Any Aspirin	58.2% (110/189)	58.7% (101/172)	0.92
325 mg Aspirin	4.2% (8/189)	4.7% (8/172)	0.85
> 1 Anti-Platelet^{+}	5.3% (10/189)	3.5% (6/172)	0.41
Month 6			
Any Aspirin	85.5% (142/166)	85.9% (122/142)	0.93
325 mg Aspirin	39.2% (65/166)	31.0% (44/142)	0.14
> 1 Anti-Platelet	8.4% (14/166)	15.5% (22/142)	0.05
Month 12			
Any Aspirin	82.5% (118/143)	83.9% (99/118)	0.77
325 mg Aspirin	35.0% (50/143)	32.2% (38/118)	0.64
> 1 Anti-Platelet	9.1% (13/143)	22.9% (27/118)	0.002
Month 18			
Any Aspirin	72.6% (90/124)	76.3% (74/97)	0.53
325 mg Aspirin	33.1% (41/124)	33.0% (32/97)	0.99
> 1 Anti-Platelet	5.6% (7/124)	22.7% (22/97)	0.0002
Month 24			
Any Aspirin	76.7% (89/116)	73.8% (62/84)	0.64
325 mg Aspirin	31.0% (36/116)	35.7% (30/84)	0.49
> 1 Anti-Platelet	6.9% (8/116)	20.2% (17/84)	0.005

* Chi-square test. $^{+}$Defined as aspirin, clopidogrel, dipyridamole, IIb/IIIa platelet inhibitor and/or cangrelor/ticagrelor.

Table S9. Subjects with Normal, Sub, and Supratherapeutic INR Values over Time (Per Protocol Population)

	Centrifugal Flow Pump (N=189)	Axial Flow Pump (N=172)	P-Value*
Baseline	n=189	n=172	0.90
INR < 2	95.8% (181/189)	94.8% (163/172)	
INR 2-3	3.7% (7/189)	4.7% (8/172)	
INR > 3	0.5% (1/189)	0.6% (1/172)	
Month 6	n=165	n=142	0.40
INR < 2	27.9% (46/165)	29.6% (42/142)	
INR 2-3	58.8% (97/165)	62.0% (88/142)	
INR > 3	13.3% (22/165)	8.5% (12/142)	
Month 12	n=143	n=118	0.17
INR < 2	24.5% (35/143)	25.4% (30/118)	
INR 2-3	61.5% (88/143)	67.8% (80/118)	
INR > 3	14.0% (20/143)	6.8% (8/118)	
Month 18	n=122	n=97	1.00
INR < 2	30.3% (37/122)	29.9% (29/97)	
INR 2-3	62.3% (76/122)	61.9% (60/97)	
INR > 3	7.4% (9/122)	8.2% (8/97)	
Month 24	n=115	n=83	0.68
INR < 2	26.1% (30/115)	30.1% (25/83)	
INR 2-3	63.5% (73/115)	62.7% (52/83)	
INR > 3	10.4% (12/115)	7.2% (6/83)	

*Fisher's Exact Test

Table S10. Renal and Hepatic Function over Time

		Centrifugal Flow Pump (N=190)		Axial Flow Pump (N=176)		
Variable	**Visit**	**n**	**Mean±SD**	**n**	**Mean±SD**	**P-Value***
Creatinine (mg/dl)	Baseline	190	1.4±0.4	176	1.4±0.4	0.84
	Month 6	165	1.3±0.4	141	1.3±0.4	0.54
	Month 12	143	1.4±0.5	118	1.3±0.4	0.37
	Month 18	122	1.4±0.4	97	1.3±0.4	0.11
	Month 24	116	1.4±0.5	83	1.3±0.5	0.54
Total Bilirubin (mg/dl)	Baseline	189	1.0±0.5	176	1.1±0.5	0.22
	Month 6	165	0.7±0.4	139	0.7±0.3	0.53^{+}
	Month 12	143	0.7±0.4	115	0.7±0.4	0.79
	Month 18	120	0.8±0.8	96	0.7±0.4	0.46^{+}
	Month 24	116	0.7±0.4	82	0.7±0.4	0.55
BUN (mg/dl)	Baseline	190	28.4±14.0	176	26.8±12.1	0.25^{+}
	Month 6	165	24.9±12.8	141	22.3±10.4	0.06^{+}
	Month 12	143	23.8±10.1	118	22.6±10.2	0.37
	Month 18	122	24.0±11.5	97	23.2±10.4	0.59
	Month 24	116	24.1±11.7	83	22.6±11.1	0.35
AST (U/L)	Baseline	188	32.0±23.4	176	33.3±62.4	0.80^{+}
	Month 6	165	30.0±15.3	139	29.3±11.9	0.68^{+}
	Month 12	143	29.3±14.7	114	29.9±12.0	0.71^{+}
	Month 18	120	27.9±13.8	96	30.0±13.2	0.26
	Month 24	116	26.7±11.2	82	30.2±12.1	0.03
ALT (U/L)	Baseline	189	40.2±65.2	176	39.6±70.4	0.94
	Month 6	165	29.4±24.3	139	27.2±19.4	0.38^{+}
	Month 12	143	27.0±15.7	115	25.6±12.2	0.40^{+}
	Month 18	120	26.2±16.0	96	27.5±17.0	0.57
	Month 24	116	23.0±11.9	82	26.4±14.7	0.08^{+}

*Two-sample t-test. $^{+}$ Satterthwaite method was used in calculating the two-sample t-test p-value due to unequal variances. BUN denotes blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Table S11. Adjudicated Causes of Death (Per Protocol Population)

Adjudicated Cause of Death	Centrifugal Flow Pump (N=189)	Axial Flow Pump (N=172)	Total
Abdominal Bleeding	1	2	3
Anoxic Brain Injury Secondary To Respiratory Failure	1	0	1
Aortic Dissection	0	1	1
Cancer	2	0	2
Pump Disconnect	2	0	2
Heart Failure	1	0	1
Hepatic Failure	0	2	2
Infection	6	6	12
Intracranial Hemorrhage Due To Trauma	0	1	1
IV drug use	1	0	1
Pneumonia	0	1	1
Pump Thrombosis	0	4	4
Respiratory Failure	1	1	2
Right Heart Failure	6	9	15
Stroke	6	6	12
Traumatic Subdural Hematoma Caused By A Fall	1	0	1
Unknown	0	2	2
Ventricular Arrhythmia	2	1	3
Total	30	36	66

REFERENCES

1. Mehra MR, Naka Y, Uriel N, et al. A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure. N Engl J Med 2017;376(5):440-50.
2. Bourque K, Cotter C, Dague C, et al. Design Rationale and Preclinical Evaluation of the HeartMate 3 Left Ventricular Assist System for Hemocompatibility. ASAIO J 2016;62(4):375-83.
3. Griffith BP, Kormos RL, Borovetz HS, et al. HeartMate II left ventricular assist system: from concept to first clinical use. Ann Thorac Surg 2001;71:S116-20; discussion S114-6.
4. Heatley G, Sood P, Goldstein D, 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.
5. Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure: the current picture. J Heart Lung Transplant 2009;28(6):535-41.