ISHLT 2021
41st Annual Meeting & Scientific Sessions
24–28 April VIRTUAL EXPERIENCE
#ISHLT2021

A Comparative Analysis of Long-Term Outcomes in the MOMENTUM 3 Pivotal Trial and Continued Access Protocol Post-Trial Study Phase: *A Study of 2200 HeartMate 3 Implants*

Authors (presenter underlined): Mandeep R. Mehra, M.D., Joseph C. Cleveland, Jr., M.D., Nir Uriel, M.D., Jennifer Cowger, M.D., Shelley Hall, M.D., Douglas Horstmanshof, M.D., Yoshifumi Naka, M.D., Ph.D., Christopher T. Salerno, M.D., Joyce Chuang, Ph.D., Christopher Williams and Daniel J. Goldstein, M.D., on behalf of the MOMENTUM 3 investigators.

MOMENTUM 3

Relevant Financial Relationship Disclosure Statement

A Comparative Analysis of Long-Term Outcomes in the MOMENTUM 3 Pivotal Trial and Continued Access Protocol Post-Trial Study Phase: *A Study of 2200 HeartMate 3 Implants*

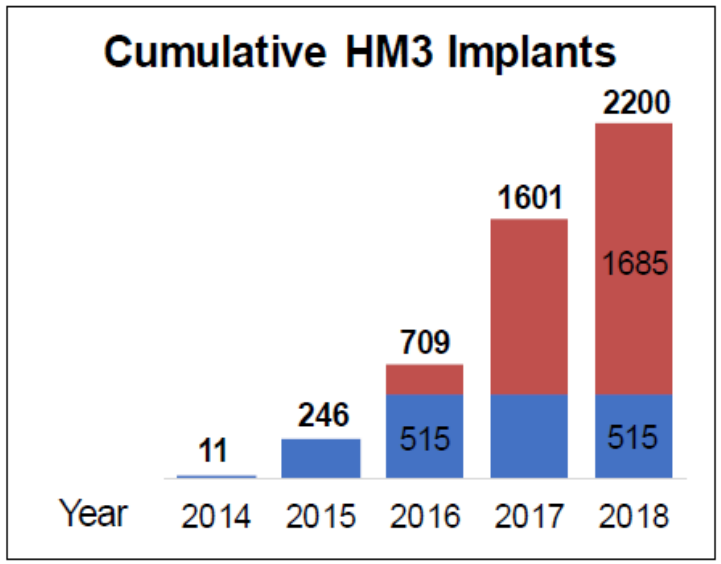
I will **not** discuss off label use and/or investigation use of any drugs or devices.

The following relevant financial relationships exist related to this presentation: **Mehra** - payment made to institution from Abbott for consulting. Consulting fees from Mesoblast, Janssen, Portola, Bayer, Triple Gene, and Baim Institute for Clinical Research. Advisory board member for NuPulseCV, Leviticus and FineHeart. **Cleveland** - grant support from Abbott. **Uriel** – grant support and consultant fees from Abbott and Medtronic. **Cowger** - consultant and speaker for Abbott and Medtronic. On steering committee/study panel for Medtronic, Abbott and Procyrion. Henry Ford receives institutional funds from Abbott, Medtronic and Procyrion. **Hall** – Speaker's Bureau fees from CareDx. Consultant fees from Abbott, Abiomed, Medtronic, CareDx and Natera. **Horstmanshof** - consultant and Speaker's bureau fees from Abbott. **Naka** – consultant fees from Abbott. **Salerno** – consultant fees from Abbott and Medtronic. **Chuang** – employee of Abbott. **Williams** – employee of Abbott. **Goldstein** - educator and surgical proctor for Abbott; consultant for Abiomed.

MOMENTUM 3 pivotal trial (NCT02224755) and CAP (NCT02892955) were sponsored by Abbott

MOMENTUM 3

MOMENTUM 3 Timeline



CAP enrollment ends
(HM3 approved for long-term use)

BTT patients excluded from CAP enrollment
(HM3 approved for short-term use)

2014 2015 2016 2017 2018 2019 2020 2021

Pivotal Trial enrollment starts

Pivotal Trial enrollment complete & CAP Cohort enrollment begins

Pivotal Trial 2-year follow-up complete

CAP Cohort 2-year follow-up complete

BTT, bridge-to-transplant; CAP, Continued Access Protocol; HM3, HeartMate 3™ left ventricular assist system.

MOMENTUM 3

Objectives

- Evaluate differences between principal outcomes with the HM3 LVAD between the early experience Pivotal Trial compared with the Post-Trial experience
  - *Is there a learning curve?*
- Determine if HM3 LVAD outcomes differ by clinical severity at implant (INTERMACS profile), or by therapeutic goal of lifelong therapy
  - *Are there sub-groups that perform differentially?*
- Outline changes in the NET-BURDEN of major adverse events over the course of the Pivotal Trial and Post-Trial cohorts
  - *Did we improve the patient experience and journey over time?*

Methods

- Patients
  - Pivotal Cohort = 515 HM3 implanted patients
  - CAP Cohort = 1685 HM3 implanted patients
  - Pooled Cohort = 2200 combined patients
- Principal endpoints *(at 2-years)*
  - Composite endpoint of survival free of disabling stroke or reoperation to replace or remove a malfunctioning pump
  - Overall survival
  - Major adverse events (hemocompatibility and non-hemocompatibility related)
- Statistical methods
  - Composite endpoint and survival assessed at 2-years with Kaplan-Meier method
    - INTERMACS subgroup analysis performed with Pooled Cohort to assess outcomes by severity
  - Hazard ratios (HR), and rate ratios *adjusted* for age, sex, race, INTERMACS profile, and intended use
  - Adverse events evaluated individually and collectively as a "Net-Burden" using events per patient year (EPPY)

Baseline Characteristics

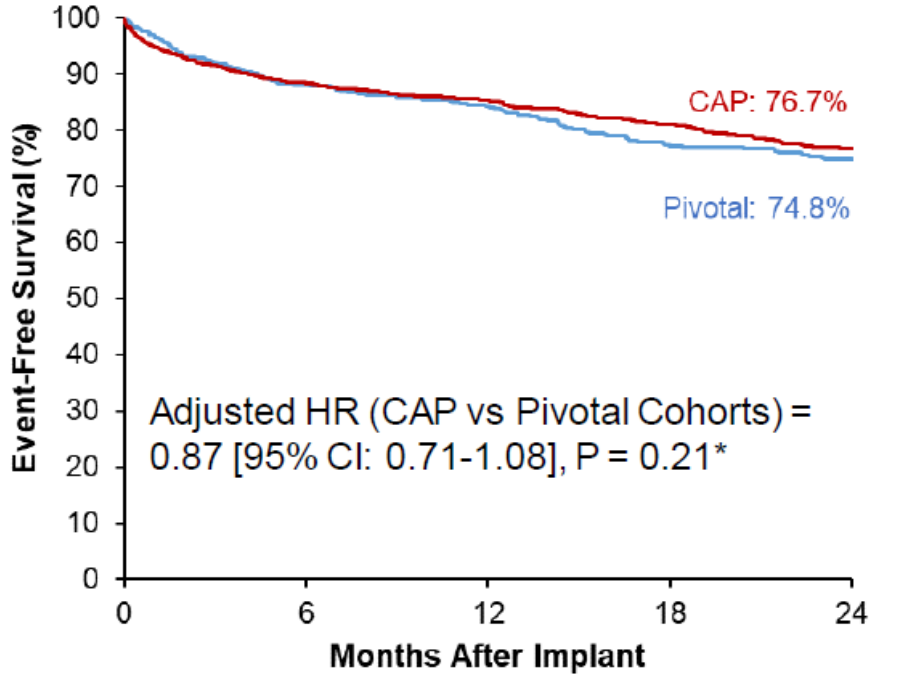
Variable	Pivotal (N=515)	CAP (N=1685)	P*
Age, years	59.2 ± 12.4	59.9 ± 12.2	0.22
BSA, m^2	2.07 ± 0.27	2.08 ± 0.29	0.86
BMI	29.2 ± 6.3	29.1 ± 6.7	0.84
Male	410 (79.6%)	1342 (79.6%)	0.99
Caucasian	341 (66.2%)	1135 (67.4%)	0.60
Ischemic HF	216 (41.9%)	760 (45.1%)	0.21
Intended use			
DT	317 (61.6%)	1274 (75.6%)	<0.001
BTT	112 (21.7%)	173 (10.3%)	<0.001
BTC	86 (16.7%)	233 (13.8%)	0.11
BTR	0 (0%)	4 (0.2%)	0.58
Rescue therapy	0 (0%)	1 (0.1%)	1.00
IABP	64 (12.4%)	282 (16.7%)	0.019
INTERMACS profile			
1	11 (2.1%)	69 (4.1%)	0.036
2	156 (30.4%)	517 (31.0%)	0.79
3	272 (52.9%)	843 (50.5%)	0.33
4-7	75 (14.6%)	241 (14.3%)	0.88

Variable	Pivotal (N=515)	CAP (N=1685)	P*
Diabetes	233 (45.2%)	690 (40.9%)	0.08
Prior stroke	50 (9.7%)	128 (7.6%)	0.12
Ace inhibitor or ARB	158 (30.7%)	338 (20.1%)	<0.001
Beta blocker	284 (55.1%)	668 (39.6%)	<0.001
CRT-P or CRT-D	188 (36.5%)	407 (24.2%)	<0.001
ICD or CRT-D	351 (68.2%)	1187 (70.4%)	0.32
CABG	102 (19.8%)	320 (19.0%)	0.68
RAP, mmHg	10.8 ± 6.5	11.1 ± 8.3	0.34
PCWP, mmHg	23.1 ± 8.6	23.4 ± 8.9	0.57
PAPI	4.14 ± 4.91	3.82 ± 4.37	0.19
eGFR, $mL/min/1.73m^2$	61.5 ± 23.8	58.8 ± 22.8	0.024
Hematocrit, %	36.5 ± 5.6	35.9 ± 5.6	0.027
WBC, $10^3/mL$	7.66 ± 2.55	7.95 ± 2.89	0.034

Continuous variables presented as mean and SD. Categorical variables presented as counts (percentage). *Chi-square/Fisher's Exact or T-test
BTR, bridge-to-recovery; IABP, intra-aortic balloon pump; CRT, cardiac resynchronization therapy; CABG, coronary artery bypass graft; RAP, right atrial pressure; PAPI, pulmonary artery pulsatility index; eGFR, estimated glomerular filtration rate; WBC, white blood cells

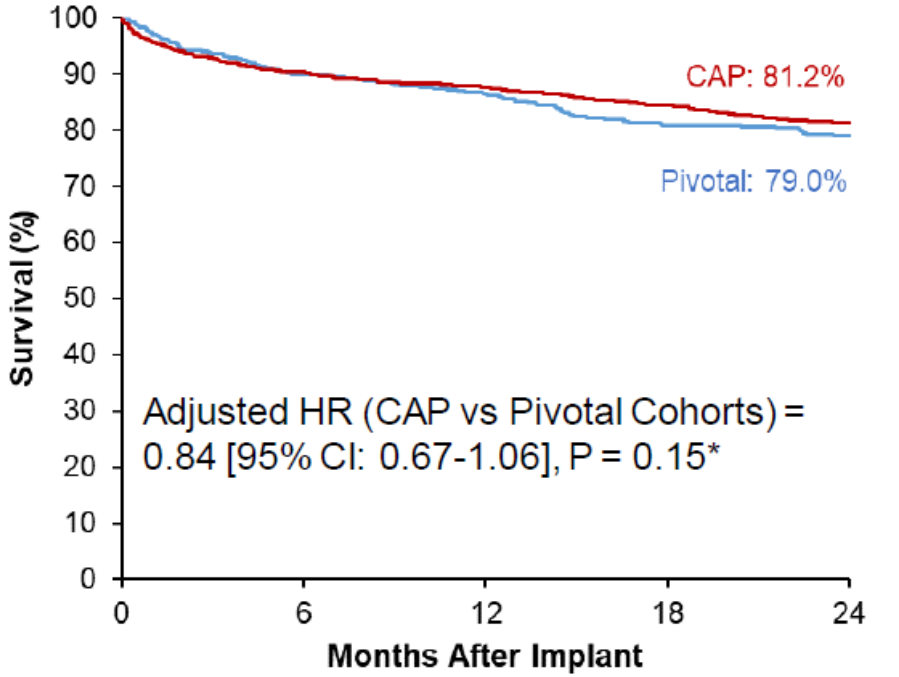
Composite Endpoint and Overall Survival

Composite Endpoint



No. at Risk:					
Pivotal	515	438	373	313	280
CAP	1685	1404	1267	1143	1050

Overall Survival



No. at Risk:					
Pivotal	515	447	383	322	289
CAP	1685	1420	1283	1163	1078

Hazard ratio presented for CAP vs Pivotal Cohorts.

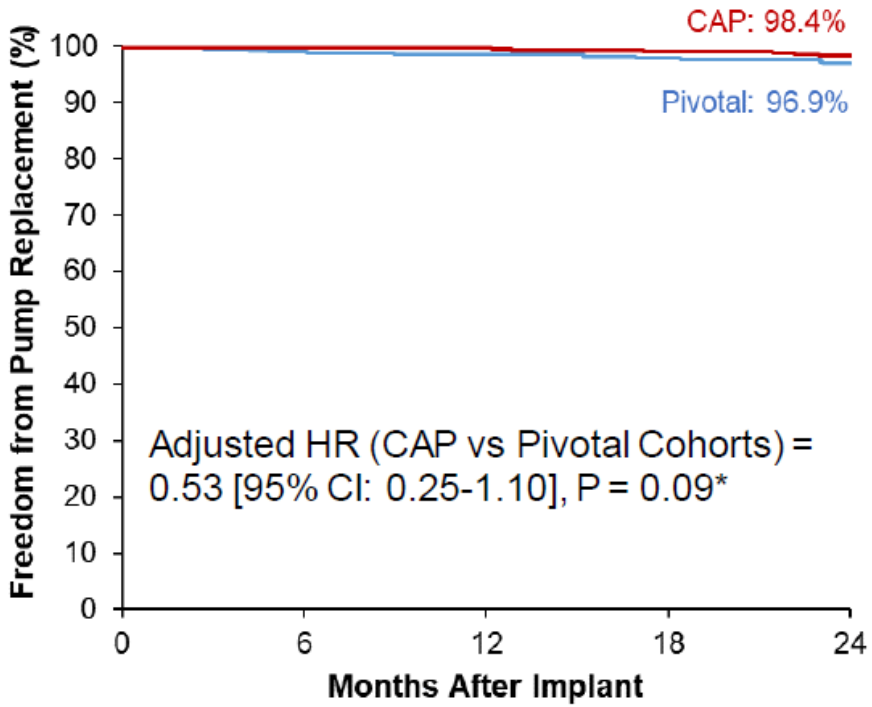
*P values were calculated with Cox regression. Models were adjusted for age, sex, race (Caucasian, non-Caucasian), intended use (BTT/BTC, DT), and INTERMACS profile (1-3, 4-7)

HR, hazard ratio; CI, confidence interval.

MOMENTUM 3

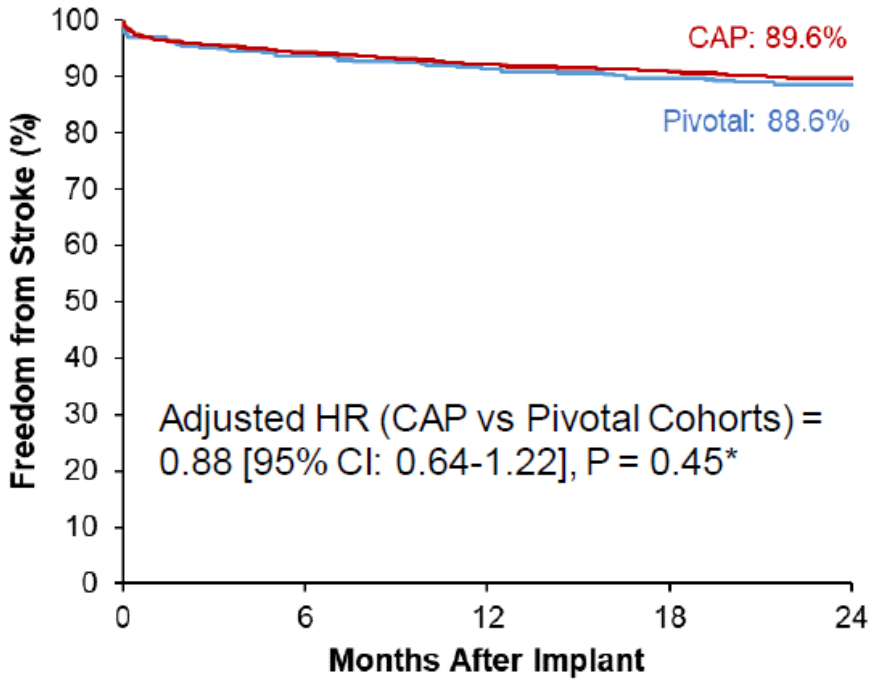
Pump Replacement and Strokes

Freedom from Pump Replacement



No. at Risk:					
Pivotal	515	444	379	317	283
CAP	1685	1418	1280	1155	1063

Freedom from Stroke

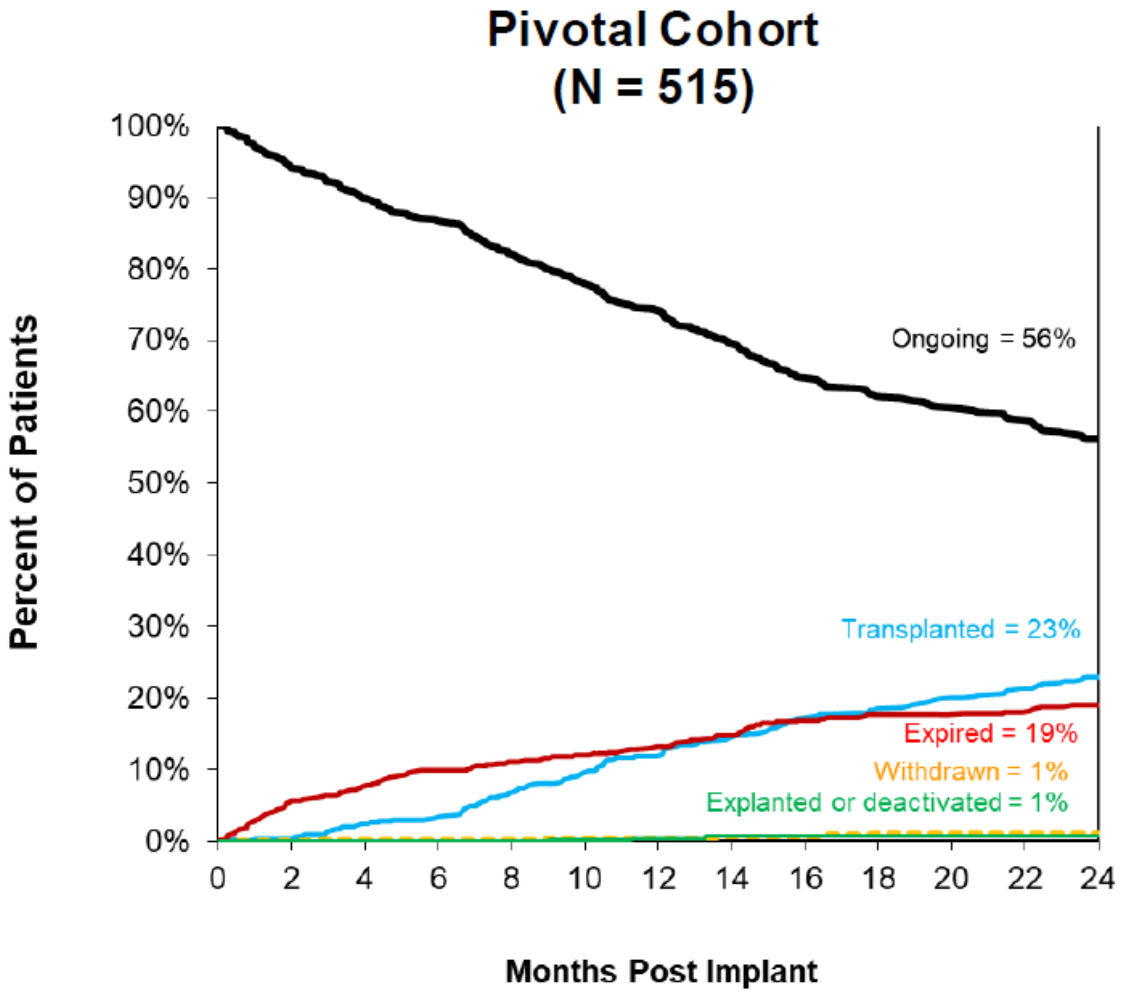


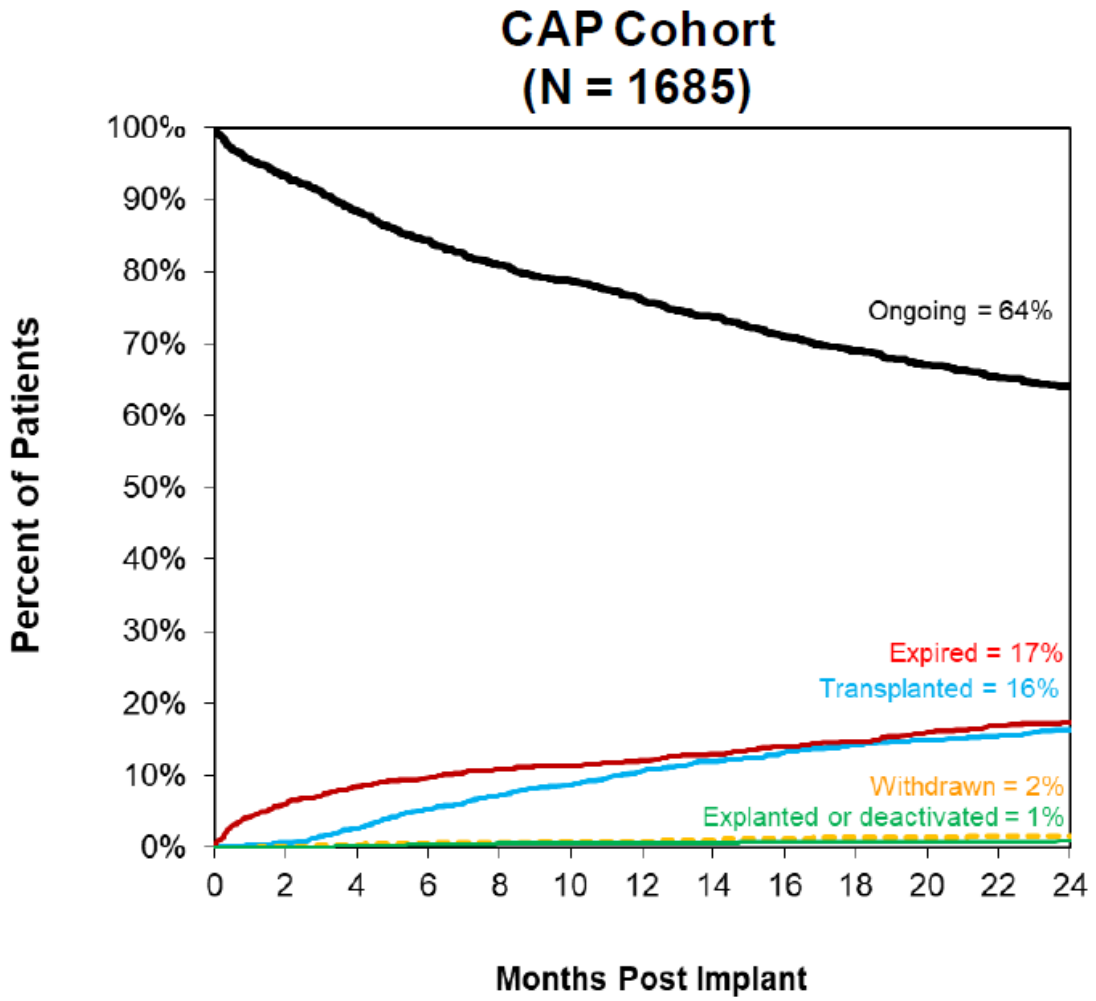
No. at Risk:					
Pivotal	515	429	361	304	270
CAP	1685	1364	1212	1092	1006

*P value was calculated with Cox regression. Model was adjusted for age, sex, race (Caucasian/non-Caucasian), intended use (BTT/BTC, DT), and INTERMACS profile (1-3, 4-7)
HR, hazard ratio; CI, confidence interval.

MOMENTUM 3

2 Year Competing Outcomes



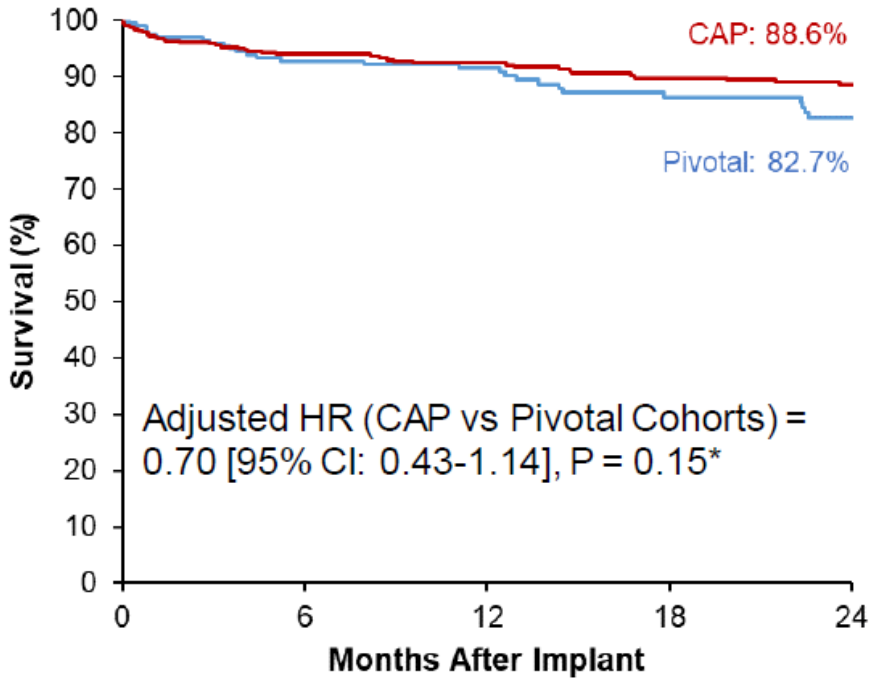


MOMENTUM 3

Overall Survival by Intended Goal of Implant

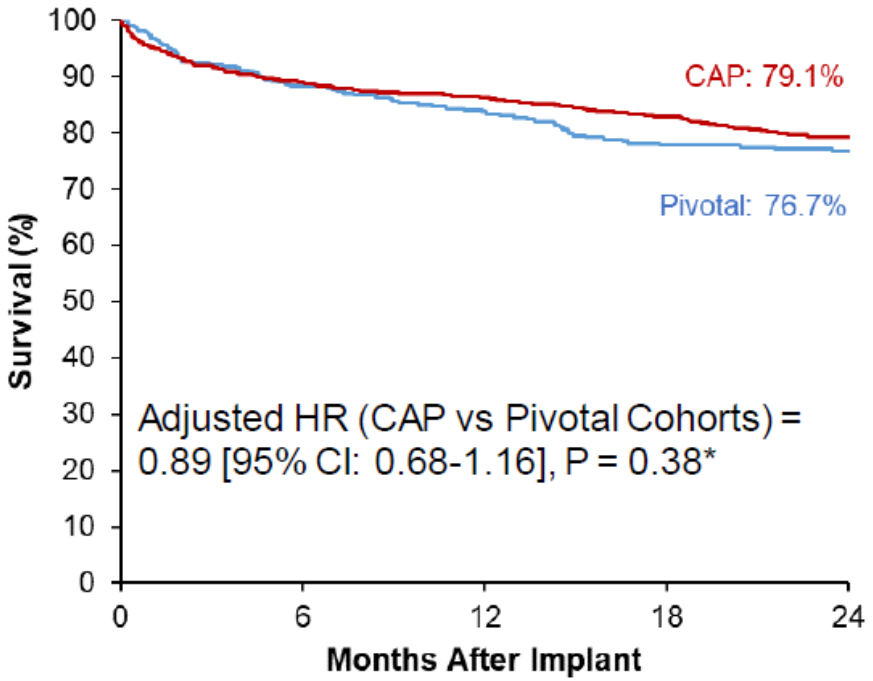
BTT/BTC and DT Subgroups

BTT/BTC: CAP vs Pivotal Cohorts



No. at Risk:					
Pivotal	198	170	134	103	87
CAP	406	323	272	235	214

DT: CAP vs Pivotal Cohorts



No. at Risk:					
Pivotal	317	277	249	219	202
CAP	1274	1092	1007	924	860

Hazard ratios presented for CAP vs Pivotal Cohorts.

*P values were calculated with Cox regression. Models were adjusted for age, sex, race (Caucasian, non-Caucasian), and INTERMACS profile (1-3, 4-7)

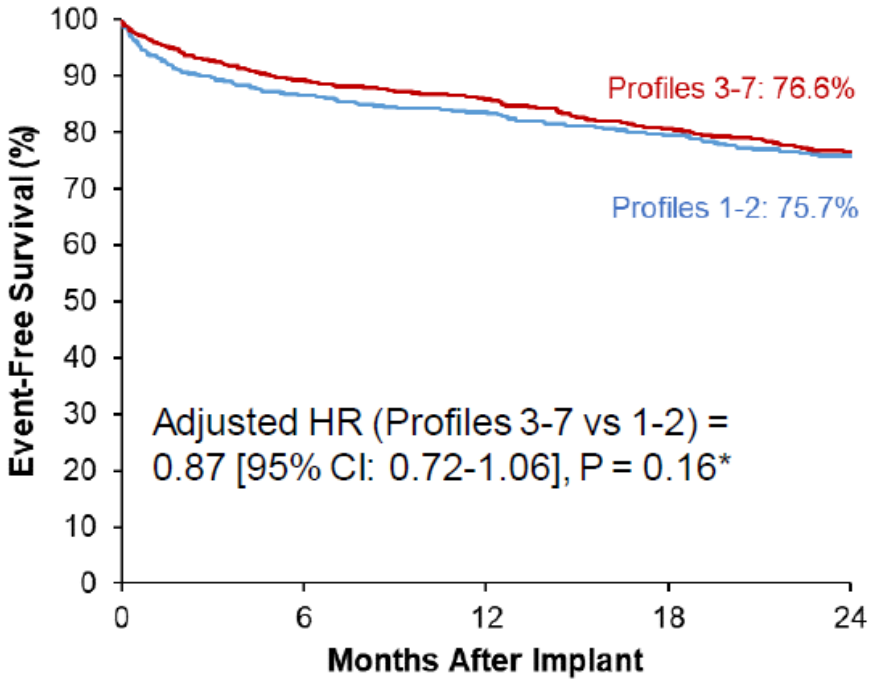
HR, hazard ratio; CI, confidence interval.

MOMENTUM 3

Clinical Severity and Outcomes

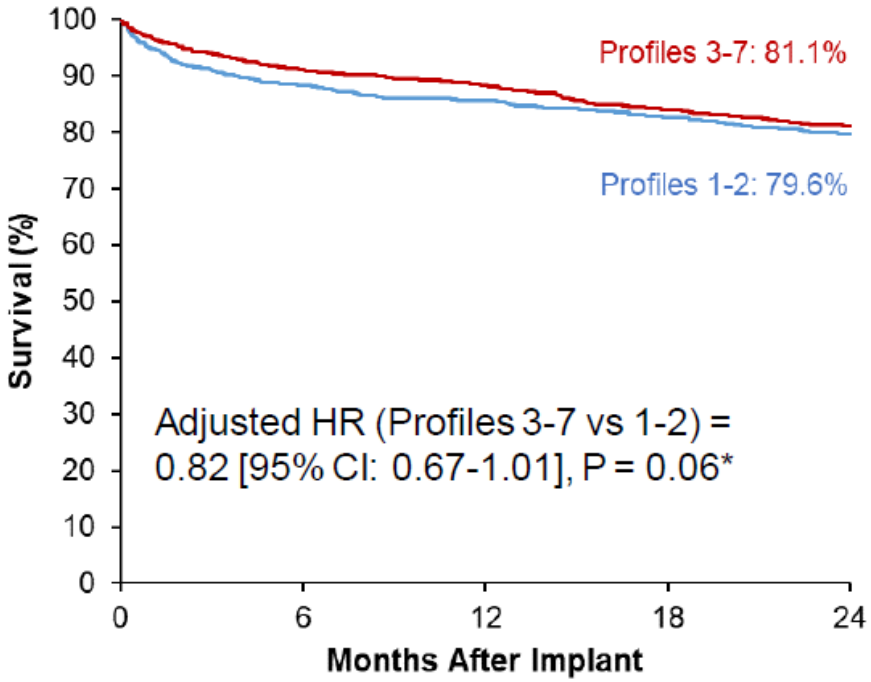
INTERMACS Profiles 1-2 ("Unstable") vs 3-7 ("Stable")

Composite Endpoint



No. at Risk:					
Profiles 1-2	753	615	552	491	445
Profiles 3-7	1431	1213	1079	956	876

Overall Survival



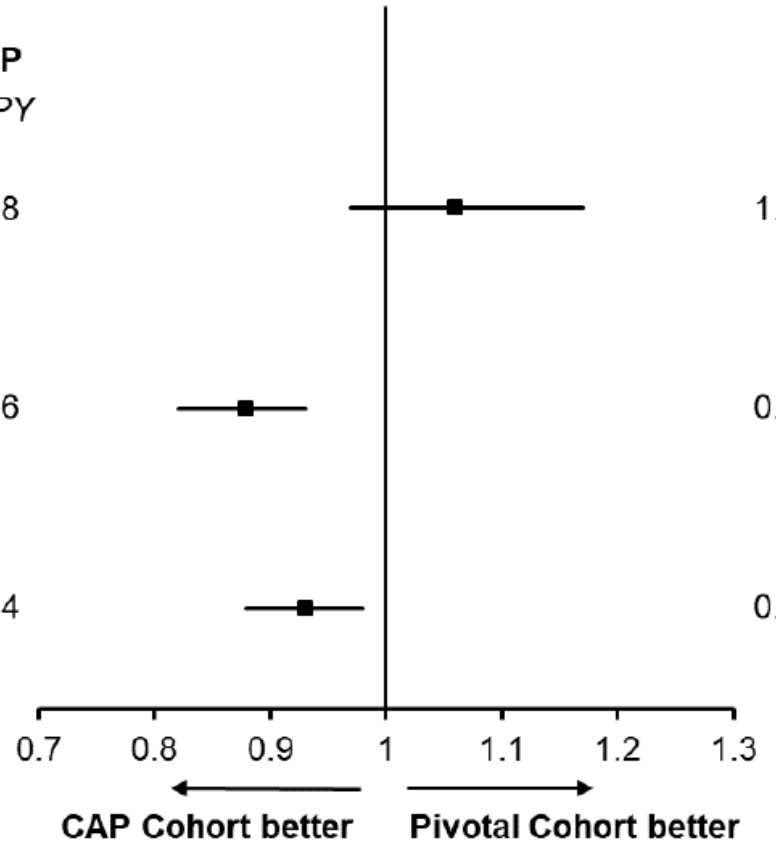
No. at Risk:					
Profiles 1-2	753	624	561	500	457
Profiles 3-7	1431	1229	1096	976	901

Hazard ratio presented for INTERMACS profiles 3-7 vs 1-2.
*P values were calculated with Cox regression. Models were adjusted for age, sex, race (Caucasian, non-Caucasian), and intended use (BTT/BTC, DT)
HR, hazard ratio; CI, confidence interval.

MOMENTUM 3

Net-Burden of Adverse Events

Adverse Event Burden	Pivotal *EPPY*	CAP *EPPY*	Adjusted Rate Ratio (95% CI)	*P-Value**
Hemocompatibility-Related (Suspected pump thrombosis, stroke, and bleeding)	0.69	0.78	1.06 (0.97 - 1.17)	0.21
Non Hemocompatibility-Related (Infection, right heart failure, cardiac arrhythmia, respiratory failure, and renal dysfunction)	1.76	1.56	0.88 (0.82 - 0.93)	<0.001
Overall (Hemocompatibility-related and non hemocompatibility-related)	2.45	2.34	0.93 (0.88 - 0.98)	0.006

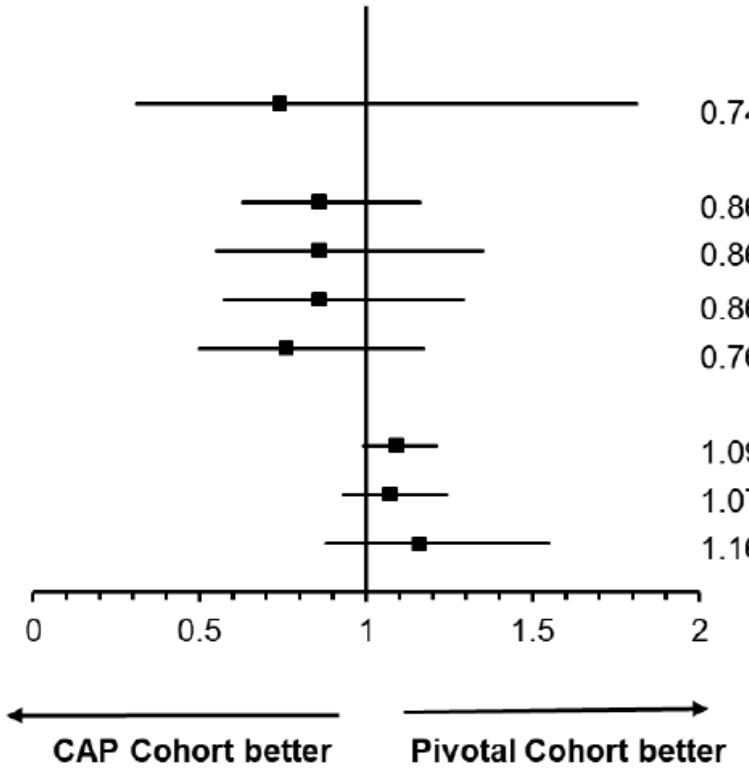


Rate ratios presented for CAP vs Pivotal Cohorts.
*P values were calculated with Poisson regression. Models were adjusted for age, sex, race (Caucasian, non-Caucasian), intended use (BTT/BTC, DT), and INTERMACS profile (1-3, 4-7)
EPPY events per patient year; CI, confidence interval.

MOMENTUM 3

Hemocompatibility-Related Adverse Events

Adverse Event	Pivotal %	CAP %	Pivotal *EPPY*	CAP *EPPY*	Adjusted Rate Ratio (95% CI)	*P-Value**
Suspected pump thrombosis	1.4	1.1	0.01	0.01	0.74 (0.31 - 1.81)	0.51
Any stroke	9.9	9.1	0.08	0.07	0.86 (0.63 - 1.16)	0.32
Hemorrhagic stroke	4.9	4.4	0.03	0.03	0.86 (0.55 - 1.35)	0.51
Ischemic stroke	5.6	5.2	0.04	0.04	0.86 (0.57 - 1.29)	0.45
Disabling stroke	5.0	4.3	0.04	0.03	0.76 (0.50 - 1.17)	0.21
Any bleeding	43.7	50.1	0.61	0.71	1.09 (0.99 - 1.21)	0.09
Gastrointestinal bleeding	24.5	29.0	0.31	0.36	1.07 (0.93 - 1.24)	0.33
Requiring surgery	9.7	13.4	0.08	0.10	1.16 (0.88 - 1.55)	0.29

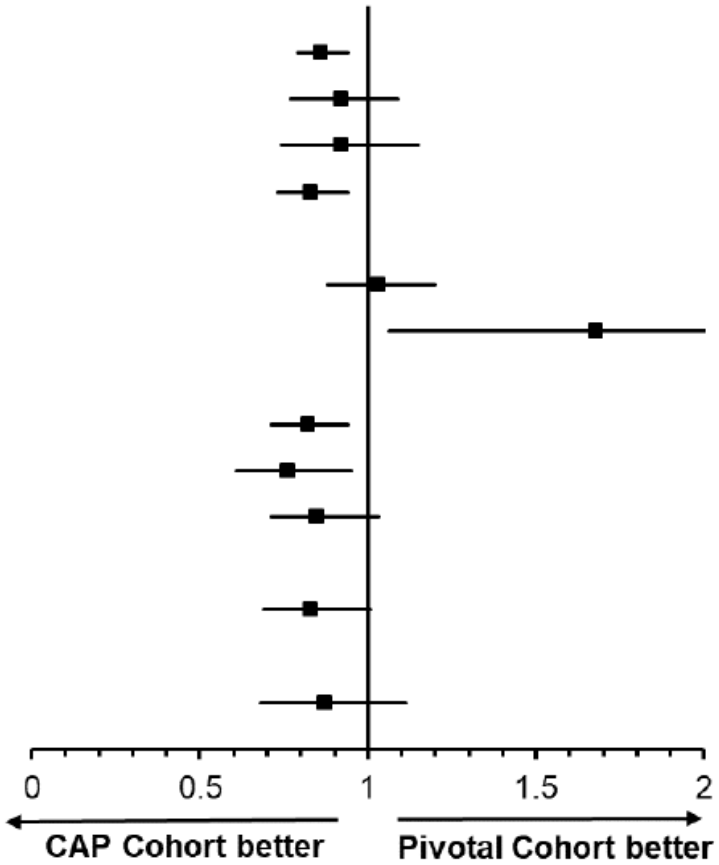


Rate ratios presented for CAP vs Pivotal Cohorts.
*P values were calculated with Poisson regression. Models were adjusted for age, sex, race (Caucasian, non-Caucasian), intended use (BTT/BTC, DT), and INTERMACS profile (1-3, 4-7)
EPPY events per patient year; CI, confidence interval.

MOMENTUM 3

Non-Hemocompatibility Adverse Events

Adverse Event	Pivotal %	CAP %	Pivotal *EPPY*	CAP *EPPY*	Adjusted Rate Ratio (95% CI)	*P-Value**
Any major infection	58.3	57.4	0.82	0.73	0.86 (0.79 - 0.94)	0.001
Driveline infection	23.3	23.1	0.23	0.21	0.92 (0.77 - 1.09)	0.32
Sepsis	15.1	15.4	0.13	0.13	0.92 (0.74 - 1.15)	0.48
Localized	40.8	36.8	0.46	0.39	0.83 (0.73 - 0.94)	0.003
Any right heart failure	34.2	37.4	0.27	0.27	1.03 (0.88 - 1.20)	0.73
Requiring RVAD	4.1	7.4	0.03	0.05	1.68 (1.06 - 2.68)	0.028
Cardiac arrhythmia	35.9	33.7	0.37	0.30	0.82 (0.71 - 0.94)	0.004
Supraventricular	18.8	16.5	0.15	0.12	0.76 (0.61 - 0.95)	0.014
Ventricular	20.8	18.6	0.20	0.17	0.85 (0.71 - 1.03)	0.09
Respiratory failure	21.6	19.8	0.19	0.16	0.83 (0.69 - 1.01)	0.06
Renal dysfunction	14.2	14.9	0.11	0.11	0.87 (0.68 - 1.11)	0.27



Rate ratios presented for CAP vs Pivotal Cohorts.

*P values were calculated with Poisson regression. Models were adjusted for age, sex, race (Caucasian, non-Caucasian), intended use (BTT/BTC, DT), and INTERMACS profile (1-3, 4-7)

EPPY events per patient year; CI, confidence interval.

Conclusions

- Survival with the HM3 LVAD is robust in this largest reported experience in 2200 implants (and is *comparable to that of heart transplantation), at 2-years*
  - Outcomes by *intended goal* of implant (BTT/BTC and DT) are similar between the pivotal trial and post-trial cohorts
  - Outcomes by *"unstable"* (INTERMACS 1-2) or *"stable"* (INTERMACS ≥3) severities were comparable with the HM3 pump

- Importantly, the "*Net-Burden"* of adverse events is markedly better in the post-trial cohort, reflecting a learning curve
  - Improvements driven by non-hemocompatibility related events, principally infection, arrhythmias, renal and respiratory failure
  - Although hemocompatibility related events maintain their improvements noted in the pivotal trial, bleeding remains a frequent adverse event and presents the greatest opportunity for improvement

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

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.

MAT-2210781 v2.0 | Item approved for U.S. use only.