LVAD as BTT or DT: An Update

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Los Angeles, April 2019
Charles Lindbergh and Alexis Carrel
John H. Gibbon, Jr., the inventor of the first successful heart-lung machine.
Domingo Liotta at his office in Baylor College of Medicine
In 1964 the NIH set a goal to developed an artificial heart by 1970.

Aug. 8, 1966.

After a four-hour surgery, Dr. DeBakey implanted an external heart pump called a LVAD in post cardiotomy shock patients. Patient was kept alive for 10 days until her own heart healed.

The first successful use of the pump.
Primary End Point Analysis (ITT)

Survival at 24 months free of disabling stroke or reoperation to replace or remove the pump

Rogers J et al NEJM 2017
ENDORSE Supplemental Trial Design

Study Population (N=494)

- Screen Failure (N=19)

Randomized 2:1

- Randomized, not implanted (N=10)

Modified ITT Population* (N=465)

- HVAD (N=308)
- HMII (control) (N=157)

* Modified Intent-to-Treat subjects in which the pump was surgically inserted and turned on. Modified ITT and As-Treated (AT) populations were identical.
Comparison of the average MAP at each follow-up

Error bars represent 95% confidence intervals
Primary Endpoint: freedom from neurologic injury (stroke with MRS > 0 at 24 weeks post stroke or a transient ischemic attack) at 12 months

Neurologic Injury was defined as any stroke with MRS > 0 at 24 weeks post-stroke, or a TIA, or spinal cord injury. Note: this endpoint does not include device exchange.

TIA: transient ischemic attack
Freedom from death, disabling stroke (MRS $\geq 4$), and device malfunction or failure requiring exchange, explant, or urgent transplant

![Graph showing event free rate over days with HVAD and Control groups, and statistical significance](image)

**Superiority P value** = 0.0354

<table>
<thead>
<tr>
<th>Days</th>
<th>HVAD</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>308</td>
<td>157</td>
</tr>
<tr>
<td>180</td>
<td>263</td>
<td>120</td>
</tr>
<tr>
<td>365</td>
<td>228</td>
<td>105</td>
</tr>
</tbody>
</table>
Background

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

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

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

¹Mehra MR. The burden of haemocompatibility with left ventricular assist systems: a complex weave. Eur Heart J 2019;40(8):673-7
HeartMate 3 LVAS

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

Bourque K et al. Design Rationale and Preclinical Evaluation of the HeartMate 3 Left Ventricular Assist System for Hemocompatibility. ASAIO J 2016;62(4):375-83
Adaptive Trial Design

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

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

Additional 72 patients enrolled

1st interim analysis of the ST cohort
(7.1%)

2nd interim analysis of the LT cohort
(35.6%)

Final analysis of the Full Cohort
(100%)

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

Additional 662 patients enrolled

Two Interim Analyses

**ST Cohort: 294 Patients at 6 Months**

HeartMate 3 superiority driven by reduction in pump thrombosis

**LT Cohort: 366 Patients at 2 Years**

Lower incidence of non-disabling stroke with HeartMate 3
## Stroke Rates Across the Duration of Support

<table>
<thead>
<tr>
<th>Time (Days)</th>
<th>Stroke Events (Pts/Patients ongoing, %)</th>
<th>Events per patient-year</th>
<th>Odds Ratio (HM3 vs HMII) OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HM3</td>
<td>HMII</td>
<td>HM3</td>
</tr>
<tr>
<td>Overall (0-733 Days)</td>
<td>22 (19/189, 10%)</td>
<td>43 (33/172, 19%)</td>
<td>0.08</td>
</tr>
<tr>
<td>- Perioperative (0-30 Days)</td>
<td>7 (7/180, 3.7%)</td>
<td>6 (6/172, 3.5%)</td>
<td>0.46</td>
</tr>
<tr>
<td>- Short-term (31-180 Days)</td>
<td>7 (7/182, 3.8%)</td>
<td>16 (13/161, 8.1%)</td>
<td>0.10</td>
</tr>
<tr>
<td>- Long-term (181-730 Days)</td>
<td>8 (5/165, 3.0%)</td>
<td>21 (17/141, 12.1%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Colombo PC / Uriel N / Mehra M Circulation 2018
Multivariable model

- Gender (Male)
  - Decreased Stroke: OR: 0.70 (0.35 - 1.40), p=0.31
  - Increased Stroke: OR: 0.1.26 (0.68 - 2.33), p=0.46

- Age (>65)
  - Decreased Stroke: OR: 0.70 (0.35 - 1.40), p=0.31
  - Increased Stroke: OR: 0.1.26 (0.68 - 2.33), p=0.46

- HM3 Treatment Group
  - Decreased Stroke: OR: 0.44 (0.24 - 0.82), p=0.01
  - Increased Stroke: OR: 1.79 (0.88 - 3.65), p=0.11

- History of Stroke/TIA
  - Decreased Stroke: OR: 0.44 (0.24 - 0.82), p=0.01
  - Increased Stroke: OR: 1.79 (0.88 - 3.65), p=0.11

Colombo PC / Uriel N / Mehra M Circulation 2018
Survival Post-Implant by Subtype: Ischemic vs. Hemorrhagic

No Stroke
- 85 ± 2%

Ischemic Stroke
- 76 ± 8%

Hemorrhagic Stroke
- 43 ± 12%

Colombo PC / Uriel N / Mehra M  Circulation 2018
Results: Survival Free of HRAEs

P = 0.012 Log-Rank
HR = 0.62 [0.42 - 0.91]

HM3 (n = 151)
HMII (n = 138)
Cumulative Costs, Hospitalizations, and Hospital Days

*Normalized over patient time in study*

### Cumulative Costs

\[ \Delta = 38,913 \quad P < 0.001 \]

### Hospitalizations

\[ \Delta = 0.6 \text{ hospitalizations} \quad P = 0.015 \]

### Hospital Days

\[ \Delta = 8.3 \text{ days} \quad P = 0.003 \]

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Difference shown is for HeartMate II – HeartMate 3. P values derived from bootstrap simulation (x1500)
Full Cohort

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

Withdrawn before implant
N = 1
Death: 1

As-Treated Population
N=1020

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

Completed study follow-up
N=509

HeartMate 3
N=516

HeartMate II
N=512

Implanted with HeartMate 3
N=515

Implanted with HeartMate II
N=505

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

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

Completed study follow-up
N=509

N=490

24-month follow-up
### Baseline Characteristics

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

There were significant differences between groups for race (P=0.04). *Assessments were not performed in 2 HeartMate 3 patients and 5 HeartMate II patients.
Primary End Point (ITT)

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

HR = 0.60 (95%CI: 0.47-0.75)
P<0.0001 by log-rank test

mRS denotes modified Rankin Score; HR, hazard ratio; CI, confidence interval
Principal Secondary End Point

Pump replacement at 2 years

<table>
<thead>
<tr>
<th>HeartMate 3</th>
<th>HeartMate II</th>
</tr>
</thead>
<tbody>
<tr>
<td>98.9%</td>
<td>95.5%</td>
</tr>
<tr>
<td>98.5%</td>
<td>92.2%</td>
</tr>
<tr>
<td>96.9%</td>
<td>84.6%</td>
</tr>
</tbody>
</table>

HR = 0.19 (95%CI: 0.10-0.35)  
P < 0.0001 by log-rank test

RR (95%CI) = 0.21 (0.11 - 0.38)  
P<0.0001

No. at Risk:
- HeartMate 3: 515, 444, 379, 317, 283
- HeartMate II: 505, 403, 322, 264, 226

RR denotes relative risk; CI, confidence interval; HR, hazard ratio
### Principal Hemocompatibility-Related Adverse Events

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

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

Freedom from All Stroke

HR = 0.47 (95%CI: 0.34-0.66)
P < 0.0001 by log-rank test

Stroke Severity

RR=0.42 (95%CI: 0.30-0.57)
P<0.0001

HeartMate 3

HeartMate II

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

No. at Risk:
HeartMate 3 515 429 361 304 270
HeartMate II 505 384 299 252 210

Stroke Rate (EPPY)

non-Disabling Stroke (Modified Rankin Score 0-3)
Disabling Stroke (Modified Rankin Score 4-5)
Death (Modified Rankin Score 6)
Gastrointestinal Bleeding

Freedom from Gastrointestinal Bleeding

HR = 0.72 (95% CI: 0.57-0.90)
P = 0.005 by log-rank test

<table>
<thead>
<tr>
<th>Months After Implant</th>
<th>HeartMate 3</th>
<th>HeartMate II</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>6</td>
<td>83.9%</td>
<td>77.4%</td>
</tr>
<tr>
<td>12</td>
<td>79.4%</td>
<td>71.5%</td>
</tr>
<tr>
<td>18</td>
<td>70.9%</td>
<td>63.2%</td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No. at Risk:

- HeartMate 3: 515, 381, 308, 251, 204
- HeartMate II: 505, 325, 248, 202, 167

GI denotes gastrointestinal; HR hazard ratio; CI, confidence interval
Other Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>HM3</th>
<th>HM II</th>
<th>Relative Risk (95% CI)</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>HM3 EPPY</td>
<td>HM II EPPY</td>
</tr>
<tr>
<td>Other neurologic event+</td>
<td>59 (11.5)</td>
<td>47 (9.3)</td>
<td>0.09</td>
<td>0.08</td>
</tr>
<tr>
<td>TIA</td>
<td>16 (3.1)</td>
<td>19 (3.8)</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Any major infection</td>
<td>300 (58.3)</td>
<td>285 (56.4)</td>
<td>0.82</td>
<td>0.82</td>
</tr>
<tr>
<td>LVAS driveline infection</td>
<td>120 (23.3)</td>
<td>98 (19.4)</td>
<td>0.23</td>
<td>0.22</td>
</tr>
<tr>
<td>Any right heart failure</td>
<td>176 (34.2)</td>
<td>143 (28.3)</td>
<td>0.27</td>
<td>0.23</td>
</tr>
<tr>
<td>Managed with RVAS</td>
<td>21 (4.1)</td>
<td>21 (4.2)</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>185 (35.9)</td>
<td>207 (41.0)</td>
<td>0.37</td>
<td>0.45</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>107 (20.8)</td>
<td>128 (25.3)</td>
<td>0.20</td>
<td>0.27</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>111 (21.6)</td>
<td>98 (19.4)</td>
<td>0.19</td>
<td>0.17</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>73 (14.2)</td>
<td>56 (11.1)</td>
<td>0.11</td>
<td>0.08</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>25 (4.9)</td>
<td>27 (5.3)</td>
<td>0.03</td>
<td>0.04</td>
</tr>
</tbody>
</table>

HM3 denotes HeartMate 3; HMII HeartMate II; EPPY events per patient year; CI, confidence interval; TIA transient ischemic attack; RVAS right ventricular assist system.

*P values were calculated with Poisson regression. +Includes TIA, encephalopathy, seizure and neurologic events other than stroke.
## Hospitalization Profiles, Days Out of the Hospital and Readmissions

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

EPPY denotes events per patient year; HR, hazard ratio; CI, confidence interval.

*P values for differences in duration are from Wilcoxon Rank Sum test. ^HR was calculated from the Andersen-Gill model.
Functional Status and Quality of Life

6 Minute Walk Distance

<table>
<thead>
<tr>
<th>Time</th>
<th>Baseline</th>
<th>6 Mo</th>
<th>12 Mo</th>
<th>24 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=471</td>
<td>N=365</td>
<td>N=306</td>
<td>N=211</td>
</tr>
<tr>
<td></td>
<td>136</td>
<td>310</td>
<td>323</td>
<td>323</td>
</tr>
</tbody>
</table>

P**<0.0001

P*=0.15

Baseline

N=452

6 Mo

N=333

12 Mo

N=268

24 Mo

N=174

P**<0.0001

P**<0.0001

P*=0.61

EQ-5D-5L Visual Analogue Scale

<table>
<thead>
<tr>
<th>Time</th>
<th>Baseline</th>
<th>6 Mo</th>
<th>12 Mo</th>
<th>24 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=486</td>
<td>N=420</td>
<td>N=358</td>
<td>N=276</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>76</td>
<td>76</td>
<td>76</td>
</tr>
</tbody>
</table>

P**<0.0001

P**<0.0001

P*=0.15

Baseline

N=475

6 Mo

N=386

12 Mo

N=311

24 Mo

N=227

P**<0.0001

P**<0.0001

P*=0.34

NYHA Class I or II

<table>
<thead>
<tr>
<th>Time</th>
<th>Baseline</th>
<th>6 Mo</th>
<th>12 Mo</th>
<th>24 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=514</td>
<td>N=428</td>
<td>N=359</td>
<td>N=275</td>
</tr>
<tr>
<td></td>
<td>79</td>
<td>81</td>
<td>80</td>
<td>80</td>
</tr>
</tbody>
</table>

P**<0.0001

P*=0.61

Baseline

N=504

6 Mo

N=392

12 Mo

N=321

24 Mo

N=229

P**<0.0001

KCCQ Overall Summary Score

<table>
<thead>
<tr>
<th>Time</th>
<th>Baseline</th>
<th>6 Mo</th>
<th>12 Mo</th>
<th>24 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=493</td>
<td>N=421</td>
<td>N=357</td>
<td>N=277</td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>70</td>
<td>68</td>
<td>69</td>
</tr>
</tbody>
</table>

P**<0.0001

P**<0.0001

P*=0.34

Baseline

N=482

6 Mo

N=388

12 Mo

N=311

24 Mo

N=227

P**<0.0001

P**<0.0001

*P-value between treatment arms over time. **P-value for treatment over time. Longitudinal changes were analyzed with linear mixed-effects models using data from baseline, 3, 6, 12, 18, and 24 month visits.
Subgroup Analyses of the Primary Endpoint (ITT)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Hazard Ratio (95% CI)</th>
<th>Interaction P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age - years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 (n = 582)</td>
<td>0.56 (0.40 - 0.78)</td>
<td>0.54</td>
</tr>
<tr>
<td>≥65 (n = 446)</td>
<td>0.65 (0.47 - 0.90)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (n= 830)</td>
<td>0.61 (0.47 - 0.79)</td>
<td>0.58</td>
</tr>
<tr>
<td>Women (n = 198)</td>
<td>0.54 (0.31 - 0.96)</td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian (n = 709)</td>
<td>0.59 (0.45 - 0.77)</td>
<td>0.70</td>
</tr>
<tr>
<td>Non-Caucasian (n = 319)</td>
<td>0.67 (0.42 - 1.07)</td>
<td></td>
</tr>
<tr>
<td><strong>Intended Use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BTT (n = 234)</td>
<td>0.51 (0.28 - 0.94)</td>
<td>0.62</td>
</tr>
<tr>
<td>BTC (n = 167)</td>
<td>0.67 (0.37 - 1.20)</td>
<td></td>
</tr>
<tr>
<td>DT (n = 627)</td>
<td>0.60 (0.45 - 0.79)</td>
<td></td>
</tr>
<tr>
<td><strong>INTERMACS Profile</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Profiles 2 or 3 (n = 825)</td>
<td>0.60 (0.46 - 0.78)</td>
<td>0.30</td>
</tr>
<tr>
<td>Profiles 4 or 5 (n = 160)</td>
<td>0.80 (0.46 - 1.38)</td>
<td></td>
</tr>
</tbody>
</table>

BTT denotes bridge to transplant; BTC, bridge to candidacy; DT, destination therapy
Results: Actuarial Survival Free of HRAEs

HRAE include: Bleeding >30 days, stroke, pump thrombosis, arterial thromboembolism, non-stroke neurological event (inconclusive or hematologic in etiology)

P < 0.0001 by log-rank test
HR: 0.70 (95%CI: 0.59-0.82) p<0.0001

No. at Risk:
- HeartMate III: 515, 342, 252, 203, 161
- HeartMate II: 505, 273, 190, 148, 114
Results: Comparison of total HCS Burden

**GEE Model**: Total Score: p<0.0001
Time to HRAE event: p<0.0001

*ordinal multinomial generalized estimating equations (GEE) repeated-measures model*
Net Clinical Benefit

- The **Number Needed to Treat** over two years to avert at least 1 hemocompatibility-related adverse event (pump thrombosis, stroke, or bleed) is **less than 1**
- For every 100 patients implanted with HeartMate 3 rather than HeartMate II over a two-year period 110 such events are averted

- **Pump Thrombosis**
  - 22 events averted

- **Stroke**
  - 20 events averted

- **Bleeding**
  - 68 events averted
    - (36 gastrointestinal)
Summary: A More Forgiving Pump

• In the largest LVAD study performed, the centrifugal-flow HeartMate 3 LVAS has demonstrated superior performance compared to the axial-flow HeartMate II pump with respect to:
  – Reduction in Pump Thrombosis and need for Pump replacement
  – Reduction in Strokes of any type and of any severity
  – Reduction in any Bleeding, particularly gastrointestinal bleeds
  – Reduction in Cardiac Arrhythmias, particularly ventricular arrhythmias
  – Reduction in re-hospitalizations and days spent in the hospital
Novel Non Invasive Arterial Pressure Technology

Monitoring of continuous blood pressure and cardiac viability metrics.

Benchmarking patients and tracking progress on the basis of deep analytics.

Patients are traced by stage of evolution from early onset, where the benefit to insurers is most compelling.

Wrist-worn device

CorMetric Herzlia Israel
Simultaneous Data Recording
Systolic Blood Pressure

\[ \text{Systolic BP} - |\text{error}| = 4.96, \text{std} = 6.61 \]
\[ N = 160, r = 0.92, p = 3.80e-67 \]

Diastolic Blood Pressure

\[ \text{Diastolic BP} - |\text{error}| = 5.22, \text{std} = 7.16 \]
\[ N = 160, r = 0.86, p = 1.28e-47 \]
Total Implanted LVAD
BiVACOR

- Long-term total artificial heart
- Can provide high flows over 12 LPM
- Wide gaps to maximize hemocompatibility
BiVACOR

- Left and right impeller blades mounted on either side of a rotating hub.
- Hub is levitated and rotated via an electromagnetic motor and bearing arrangement on top of pump casings.
We Need Pulsatility?
Successful Pregnancy
Improvement in Survival Rates through Time

A new standard has been set

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2. Slaughter, et al. NEJM


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Nitasha Sarswat
Jayant Raikhelkar
Sara Kalantari
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