HEART FAILURE

F. Ruschitzka (Zurich, CH)
Professor of Cardiology
Co-Head, Dept of Cardiology
President-elect HFA
University Heart Center
University Hospital
Zürich, Switzerland

Conflicts of Interest
Aventis, Bayer, Biotronik, Cardiorentis, Merck, Novartis, Pfizer, SJM, Servier
Interest in Conflict: none
Peri-infarct Zone Pacing to Prevent Adverse Left Ventricular Remodeling in Patients with Large Myocardial Infarction

**Results from the PRomPT Trial**

**Gregg W. Stone, MD**  
Eugene S. Chung, Branislav Stancak, Jesper H. Svendsen, Trent M. Fischer, Fred Kueffer, Thomas Ryan, Jeroen Bax, and Angel Leon, for the Post-Myocardial Infarction Remodeling Prevention Therapy (PRomPT) Trial Investigators

Stone GW et al. Eur Heart J 2015; DOI: [http://dx.doi.org/10.1093/eurheartj/ehv436](http://dx.doi.org/10.1093/eurheartj/ehv436), FP 7065

**ALBATROSS**

Aldosterone Lethal effects Blockade in Acute myocardial infarction Treated with or without Reperfusion to improve Outcome and Survival at Six months follow-up


On behalf of the ALBATROSS investigators

Between December 2010 and October 2013, 126 patients were randomized at 27 sites in Europe, the Middle East, and the United States.

**Randomized 1:1:1**
- LV and RV pacing (n=41)
  - 1 withdrew
  - 1 withdrawn
  - Successful implant (n=37)
    - 1 withdrew
    - 18-month FU (n=38)
      - As-treated (n=37)
      - ITT (n=41)

- LV pacing only (n=40)
  - 1 withdrew
  - 1 withdrawn
  - Successful implant (n=38)
    - 18-month FU (n=36)
      - As-treated (n=38)
      - ITT (n=40)

- No implant (n=45)
  - 5 withdrew
  - 3 lost to FU
  - 1 missed
  - 18-mo FU

**Stone GW et al. Eur Heart J 2015; DOI: http://dx.doi.org/10.1093/eurheartj/ehv436, FP 7065**
Paired echocardiographic results between the baseline and 18-month follow-up visits

PRomPT: PRIMARY ENDPOINT – ΔLVEDV

Mean ΔLVEDV (mL)

Control  Single Site  Dual Site

Months after randomization

N with data:

<table>
<thead>
<tr>
<th>Single-site</th>
<th>37</th>
<th>32</th>
<th>27</th>
<th>27</th>
<th>29</th>
<th>31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dual-site</td>
<td>37</td>
<td>33</td>
<td>34</td>
<td>28</td>
<td>25</td>
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<tr>
<td>Control</td>
<td>44</td>
<td>34</td>
<td>34</td>
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</table>

Stone GW et al. Eur Heart J 2015; DOI: http://dx.doi.org/10.1093/eurheartj/ehv436, FP 7065
**ALBATROSS STUDY DESIGN**

**AMI (ST+ or ST-) in the first 72hrs**

- **Aldosterone blockade**
  - iv K⁺ canrenoate* 
  - then 
  - spironolactone**

- **control**

  - Randomized Open label N=1600

- Randomized Open label N=1600

- * Soludactone 200mg

- ** Aldactone 25mg od

**1° End Point:** death, resuscitated cardiac death, VF/VT, indication for defibrillator, heart failure *up to 6-month FU*
PRIMARY END POINT

Death, resuscitated death, VF/VT, indication for ICD or heart failure

N at risks

<table>
<thead>
<tr>
<th></th>
<th>Standard Therapy</th>
<th>MRA Regimen</th>
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</thead>
<tbody>
<tr>
<td>Follow-up (days)</td>
<td>801</td>
<td>802</td>
</tr>
<tr>
<td>0</td>
<td>687</td>
<td>705</td>
</tr>
<tr>
<td>50</td>
<td>669</td>
<td>683</td>
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<td>100</td>
<td>645</td>
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<tr>
<td>150</td>
<td></td>
<td>273</td>
</tr>
<tr>
<td>200</td>
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<td>183</td>
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</tbody>
</table>

HR = 0.97 [0.73-1.28]
P = 0.81

MRA: Mineralocorticoid Receptor Antagonist; VF: Ventricular Fibrillation; VT: Ventricular Tachycardia; ICD: Implantable Cardioverter Defibrillator

G. Montalescot (Paris, FR), FP 1167
## DEATH IN PRE-SPECIFIED SUBGROUPS

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Death</th>
<th>Hazard ratio [95% confidence interval]</th>
<th>P for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td>0.65 [0.30, 1.38]</td>
<td>0.57</td>
</tr>
<tr>
<td>Age &gt;= 65</td>
<td></td>
<td>0.68 [0.30, 1.54]</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 65</td>
<td></td>
<td>0.34 [0.04, 2.36]</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td>0.73 [0.13, 4.37]</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td>0.63 [0.27, 1.46]</td>
<td>0.88</td>
</tr>
<tr>
<td>STEMI</td>
<td></td>
<td>0.20 [0.06, 0.70]</td>
<td>0.01</td>
</tr>
<tr>
<td>NSTEMI</td>
<td></td>
<td>3.47 [0.72, 16.72]</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td></td>
<td>0.50 [0.20, 1.25]</td>
<td>0.50</td>
</tr>
<tr>
<td>ACE or ARB before randomization</td>
<td></td>
<td>0.83 [0.25, 2.71]</td>
<td>0.60</td>
</tr>
<tr>
<td>Neither ACE nor ARB before randomization</td>
<td></td>
<td>0.55 [0.20, 1.48]</td>
<td></td>
</tr>
<tr>
<td>ACE or ARB after randomization</td>
<td></td>
<td>0.47 [0.14, 1.51]</td>
<td></td>
</tr>
<tr>
<td>Neither ACE nor ARB after randomization</td>
<td></td>
<td>0.94 [0.30, 2.96]</td>
<td>0.40</td>
</tr>
<tr>
<td>BB after randomization</td>
<td></td>
<td>0.72 [0.23, 2.27]</td>
<td>0.96</td>
</tr>
<tr>
<td>No BB after randomization</td>
<td></td>
<td>0.75 [0.25, 2.23]</td>
<td></td>
</tr>
<tr>
<td>ACE/ARB and BB after randomization</td>
<td></td>
<td>0.63 [0.15, 2.64]</td>
<td>0.95</td>
</tr>
<tr>
<td>no ACE/ARB or no BB or neither after randomization</td>
<td></td>
<td>0.67 [0.26, 1.74]</td>
<td></td>
</tr>
<tr>
<td>Killip class &gt;= 2</td>
<td></td>
<td>0.71 [0.24, 2.11]</td>
<td>0.97</td>
</tr>
<tr>
<td>Killip class = 1</td>
<td></td>
<td>0.73 [0.25, 2.11]</td>
<td></td>
</tr>
<tr>
<td>Pulsed blood pressure &lt; 45mmHg</td>
<td></td>
<td>0.96 [0.28, 3.33]</td>
<td>0.51</td>
</tr>
<tr>
<td>Pulsed blood pressure &gt;= 45mmHg</td>
<td></td>
<td>0.56 [0.21, 1.52]</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction &lt; 40%</td>
<td></td>
<td>0.62 [0.20, 1.94]</td>
<td>0.98</td>
</tr>
<tr>
<td>Left ventricular ejection fraction &gt;= 40%</td>
<td></td>
<td>0.63 [0.21, 1.92]</td>
<td></td>
</tr>
<tr>
<td>Admission creatinine clearance &gt; 60ml/min</td>
<td></td>
<td>0.88 [0.32, 2.43]</td>
<td>0.40</td>
</tr>
<tr>
<td>Admission creatinine clearance &lt;= 60ml/min</td>
<td></td>
<td>0.45 [0.14, 1.49]</td>
<td></td>
</tr>
<tr>
<td>Admission plasma potassium level &lt;4 mmol/l</td>
<td></td>
<td>0.70 [0.20, 2.49]</td>
<td>0.96</td>
</tr>
<tr>
<td>Admission plasma potassium level &gt;=4 mmol/l</td>
<td></td>
<td>0.67 [0.26, 1.77]</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>1.33 [0.30, 5.00]</td>
<td>0.27</td>
</tr>
<tr>
<td>No Diabetes</td>
<td></td>
<td>0.50 [0.20, 1.24]</td>
<td></td>
</tr>
<tr>
<td>Pre-hospital randomization</td>
<td></td>
<td>1.33 [0.41, 3.18]</td>
<td>0.08</td>
</tr>
<tr>
<td>In-hospital randomization</td>
<td></td>
<td>0.50 [0.18, 1.07]</td>
<td></td>
</tr>
<tr>
<td>BMI &lt;= 25</td>
<td></td>
<td>0.55 [0.20, 1.51]</td>
<td>0.70</td>
</tr>
<tr>
<td>BMI &gt; 25</td>
<td></td>
<td>0.74 [0.23, 2.32]</td>
<td></td>
</tr>
</tbody>
</table>

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G. Montalescot (Paris, FR), FP 1167
Finerenone (BAY 94-8862) is a novel non-steroidal MRA that has greater receptor selectivity than spironolactone and better receptor affinity than eplerenone \textit{in vitro} \textsuperscript{1}

\textbf{Study objective:} to compare the safety and efficacy of different once-daily oral doses of finerenone with eplerenone in patients who presented in emergency departments with worsening chronic HFrEF with type 2 diabetes mellitus and/or chronic kidney disease (CKD)
ARTS-HF: STUDY FLOW

Enrolment
- Assessed for eligibility (n = 1286)
  - Excluded (n = 220)
    - Did not meet inclusion criteria (n = 191)
    - Declined to participate (n = 21)
    - Other reasons (n = 8)
  - Randomized (n = 1066)

Allocation
- Eplerenone
  - n = 224
  - 2.5–5 mg, n = 173
  - 5–10 mg, n = 165
- Finerenone
  - 2.5–5 mg, n = 173
  - 5–10 mg, n = 165
  - 7.5–15 mg, n = 169
  - 10–20 mg, n = 170
  - 15–20 mg, n = 165

Follow-up
- Discontinued study drug (n = 298 [AE, n = 145; death, n = 29; patient withdrawal, n = 99; other reasons, n = 25])
- Completed (n = 768)

Completed
- Eplerenone
  - n = 144
  - 2.5–5 mg, n = 121
- Finerenone
  - 2.5–5 mg, n = 121
  - 5–10 mg, n = 122
  - 7.5–15 mg, n = 123
  - 10–20 mg, n = 134
  - 15–20 mg, n = 124

AE, adverse event; FAS, full analysis set; PPS, per protocol analysis set; SAF, safety analysis set

G. Filippatos et al. (Athens, GR) FP 3150
The proportion of patients who had an NT-proBNP decrease of more than 30% at day 90 compared with baseline was similar in the finerenone groups and the eplerenone group in the full analysis set.

Error bars show 90% confidence intervals. NT-proBNP, N-terminal of prohormone B-type natriuretic peptide.

G. Filippatos et al. (Athens, GR) FP 3150
ARTS-HF: DEATH FROM ANY CAUSE, CV HOSPITALIZATION, OR WORSENING CHF

Study period

Follow-up

Probability of survival (%)

Time (days)

Eplerenone (n = 207)

Finerenone 7.5–15 mg (n = 158)

Finerenone 2.5–5 mg (n = 162)

Finerenone 10–20 mg (n = 160)

Finerenone 5–10 mg (n = 157)

Finerenone 15–20 mg (n = 158)

G. Filippatos et al. (Athens, GR) FP 3150
Patients with Chronic Chagas Cardiomyopathy
Aged 18 to 75 years, ≥2 positive serological tests for *T. cruzi*, ECG Abnormalities

BNZ 300 mg daily

Placebo

Follow-up
11, 21 days, end of treatment, 6-mos, annually until study end

Primary Outcome
composite of death, resuscitated cardiac arrest, pacemaker/ICD, sustained VT, cardiac transplant, new HF, stroke/TIA and systemic or pulmonary thromboembolic event.

BENEFIT TRIAL: RATIONALE

- **Chagas disease**
  - Third commonest parasitic disease globally
  - Most common form of non-ischemic cardiomyopathy in Latin America
  - 5–7 million infected, 1.4 - 2.1 million develop cardiomyopathy <20-30 yr.

- *T. cruzi* low level parasitemia may be a key factor

- Role of trypanocidal therapy in established Chagas cardiomyopathy is unknown

## BENEFIT TRIAL: BASELINES

<table>
<thead>
<tr>
<th></th>
<th>Benznidazole N=1431</th>
<th>Placebo N=1423</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>55.4 years</td>
<td>55.2 years</td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>93.3%</td>
<td>94.8%</td>
</tr>
<tr>
<td>Previous Heart Failure</td>
<td>9.9%</td>
<td>9.0%</td>
</tr>
<tr>
<td>NYHA Class I</td>
<td>74.4%</td>
<td>73.5%</td>
</tr>
<tr>
<td>Mean LVEF</td>
<td>54.4</td>
<td>54.6</td>
</tr>
<tr>
<td>Wall-motion Abnormality</td>
<td>38.3%</td>
<td>37.6%</td>
</tr>
<tr>
<td>Diuretics</td>
<td>30.4%</td>
<td>29.9%</td>
</tr>
<tr>
<td>ACE-Inhibitor or ARB</td>
<td>49.6%</td>
<td>49.2%</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>31.0%</td>
<td>30.3%</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>19.9%</td>
<td>18.8%</td>
</tr>
</tbody>
</table>

BENEFIT TRIAL: PRIMARY OUTCOME

(death, resuscitated cardiac arrest, sustained VT, pacemaker/ICD, new HF, cardiac transplant, and stroke/TIA and SE)

Log-Rank p-value=0.31

Proportion with Events

Years of Follow-up

# at Risk

<table>
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<tr>
<th></th>
<th>BNZ</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>1431</td>
<td>1423</td>
</tr>
<tr>
<td>1</td>
<td>1312</td>
<td>1316</td>
</tr>
<tr>
<td>2</td>
<td>1246</td>
<td>1233</td>
</tr>
<tr>
<td>3</td>
<td>1178</td>
<td>1155</td>
</tr>
<tr>
<td>4</td>
<td>936</td>
<td>881</td>
</tr>
<tr>
<td>5</td>
<td>695</td>
<td>649</td>
</tr>
<tr>
<td>6</td>
<td>484</td>
<td>459</td>
</tr>
<tr>
<td>7</td>
<td>323</td>
<td>294</td>
</tr>
</tbody>
</table>

BNZ with a 40-80 day course in established Chagas cardiomyopathy did not significantly reduce clinical progression, despite significantly reducing PCR blood *T. cruzi* detection.

BNZ was well tolerated and permanent discontinuation was lower than previously reported (13.4%).

50–75% of all patients with HF suffer from Sleep-Disordered Breathing

- Obstructive sleep apnoea (OSA)
- Central sleep apnoea (CSA) which may manifest as Cheyne–Stokes respiration
- resulting in tissue hypoxia, repetitive arousal from sleep with increased sympathetic nervous system activity

Small and/or uncontrolled studies (and meta-analyses) suggest multiple beneficial effects of ASV on surrogates in HF

Post-hoc data from CANPAP (N=258) suggest that CPAP might improve mortality when CSA was controlled (AHI < 15) in HF patients with CSA and EF < 40%

SERVE-HF: ADAPTIVE SERVO-VENTILATION

- Non-invasive ventilatory therapy that supports inspiration when breathing amplitude is reduced and ensures sufficient respiration when respiratory effort is absent (Variable IPAP)

- Upper airway patency is ensured by provision of end-expiratory pressure

- Although algorithms employed by different ASV devices vary slightly, the principle of treatment is the same: back-up rate ventilation with adaptive pressure support

## SERVE-HF: BASELINE

<table>
<thead>
<tr>
<th></th>
<th>Control (n=659)</th>
<th>ASV (n=666)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>69.3±10.4</td>
<td>69.6±9.5</td>
</tr>
<tr>
<td>Male</td>
<td>90.0%</td>
<td>89.9%</td>
</tr>
<tr>
<td>NYHA class III or IV, n (%)</td>
<td>70.3%</td>
<td>70.5%</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>32.5±8.0</td>
<td>32.2±7.9</td>
</tr>
<tr>
<td>Ischaemic HF aetiology, n (%)</td>
<td>57.0%</td>
<td>59.7%</td>
</tr>
<tr>
<td>Implanted device, n (%)</td>
<td>55.2%</td>
<td>54.5%</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73m²</td>
<td>59.3±20.8</td>
<td>57.8±21.1</td>
</tr>
<tr>
<td>Six-minute walk distance, m</td>
<td>337.9±127.5</td>
<td>334.0±126.4</td>
</tr>
<tr>
<td>ACEI/ARB, n (%)</td>
<td>91.5%</td>
<td>92.0%</td>
</tr>
<tr>
<td>β-blockers, n (%)</td>
<td>92.7%</td>
<td>91.9%</td>
</tr>
<tr>
<td>Antiarrhythmics, n (%)</td>
<td>13.5%</td>
<td>19.2%</td>
</tr>
</tbody>
</table>

**p=0.005**

SERVE-HF: PRIMARY ENDPOINT NEUTRAL
TIME TO FIRST EVENT OF ALL-CAUSE DEATH, LIFE-SAVING CARDIOVASCULAR INTERVENTION, OR UNPLANNED HOSPITALIZATION FOR WORSENING CHRONIC HF

Hazard ratio, 1.13 (95% CI, 0.97-1.31)

SERVE-HF: A RUDE AWAKENING

Death from any cause

Cardiovascular Death

Hazard ratio, 1.28 (95% CI, 1.06–1.55)
P = 0.01

Hazard ratio, 1.34 (95% CI, 1.09–1.65)
P = 0.006

Heart Failure 2016
21 – 24 May, FLORENCE, Italy

4 700+ healthcare professionals
90+ countries represented
4 days of science
1 700+ abstracts and cases submitted
300+ expert faculty members
100+ scientific sessions
40+ industry sessions and workshops

ESC/ HFA Guidelines on HEART FAILURE

FOCUS ON: ACUTE HEART FAILURE

« Heart failure: State of the Art »
Merci

Frank Ruschitzka, MD, FRCP, FESC
Professor of Cardiology
University Zürich
E-mail: frank.ruschitzka@usz.ch
Access arm:
- Telemedicine guided,
- No audible alert for fluid retention

Control arm:
- Standard clinical assessment,
- No alert for fluid retention

Risk stratified:
- NYHA II vs. III,
- Ischemic vs. Non-Ischemic,
- Atrial Fibrillation,
- Primary vs. Secondary Prevention (VT/VF before Implant)
OPTILINK HF: PRIMARY ENDPOINT: ALL-CAUSE DEATH OR CV HOSPITALISATION

Hazard ratio = 0.867 (0.72, 1.044)
Stratified log-rank p-value = 0.132

Number at risk
Control 497 361 302 175 84 64 45 29
Intervention 505 361 310 183 94 80 58 35
SERVE-HF: ALL-CAUSE DEATH

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>ASV</th>
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<tbody>
<tr>
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<td>48</td>
<td>213</td>
<td>189</td>
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<tr>
<td>60</td>
<td>117</td>
<td>97</td>
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</tbody>
</table>

SERVE-HF: PRIMARY ENDPOINT NEUTRAL
TIME TO FIRST EVENT OF ALL-CAUSE DEATH, LIFE-SAVING CARDIOVASCULAR INTERVENTION, OR UNPLANNED HOSPITALIZATION FOR WORSENING CHRONIC HF

Cumulative incidence rate (%)

Months since Randomisation

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>ASV</th>
</tr>
</thead>
<tbody>
<tr>
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<td>136</td>
<td>122</td>
</tr>
<tr>
<td>48</td>
<td>77</td>
<td>52</td>
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</table>

HEART FAILURE

F. Ruschitzka (Zurich, CH)
Professor of Cardiology
Co-Head, Dept of Cardiology
President-elect HFA
University Heart Center
University Hospital
Zürich, Switzerland

Conflicts of Interest
Aventis, Bayer, Biotronik, Cardiorentis, Merck, Novartis, Pfizer, SJM, Servier
Interest in Conflict: none