The new boy in town:

Serelaxin Therapy in Acute Heart Failure

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Clinical Military Hospital
Wroclaw, Poland
Disclosure

Consultancy fees and speaker’s honoraria from: Corthera, Novartis
Acute Heart Failure: landscape at the beginning of the 21\textsuperscript{st} century

EURObservational Research Program: The Heart Failure Pilot Survey

All-cause death or HF hospitalization
1892 pts with acute HF & 3226 pts with chronic HF

Acute HF: 35.1%

Chronic HF: 17.2%

1-year all cause mortality:
acute HF – 16.8%
chronic HF – 6.8%

Cardiologist’s summary:
„broadly speaking, the pharmacological armamentarium for AHFS – loop diuretics, vasodilators and inotropes – is largely unchanged from 1970s…”

Felker GM et al., Circ Heart Fail 2010;3:314-25

Cardiologist’s question:
Why all successful phase II studies are followed by failures in phase III trials?
Do we need shift in a „AHF paradigm”?

A. Maggioni ESC 2011
**Long-term benefit from short-term intervention: ever possible?**

Initial, short-term therapies (hours-days)

<table>
<thead>
<tr>
<th>Target</th>
<th>„Traditional” therapeutic approach</th>
<th>Effects on long-term outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alleviate congestion</td>
<td>i.v. diuretics</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May be detrimental</td>
</tr>
<tr>
<td>Reduce ↑ LV filling pressure</td>
<td>i.v. nitrates</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potentially favourable</td>
</tr>
<tr>
<td>Hypoperfusion</td>
<td>i.v. inotropes</td>
<td>Detrimental</td>
</tr>
<tr>
<td>Poor cardiac performance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Dissociation between symptomatic improvement & clinical stabilisation and better long-term outcome**

Modified from Pang PS et al. Eur Heart J 2010;31:784-93
Lessons from ACS trials: short-term intervention can result in long-term benefit

**GISSI**
- 21-day mortality: Control/placebo (15%) vs. STK (10%)
- 5-week vascular mortality: Control/placebo (10%) vs. STK (5%)

**ISIS-2**
- 21-day mortality: Control/placebo (15%) vs. STK (10%)
- 5-week vascular mortality: Control/placebo (10%) vs. STK (5%)

**ISIS-2 follow-up**

<table>
<thead>
<tr>
<th>Period of follow up</th>
<th>No of deaths/No of patients (% dead)</th>
<th>Death rate ratio (CI*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptokinase infusion</td>
<td>796/8592 (9.3)</td>
<td>0.75 (0.69 to 0.83)</td>
</tr>
<tr>
<td>Placebo infusion</td>
<td>1045/8595 (12.2)</td>
<td>0.89 (0.75 to 1.05)</td>
</tr>
</tbody>
</table>

Grines CL et al. NEJM 1993;328:673-9

Need for paradigm shifting in acute heart failure: short-term intervention and long-term goals (?)

What is needed?

- **Targeted-approach** = characterizing patient’s clinical profile
different pathophysiology & therapies for different clinical profiles (?)

- **An ideal drug / intervention**
symptomatic improvement, „end-organ” protection,
improvement in neurohumoral and proinflammatory profile

- **Appropriate timing** = early administration of therapy
  „the earlier the better” (?)
  → prevention of tissue damage;
  → phase of severe symptoms;
  → early clinical stabilization & chance to introduce disease-modifying therapies
Serelaxin is a recombinant form of human relaxin-2

- Relaxin-2 is a naturally occurring peptide hormone which mediates systemic hemodynamic and renal adaptive changes during pregnancy
- Structure of human relaxin-2: 53 amino acids (2 chains connected by 2 disulphide bonds)
- Human relaxin-2 is one of seven peptides in the relaxin family of hormones
- Each of these seven peptides is structurally and functionally distinct
- Relaxin-2 mediates its effects via specific G-protein-coupled receptors: RXFP1 (LGR7) and RXFP2 (LGR8)
- Relaxin-2 receptors are localized in many blood vessels

Kong et al. Moll Cell Endocrinol 2010;320:1–15
Levels are elevated in circulation in the first trimester of pregnancy and throughout 9 months.

- Cardiac output (L/min): 20% increase
- Systemic vascular resistance (dyn.s.cm²): 30% decrease
- Global arterial compliance (mL/mmHg): 30% increase
- Creatinine clearance (mL/min): 45% increase

Serelaxin Is NOT Just Another Vasodilator

Non-clinical and clinical evidence suggest that relaxin-2 may have additional effects

- The mechanism of action of relaxin/serelaxin involves upregulation of the endothelin type B (ET\textsubscript{B}) receptor
- The ET\textsubscript{B} receptor mediates: (1) increased systemic and renal vasodilation, (2) natriuresis, and (3) clearance of ET-1

ET\textsubscript{B} receptor = endothelin receptor type B; ET-1 = endothelin-1; MMP = matrix metalloproteinase; NO = nitric oxide; NOS = nitric oxide synthase; TGF = transforming growth factor; TNF = tumor necrosis factor; VEGF = vascular endothelial growth factor
Serelaxin: proof of concept in heart failure

Reduction in left ventricular filling pressure

Open-label pilot study of serelaxin in 16 patients with stable chronic HF‡

Serelaxin:
- reduced pulmonary capillary wedge pressure
- increased cardiac output
- improved renal function during infusion
- no abnormalities regarding vital signs, clinical status, electrocardiogram, serum chemistry, and hematology parameters, and no relevant adverse events at the doses tested (10–960 µg/kg/day)

*\(p<0.05\) vs. baseline
‡3 dose escalation cohorts: Group A (8-hour sequential i.v. infusions at 10, 30, 100 µg/kg/day); Group B (240, 480, 960 µg/kg/day); Group C (24-hour infusion at 960 µg/kg/day)

Pre-RELAX-AHF and RELAX-AHF: clinical trials testing the efficacy of serelaxin in AHF

Timeline:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 14</th>
<th>Day 60</th>
<th>Day 180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment (within 16h of symptoms)</td>
<td>48h i.v.</td>
<td>„the earlier the better”</td>
<td>Early Relief (Likert)</td>
<td>6, 12, 24 h</td>
<td></td>
</tr>
<tr>
<td>Primary EP1</td>
<td>△ Dyspnea</td>
<td>Sustained Effect (VAS AUC)</td>
<td>0-100 mm; 0, 6, 12, 24h, D2-D5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary EP2</td>
<td>△ Worsening HF (%)</td>
<td>Creatinine changes</td>
<td>LoS (days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>Days alive out of hospital</td>
<td>CV mortality or re-hospitalization for HF or renal failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HE</td>
<td>CV Mortality (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary EP1</td>
<td>Hospital admission</td>
<td>Hospital discharge</td>
<td>Day 60 analysis</td>
<td>Follow-up</td>
<td></td>
</tr>
<tr>
<td>Secondary EP2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pre-RELAX-AHF

- 234 patient, dose-finding, Phase II study
- Optimal dose across multiple clinical outcome domains was 30 mcg/kg/d
- Serelaxin had trends to:
  - Improve dyspnea relief
  - Decrease congestion
  - Reduce diuretic use
  - Limit worsening of heart failure
  - Shorten length of stay
  - Increase days alive out of hospital
  - Improve cardiovascular and all-cause survival
- Safe and well-tolerated without significant hypotension

CV Death (KM)

Placebo (n=62)
Serelaxin (n=172)

HR 0.25 (0.08-0.79) P=0.019

Events n (KM%)
Placebo 7 (14%)
Serelaxin 5 (3%)

Teerlink J. LBCT Presentation, AHA 2012
RELAX-AHF: Study Design

Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study

AHF (dyspnea, BNP, CXR)
SBP > 125 mmHg
Within 16 hours of presentation
eGFR 30-75 ml/m/m^2

Placebo (n=580)
Relaxin 30 µg/kg/d (n=580)

Hospitalization

48 h Study Drug Infusion
Post-discharge Evaluations

Ponikowski et al. Am Heart J 2012;163:149-155.e1
1° Endpoint: Dyspnea Relief (VAS AUC)

- AUC with placebo, $2308 \pm 3082$
- AUC with serelaxin, $2756 \pm 2588$

*P=0.0075

19.4% increase in AUC with serelaxin from baseline through day 5 (Mean difference of 448 mm-hr)
### VAS Results Consistent across all Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo N</th>
<th>Serelaxin N</th>
<th>Favors placebo</th>
<th>Favors Serelaxin</th>
<th>LS mean difference Estimate (95%CI)</th>
<th>Interaction P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total population</strong></td>
<td>580</td>
<td>581</td>
<td></td>
<td></td>
<td>448 (120, 775)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>357</td>
<td>368</td>
<td></td>
<td></td>
<td>441 (26, 855)</td>
<td>0.92</td>
</tr>
<tr>
<td>Female</td>
<td>223</td>
<td>213</td>
<td></td>
<td></td>
<td>474 (61, 1009)</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;75 years</td>
<td>296</td>
<td>315</td>
<td></td>
<td></td>
<td>192 (–260, 644)</td>
<td>0.11</td>
</tr>
<tr>
<td>≥75 years</td>
<td>284</td>
<td>266</td>
<td></td>
<td></td>
<td>725 (249, 1202)</td>
<td></td>
</tr>
<tr>
<td><strong>eGFR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 mL/min</td>
<td>408</td>
<td>409</td>
<td></td>
<td></td>
<td>504 (113, 895)</td>
<td>0.55</td>
</tr>
<tr>
<td>≥60 mL/min</td>
<td>160</td>
<td>155</td>
<td></td>
<td></td>
<td>280 (–350, 910)</td>
<td></td>
</tr>
<tr>
<td><strong>SBP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;140 mmHg</td>
<td>284</td>
<td>298</td>
<td></td>
<td></td>
<td>436 (–27, 899)</td>
<td>0.82</td>
</tr>
<tr>
<td>≥140 mmHg</td>
<td>294</td>
<td>279</td>
<td></td>
<td></td>
<td>513 (47, 980)</td>
<td></td>
</tr>
<tr>
<td><strong>HF Past Year Hospitalization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>180</td>
<td>214</td>
<td></td>
<td></td>
<td>488 (–75, 1051)</td>
<td>0.88</td>
</tr>
<tr>
<td>No</td>
<td>400</td>
<td>367</td>
<td></td>
<td></td>
<td>433 (28, 838)</td>
<td></td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40%</td>
<td>295</td>
<td>303</td>
<td></td>
<td></td>
<td>378 (–71, 828)</td>
<td>0.83</td>
</tr>
<tr>
<td>≥40%</td>
<td>244</td>
<td>249</td>
<td></td>
<td></td>
<td>454 (–41, 949)</td>
<td></td>
</tr>
<tr>
<td><strong>IV nitrates at baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>42</td>
<td>39</td>
<td></td>
<td></td>
<td>808 (–435, 2050)</td>
<td>0.56</td>
</tr>
<tr>
<td>No</td>
<td>538</td>
<td>542</td>
<td></td>
<td></td>
<td>421 (81, 761)</td>
<td></td>
</tr>
</tbody>
</table>

Metra et al., EHJ, 2013

AUC = area under the curve; HF = heart failure; LS = least squares; VAS = visual analogue scale;
1° Endpoint: Dyspnea Relief (Likert)

Proportion of subjects with moderately or markedly better dyspnea by Likert by time point

- **6 hr:**
  - Placebo: n=180
  - Serelaxin: n=205
  - p=0.113

- **12 hr:**
  - Placebo: n=256
  - Serelaxin: n=288
  - p=0.051

- **24 hr:**
  - Placebo: n=362
  - Serelaxin: n=389
  - p=0.086

- **6, 12, and 24 hr:**
  - Placebo: n=150
  - Serelaxin: n=156
  - p=0.702

Teerlink J. LBCT Presentation, AHA 2012
Moderately or Markedly Worsening of Dyspnea on the Likert Scale

Less worsening than placebo at all time points through Day 5

<table>
<thead>
<tr>
<th>Time Since Treatment Initiation</th>
<th>Placebo</th>
<th>Serelaxin</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6h</td>
<td>n=573</td>
<td>n=572</td>
<td>P=0.0377</td>
</tr>
<tr>
<td>12h</td>
<td>n=574</td>
<td>n=574</td>
<td>P=0.0136</td>
</tr>
<tr>
<td>1d</td>
<td>n=574</td>
<td>n=573</td>
<td>P=0.0014</td>
</tr>
<tr>
<td>2d</td>
<td>n=575</td>
<td>n=573</td>
<td>P=0.0003</td>
</tr>
<tr>
<td>3d</td>
<td>n=575</td>
<td>n=573</td>
<td>P=0.0003</td>
</tr>
<tr>
<td>4d</td>
<td>n=576</td>
<td>n=573</td>
<td>P=0.0040</td>
</tr>
<tr>
<td>5d</td>
<td>n=577</td>
<td>n=574</td>
<td>P=0.0013</td>
</tr>
</tbody>
</table>
### RELAX-AHF: Worsening of Heart Failure

#### Cumulative proportion of worsening heart failure to Day 5 (%)

<table>
<thead>
<tr>
<th>Time</th>
<th>Placebo (N=573)</th>
<th>Serelaxin (N=570)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 hr</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>12 hr</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Day 1</td>
<td>31</td>
<td>10</td>
</tr>
<tr>
<td>Day 2</td>
<td>44</td>
<td>17</td>
</tr>
<tr>
<td>Day 3</td>
<td>57</td>
<td>25</td>
</tr>
<tr>
<td>Day 4</td>
<td>64</td>
<td>36</td>
</tr>
<tr>
<td>Day 5</td>
<td>69</td>
<td>37</td>
</tr>
</tbody>
</table>

*P<0.001 through Day 5

#### Kaplan-Meier estimate for time to WHF (%)

<table>
<thead>
<tr>
<th>Time</th>
<th>Placebo (N=573)</th>
<th>Serelaxin (N=570)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 5</td>
<td>573</td>
<td>570</td>
</tr>
<tr>
<td>Day 14</td>
<td>573</td>
<td>570</td>
</tr>
</tbody>
</table>

**HR 0.7 (0.51, 0.96); p=0.024

Worsening Heart Failure (WHF) - worsening signs and/or symptoms of HF that required an intensification of IV therapy for heart failure or mechanical ventilatory or circulatory support.

*p value by Wilcoxon test **p value by log rank test for Serelaxin vs. Placebo; HR estimate by Cox model, HR<1.0 favors Serelaxin

Teerlink J. LBCT Presentation, AHA 2012
Variability in the clinical course of AHF: steady improvement vs. worsening

\(~10\text{–}30\% \text{ of patients develop WHF}\)

\text{Intensification of treatment}

\text{WHF = worsening heart failure}

\text{J Card Fail 2009;15: 639-44}
\text{Fundam Clin Pharmacol 2009;23:633-9 f}
2° Endpoint: CV Death or Heart Failure / Renal Failure Re-hospitalization through Day 60

K-M estimate for time to first CV Death or HF/RF re-hosp (%)

Composite event components (%)

CV death: (% subjects) HF/RF re-hospitalization (% subjects)

Placebo Serelaxin Placebo Serelaxin

HR 1.02 (0.74, 1.41) HR=0.7
p=0.89 p=0.23

n=27 n=19

n=50 n=60

RELAX-AHF

Teerlink J. LBCT Presentation, AHA 2012
**All-cause Death through Day 180**

K-M estimate for All-cause Death ITT (%)

**HR 0.63 (CI 0.43, 0.93); p=0.020**

**NNT = 25**

Placebo (N=580) - 65 (11.3%)

Serelaxin (N=581) - 42 (7.3%)

Teerlink J. LBCT Presentation, AHA 2012
# RELAX-AHF: Incidence of AEs/SAEs to Day 14

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=570) n (%)</th>
<th>Serelaxin (N=568) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with any AE</td>
<td>320 (56.1)</td>
<td>305 (53.7)</td>
</tr>
<tr>
<td>Subjects with any drug-related AE</td>
<td>46 (8.1)</td>
<td>47 (8.3)</td>
</tr>
<tr>
<td>Subjects with AE leading to study drug d/c</td>
<td>22 (3.9)</td>
<td>26 (4.6)</td>
</tr>
<tr>
<td>Hypotension-related AE (through day 5)</td>
<td>25 (4.4)</td>
<td>28 (4.9)</td>
</tr>
<tr>
<td>Renal Impairment-related AE (through day 5)</td>
<td>49 (8.6)</td>
<td>26 (4.6)*</td>
</tr>
<tr>
<td>Subjects with any SAE</td>
<td>78 (13.7)</td>
<td>86 (15.1)</td>
</tr>
<tr>
<td>Subjects with any drug-related SAEs</td>
<td>2 (0.4)</td>
<td>3 (0.5)</td>
</tr>
<tr>
<td>Subjects with SAE leading to drug d/c</td>
<td>3 (0.5)</td>
<td>5 (0.9)</td>
</tr>
<tr>
<td>Serious AE with an outcome of death</td>
<td>15 (2.6)</td>
<td>10 (1.8)</td>
</tr>
</tbody>
</table>

The number of subjects with any AE includes all AEs and SAEs reported through Day 14. Non-serious AEs were collected through Day 5, SAEs through Day 14.

* Teerlink J. LBCT Presentation, AHA 2012
Mechanisms of Action of Serelaxin

- Beneficial effects of serelaxin in patients with AHF
  - Improvement in dypsnea
  - Improvement in signs and symptoms of heart failure
  - Preventing worsening heart failure
  - Reducing (CV) mortality
- How is serelaxin doing this?
Changes from baseline in biomarkers related to organ damage in the RELAX-AHF study

- Cardiac damage:
  - hs-cTnT ≥20% increase at day 2

- Renal damage:
  - Cystatin C ≥0.3 mg/l increase at day 2
  - Creatinine ≥0.3 mg/dl increase at day 2

- Liver damage:
  - AST ≥20% increase at day 2

Metra M et al. JACC 2013;61:196-206
CRLX030A2201: Study objective and design

Study objective: to evaluate the hemodynamic effects of serelaxin in 71 patients with AHF at a dose rate of 30 µg/kg/day.

Patients hospitalized with AHF, mean PCWP ≥ 18 mmHg, SBP ≥ 115 mmHg, and estimated glomerular filtration rate ≥ 30 ml/min/1.73 m².

Screening

Swan-Ganz catheter inserted ≥ 1 h prior to randomization.

Double-blind, randomized treatment period

Placebo

Serelaxin 30 µg/kg/d

Washout

Serelaxin 100 µg/kg/d (n=37)

Serelaxin 250 µg/kg/d (n=49)

Presentation

Randomized 1:1

≤ 48 h

0 h

8 h

20 h

24 h

30 d

20 h study drug infusion

4th post-infusion

Safety evaluation

Ponikowski P et al. Eur Heart J 2013
Hemodynamic results: Change in PCWP

Data represented as mean ± SE; *p<0.05

<table>
<thead>
<tr>
<th>Time-weighted average change from baseline</th>
<th>Serelaxin (n=32)</th>
<th>Placebo (n=31)</th>
<th>Treatment difference [95% confidence interval]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-8 h</td>
<td>-3.79 (0.50)</td>
<td>-1.08 (0.51)</td>
<td>-2.70 [-4.10, -1.31]</td>
<td>0.0001</td>
</tr>
<tr>
<td>8-20 h</td>
<td>-4.90 (0.73)</td>
<td>-2.67 (0.74)</td>
<td>-2.24 [-4.28, -0.19]</td>
<td>0.0322</td>
</tr>
<tr>
<td>20-24 h</td>
<td>-4.41 (0.83)</td>
<td>-3.11 (0.85)</td>
<td>-1.30 [-3.63, 1.03]</td>
<td>0.27</td>
</tr>
</tbody>
</table>

PCWP, pulmonary capillary wedge pressure; SE, standard error. Data represented in mmHg as least squares mean (SE) change from baseline. Time-weighted average is based on area under the effect curve for the corresponding time interval.

Ponikowski P et al. Eur Heart J 2013
Hemodynamic results: Change in mean PAP

Data represented in mmHg as least squares mean (SE) change from baseline. Time-weighted average is based on area under the effect curve for the corresponding time interval.

Data represented as mean ± SE; *p<0.05

<table>
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<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-8 h</td>
<td>-3.98 (0.65)</td>
<td>0.06 (0.66)</td>
<td>-4.04 [-5.86, -2.22]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>8-20 h</td>
<td>-4.56 (0.88)</td>
<td>-0.80 (0.89)</td>
<td>-3.76 [-6.22, -1.29]</td>
<td>0.0028</td>
</tr>
<tr>
<td>20-24 h</td>
<td>-4.29 (0.96)</td>
<td>-1.67 (0.98)</td>
<td>-2.62 [-5.31, 0.07]</td>
<td>0.06</td>
</tr>
</tbody>
</table>

PAP, pulmonary arterial pressure; SE, standard error. Data represented in mmHg as least squares mean (SE) change from baseline. Time-weighted average is based on area under the effect curve for the corresponding time interval.

Ponikowski P et al. Eur Heart J 2013
**RELAX-AHF: Benefit-Risk Conclusion**

**Improvement in current clinical status**
- Patient-reported dyspnea ↓
- Physician-assessed signs and symptoms of congestion
  - NT-pro-BNP ↓, PCWP ↓, troponin ↓
  - Less diuretics required

**Prevention of worsening clinical status**
- Worsening HF ↓, NNT 15 by Day 5
  - Length of hospital stay ↓
  - Length of time in critical care unit ↓
  - Less worsening renal function

**Reduction in risk of death**
- ↓ Cardiovascular mortality at Day 180
  - ↓ All cause mortality at Day 180

**Safety profile comparable to placebo**
- BP decreases manageable
- Strong evidence of no harm in AHF patients with high unmet medical need
Short-term relief, long-term goals – the cardiologist’s perspective on a novel therapeutic approach to acute heart failure

„broadly speaking, the pharmacological armamentarium for AHFS – loop diuretics, vasodilators and inotropes – is largely unchanged from 1970s…”

Will it be changed after RELAX?

Sunrise or sunset?
HFA Congress 17-20 May 2014 – Athens

Will publish then:

International Consensus Document on the Diagnosis & Treatment of Acute Heart Failure

www.escardio.org