'12 HighLights

Insuficiencia Cardiaca

American Heart Association
Learn and Live

SCIENTIFIC SESSIONS 2012
EXHIBITS: NOVEMBER 4-6
SESSIONS: NOVEMBER 3-7
RESUSCITATION SCIENCE SYMPOSIUM: NOVEMBER 3-4

UMPIRE

Objetivo y diseño

Objetivo: Valorar la adherencia al tratamiento (reportada por el paciente) y el efecto sobre la presión arterial y el LDL-col
2.004 pacientes, 88% con ECV previa, 28% DM
Europa e India. Seguimiento 15 meses

Usual care

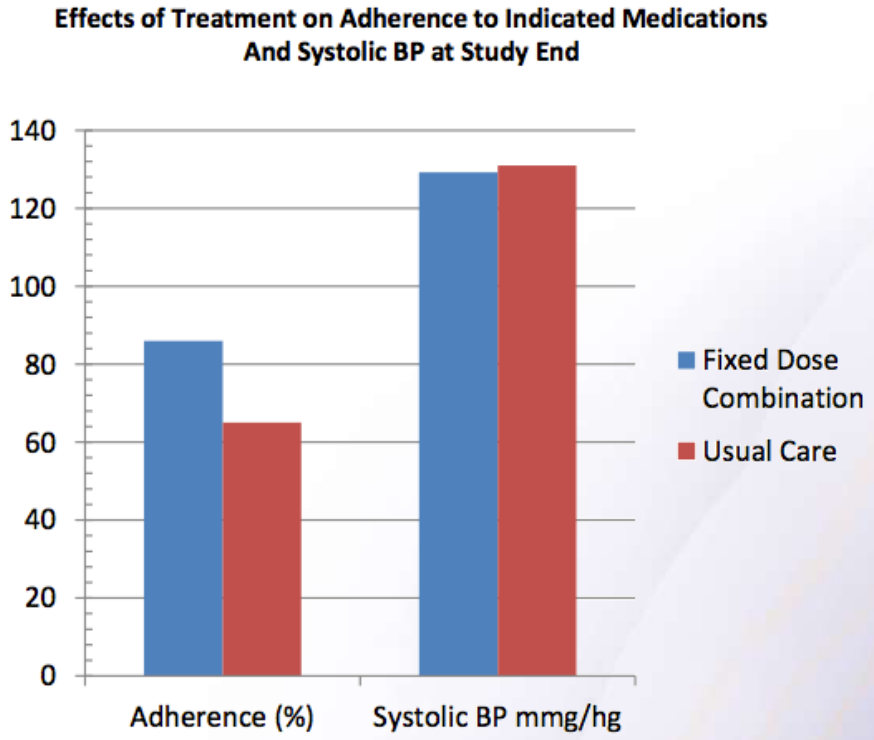
VS.

Aspirina 75 mg	Aspirina 75 mg
Simvastatina 40 mg	Simvastatina 40 mg
Lisinopril 10 mg	Lisinopril 10 mg
Atenolol 50 mg	HCTZ 12,5 mg

Se puede elegir entre las dos versiones de la polypill, cambiar entre ellas, o añadir tratamiento si fuera necesario

UMPIRE

Resultados



- La Polypill mejora la adherencia al tratamiento (33% a 15 meses) y resulta en una discreta mejoría en TA y LDL (faltaría ver el impacto clínico en eventos)
- Hay que tener en cuenta que el tratamiento era gratuito (¿qué pasaría en un entorno con copago?)

Outcome	Fixed-dose combination (n=1002)	Usual care (n=1002)	Treatment effect (95% CI)
Adherence (%)	86	65	1.33 (1.26 to 1.41)
Systolic blood pressure (mm Hg)	129.2	131.7	-2.6 (-4.0 to -1.1)
LDL cholesterol, mmol/L (mg/dL)	2.18 (84.3)	2.29 (88.5)	-0.11 (-0.17 to -0.05)

A Randomized Trial of a Multivitamin in the Prevention of Cardiovascular Disease in Men: The Physicians' Health Study II

HD Sesso, WC Christen, V Bubes, JP Smith,
J MacFadyen, M Schvartz, JE Manson, RJ Glynn,
JE Buring, JM Gaziano

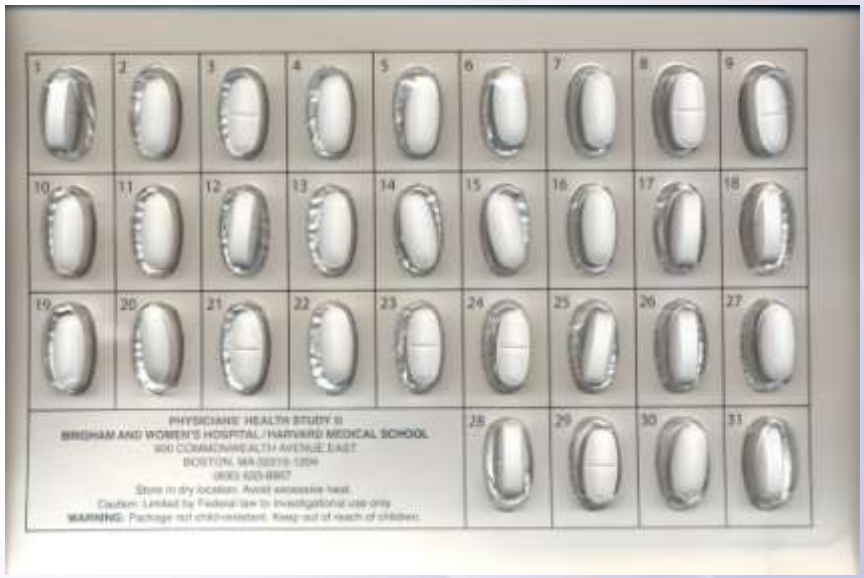
Division of Preventive Medicine
Brigham and Women's Hospital
Boston, MA

Funding: NIH (NCI, NHLBI, NIA, and NEI) and an investigator-initiated grant from BASF Corporation. Pills and/or packaging were provided by BASF, Pfizer and DSM Nutritional Products.

- Más de la mitad de la población americana toma vitaminas
- Investigación básica: pueden reducir la ECV

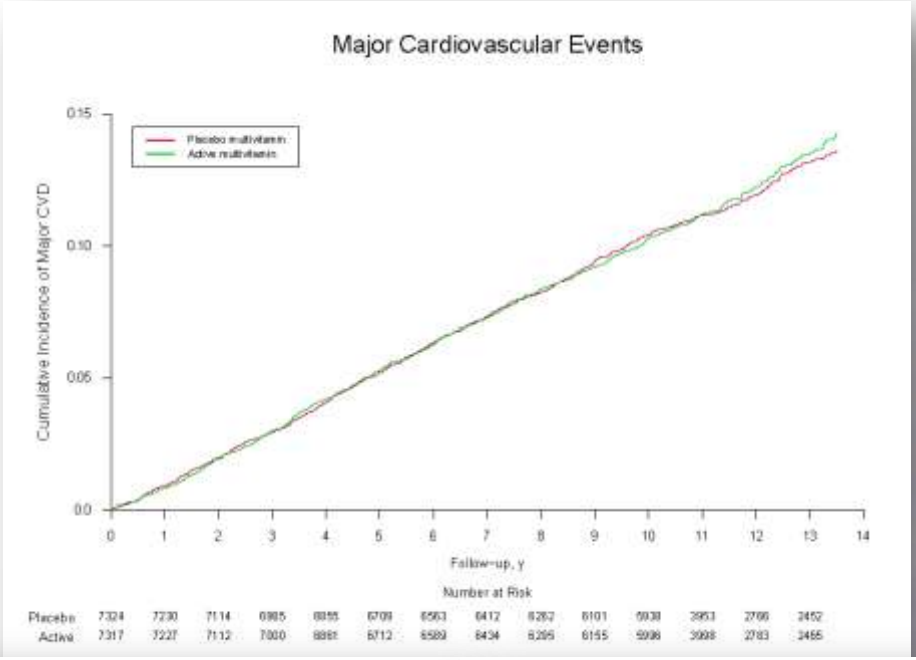
Physicians' Health Study (PHS) II:

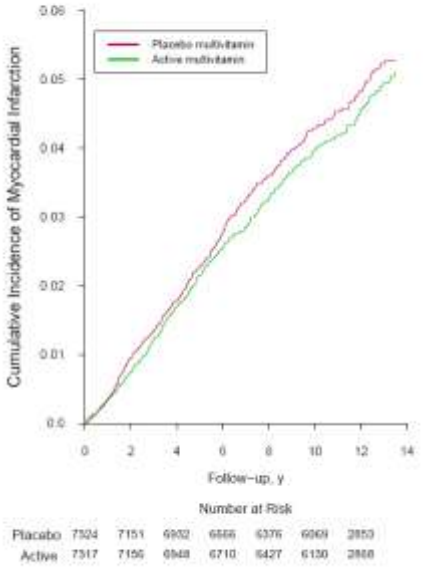
- 14.641 médicos (7.000 placebo, 7.641 multivitaminas)
- Seguimiento: 11,2 años
- Objetivo Primario: IAM no fatal, Ictus no fatal y Muerte CV
- Cumplimiento: 77% 4 años, 72% 8 años, 67% final

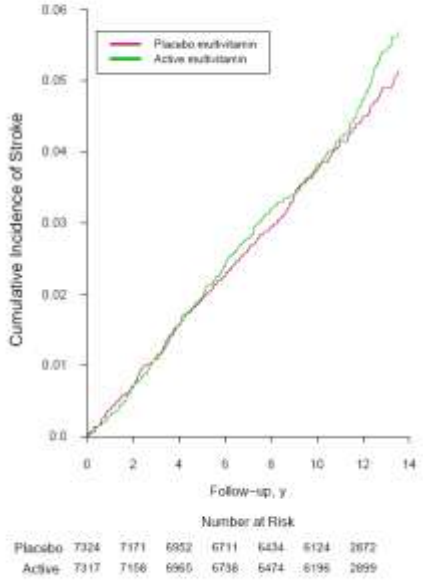


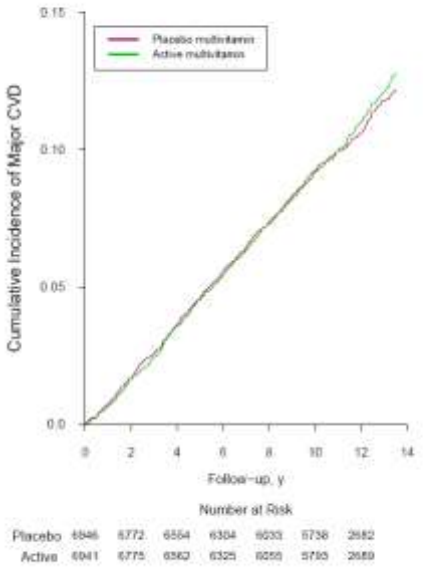
Características basales

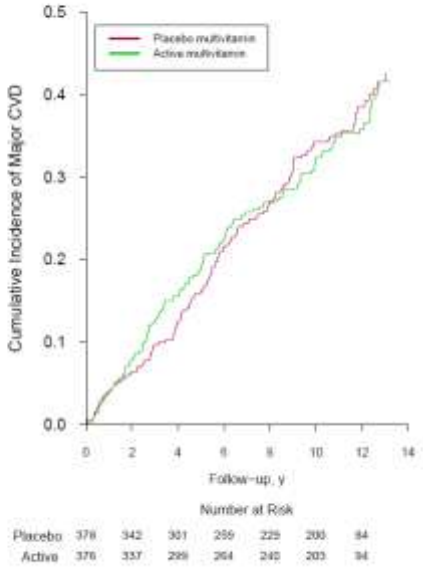
	Active (n = 7317)	Placebo (n = 7324)
Age, mean (SD)	64.2 (9.1)	64.3 (9.2)
BMI, mean (SD)	25.9 (3.4)	26.0 (3.4)
Current smoker, %	3.5	3.7
Exercise ≥1 time/wk, %	62.2	60.7
Current aspirin use, %	77.5	77.3
History of hypertension, %	41.8	42.7
History of high cholesterol, %	36.0	37.3
History of diabetes, %	6.5	5.9
Plasma TC, mean (SD)	203.5 (35.5)	203.7 (36.0)
Fruits & vegetables, servings/d (IQR)	4.26 (2.95-5.75)	4.19 (2.94-5.77)
Whole grains, servings/d (IQR)	1.13 (0.49-2.00)	1.07 (0.49-1.99)


Major Cardiovascular Events
Placebo multivitamin
Active multivitamin
Cumulative Incidence of Major CVD
0.15
0.10
0.05
0.0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Follow-up, y
Number at Risk
Placebo 7324 7230 7114 6985 6855 6709 6563 6412 6262 6101 5938 3953 2766 2452
Active 7317 7227 7112 7000 6861 6712 6589 6434 6295 6155 5996 3998 2783 2465


Total Myocardial Infarction
Placebo multivitamin
Active multivitamin
Cumulative Incidence of Myocardial Infarction
0.06
0.05
0.04
0.03
0.02
0.01
0.0
0 2 4 6 8 10 12 14
Follow-up, y
Number at Risk
Placebo 7324 7151 6952 6666 6376 6069 2853
Active 7317 7156 6948 6710 6427 6130 2868


Total Stroke
Placebo multivitamin
Active multivitamin
Cumulative Incidence of Stroke
0.06
0.05
0.04
0.03
0.02
0.01
0.0
0 2 4 6 8 10 12 14
Follow-up, y
Number at Risk
Placebo 7324 7171 6952 6711 6434 6124 2872
Active 7317 7156 6965 6738 6474 6195 2899


Primary Prevention
(N=13,887)
Placebo multivitamin
Active multivitamin
Cumulative Incidence of Major CVD
0.15
0.10
0.05
0.0
0 2 4 6 8 10 12 14
Follow-up, y
Number at Risk
Placebo 6946 6772 6554 6304 6033 5738 2682
Active 6941 6775 6562 6325 6055 5765 2689


Secondary Prevention
(N=754)
Placebo multivitamin
Active multivitamin
Cumulative Incidence of Major CVD
0.5
0.4
0.3
0.2
0.1
0.0
0 2 4 6 8 10 12 14
Follow-up, y
Number at Risk
Placebo 378 342 301 259 225 200 84
Active 376 337 299 264 240 203 94

Cáncer

Outcome	Active (n = 7317)	Placebo (n = 7324)	HR (95% CI)	*P*
Total cancer	1290	1379	0.92 (0.86-0.998)	.04
Total epithelial cell cancer	1158	1244	0.92 (0.85-0.997)	.04
Prostate cancer	683	690	0.98 (0.88-1.09)	.76
Total cancer minus prostate	641	715	0.88 (0.79-0.98)	.02
Cancer mortality	403	456	0.88 (0.77-1.01)	.07
Total mortality	1345	1412	0.94 (0.88-1.02)	.13
By baseline history of cancer				
Yes (n=1312)	95	126	0.73 (0.56-0.96)	.02
No (n=13329)	1195	1253	0.94 (0.87-1.02)	.15

Conclusiones

- PHS II: único estudio aleatorizado a gran escala y largo plazo sobre el uso de multivitaminas:
  - Sin beneficios CV

- Razones para tomar diariamente multivitaminas:
  - Prevenir estados carenciales
  - Beneficio modesto en el cáncer

5 Estudios de Regeneración

	n	Aleator.	IAM	Células	Vía	Objetivo
SWISS AMI	200	Sí, controlado	5-7 días vs 3-4 semanas, reperfundido	Mononucleares autólogas	Intracoronaria	Cambios en la FEVI a los 4 meses
ALCADIA	6	No	Miocardiopatía isquémica	Cardiac derived stem cells + bFGF, derivadas de biopsia endomiocárdica	Transendocárdica	Seguridad
TIME	120	SÍ, controlado	3 ó 7 días, anterior, reperfundido	Mononucleares autólogas Dosis fija	Intracoronaria	Timing de la infusión
POSEIDON	30	Sí, no controlado	Años Miocardiopatía isquémica	Mesenquimales autólogas o alogénicas (6 tipos de células y dosis)	Transendocárdica	Autólogo vs. alogénico
SCIPIO	33	Sí, controlado	Miocardiopatía isquémica, CABG en las semanas previas	Cardiac stem cell	Intracoronaria	Cambios en RM y clínicos

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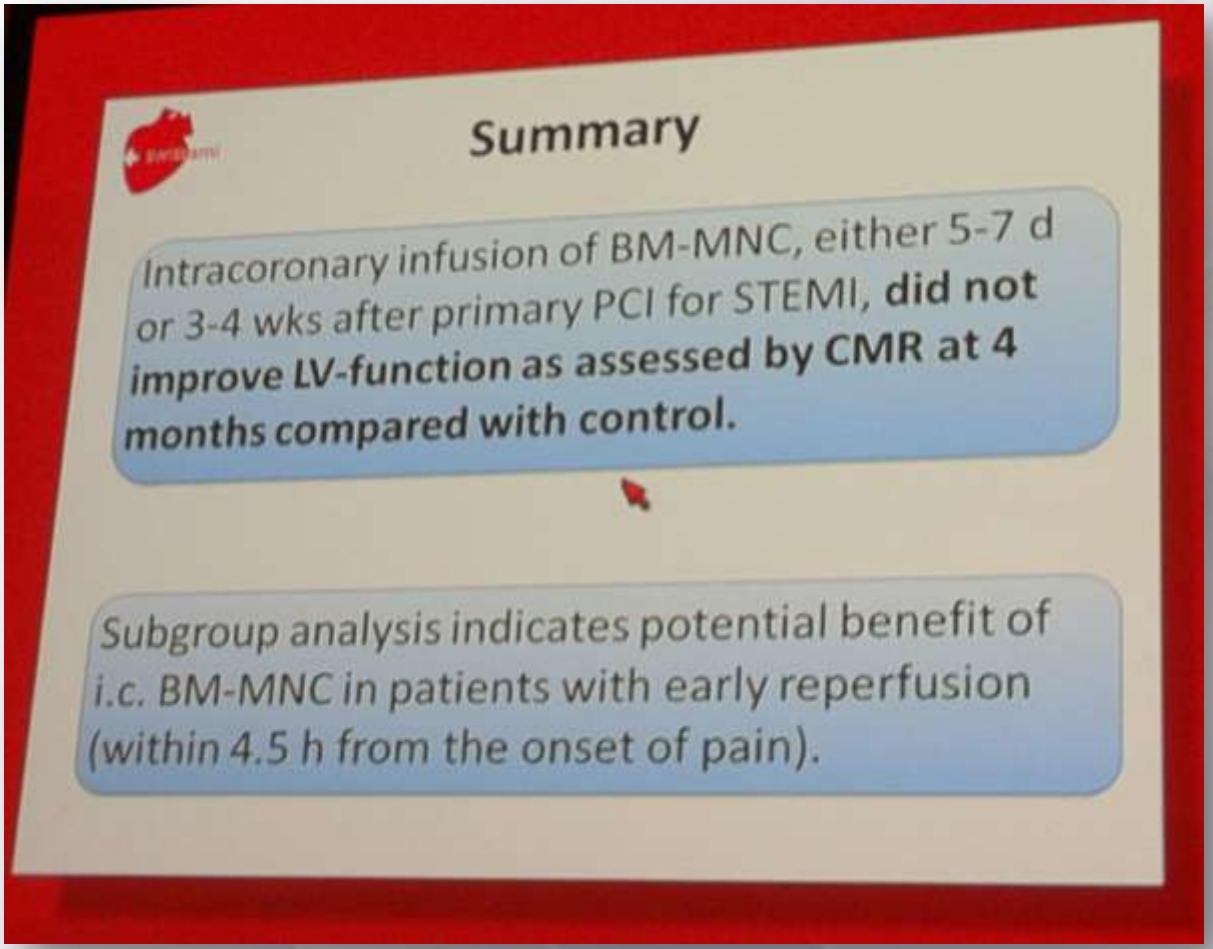
SWISS AMI	200	Sí, controlado	5-7 días vs 3-4 semanas, reperfundido	Mononucleares autólogas	Intracoronaria	Cambios en la FEVI a los 4 meses



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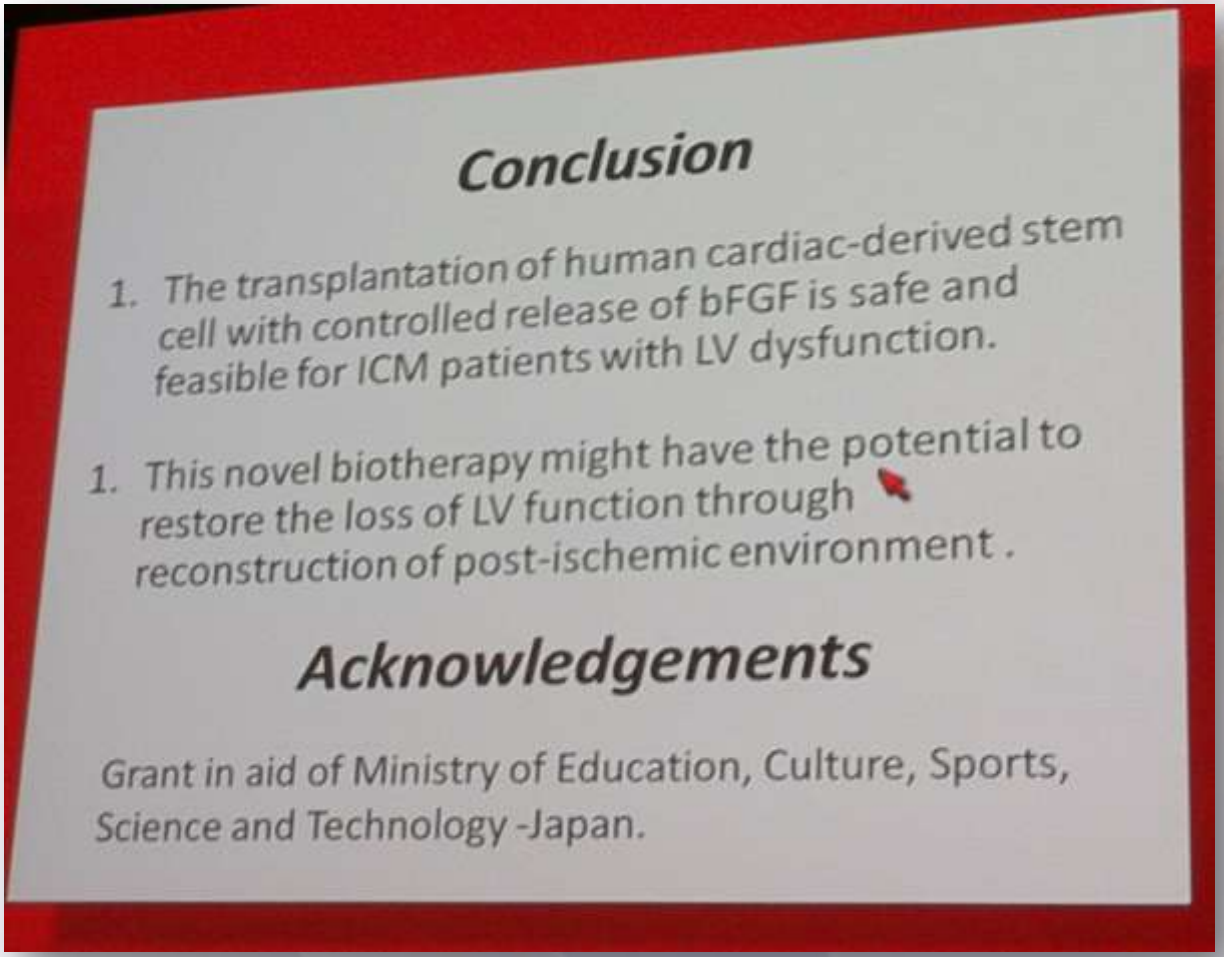

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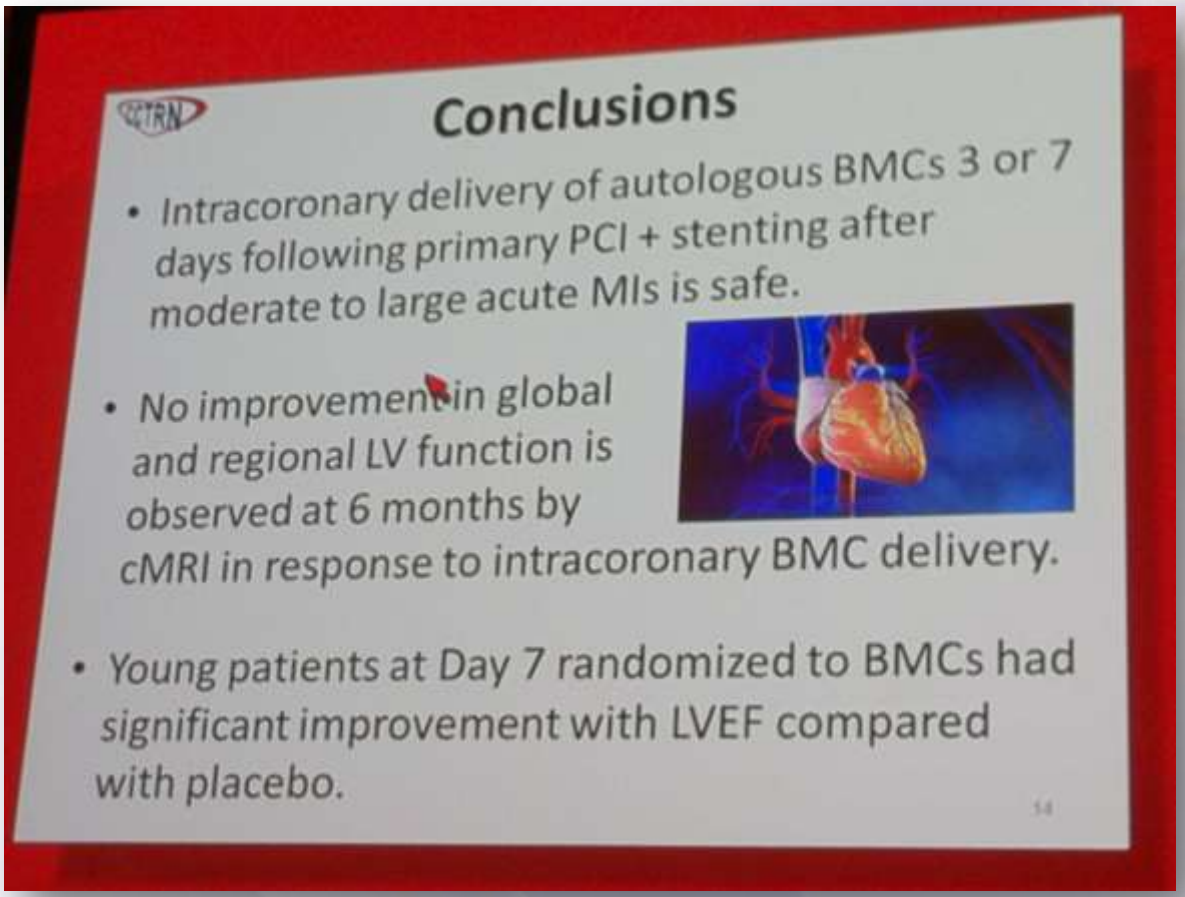

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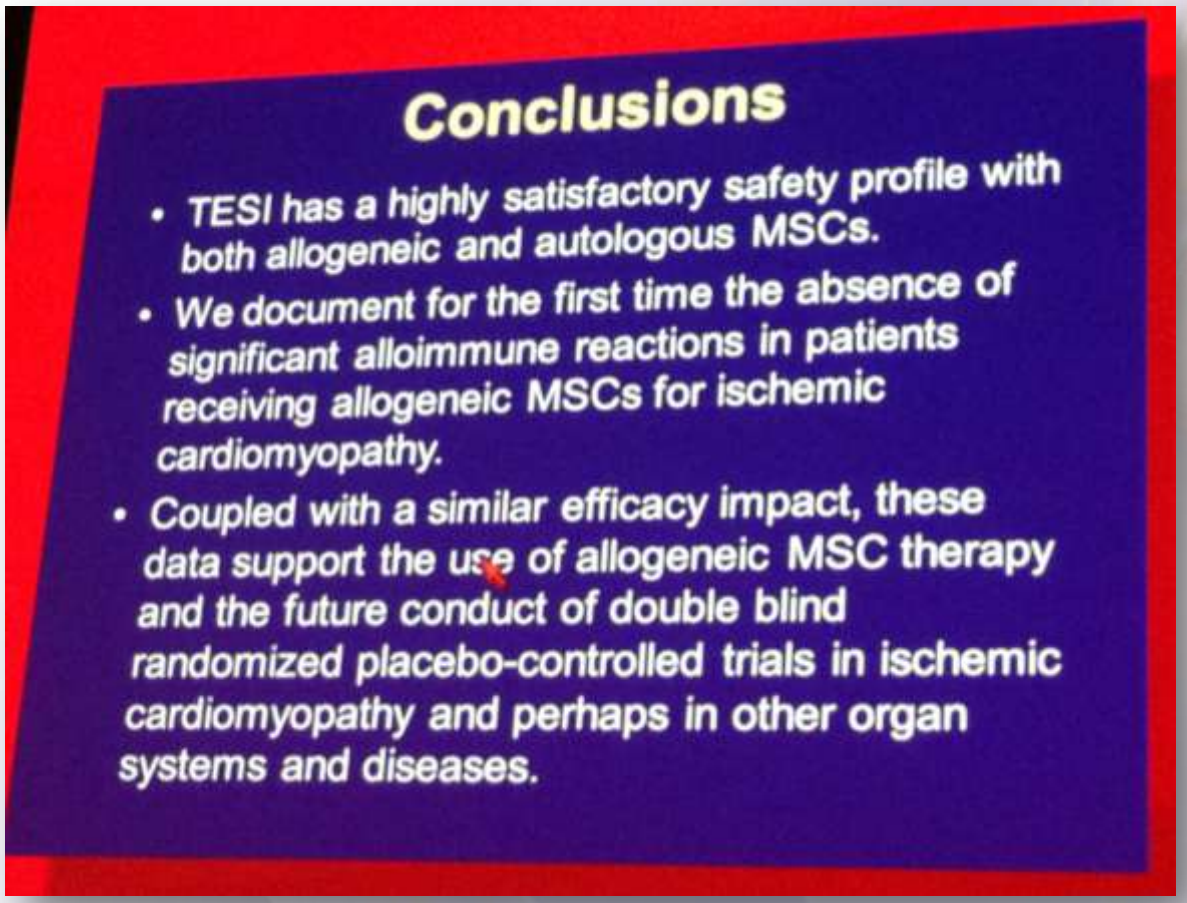
POSEIDON	30	Sí, no controlado	Años Miocardiopatía isquémica	Mesenquimales autólogas o alogénicas (6 tipos de células y dosis)	Transendocárdica	Autólogo vs. alogénico



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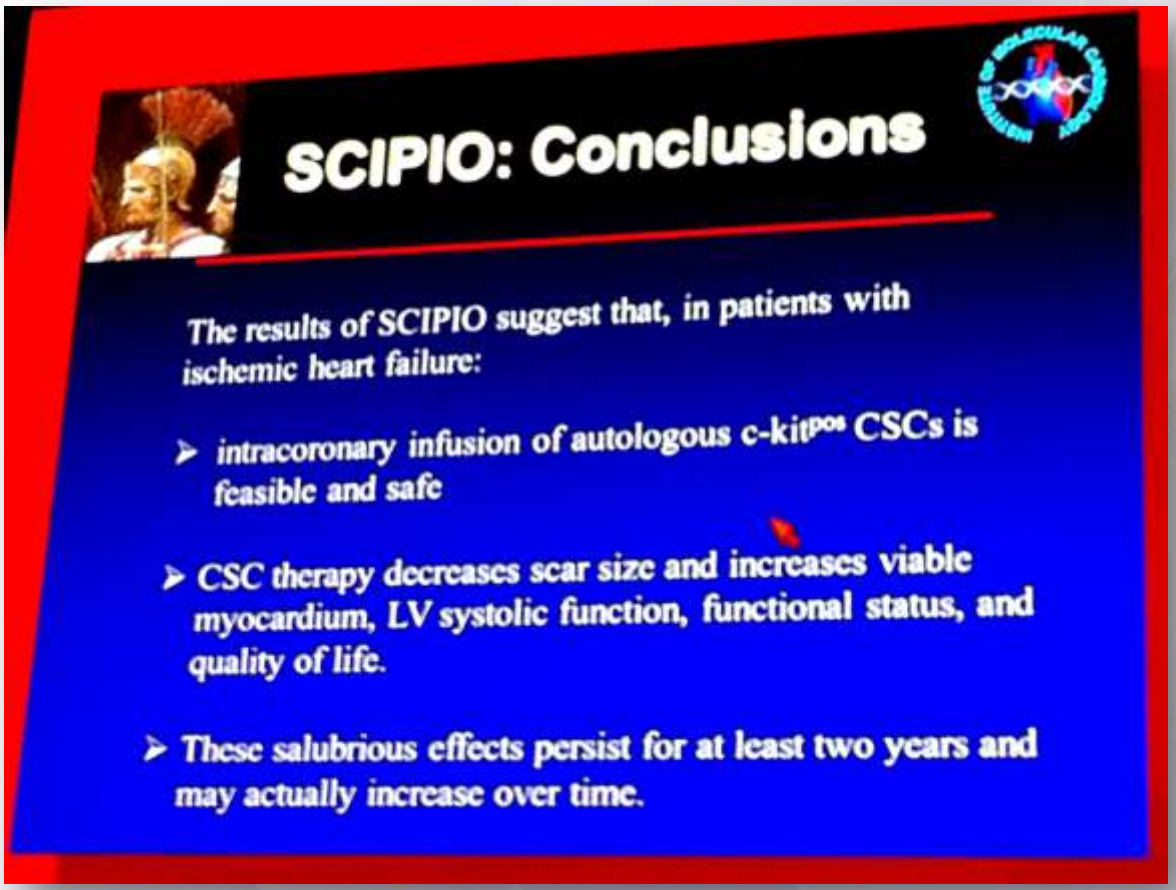
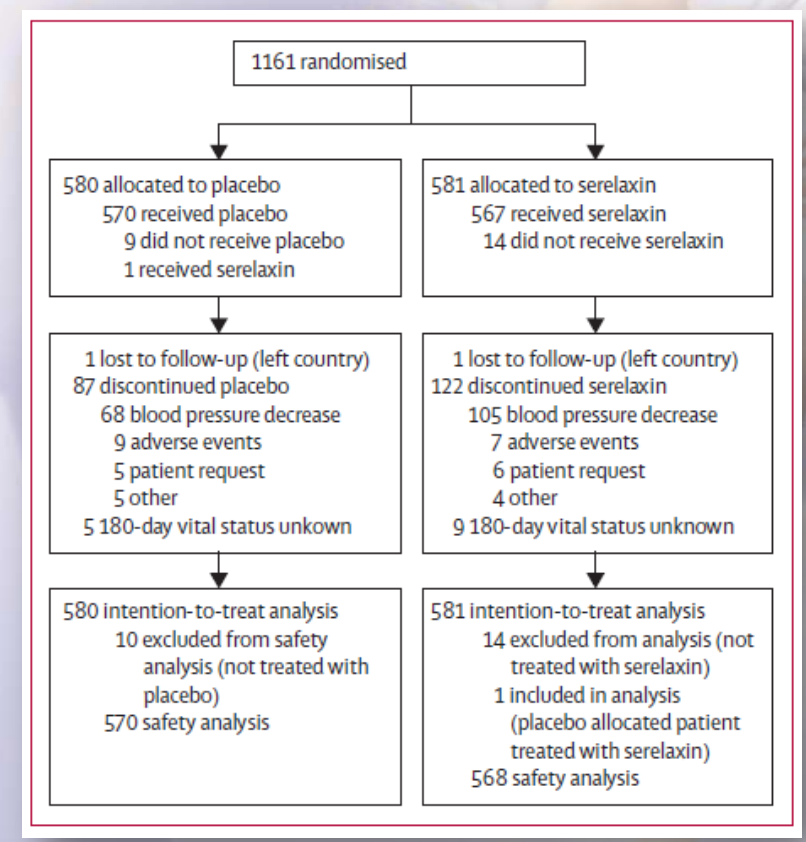
SCIPIO	33	Sí, controlado	Miocardiopatía isquémica, CABG en las semanas previas	Cardiac stem cell	Intracoronaria	Cambios en RM y clínicos



Serelaxin, recombinant human relaxin-2, for treatment of acute heart failure (RELAX-AHF): a randomised, placebo-controlled trial

John R Teerlink, Gad Cotter, Beth A Davison, G Michael Felker, Gerasimos Filippatos, Barry H Greenberg, Piotr Ponikowski, Elaine Unemori, Adriaan A Voors, Kirkwood F Adams Jr, Maria I Dorobantu, Liliana R Grinfeld, Guillaume Jondeau, Alon Marmor, Josep Masip, Peter S Pang, Karl Werdan, Sam L Teichman, Angelo Trapani, Christopher A Bush, Rajnish Saini, Christoph Schumacher, Thomas M Severin, Marco Metra, for the RELAXin in Acute Heart Failure (RELAX-AHF) Investigators

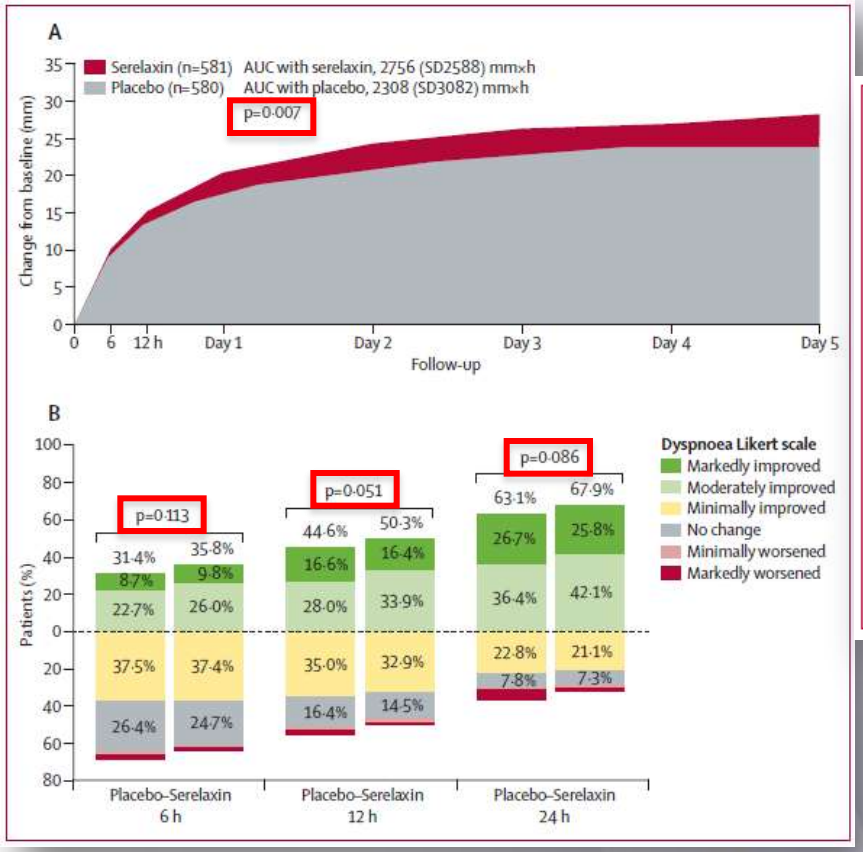
- Relaxina: vasodilatadora, antiinflamatoria, antiisquémica, antiapoptótica, antifibrótica
- Pacientes con AHF, TAS > 125 mmHg, primeras 16 horas tras ingreso
- Infusión 48 horas, 30 µg/k
- Objetivo primario: mejoría de la disnea en la escala de Likert 24h, y en la VAS AUC a los 5 días

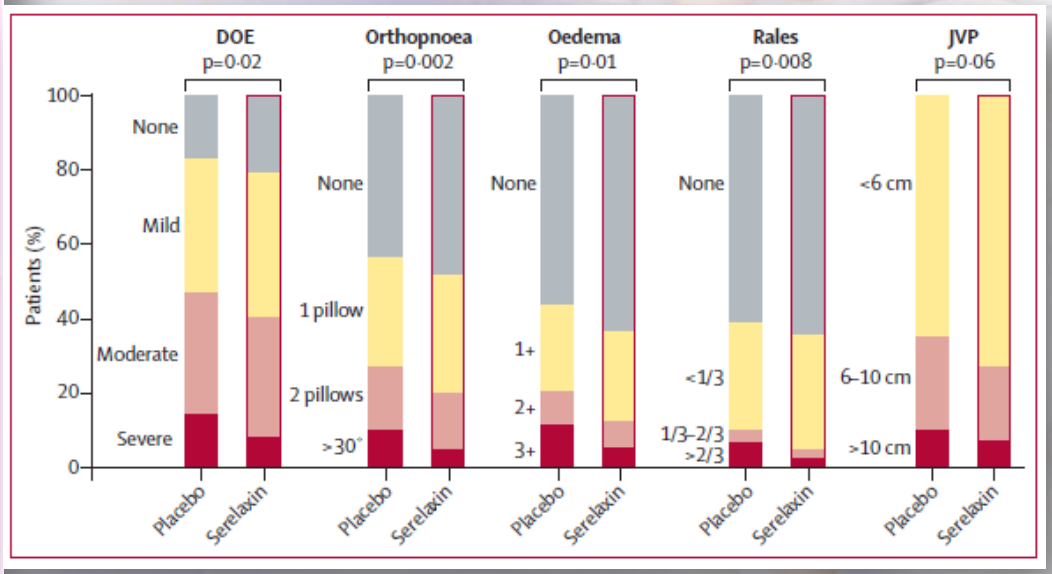


RELAX-AHF

RESULTADOS

- Mejoría de la disnea, síntomas y signos de IC





RELAX-AHF

RESULTADOS

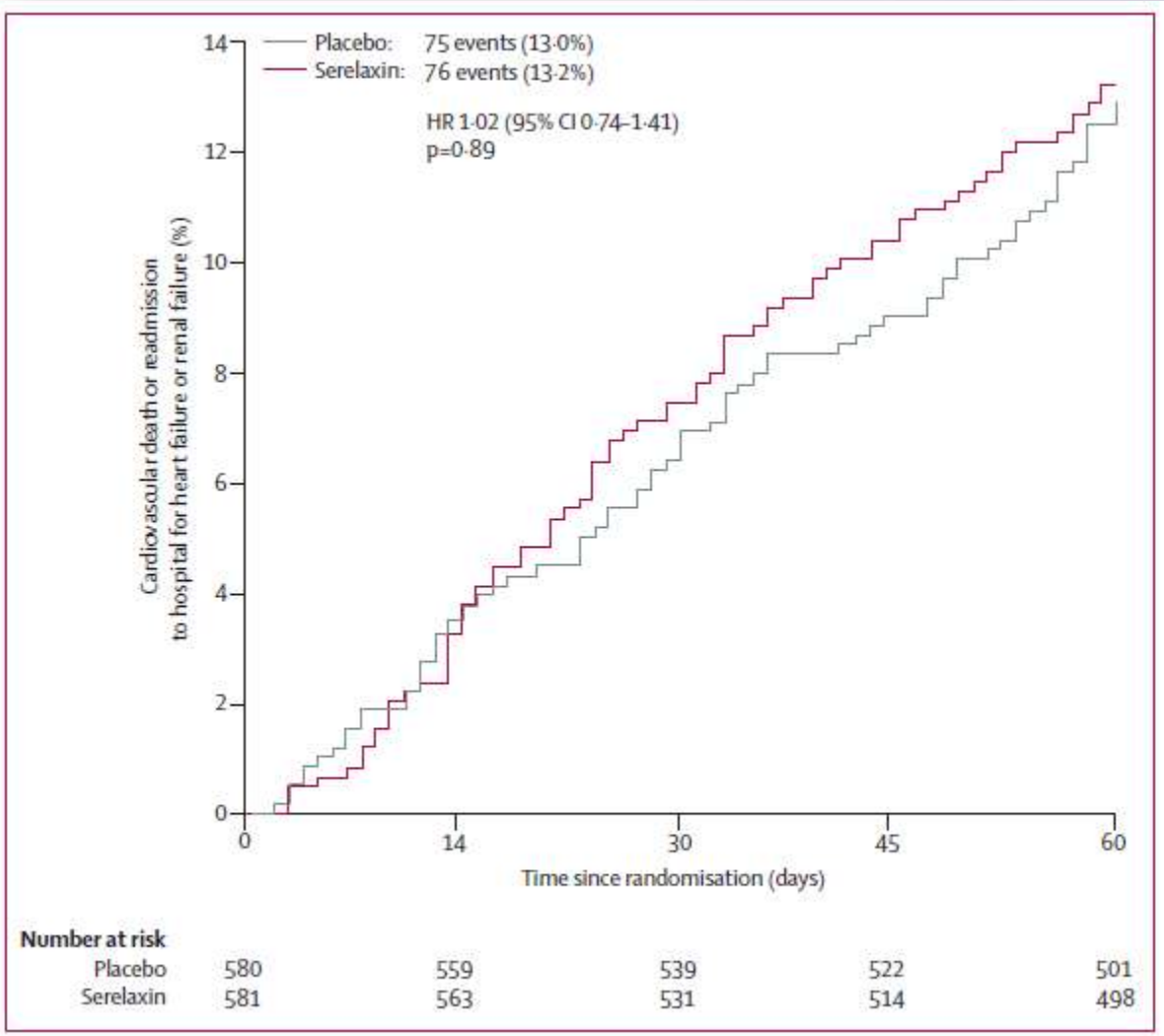


Figure 3: Cardiovascular death or readmission to hospital for heart failure or renal failure during 60-day follow-up

RELAX-AH

RESULTADOS

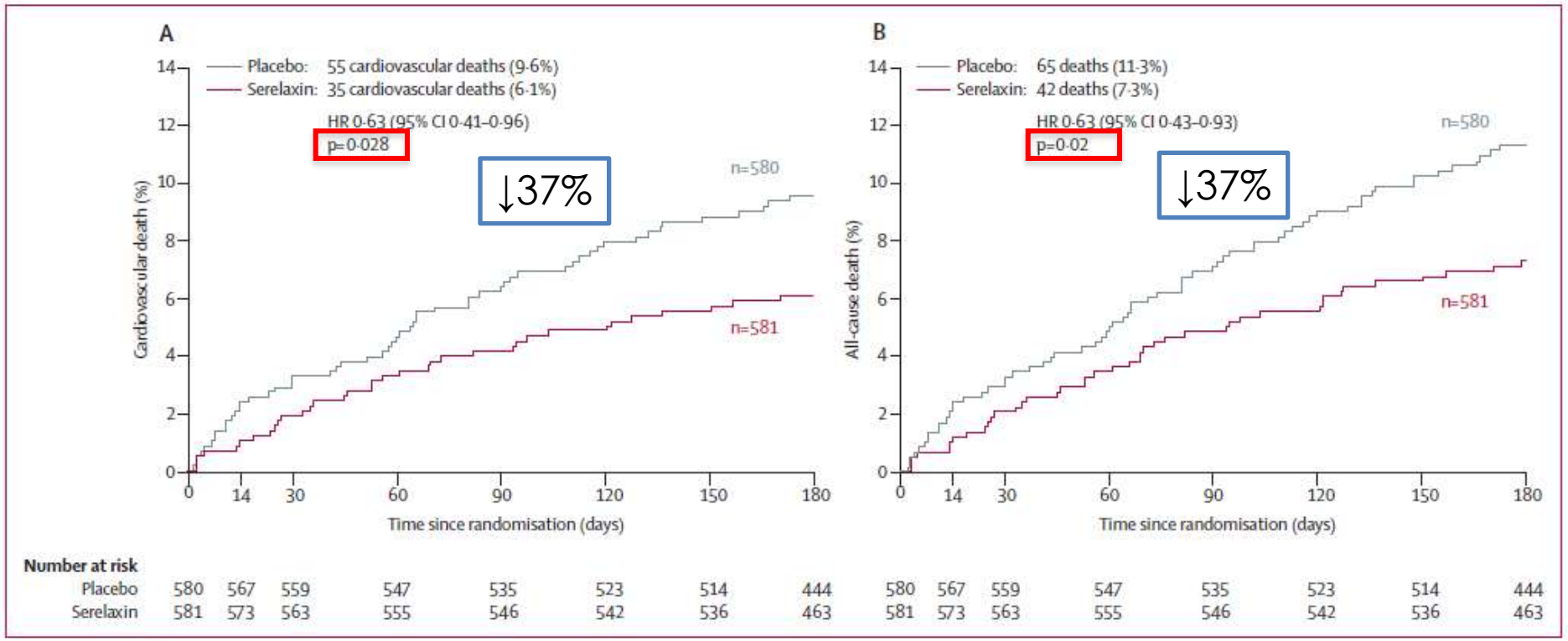


Figure 5: Kaplan-Meier analysis of death

RELAX-AH

CONCLUSIONES

Interpretation Treatment of acute heart failure with serelaxin was associated with dyspnoea relief and improvement in other clinical outcomes, but had no effect on readmission to hospital. Serelaxin treatment was well tolerated and safe, supported by the reduced 180-day mortality.

CARRESS-HF

HEART FAILURE NETWORK

Randomized Trial of Ultrafiltration versus Pharmacologic Care in Patients with Acute Decompensated Heart Failure and Cardiorenal Syndrome: **Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF)**

Bradley A. Bart, MD
on behalf of the
NHLBI Heart Failure Clinical Research Network

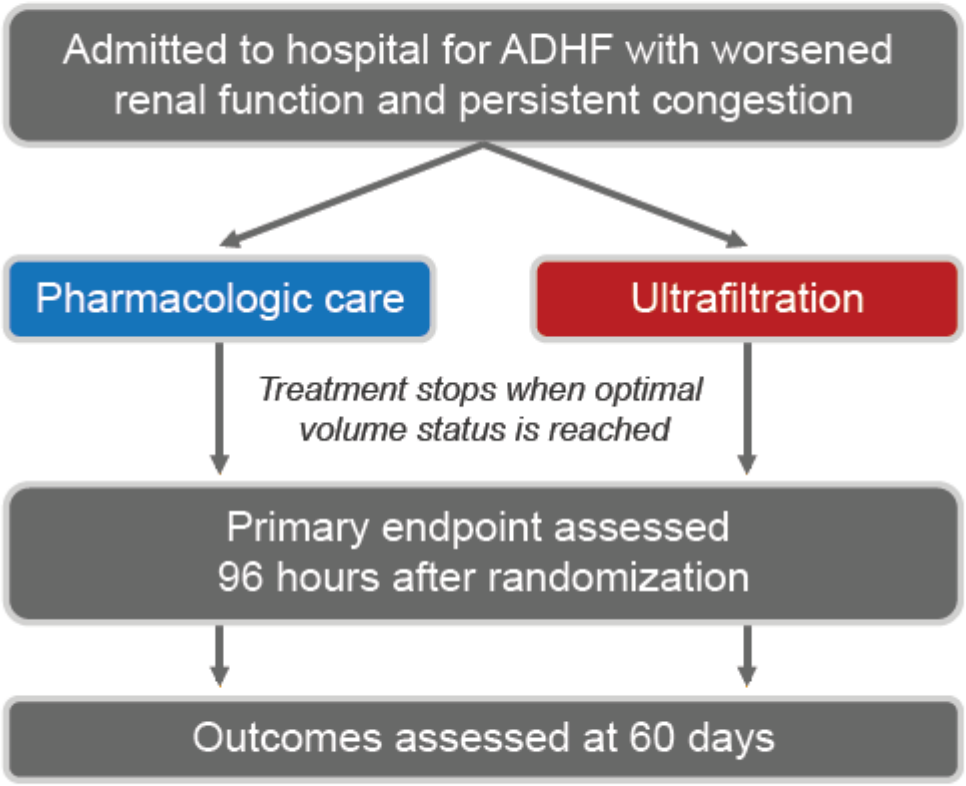
U.S. Department of Health and Human Services
National Institutes of Health

National Heart Lung and Blood Institute
People Science Health

CARRESS-HF

Study Design

HEART FAILURE NETWORK



CARRESS-HF

Patient Selection

HEART FAILURE NETWORK

Inclusion

- Age 18 or older
- Admitted to hospital with ADHF
- Worsened renal function with increase in creatinine ≥ 0.3 mg/dL
- Persistent congestion

Exclusion

- Creatinine > 3.5 mg/dL
- Alternate explanation for worsening renal function
- Systolic blood pressure < 90 mm Hg
- Hematocrit > 45%
- Need for IV vasoactive drugs

CARRESS-HF

Primary Endpoint

HEART FAILURE NETWORK

Change in serum creatinine AND change in weight between randomization and 96 hours, considered as a bivariate response

- Intention to treat
- Multivariate linear regression model, adjusting for baseline values of weight and creatinine

CARRESS-HF

Randomized Treatment Arms

HEART FAILURE NETWORK

Ultrafiltration

- IV access
- Stop all diuretics for duration of UF
- Heparin for PTT 2.0–2.5 x normal
- UF rate 200 mL/hr
- Use of IV inotropes or vasodilators prohibited

CARRESS-HF

Randomized Treatment Arms

HEART FAILURE NETWORK

Stepped Pharmacologic Care

First 2 days

- Adjust diuretics to maintain 3–5 liters urine/day

After 48 hours if urine output still inadequate

- Consider dopamine or dobutamine if SBP < 110 mm Hg and EF < 40%
- Nitroglycerin or nesiritide if SBP > 120 and severe symptoms

After 72 hours if urine output still inadequate

- Consider hemodynamic guided IV therapy, crossover to UF, or dialysis

CARRESS-HF

Baseline Features

HEART FAILURE NETWORK

Characteristic	Pharmacologic Care (N = 94)	Ultrafiltration (N = 94)
Age — years	66	69
Male	72%	78%
White race	71%	72%
Ejection fraction	35%	30%
HF hospitalization in past year	79%	75%
Ischemic etiology	51%	70%*
Diabetes mellitus	67%	65%
H.O. hypertension	84%	85%
Serum creatinine — mg/dL	2.09	1.90
Qualifying creatinine inc — mg/dL	0.46	0.43

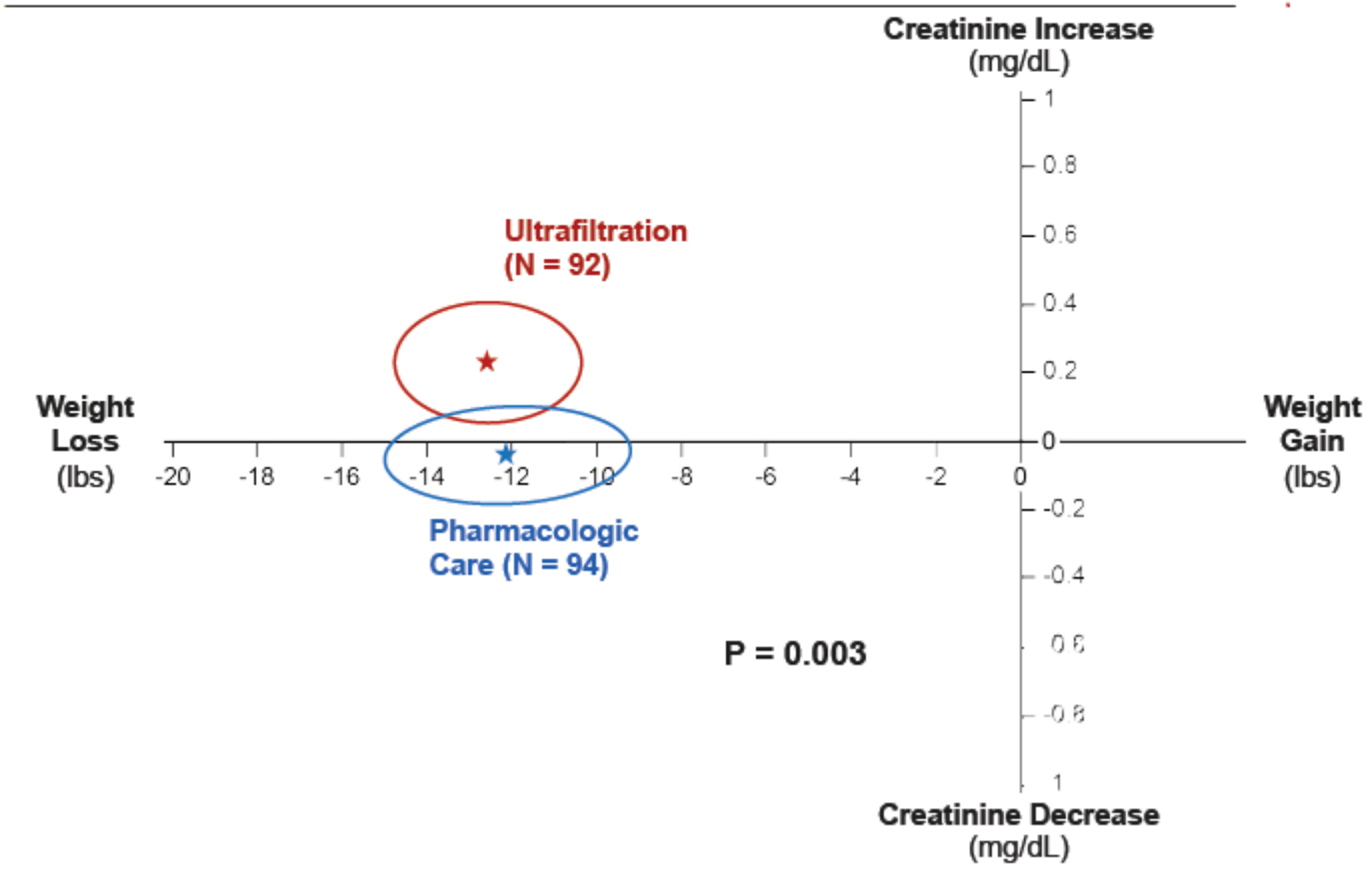
p-value < 0.05

CARRESS-HF

Results: Primary Endpoint

Mean changes in creatinine and weight at 96 hours

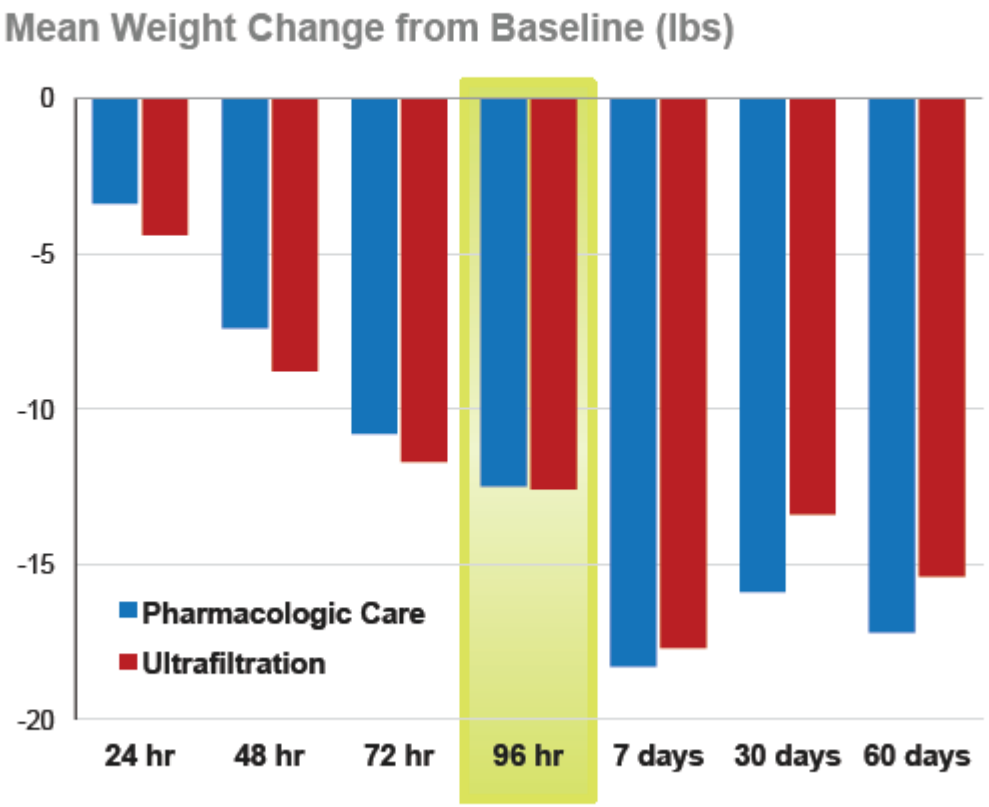
HEART FAILURE NETWORK



CARRESS-HF

Change in Weight

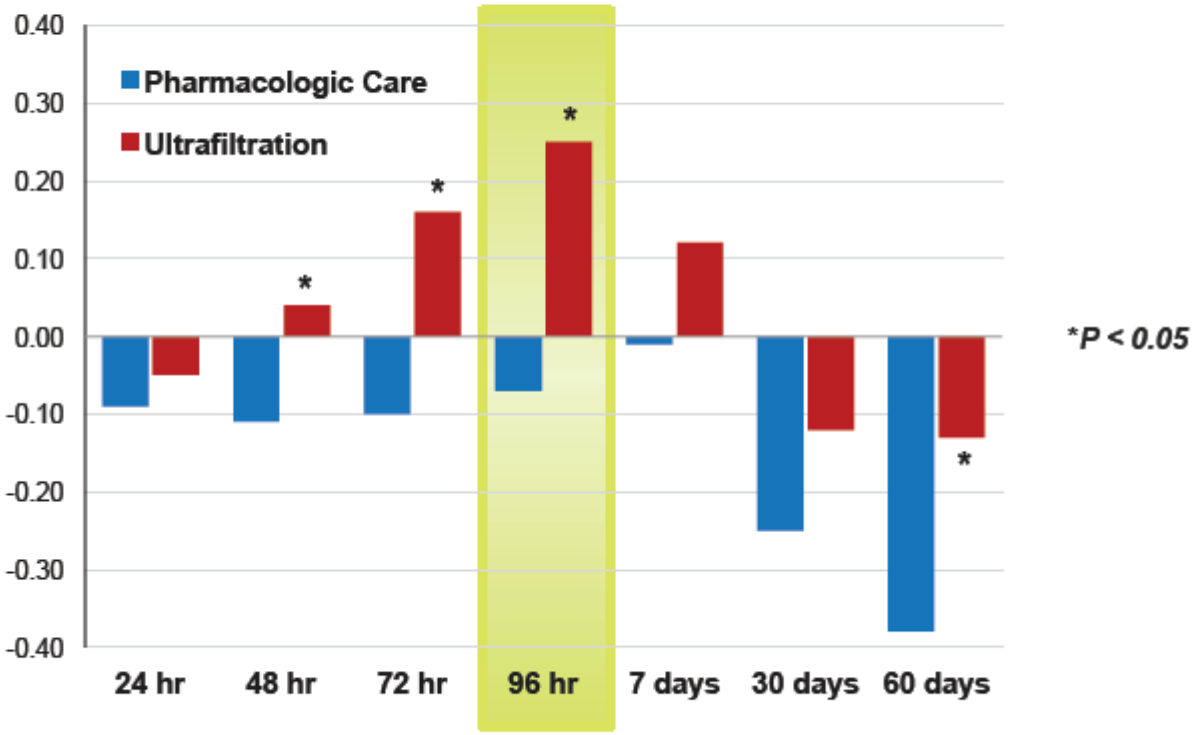
HEART FAILURE NETWORK



CARRESS-HF

Change in Creatinine

HEART FAILURE NETWORK

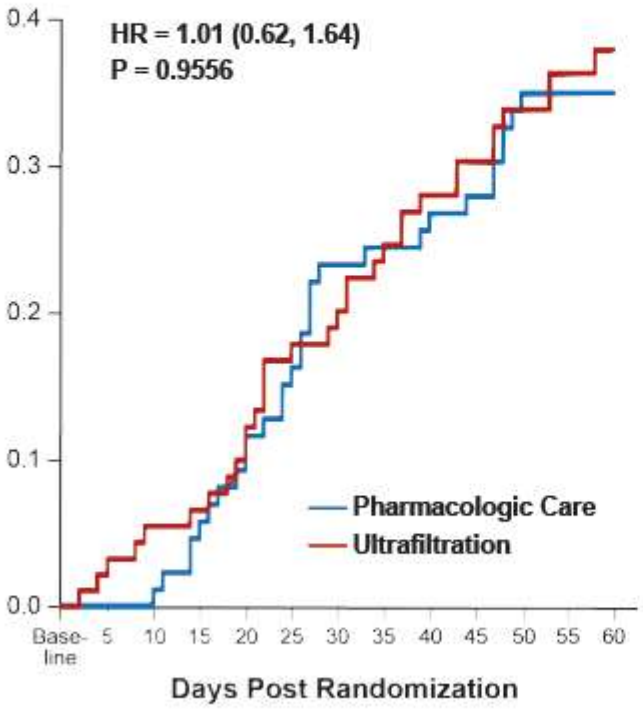


CARRESS-HF

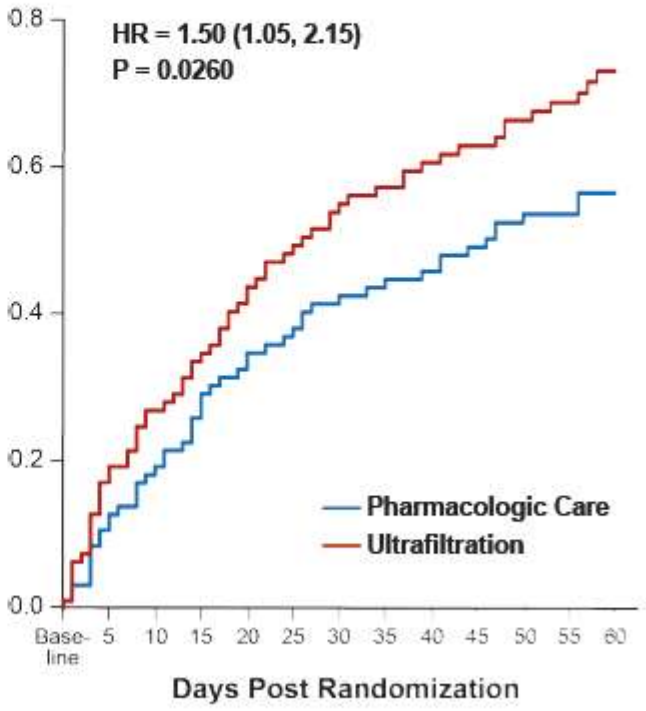
60-day Event Rates

HEART FAILURE NETWORK

Death or HF Rehospitalization



Death or Serious Adverse Event



CARRESS-HF

Table 3. Serious Adverse Events.

Event	Pharmacologic Therapy (N=94)	Ultrafiltration (N=94)
	no. of patients (%)	
Any	54 (57)	68 (72)
Heart failure	28 (30)	31 (33)
Other cardiovascular disorder	5 (5)	6 (6)
Renal failure	14 (15)	17 (18)
Anemia or thrombocytopenia	5 (5)	8 (9)
Catheter-site hemorrhage	0	2 (2)
Electrolyte disorder*	3 (3)	0
Gastrointestinal hemorrhage	3 (3)	7 (7)
Pneumonia or other respiratory disorder	6 (6)	10 (11)
Sepsis, bacteremia, or cellulitis	4 (4)	8 (9)
Other	19 (20)	17 (18)

CARRESS-HF

Conclusions

HEART FAILURE NETWORK

- Pharmacologic care was superior to ultrafiltration at 96 hours for preservation of renal function with similar weight loss
- Ultrafiltration, as administered in this study, had higher rates of adverse events and therefore offers no advantage to stepped pharmacologic care in patients with ADHF, worsened renal function, and persistent congestion
- Treatment of these patients remains a challenging clinical problem in need of better therapy