

Novetats en el Tractament Farmacològic i amb l'ús de Dispositius en HTAP

Sessions d'Actualització de la Societat Catalana de Cardiologia
Acadèmia de les Ciències Mèdiques

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1 TRACTAMENT FARMACOLÒGIC EN LA HTAP TIPUS 2

2 SUPORT CIRCULATORI MECÀNIC EN HTAP TIPUS 2

3 EL FUTUR INMEDIAT EN DISPOSITIUS

4 CONCLUSIONS

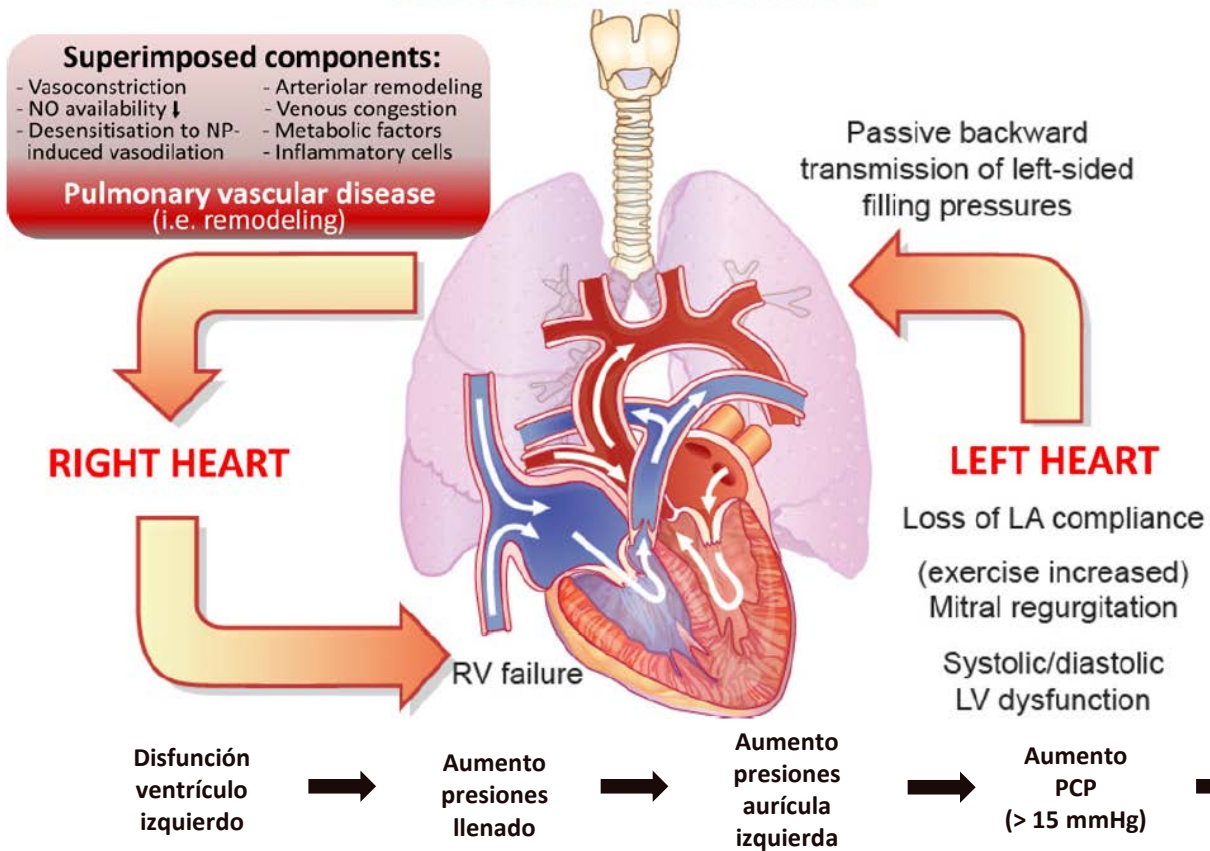
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TRACTAMENT FARMACOLÒGIC DE LA HTAP

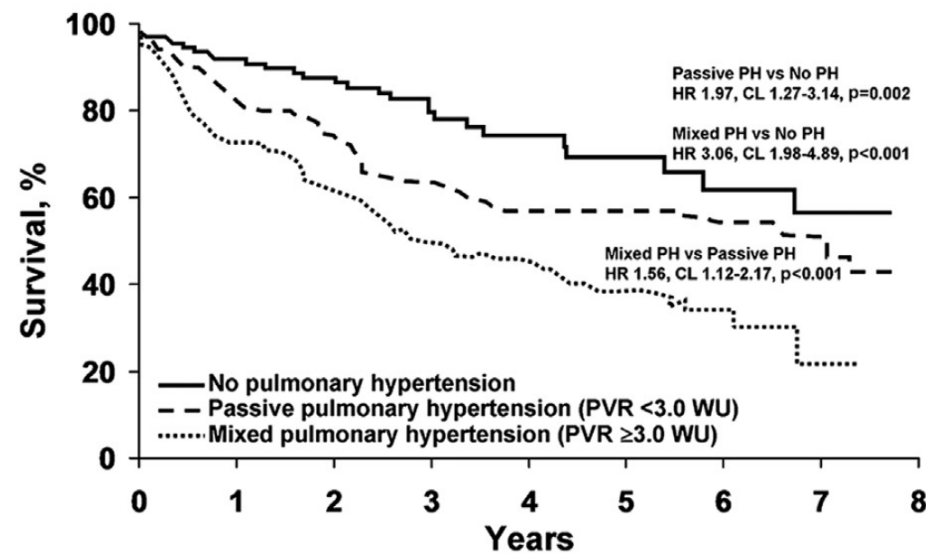


Fisiopatologia i Pronòstic de la HTAP tipus 2

PULMONARY CIRCULATION



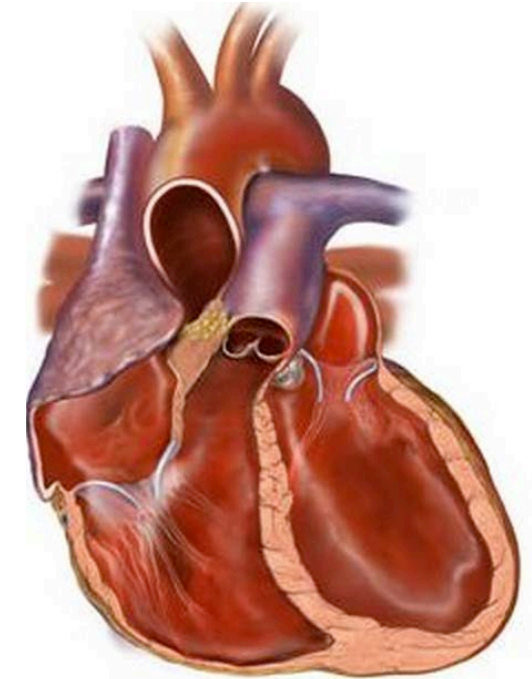
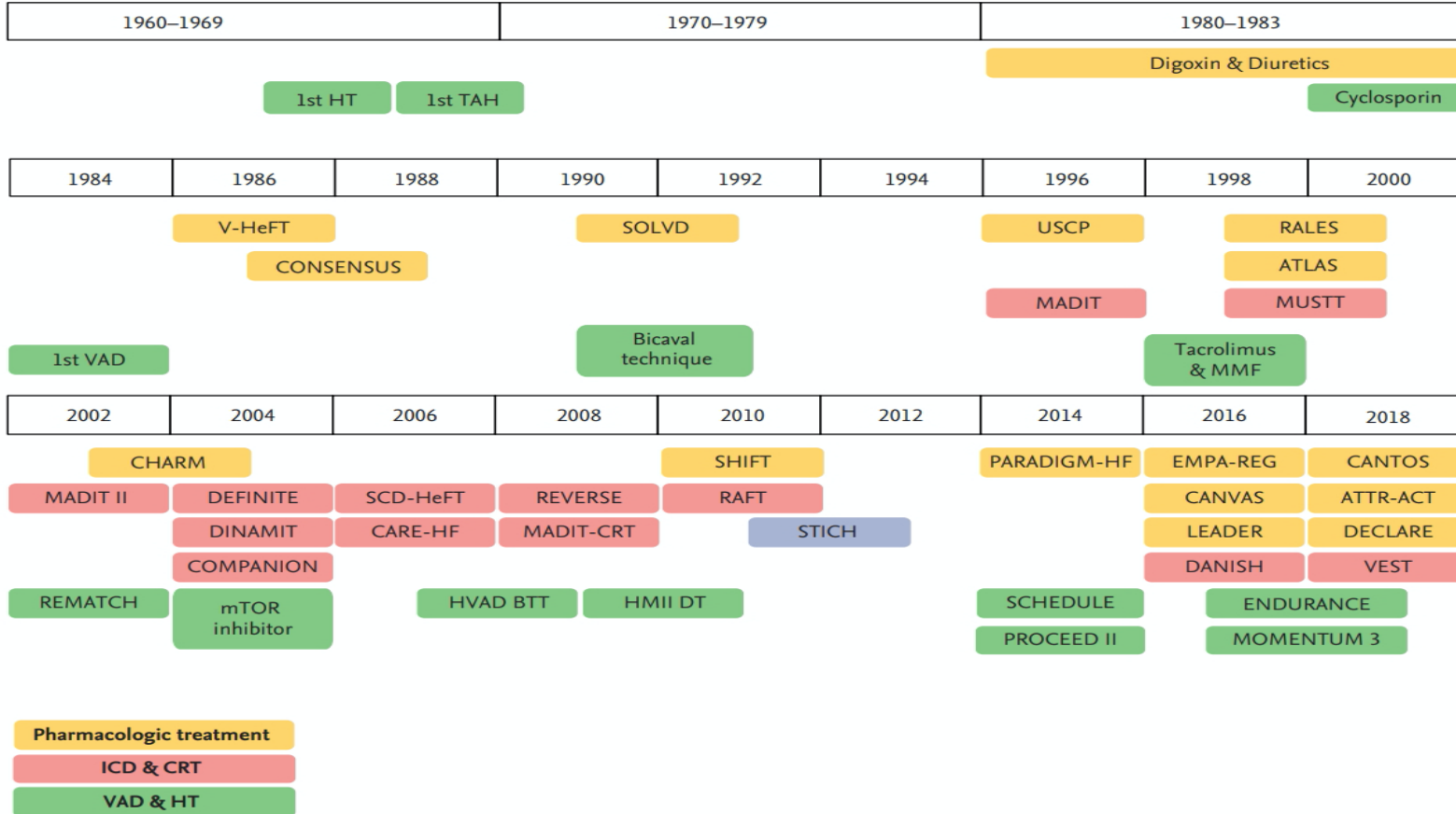
Risk of Death Using Mixed PH Defined by PVR



Rosenkranz et al. European Heart Journal 2017



Evolució del tractament de la IC FE reduïda



Adaptado de Choi HM et al. Korean J Intern Med. 2019 Jan;34(1):11-43



Sacubitril / Valsartan hipertensió pulmonar

Circulation: Heart Failure

Volume 12, Issue 11, November 2019

<https://doi.org/10.1161/CIRCHEARTFAILURE.119.005819>



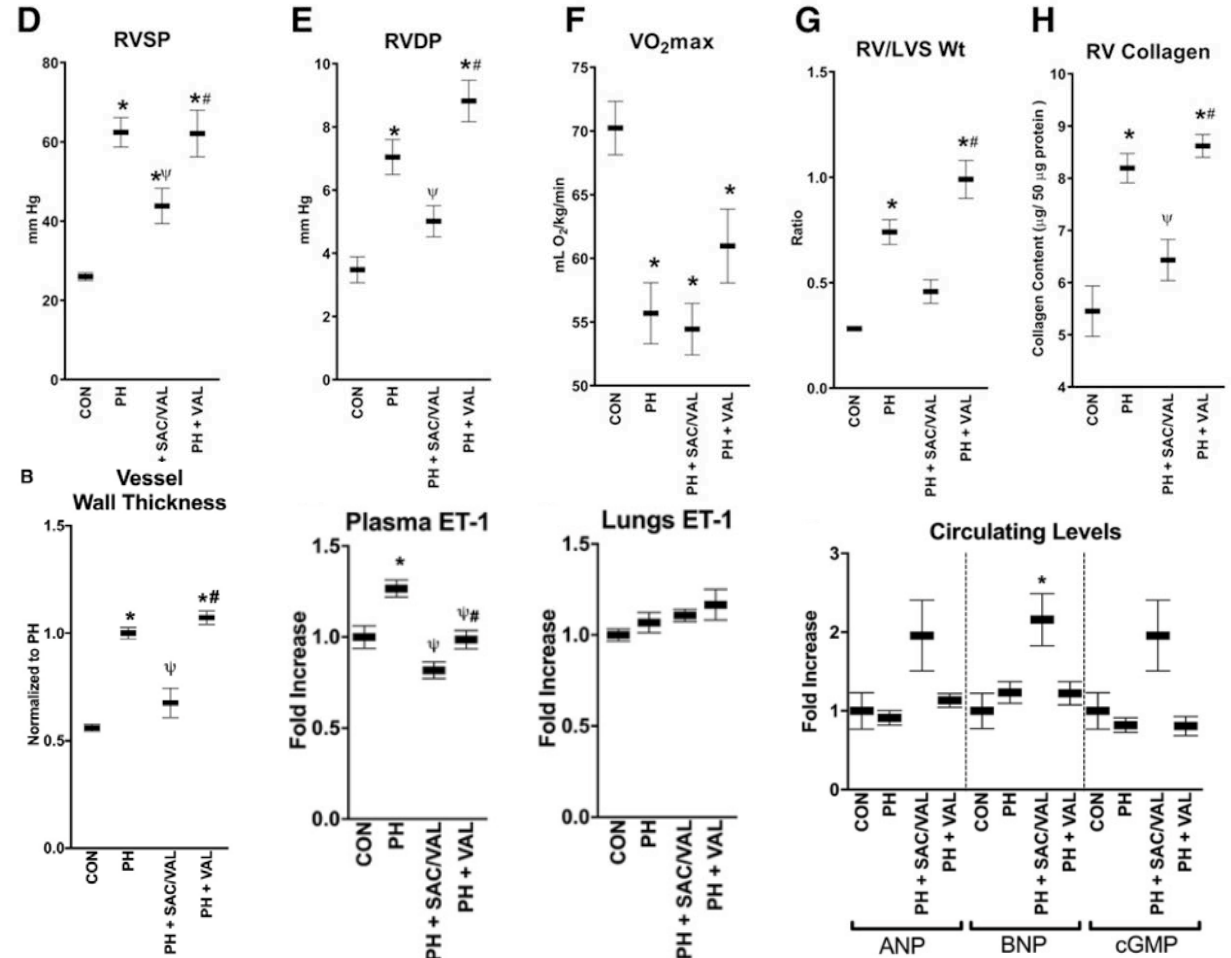
SHORT COMMUNICATION

Treatment of Pulmonary Hypertension With Angiotensin II Receptor Blocker and Neprilysin Inhibitor Sacubitril/Valsartan

Richard T. Clements, PhD, Alexander Vang, AB, Ana Fernandez-Nicolas, PhD, Nouaying R.

METHODS: PH was induced in rats using the SU5416/hypoxia model (Su/Hx), followed by 6-week treatment with placebo, Sac/Val, or Val alone. There were 4 groups: CON—normoxic animals with placebo (n=18); PH—Su/Hx rats+placebo (n=34); PH+Sac/Val (N=24); and PH+Val (n=16).

RESULTS: In animals with PH, treatment with Sac/Val but not Val resulted in significant reduction in RV pressure (mmHg: PH: 62±4, PH+Sac/Val: 46±5), hypertrophy (RV/LV+S: PH: 0.74±0.06, PH+Sac/Val: 0.46±0.06), collagen content (µg/50 µg protein: PH: 8.2±0.3, PH+Sac/Val: 6.4±0.4), pressures and improvement in RVs (mm/s: PH: 31.2±1.8, PH+Sac/Val: 43.1±3.6) compared with placebo. This was associated with reduced pulmonary vascular wall thickness, increased lung levels of ANP (atrial natriuretic peptide), BNP (brain-type natriuretic peptide), and cGMP, and decreased plasma endothelin-1 compared with PH alone. Also, PH+Sac/Val animals had altered expression of PKC isozymes in RV tissue compared with PH alone.





RESEARCH ARTICLE

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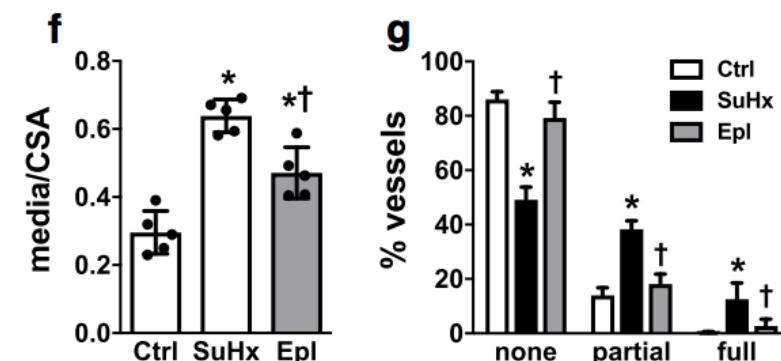
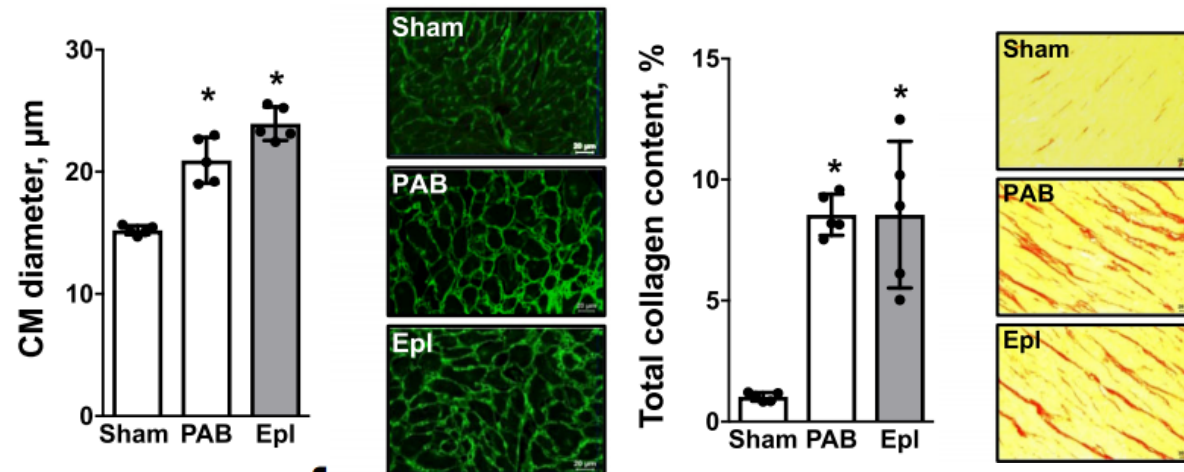
Eplerenone attenuates pathological pulmonary vascular rather than right ventricular remodeling in pulmonary arterial hypertension

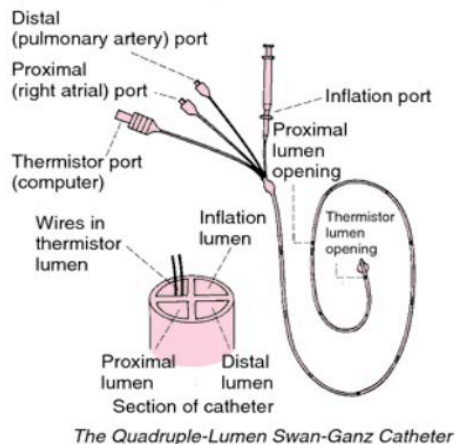
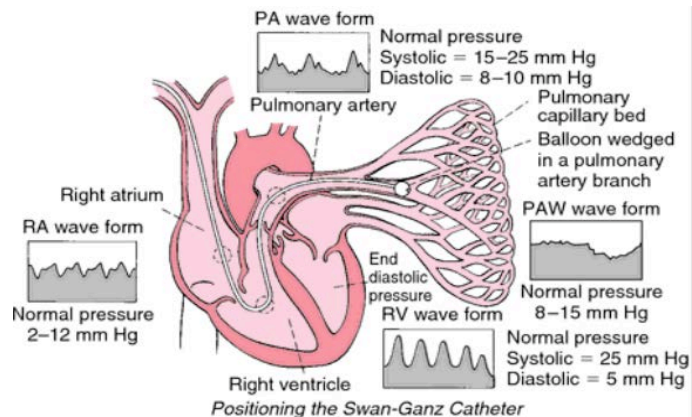
Mario Boehm¹, Nadine Arnold², Adam Braithwaite², Josephine Pickworth², Changwu Lu¹, Tatyana Novoyatleva¹,

Methods: The effects of Eplerenone (0.1% Inspra® mixed in chow) on pulmonary vascular and RV remodeling were evaluated in mice with pulmonary hypertension (PH) caused by Sugen5416 injection with concomitant chronic hypoxia (SuHx) and in a second animal model with established RV dysfunction independent from lung remodeling through surgical pulmonary artery banding.

Results: Preventive Eplerenone administration attenuated the development of PH and pathological remodeling of pulmonary arterioles. Therapeutic aldosterone antagonism – starting when RV dysfunction was established - normalized mineralocorticoid receptor gene expression in the right ventricle without direct effects on either RV structure (Cardiomyocyte hypertrophy, Fibrosis) or function (assessed by non-invasive echocardiography along with intra-cardiac pressure volume measurements), but significantly lowered systemic blood pressure.

Conclusions: Our data indicate that aldosterone antagonism with Eplerenone attenuates pulmonary vascular rather than RV remodeling in PAH.





RHC is recommended in patients with congenital cardiac shunts to support decisions on correction (Table 24)	I	C	
RHC is recommended in patients with PH due to left heart disease (group 2) or lung disease (group 3) if organ transplantation is considered	I	C	
When measurement of PAWP is unreliable, left heart catheterization should be considered to measure LVEDP	IIa	C	
RHC may be considered in patients with suspected PH and left heart disease or lung disease to assist in the differential diagnosis and support treatment decisions	IIb	C	

Vasoreactivity testing is indicated only in expert centres **I C 69**

A positive response to vasoreactivity testing is defined as a reduction of mean PAP ≥ 10 mmHg to reach an absolute value of mean PAP ≤ 40 mmHg with an increased or unchanged cardiac output **I C 85,86**

Table 5 Selective Intravenous Pulmonary Vasodilators

Agent	PVR	mPAP	PCWP	CI	SVR	Notes
Nitroprusside	↓↓↓	↓↓	↓↓	↑↑	↓↓↓	0.5–5.0 $\mu\text{g}/\text{kg}/\text{min}$
Milrinone	↓↓↓	↓	↓	↑↑↑	↓↓↓	50 $\mu\text{g}/\text{kg}$ IV bolus
Nitric oxide	↓↓↓	↔	↑↑	↓	↔	80 ppm over 10 min
Prostaglandin E1	↓↓↓	↓↓	↑	↑↑	↓↓↓	0.02–0.30 $\mu\text{g}/\text{kg}/\text{min}$
Adenosine	↓↓↓	↔	↑	↑	↔	100 $\mu\text{g}/\text{kg}/\text{min}$

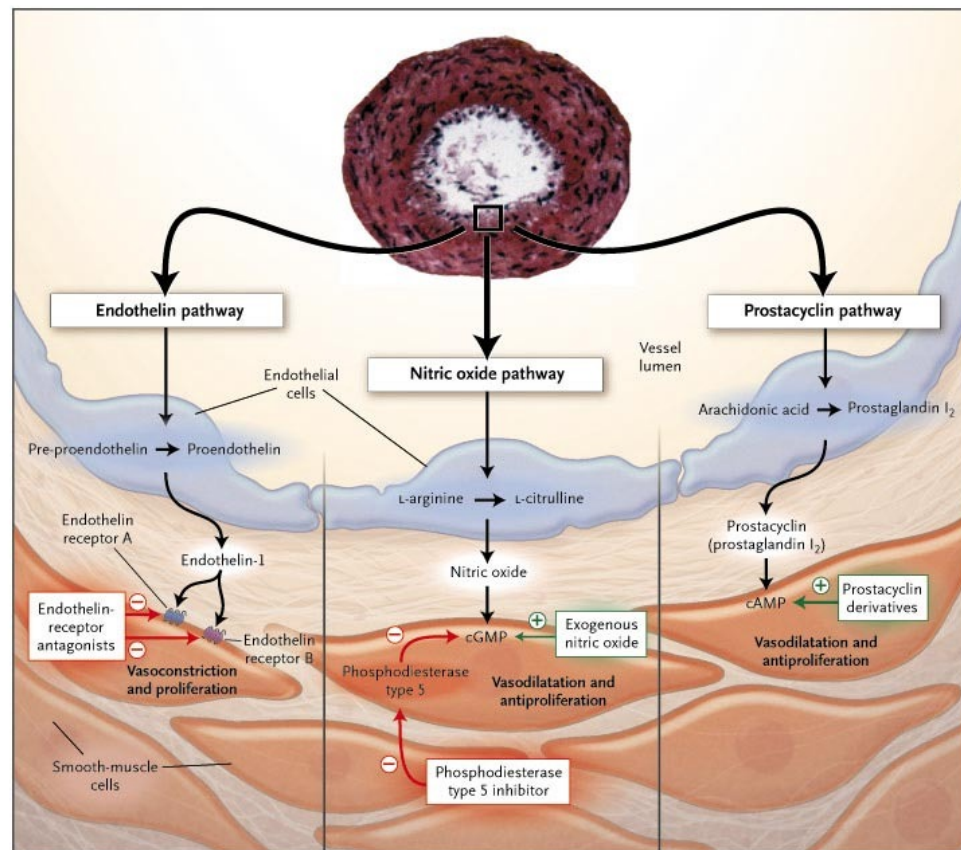
CI, cardiac index; IV, intravenous; mPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PVR, peripheral vascular resistance; SVR, systemic vascular resistance.
Adapted from Bain DS, editor. Grossman's cardiac catheterization, angiography, and intervention. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. Used with permission.

ESC/ERS Guidelines in the Management of PHT; European Heart Journal (2016) 37, 67–119
 Conferencia Consenso de los Grupos Españoles de Trasplante Cardíaco. Rev Esp Cardiol Supl. 2007;7:4B-54B



Teràpia Farmacològica amb Vasodilatadors Pulmonars

Ant ET-1 (A i B)
Bosentan
Macintentan
Darusentan



Prostaciclins
Epoprostenol
Iloprost
Alprostadil

Via del ON-GMPc
Sildenafil, Tadalafil (iPD5)
Riociguat, Vericiguat (GMPc)

Humbert et al. NEJM. 2004.

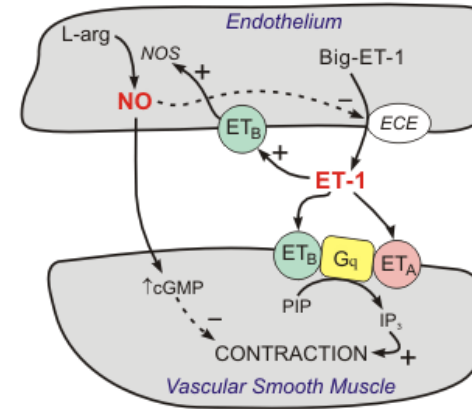
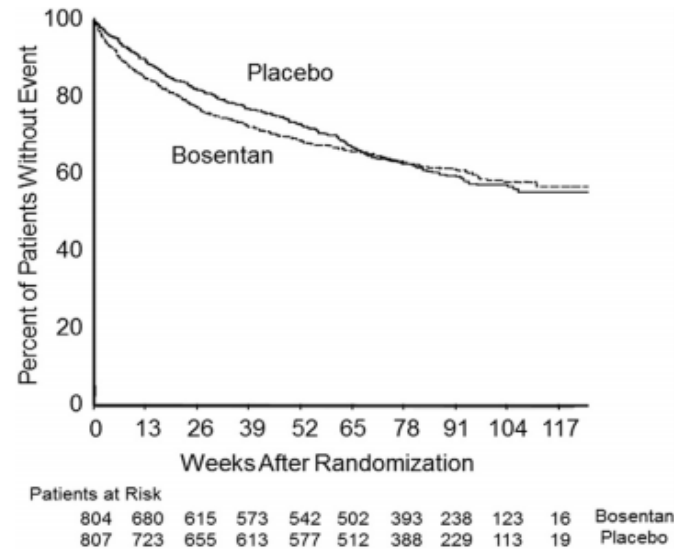


Enable Study: Bosentan en pacients amb FE reduïda

Long-Term Effect of Endothelin Receptor Antagonism With Bosentan on the Morbidity and Mortality of Patients With Severe Chronic Heart Failure

Primary Results of the ENABLE Trials

FIGURE 1 Freedom From All-Cause Mortality or Hospitalization for Heart Failure (Coprimary Endpoint)



Efecte agut de ET1:
- Estimula ON (GMPc) en vasos sense múscul llis

Efecte perllongat de ET1:
- VC dels vasos amb múscul llis

- Anàlisi estadística dels estudis ENABLE 1 i 2.
- En cap assaig es varen demostrar millores en l'estat clínic dels pacients en quant a mortalitat o hospitalització per IC
- El grup de pacients tractats amb Bosentan, va presentar més episodis de congestió en forma d'augment de pes, edemes i hospitalització per IC, inclús augmentant l'ús de diürètics.
- El 10% dels pacients amb Bosentan varen presentar augment d'enzims hepàtics.



Macitentan in pulmonary hypertension due to left ventricular dysfunction

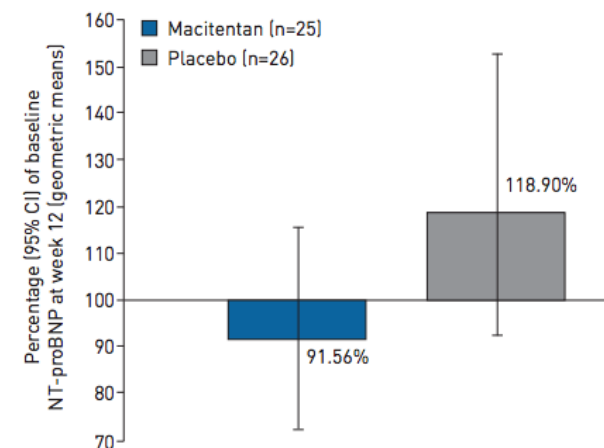
Jean-Luc Vachiéry¹, Marion Delcroix², Hikmet Al-Hiti³, Michela Efficace⁴, Martin Hutyra⁵, Gabriela Lack⁶, Kelly Papadakis⁷ and Lewis J. Rubin⁸

63 patients with PH-LHD and diastolic pressure gradient ≥ 7 mmHg and pulmonary vascular resistance (PVR) > 3 WU were randomised to macitentan 10 mg (n=31) or placebo (n=32) for 12 weeks. The main end-point assessed a composite of significant fluid retention (weight gain $\geq 5\%$ or ≥ 5 kg because of fluid overload or parenteral diuretic administration) or worsening in New York Heart Association functional class from baseline to end of treatment. Exploratory end-points included changes in N-terminal pro-brain natriuretic peptide (NT-proBNP) and haemodynamics at week 12.

- Pacients amb IC i FE $> 30\%$, la major part $> 50\%$
- Augment de descompensacions (edemes i necessitat de diürètic)
- Empitjorament del 6'WT

TABLE 4 Treatment effect for haemodynamic parameters at week 12

	Mean absolute change from baseline (95% CI)
PVR dyn·s·cm ⁻⁵	0.93 (0.64–1.36) ^{#,†1}
mPAP mmHg	0.3 (–4.3–4.9)
mRAP mmHg	0.7 (–2.2–3.6)
PAWP mmHg	–0.3 (–4.2–3.7)
TPR dyn·s·cm ⁻⁵	–162.2 (–318.0–6.5)
Cardiac index L·min ⁻¹ ·m ⁻²	0.4 (0.1–0.7)
Cardiac output L·min ⁻¹	0.8 (0.3–1.4)
TPG mmHg	0.7 (–3.7–5.1)
DPG mmHg	–0.4 (–4.5–3.6)
Mixed venous oxygen saturation %	–0.4 (–4.6–3.8)

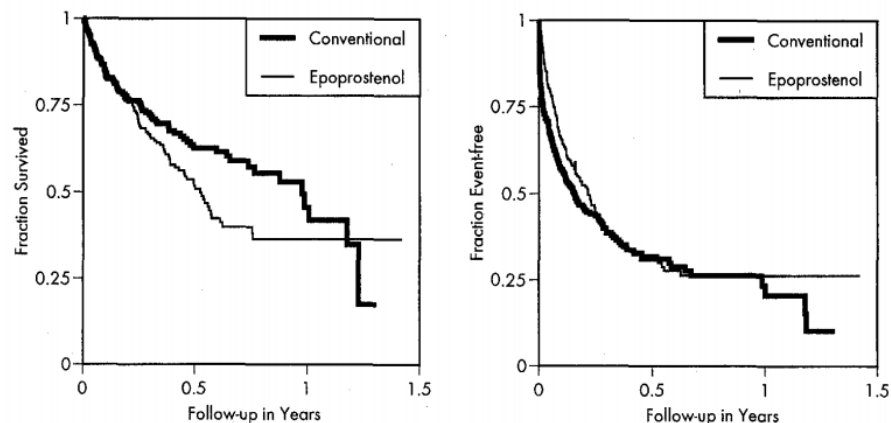




Epoprosterenol: Prostanoides en el tractament de la ICFEr

A randomized controlled trial of epoprostenol therapy for severe congestive heart failure: The Flolan International Randomized Survival Trial (FIRST)

Robert M. Califf, MD,^a Kirkwood F. Adams, MD,^b William J. McKenna, MD,^c Mihai Gheorghiade, MD,^d Barry F. Uretsky, MD,^e Steven E. McNulty, MS,^a Harald Darius, MD,^f Kevin Schulman, MD,^g Faiez Zannad, MD,^h Eileen Handberg-Thurmond, RN,ⁱ Frank E. Harrell Jr., PhD,^j William Wheeler, MD,^k Jordi Soler-Soler, MD,^l and Karl Swedberg, MD^m *Durham, Chapel Hill, and Triangle Park, N.C.; London, United Kingdom; Chicago, Ill.; Pittsburgh, Pa.; Mainz, Germany; Washington, D.C.; Nancy, France; Gainesville, Fla.; Charlottesville, Va.; Barcelona, Spain; and Gothenberg, Sweden*



Kaplan-Meier plots demonstrating time to death (*left*) and time to first event (death, worsening heart failure requiring hospitalization, initiation of intravenous inotropic support, mechanical assisted circulation, tracheotomy, resuscitation, or myocardial infarction) (*right*) by intention to treat.

- Al voltant de 470 pacients amb IC i FE reduïda amb símptomes avançats (CF III-IV)
- L'objectiu principal de l'estudi: supervivència;
- Objectius secundaris: empitjorament de IC, 6'WT, QoL.

- Es va demostrar millora dels paràmetres hemodinàmics (PAP, PCP i índex cardíac)

- Es va aturar precoçment l'estudi per excés de mortalitat en el grup tractat



Inhibidors de la fosfodiesterasa 5: Sildenafil

Additional use of a phosphodiesterase 5 inhibitor in patients with pulmonary hypertension secondary to chronic systolic heart failure: a meta-analysis

Xiaojing Wu^{1*}, Te Yang¹, Qi Zhou², Shuangfei Li¹, and Lan Huang^{1*}

¹Cardiovascular Department of Xinqiao Hospital, Third Military Medical University, No.183 Xinqiao Street, Chongqing, China; and ²Cardiovascular Department of the Second Affiliated Hospital, Chongqing Medical University, Chongqing, China

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- Metanàlisi d'estudis caracteritzats per escassa randomització.
- Heterogeneïtat de la causa de la miocardiopatia
- Objectius primaris diferents entre els estudis

Table 1 Characteristics of randomized controlled trials included in the meta-analysis

Corresponding author, year	Individuals randomized (n)		Gender (male/female)		Age (mean, years)		LVEF (mean, %)		NYHA	mPAP (mmHg)		PASP (mmHg)	
	Sildenafil	Placebo	Sildenafil	Placebo	Sildenafil	Placebo	Sildenafil	Placebo		Sildenafil	Placebo	Sildenafil	Placebo
Marco Guazzi 2012	16	16	16/0	16/0	66	68	29	28	III/IV	35	34	—	—
Marco Guazzi 2011	23	22	23/0	22/0	60	61	29	30	II/III	—	—	37	37
Nadine Clausell 2008	11	8	9/2	4/4	45	53	27	30	I/III	—	—	62	56
Marc J. Semigran 2007	17	17	14/3	15/2	54	62	19	20	II/IV	30	33	—	—
Maurizio D. Guazzi 2007	23	23	23/0	23/0	62	63	31	32	II/III	—	—	42	44
Gregory D. Lewis 2008	15	15	27/3 (overall) ^a			58	27	28	II/IV	30	33	—	—

Corresponding author, year	Aetiology (ischaemic, %)	Basic treatment (percentage of patients)	Dose of sildenafil	Follow-up	Endpoints
Marco Guazzi 2012	38	Beta-blockers (78%), ACEI (75%), ARB (25%), aldosterone antagonist (50%), digitalis (9%), CRT (53%)	50 mg three times daily	1 year	Adverse events, hospital admission, haemodynamic assessment, CPX, QOL
Marco Guazzi 2011	51	Beta-blockers (84%), ACEI (86%), ARB (24%), aldosterone antagonist (42%), digitalis (11%), CRT (38%)	50 mg three times daily	1 year	Adverse events, hospital admission, LV function, PASP, plasma NT-proBNP, CPX, QOL
Nadine Clausell 2008	32	Beta-blocker (89%), ACEI (100%), diuretics (100%), digitalis (84%)	50 mg three times daily	4 weeks	Adverse events, CPX, PASP, endothelial function
Marc J. Semigran 2007	50	Beta-blockers (97%), ACEI or ARB (82%), diuretics (100%), digitalis (68%), aldosterone antagonist (53%), CRT (29%)	Initial dose: 25 mg three times daily, titrated every 2 weeks to 75 mg three times daily	12 weeks	Adverse events, hospital admission, haemodynamic assessment, CPX, 6 min walking distance, NYHA, QOL
Maurizio D. Guazzi 2007	46	Beta-blockers (65%), ACEI (80%), ARB (17%), diuretics (67%), digitalis (26%)	50 mg twice daily	6 months	Adverse events, hospital admission, LVr function, PASP, CPX, QOL
Gregory D. Lewis 2008	50	Beta-blockers (97%), ACEI or ARB (83%), aldosterone antagonist (57%), diuretics (100%), digitalis (73%), CRT (27%)	Initial dose: 25 mg three times daily, titrated every 2 weeks to 75 mg three times daily	12 weeks	Haemodynamic assessment, CPX, LV function

ACEI, ACE inhibitor; CPX, cardiopulmonary exercise testing; mPAP, mean pulmonary artery pressure; PASP, pulmonary artery systolic pressure; QOL, quality of life.
^aPercentage in all included patients.



Inhibidors de la fosfodiesterasa 5: Sildenafil



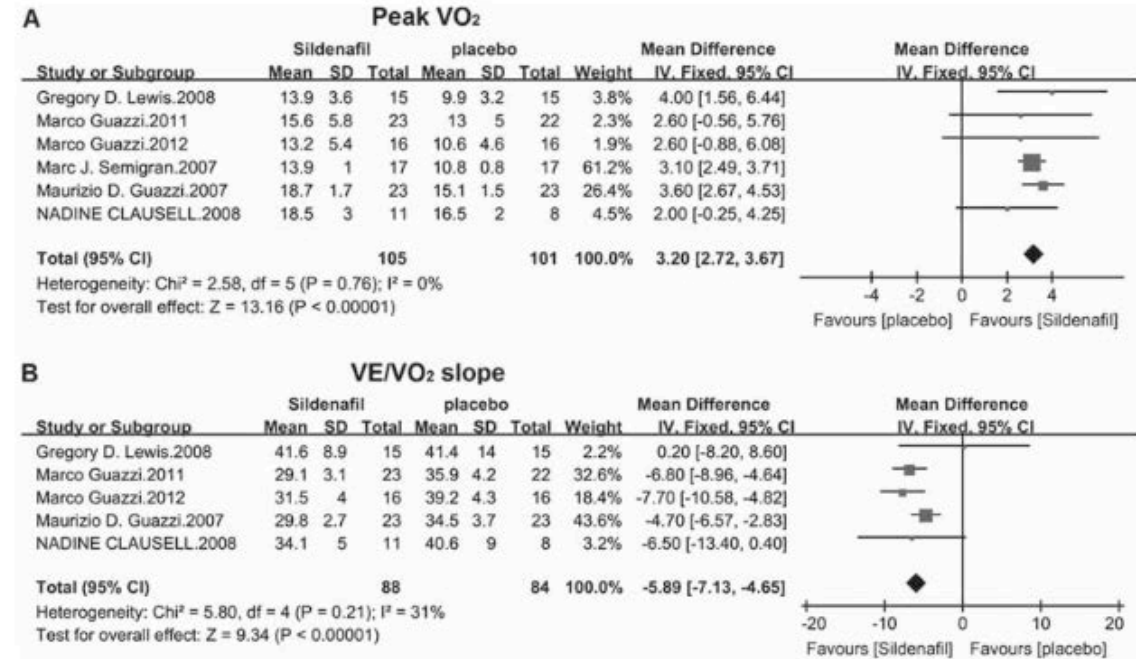
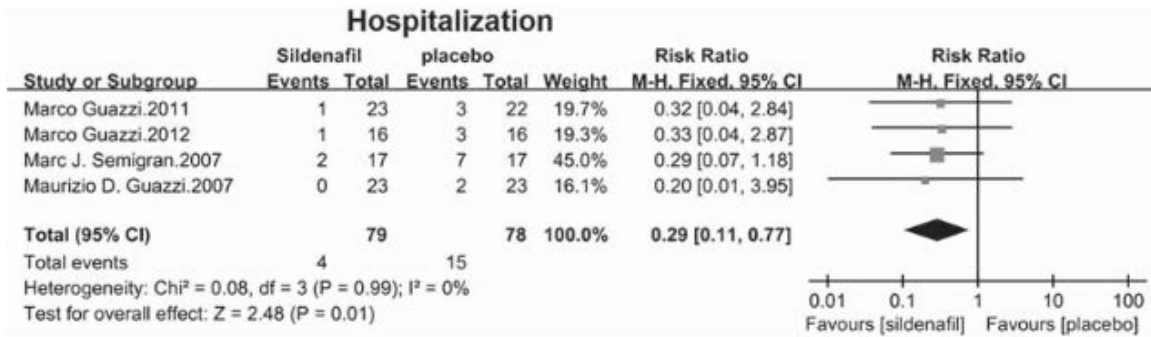
European Journal of Heart Failure (2014) 16, 444–453
doi:10.1002/ejhf.47

Additional use of a phosphodiesterase 5 inhibitor in patients with pulmonary hypertension secondary to chronic systolic heart failure: a meta-analysis

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¹Cardiovascular Department of Xinqiao Hospital, Third Military Medical University, No.183 Xinqiao Street, Chongqing, China; and ²Cardiovascular Department of the Second Affiliated Hospital, Chongqing Medical University, Chongqing, China

Received 17 September 2013; revised 10 November 2013; accepted 15 November 2013; online publish-ahead-of-print 31 December 2013



Reducció de ingressos per IC, PAPm, RVP. PCP sense canvis. Augment de consum pic de O₂ i Slope favorable



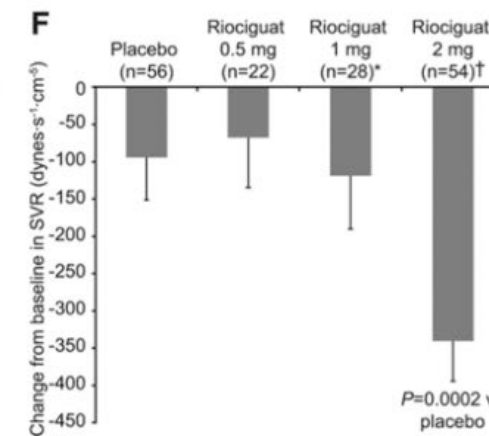
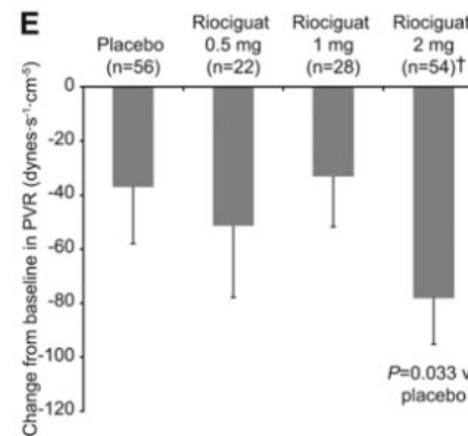
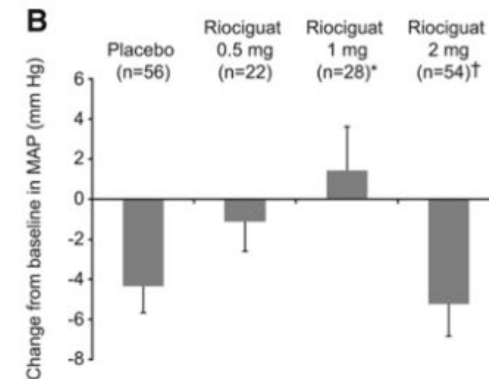
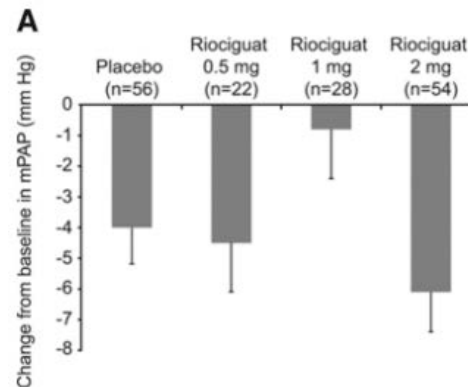
Estimuladors de GMPc en ICFeR: Riociguat (LEPTH Trial)

Heart Failure

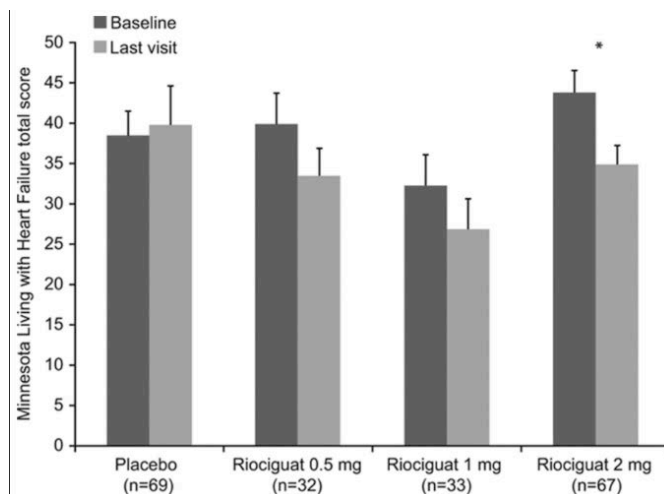
Riociguat for Patients With Pulmonary Hypertension Caused by Systolic Left Ventricular Dysfunction

A Phase IIb Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging Hemodynamic Study

Diana Bonderman, MD; Stefano Ghio, MD; Stephan B. Felix, MD; Hossein-Ardeschir Ghofrani, MD; Evangelos Michelakis, MD; Veselin Mitrovic, MD; Ronald J. Oudiz, MD; Francis Boateng, PhD; Andrea-Viviana Scalise, MD; Lothar Roessig, MD; Marc J. Semigran, MD; on behalf of the Left Ventricular Systolic Dysfunction Associated With Pulmonary Hypertension Riociguat Trial (LEPHT) Study Group



- No es va assolir l'objectiu primari (descens PAPm)
- Perfil hemodinàmic favorable (UW, dosis)
- Millora de la qualitat de vida (dosis alta)
- Sense events adversos significatius



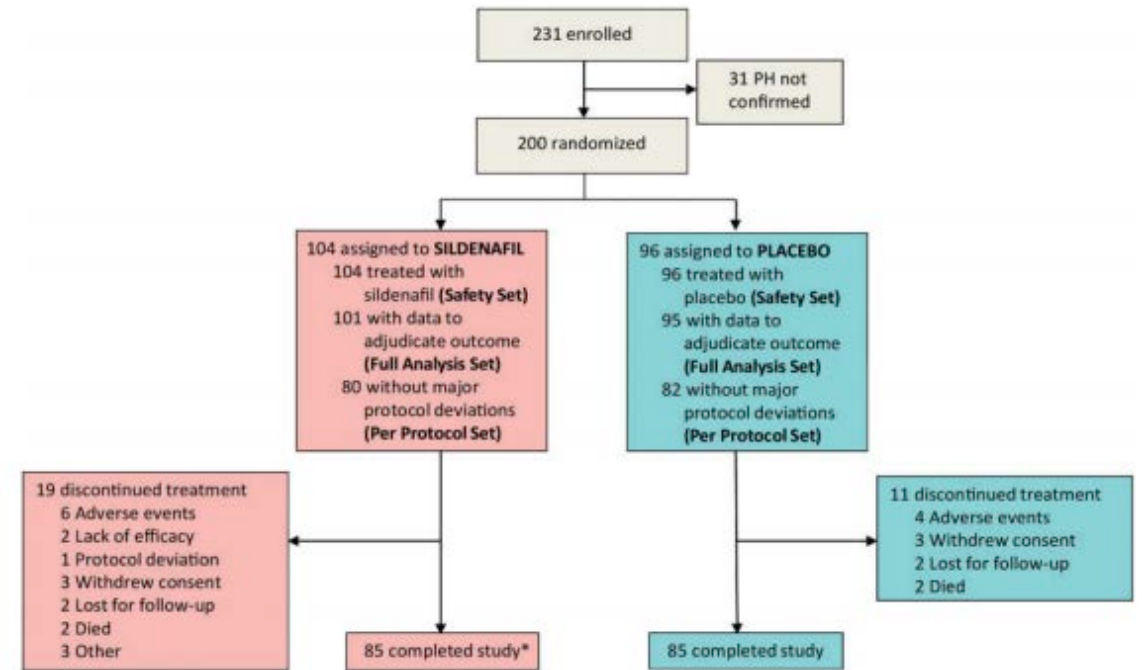


iDP5 (Sildenafil) en HTAP en cardiopatia valvular

Sildenafil for improving outcomes in patients with corrected valvular heart disease and persistent pulmonary hypertension: a multicenter, double-blind, randomized clinical trial

Javier Bermejo^{1*}, Raquel Yotti¹, Rocío García-Orta², Pedro L. Sánchez-Fernández³,

Heart valve procedures				
Time from last valvular surgery (years), median (IQR)	7.5 (4.2, 13.1)	5.8 (3.0, 12.3)		0.12
Isolated mitral valve surgery, n (%)	27 (26)	33 (34)		0.22
Isolated aortic valve replacement, n (%)	8 (8)	9 (9)		0.80
Mitral and aortic valve surgery, n (%)	29 (28)	16 (17)		0.06
Mitral and tricuspid valve surgery, n (%)	26 (25)	23 (24)		0.87
Aortic and tricuspid valve surgery, n (%)	0 (0)	1 (1)		0.48
Mitral, aortic and tricuspid valve surgery, n (%)	14 (14)	14 (15)		0.84
Patients with re-interventions, n (%)	39 (38)	24 (25)		0.07



Estudi Basal: PAP 64/39/23mmHg, PCP 22-23mmHg, GTP 15-16mmHg, GTPd 2-3mmHg. UW 3.4-3,1. PVC 12mmHg, IC 2.8.



iDP5 (Sildenafil) en HTAP en cardiopatia valvular

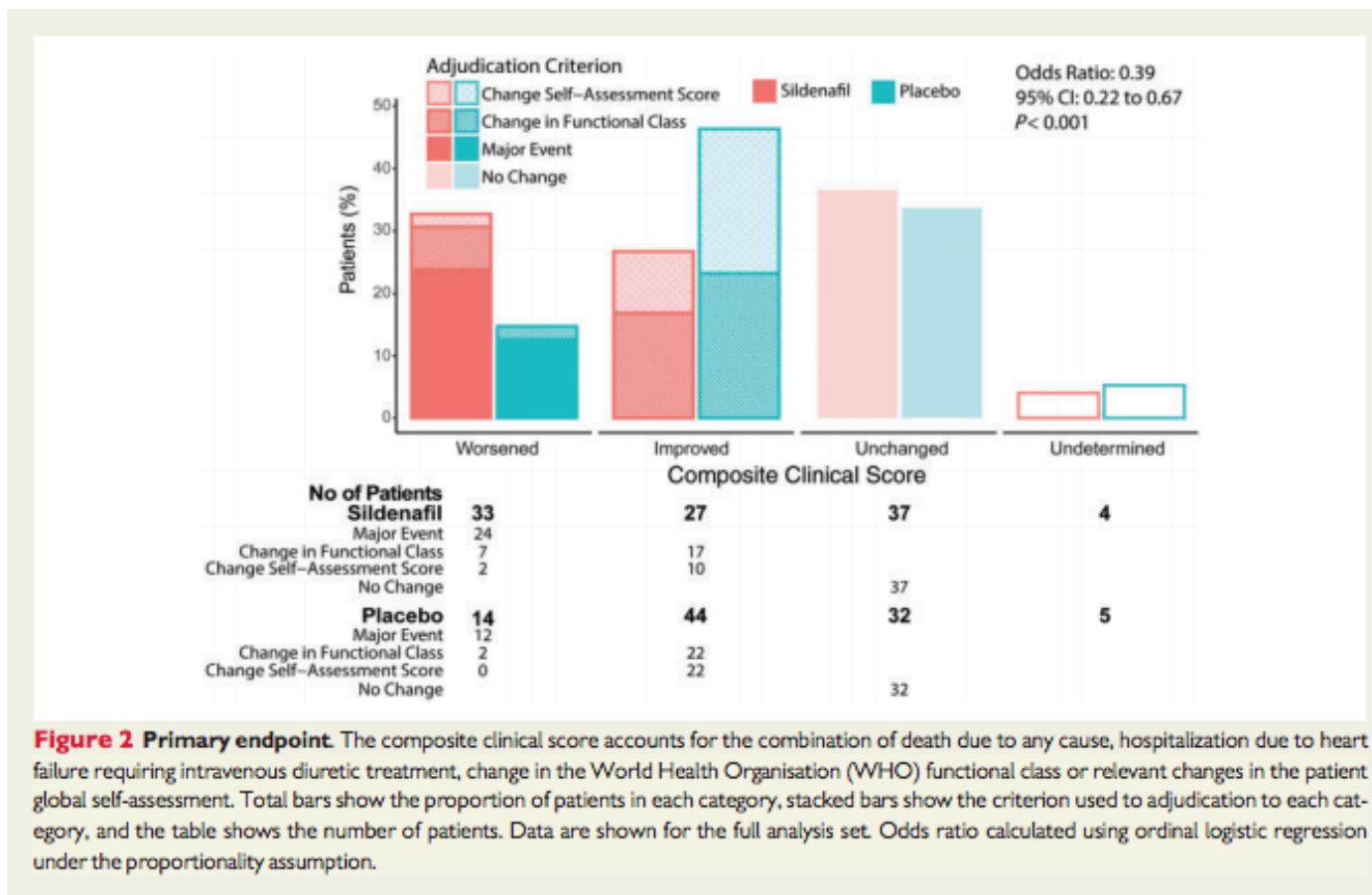
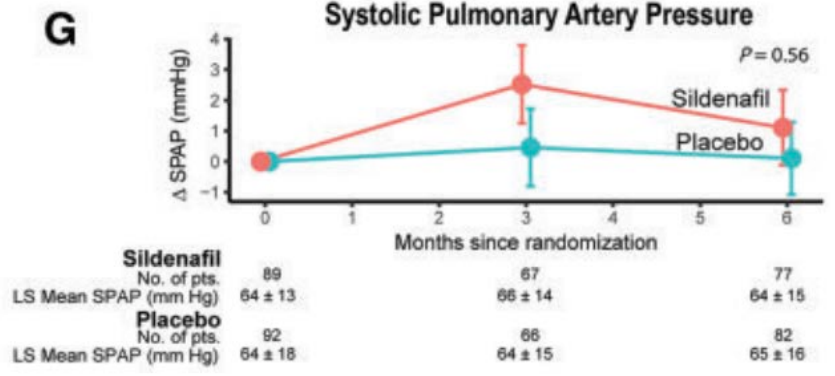
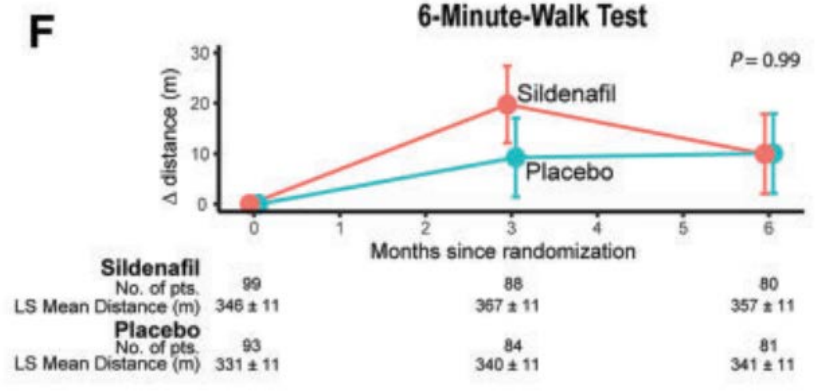
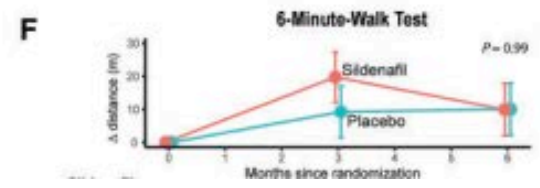
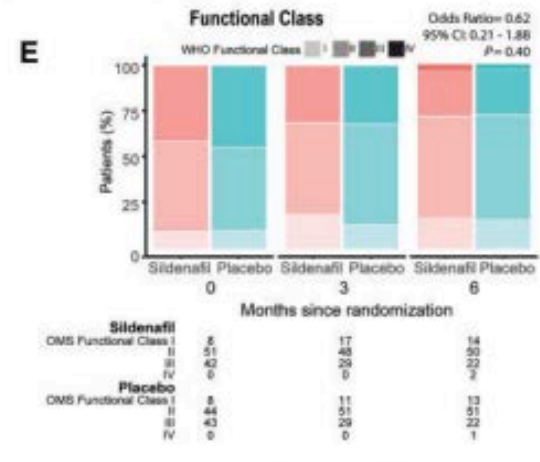
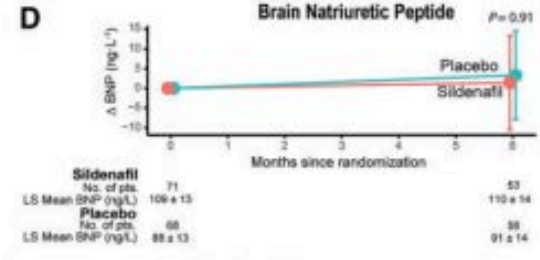
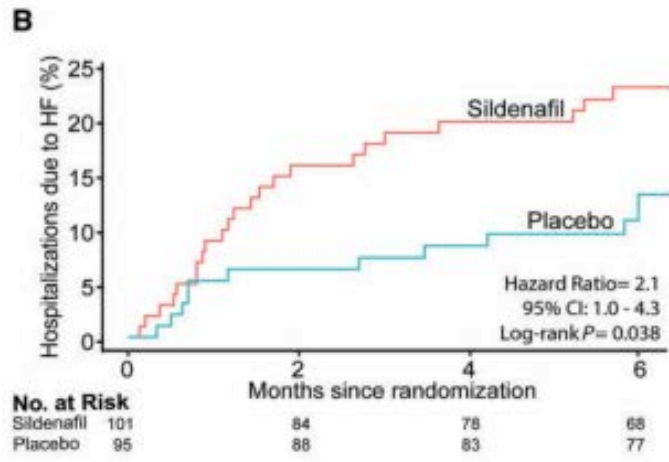
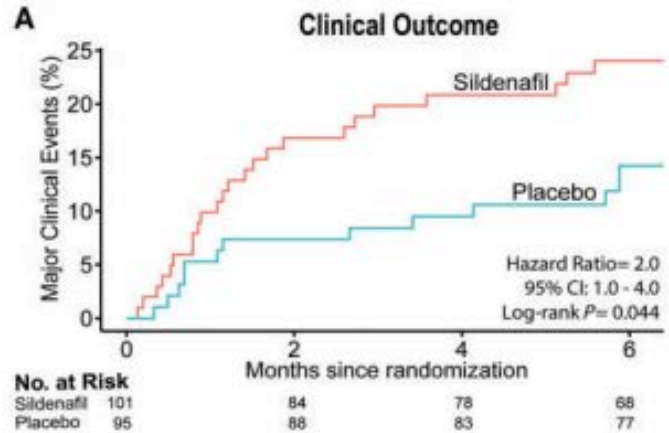


Figure 2 Primary endpoint. The composite clinical score accounts for the combination of death due to any cause, hospitalization due to heart failure requiring intravenous diuretic treatment, change in the World Health Organisation (WHO) functional class or relevant changes in the patient global self-assessment. Total bars show the proportion of patients in each category, stacked bars show the criterion used to adjudication to each category, and the table shows the number of patients. Data are shown for the full analysis set. Odds ratio calculated using ordinal logistic regression under the proportionality assumption.

Empitjorament de la situació clínica global mitjançant Score (Mort, hIC, CF, QoL)
Tendència a major taxa d'aconteixements adversos (principalment IC)



iDP5 (Sildenafil) en HTAP en cardiopatia valvular





Situació actual del tractament farmacològic

The use of PAH-approved therapies is not recommended in PH-LHD	III	C	396
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Inhibidors de la fosfodiesterasa 5 en HFpEF: Sildenafil

ONLINE FIRST

Effect of Phosphodiesterase-5 Inhibition on Exercise Capacity and Clinical Status in Heart Failure With Preserved Ejection Fraction A Randomized Clinical Trial

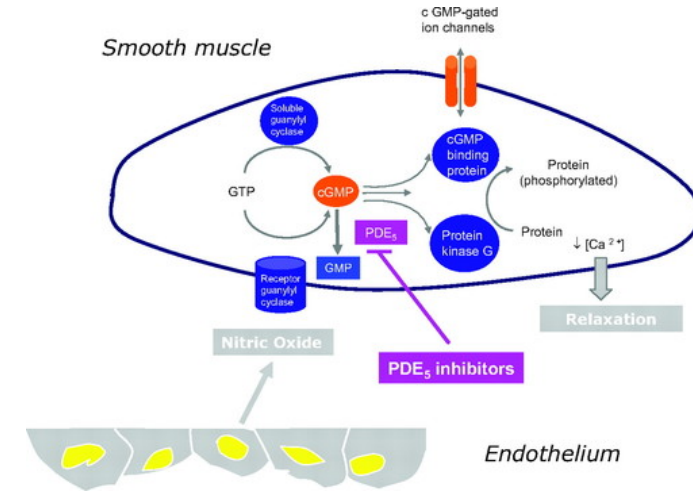
Table 3. Primary, Secondary, and Safety End Points

	Placebo		Sildenafil		P Value
	No. of Patients	Variable	No. of Patients	Variable	
Primary end point					
Change in peak oxygen consumption at 24 wk, median (IQR), mL/kg/min	94	-0.20 (-0.70 to 1.00)	91	-0.2 (-1.70 to 1.11)	.90
Secondary end points					
Clinical rank score, mean ^a	94	95.8	95	94.2	.85
Change in 6-minute walk distance at 24 wk, median (IQR), m	95	15.0 (-26.0 to 45.0)	90	5.0 (-37.0 to 55.0)	.92
Change in peak oxygen consumption at 12 wk, median (IQR), mL/kg/min	96	0.03 (-1.10 to 0.67)	97	0.01 (-1.35 to 1.25)	.98
Change in 6-minute walk distance at 12 wk, median (IQR), m	96	18.0 (-14.5 to 48.0)	99	10.0 (-25.0 to 36.0)	.13
Components of clinical rank score at 24 wk					
Death, No. (%) ^b	103	0	113	3 (3)	.25
Hospitalization for cardiovascular or renal cause, No. (%)	103	13 (13)	113	15 (13)	.89
Change in MLHFQ, median (IQR)	91	-8 (-21 to 5)	91	-8 (-19 to 0)	.44
Safety end points, No. (%)					
Adverse events	103	78 (76)	113	90 (80)	.49
Serious adverse events	103	16 (16)	113	25 (22)	.22

Abbreviations: IQR, interquartile range; MLHFQ, Minnesota Living with Heart Failure Questionnaire.

^aA mean value of 95 in each group is expected under the null hypothesis of no treatment effect.

^bSite investigator identified causes of death were sudden death (n=1), progressive cardiorenal failure (n=1), and noncardiovascular (n=1).



- No es va observar millora significativa en la capacitat funcional.
- Sense canvis significatius en el perfil de biomarcadors
- Sense diferències significatives en els events adversos



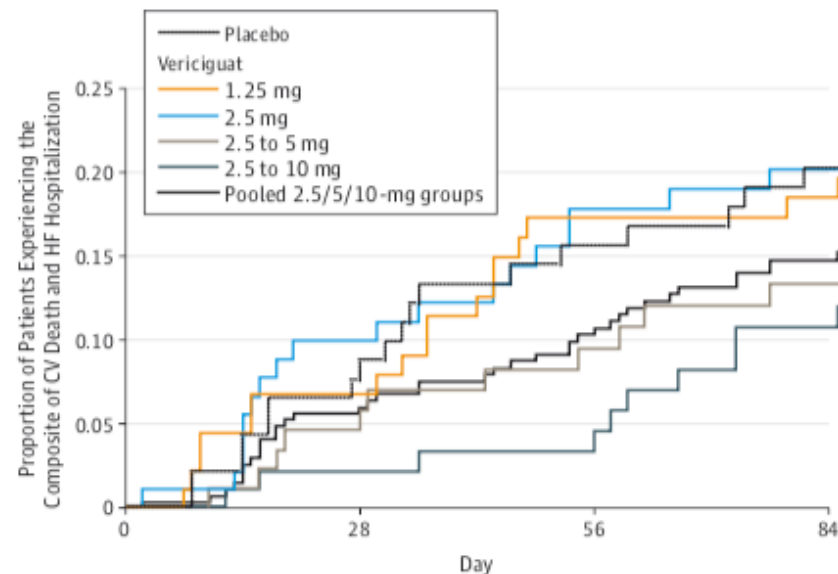
Estimuladors de GMPc en ICFEr: SOCRATES REDUCED

Original Investigation

Effect of Vericiguat, a Soluble Guanylate Cyclase Stimulator, on Natriuretic Peptide Levels in Patients With Worsening Chronic Heart Failure and Reduced Ejection Fraction The SOCRATES-REDUCED Randomized Trial

Mihai Gheorghiu, MD; Stephen J. Greene, MD; Javed Butler, MD, MPH, MBA; Gerasimos Filippatos, MD; Carolyn S. P. Lam, MBBS; Aldo P. Maggioni, MD;

CONCLUSIONS AND RELEVANCE Among patients with worsening chronic HF and reduced LVEF, compared with placebo, vericiguat did not have a statistically significant effect on change in NT-proBNP level at 12 weeks but was well-tolerated. Further clinical trials of vericiguat based on the dose-response relationship in this study are needed to determine the potential role of this drug for patients with worsening chronic HF.

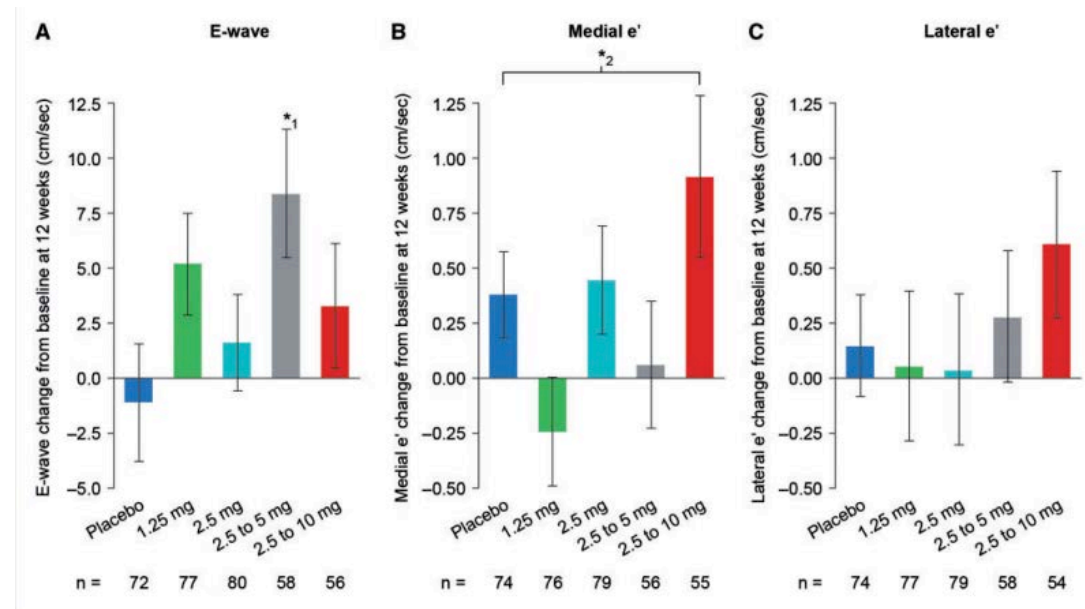




Estimuladors de GMPc en ICFeR: SOCRATES PRESERVED

Vericiguat in patients with worsening chronic heart failure and preserved ejection fraction: results of the SOLuble guanylate Cyclase stimulator in heArT failurE patientS with PRESERVED EF (SOCRATES-PRESERVED) study

Burkert Pieske^{1*}, Aldo P. Maggioni², Carolyn S.P. Lam³, Elisabeth Pieske-Kraigher⁴,



Conclusion

Vericiguat was well tolerated, did not change NT-proBNP and LAV at 12 weeks compared with placebo but was associated with improvements in quality of life in patients with HFpEF. Given the encouraging results on quality of life, the effects of vericiguat in patients with HFpEF warrant further study, possibly with higher doses, longer follow-up and additional endpoints.



Published on *Merck Newsroom Home* (<https://www.mrknewsroom.com>) on 11/18/19 6:30 am EST

Merck and Bayer's Investigational Drug Vericiguat Meets Primary Endpoint in Phase 3 Study of Patients with Worsening Chronic Heart Failure

Release Date:

Monday, November 18, 2019 6:30 am EST

Terms:

[Research and Development News](#) [Corporate News](#) [#Merck](#) [#MRK](#) [\\$MRK](#) [Merck](#) [MRK](#) [NYSE:MRK](#)

Dateline City:

KENILWORTH, N.J.

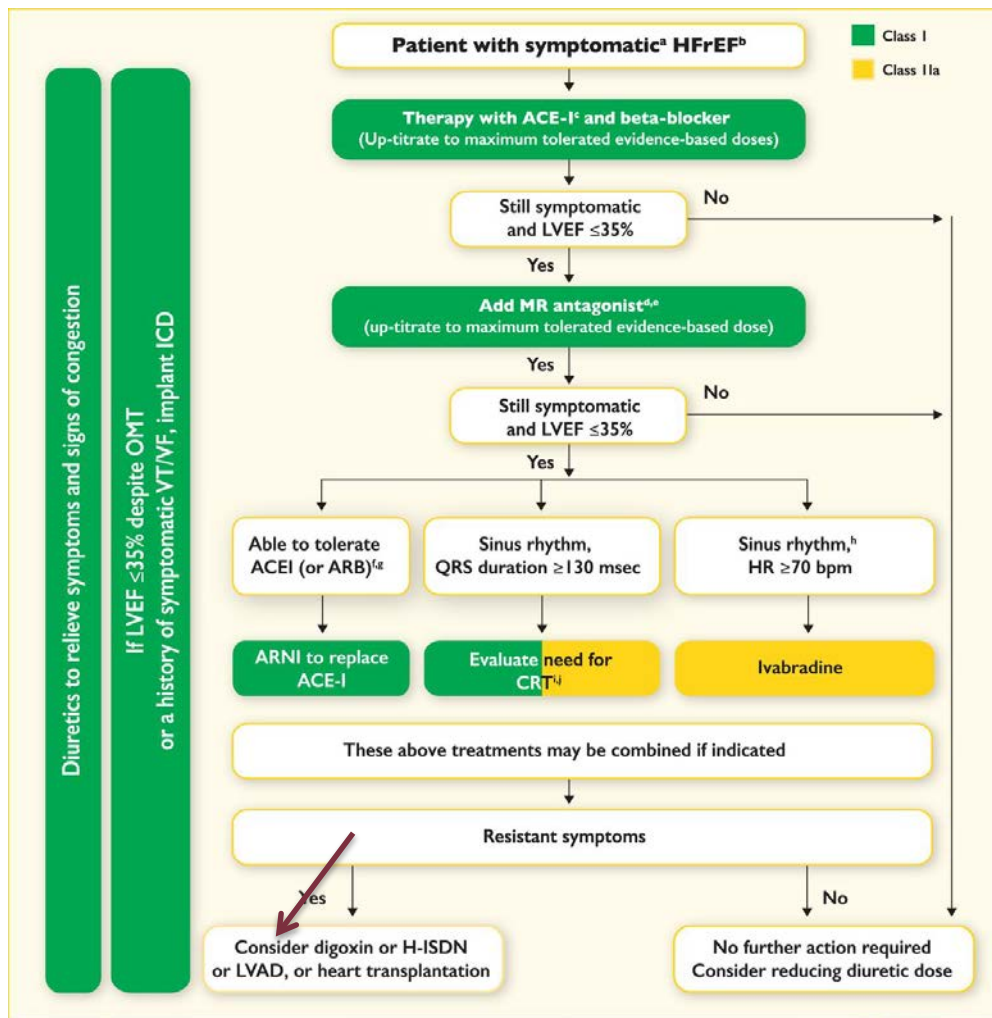
Vericiguat Reduced the Risk of Heart Failure Hospitalization or Cardiovascular Death in Patients with Worsening Chronic Heart Failure with Reduced Ejection Fraction, Compared to Placebo When Added to Available Heart Failure Therapies

2

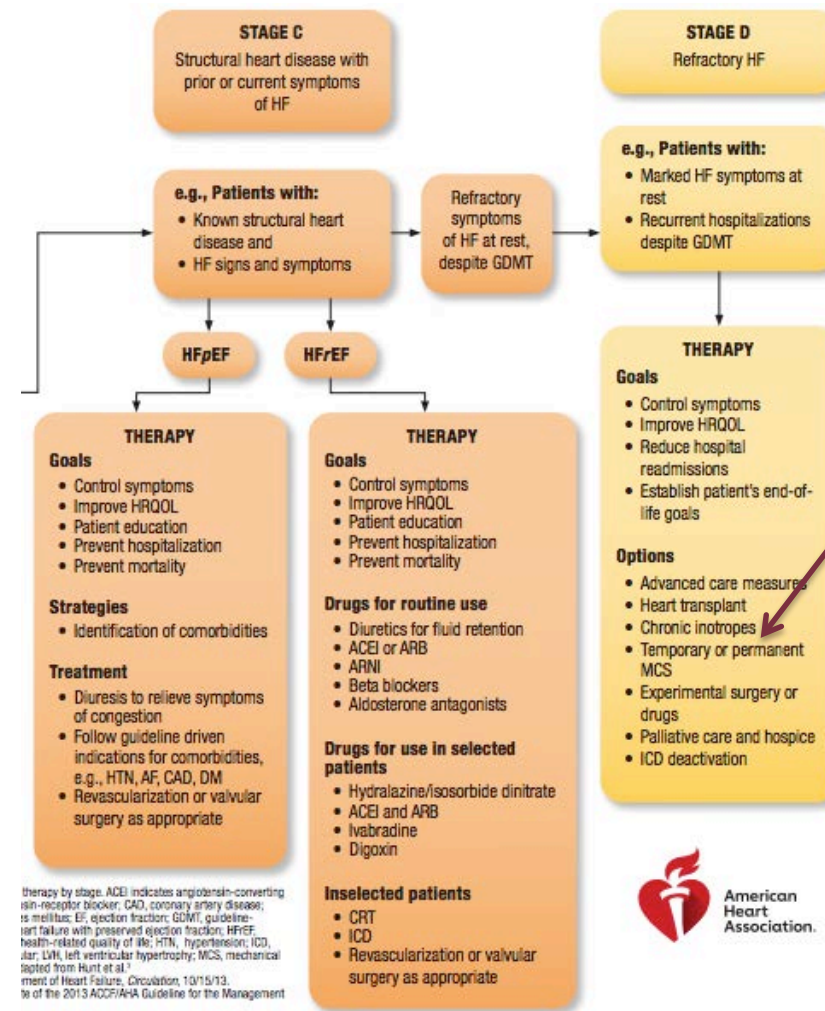
SUPPORT CIRCULATORI MECÀNIC EN HIPERTENSIÓ PULMONAR TIPUS 2



Consta a les guies de IC tractament per a la HTAP?



European Heart Journal, Volume 37, Issue 27, 14 July 2016

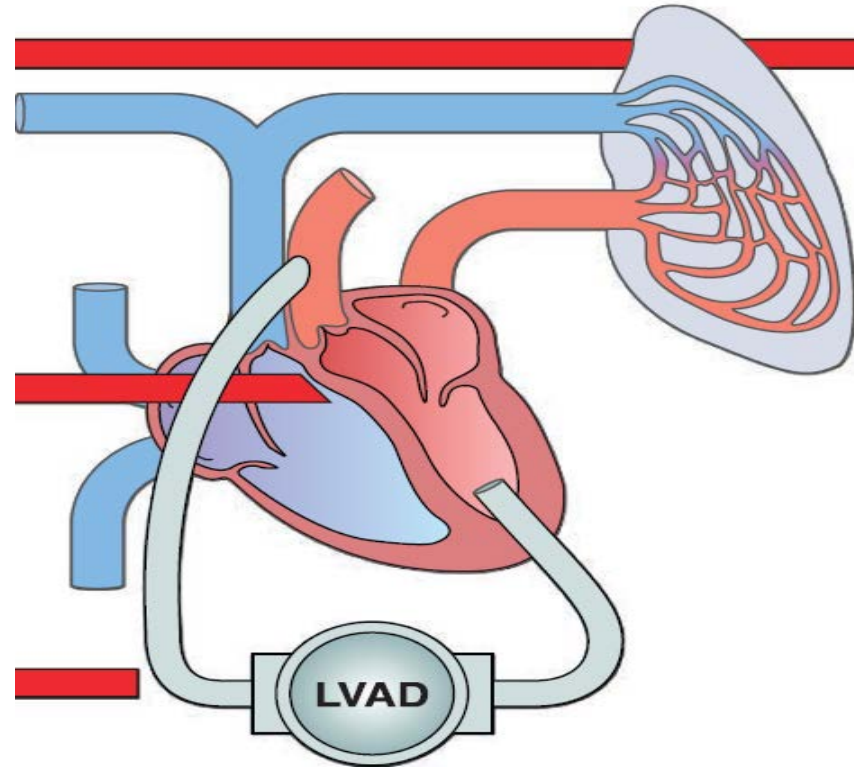


Focused Update of the 2013 ACCF/AHA HF Guideline, Circulation;2017



Suport Circulatori Mecànic en IC Avançada i HTAP

Bridge to decision (BTD)/ Bridge to bridge (BTB)	Use of short-term MCS (e.g. ECLS or ECMO) in patients with cardiogenic shock until haemodynamics and end-organ perfusion are stabilized, contra-indications for long-term MCS are excluded (brain damage after resuscitation) and additional therapeutic options including long-term VAD therapy or heart transplant can be evaluated.
Bridge to candidacy (BTC)	Use of MCS (usually LVAD) to improve end-organ function in order to make an ineligible patient eligible for heart transplantation.
Bridge to transplantation (BTT)	Use of MCS (LVAD or BiVAD) to keep patient alive who is otherwise at high risk of death before transplantation until a donor organ becomes available.
Bridge to recovery (BTR)	Use of MCS (typically LVAD) to keep patient alive until cardiac function recovers sufficiently to remove MCS.
Destination therapy (DT)	Long-term use of MCS (LVAD) as an alternative to transplantation in patients with end-stage HF ineligible for transplantation or long-term waiting for heart transplantation.



Disminució PCP

↑

Disminució pressions Aurícula esquerra

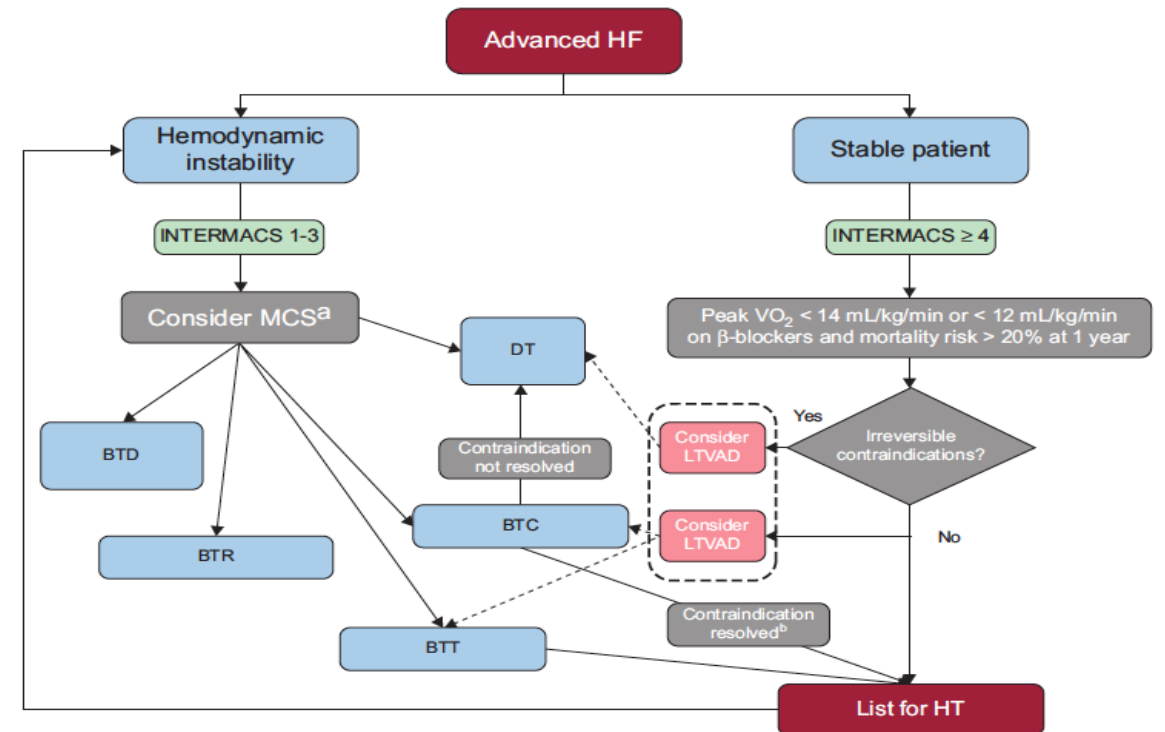
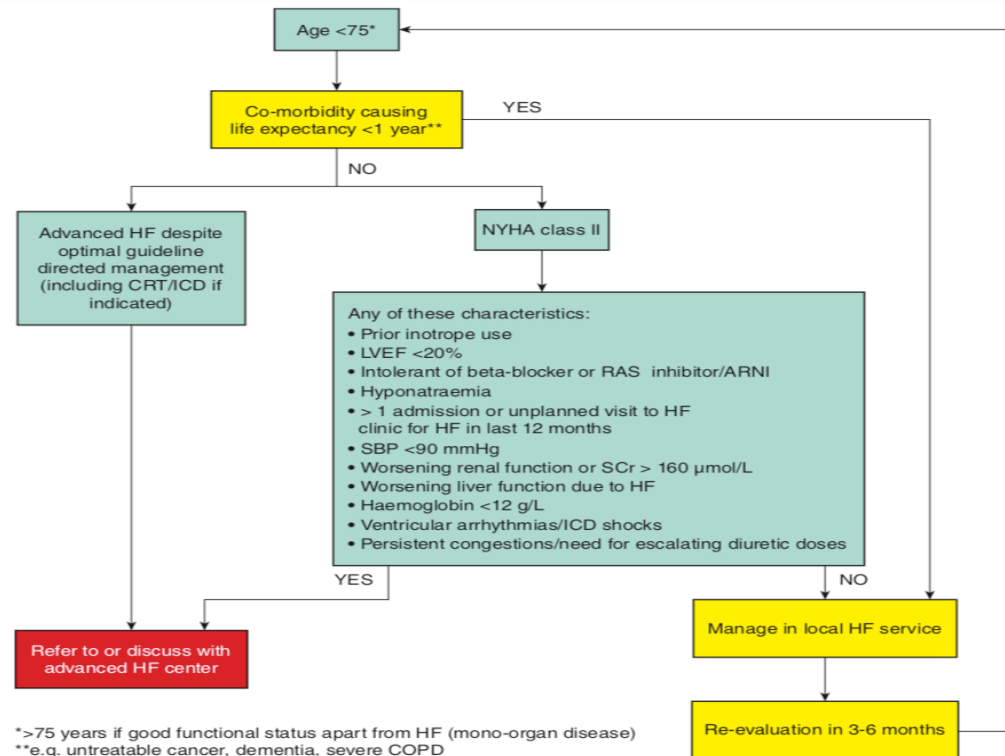
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Disminució pressions Ventricle esquerra

European Heart Journal, Volume 37, Issue 27, 14 July 2016



Assistència Circulatòria Mecànica: Qui / Quan / Com?



Crespo-Leiro MG et al. Advanced HF. A position Statement of the HFA-ESC. Eur J Heart Fail. 2018
Sanchez-Enrique C, Gonzalez-Costello J, Jorde U. Rev Esp Cardiol.2017;70:371–381



Primeres Experiències amb LVAD



European Journal of Cardio-thoracic Surgery 25 (2004) 971–977

EUROPEAN JOURNAL OF
CARDIO-THORACIC
SURGERY

www.elsevier.com/locate/ejcts

Implantable left ventricular assist device for treatment of pulmonary hypertension in candidates for orthotopic heart transplantation—a preliminary study[☆]

Juergen Martin^{a,*}, Michael P. Siegenthaler^a, Ortwin Friesewinkel^a, Tina Fader^a, Andreas van de Loo^b, Georg Trummer^a, Michael Berchtold-Herz^a, Friedhelm Beyersdorf^a

^aDepartment of Cardiovascular Surgery, Albert-Ludwigs-University Medical Center, Hugstetter Str. 55, D-79106 Freiburg, Germany

^bDepartment of Cardiology, Albert-Ludwigs-University Medical Center, Freiburg, Germany

Received 21 October 2003; received in revised form 26 January 2004; accepted 28 January 2004

LVAD:

- 6 pacientes con ICC NYHA IV candidatos a Trasplante Hipertensión pulmonar irreversible (RVP>3 UW)
- Implante de LVAD pulsátil (5 TCI Heartmate/1 Novacor)
- Todos ellos recibieron trasplante cardiaco
5 alta a domicilio
1 exitus por rechazo humoral

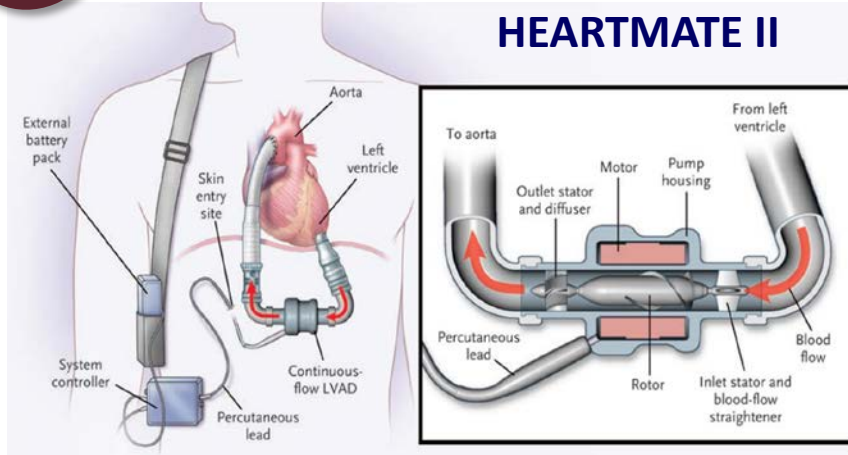
Table 2
Hemodynamic parameters before LVAD implantation and prior to orthotopic heart transplantation

Patient no	Baseline					Prior to HTX				
	PVR	CI	PAs	PAm	PC	PVR	CI	PAs	PAm	PC
1	5.9/5.1 ^a	1.75	63	47	28	3.6/2.2 ^a	2.5	30	18	2
2	6.25	1.7	60	52	37	1.1	3.0	31	26	18
3	4.4/3.9 ^a	1.5	39	29	16	2.3	2.6	23	18	7
4	5.5/4.5 ^a	1.8	70	38	21	1.2	3.9	27	22	9
5	6.5/4.1 ^a	1.8	88	61	40	0.8	2.8	27	23	9
6	5.8	1.9	65	50	26	3.3	2.5	31	20	10
Total	5.7 ± 0.7	1.7 ± 0.1	64 ± 16	46 ± 11	28 ± 9	2.0 ± 1.2^b	2.9 ± 0.5^b	28 ± 3^b	21 ± 3^b	9 ± 5^b

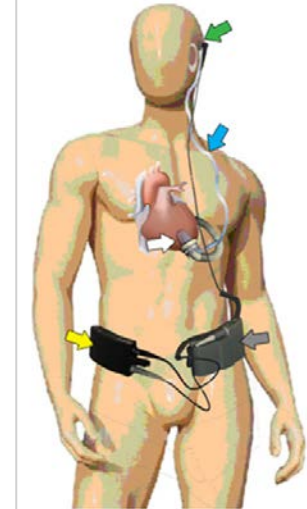
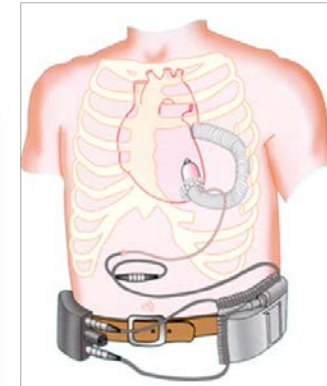
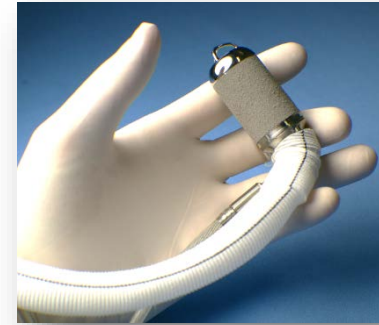


Dispositius d'Assistència Circulatòria Mecànica (Flux continu)

HEARTMATE II



JARVIK 2000

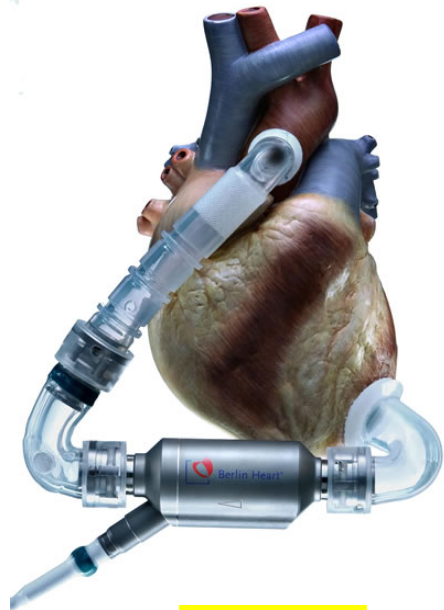
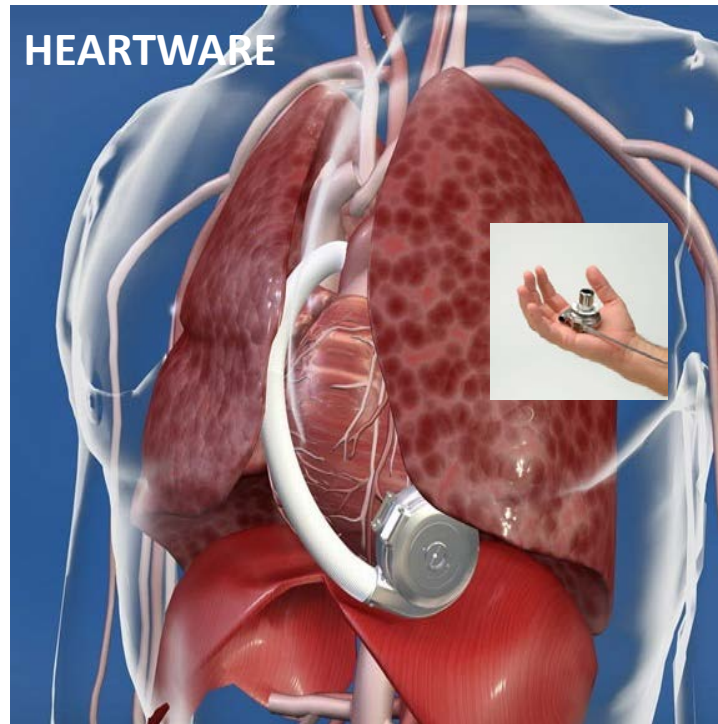


Abdominal Driveline*

Post-Auricular Driveline*

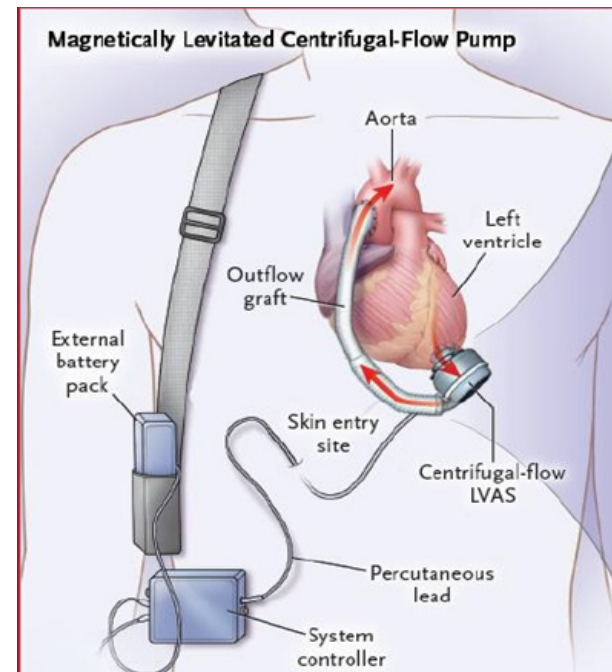
Two Product Options Available Today

HEARTWARE

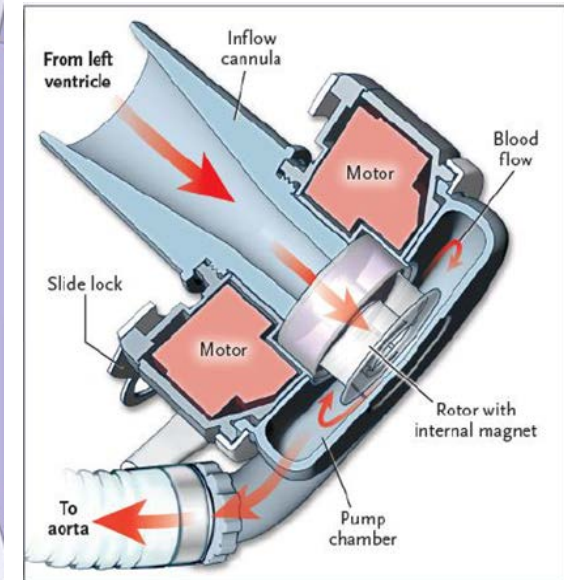


INCOR

Magnetically Levitated Centrifugal-Flow Pump



HEARTMATE III



Mechanical Circulatory Support as a Bridge to Transplant Candidacy

Ab
Ma
Ro
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He
He



EUROPEAN JOURNAL OF
CARDIO-THORACIC

Use of centrifugal left ventricular assist device as a bridge to candidacy for heart transplantation in patients with dilated cardiomyopathy or peripartum cardiomyopathy.^{608,609} LVADs may also be used as a 'bridge to candidacy' (BTC) in order to permit recovery of end-organ dysfunction, improve RV function and relieve pulmonary hypertension, which may allow initially ineligible patients to become eligible for heart transplantation.

Ramesh

ne D. Sudarshan,

Department of Cardiothoracic Surgery, The Transplant Unit, Papworth Hospital, Cambridge, UK

* Corresponding author. Department of Cardiothoracic Surgery, Papworth Hospital, Papworth Everard, Cambridge CB23 3RE, UK. Tel: +44-1480-830541; e-mail: ramesh.kutty@papworth.nhs.uk (R.S. Kutty).

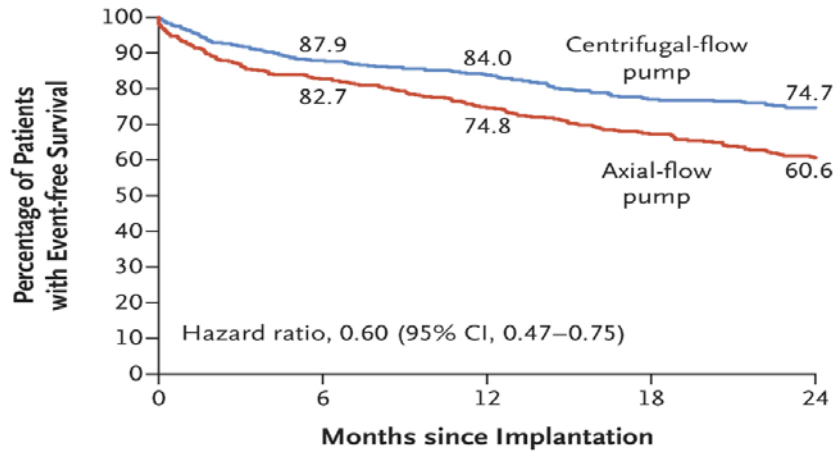
Received 16 January 2012; received in revised form 11 August 2012; accepted 14 October 2012

Pulmonary hypertension ESC guidelines 2015 & Heart failure ESC guidelines 2016.



MOMENTUM 3: 2-y Outcome (HeartMate 3 LVAD)

The primary end point was a composite of survival free of disabling stroke or survival free of reoperation to replace or remove a malfunctioning device at 24 months after implantation

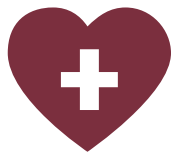


No. at Risk

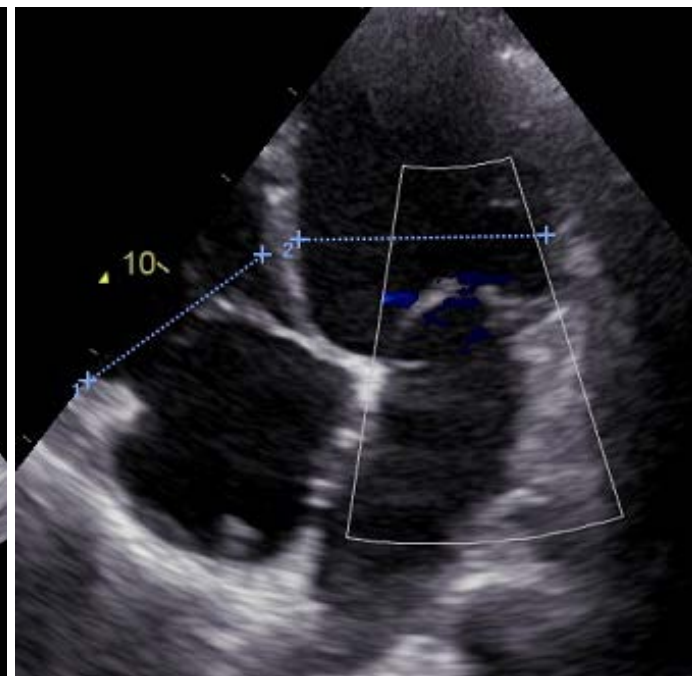
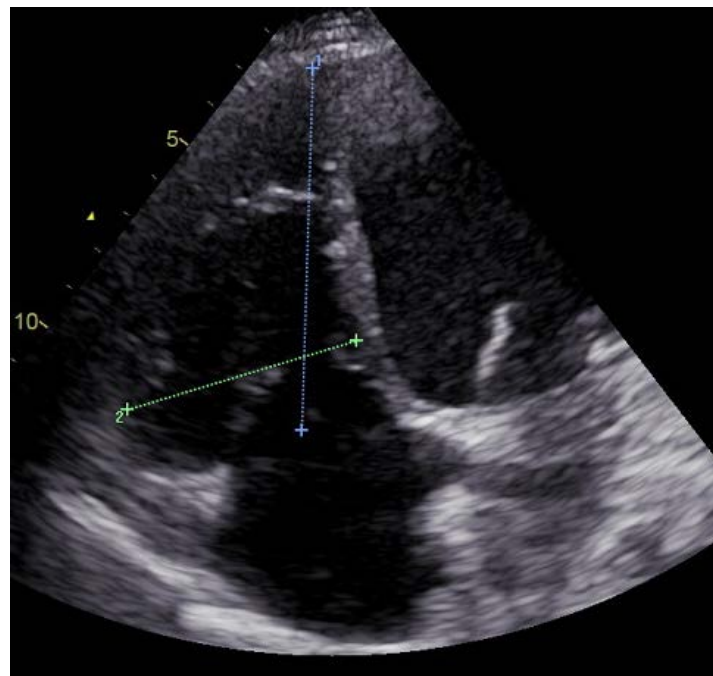
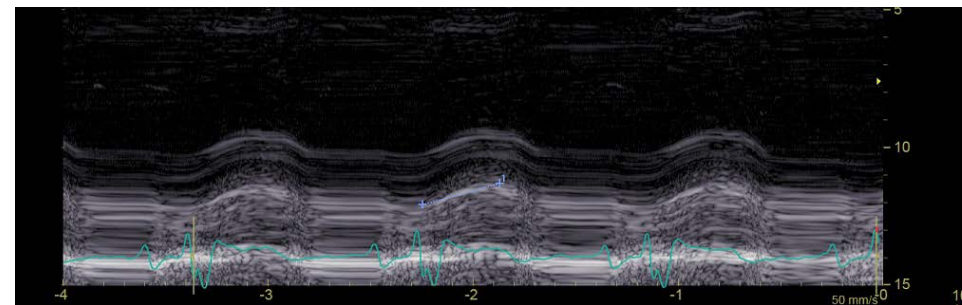
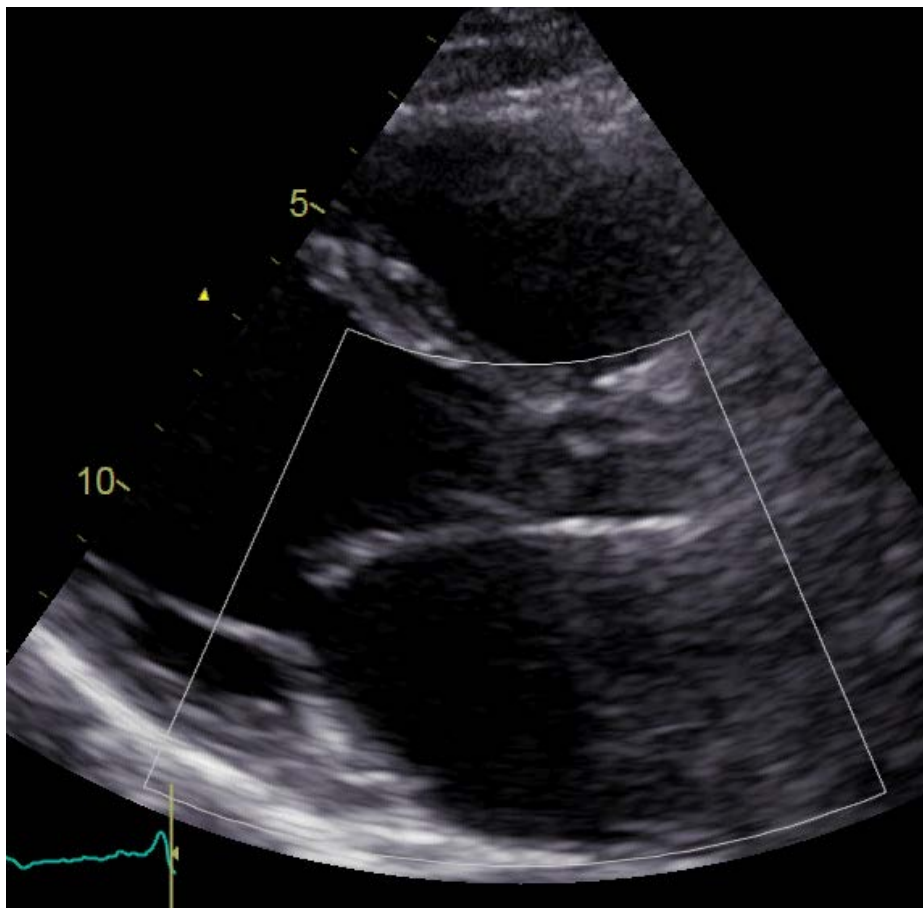
	0	6	12	18	24
Centrifugal-flow pump	516	438	373	313	280
Axial-flow pump	512	401	321	264	223

Adverse Event	Centrifugal-Flow Pump	Axial-Flow Pump	Centrifugal-Flow Pump	Axial-Flow Pump	Relative Risk (95% CI)	P Value
	no. of patients with events (%)	no. of patients with events (%)	events per patient-yr	events per patient-yr		
Suspected or confirmed pump thrombosis	7 (1.4)	70 (13.9)	0.01	0.12	0.08 (0.04–0.16)	<0.001
Any stroke	51 (9.9)	98 (19.4)	0.08	0.18	0.42 (0.30–0.57)	<0.001
Disabling stroke	26 (5.0)	38 (7.5)	0.04	0.07	0.54 (0.34–0.85)	0.008
Any bleeding	225 (43.7)	278 (55.0)	0.61	0.95	0.64 (0.57–0.72)	<0.001
Gastrointestinal bleeding	126 (24.5)	156 (30.9)	0.31	0.49	0.64 (0.54–0.75)	<0.001
Other neurologic event	59 (11.5)	47 (9.3)	0.09	0.08	1.25 (0.88–1.79)	0.21
Any major infection	300 (58.3)	285 (56.4)	0.82	0.82	1.00 (0.89–1.12)	0.96
Right heart failure	176 (34.2)	143 (28.3)	0.27	0.23	1.15 (0.94–1.42)	0.18
Cardiac arrhythmia	185 (35.9)	207 (41.0)	0.37	0.45	0.82 (0.70–0.97)	0.02
Respiratory failure	111 (21.6)	98 (19.4)	0.19	0.17	1.10 (0.86–1.40)	0.44
Renal dysfunction	73 (14.2)	56 (11.1)	0.11	0.08	1.36 (0.98–1.89)	0.07
Hepatic dysfunction	25 (4.9)	27 (5.3)	0.03	0.04	0.78 (0.46–1.34)	0.38

Mehra MR et al. N Engl J Med 2019

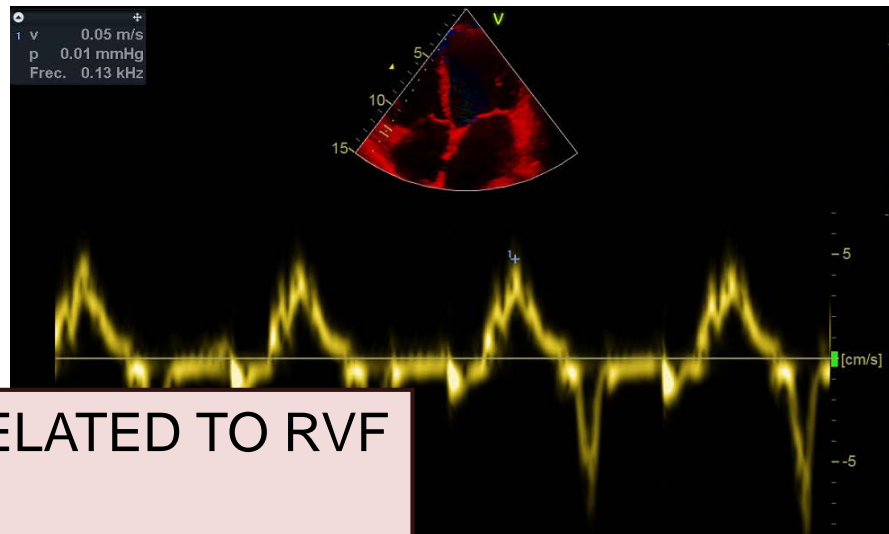
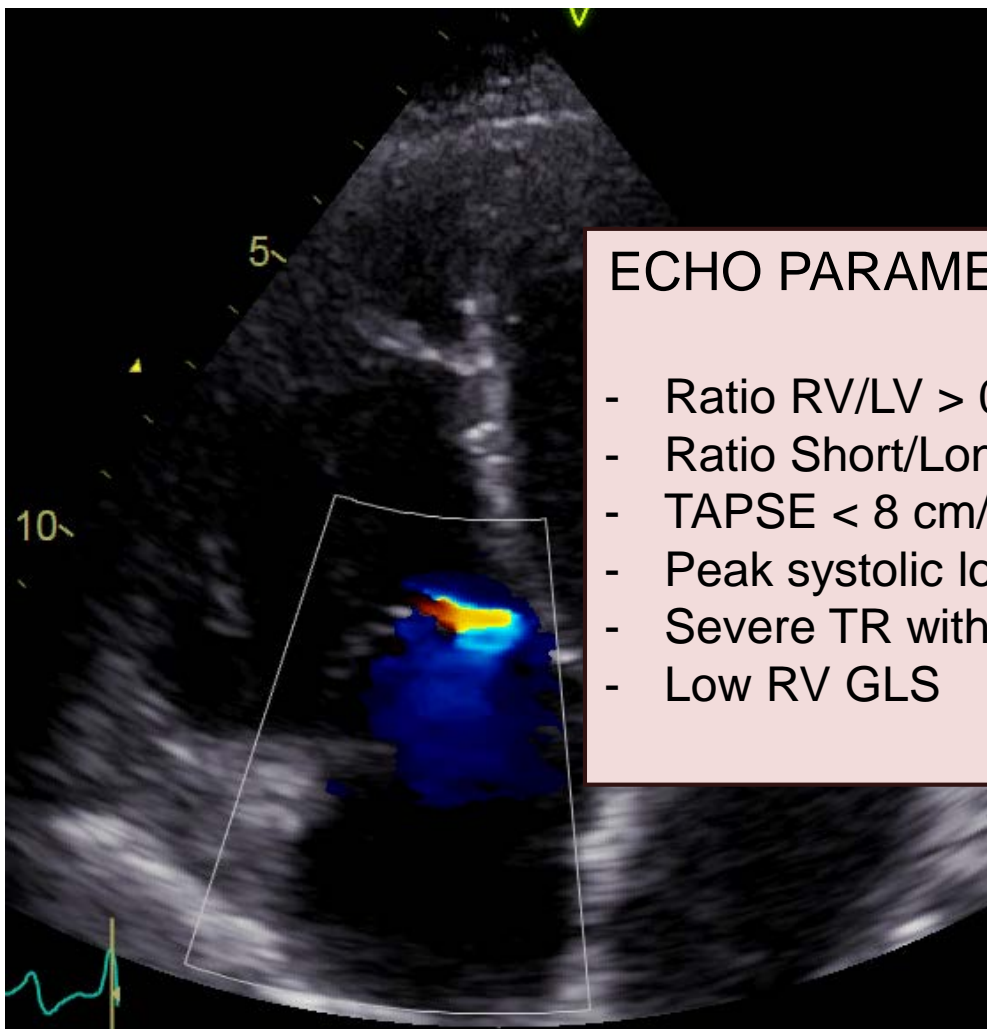


Important: Valoració del VD en SCM



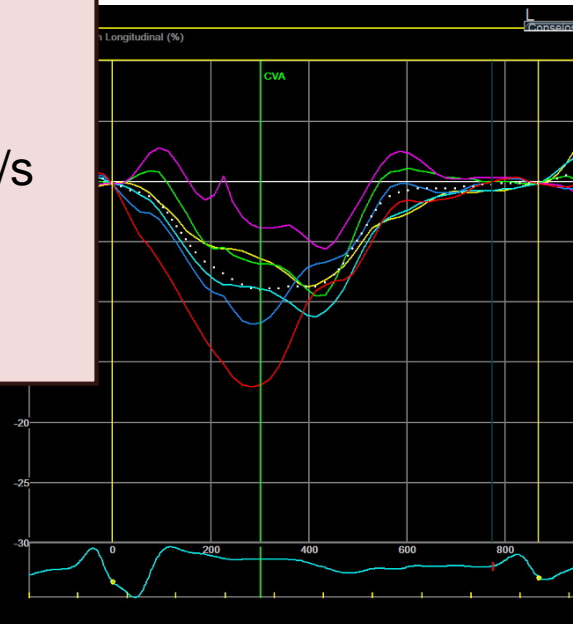
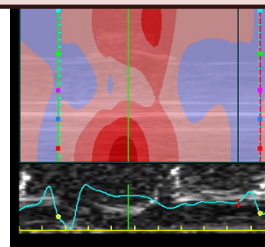


Valoració del VD en SCM



ECHO PARAMETERS RELATED TO RVF

- Ratio RV/LV > 0,72
- Ratio Short/Long del VD > 0,6
- TAPSE < 8 cm/s
- Peak systolic longitudinal strain < 0.6/cm/s
- Severe TR with sPAP < 50mmHg
- Low RV GLS





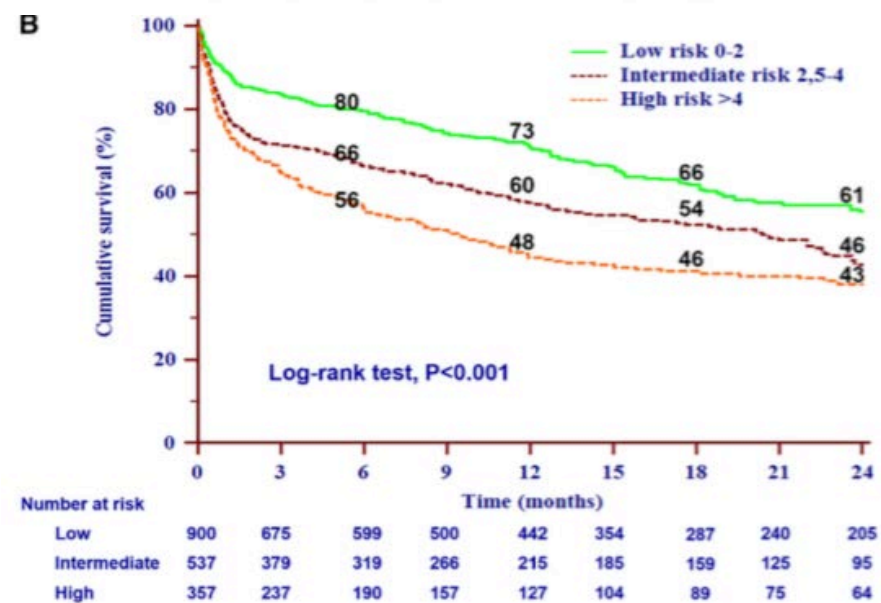
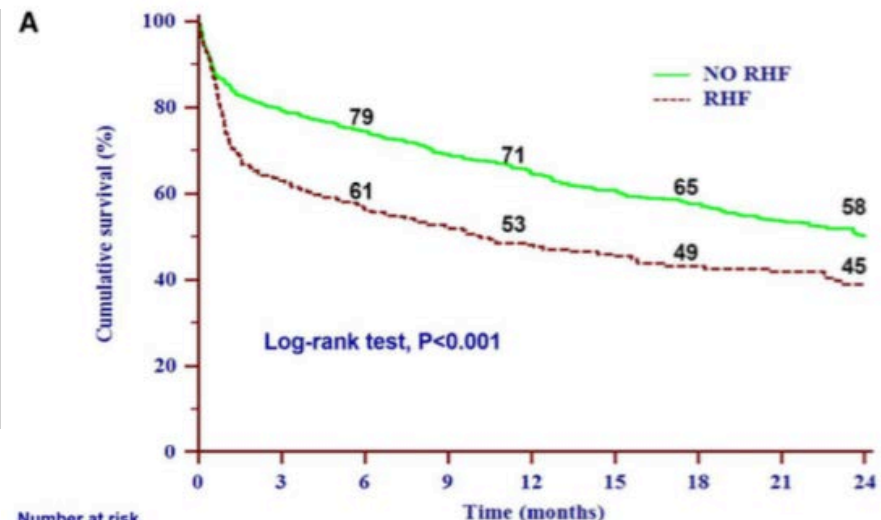
Derivation and Validation of a Novel Right-Sided Heart Failure Model After Implantation of Continuous Flow Left Ventricular Assist Devices

The EUROMACS (European Registry for Patients with Mechanical Circulatory Support) Right-Sided Heart Failure Risk Score

ORIGINAL RESEARCH ARTICLE

Table 6. European Registry for Patients with Mechanical Circulatory Support Multivariable Model for Right-Sided Heart Failure Derived From the Derivation Cohort

Variables	OR	Lower 95% CI	Upper 95% CI	χ^2 Value ($\chi^2=56.9$)	Coefficients	Score
Preoperative model						
RA/PCWP >0.54	2.075	1.383	3.112	12.441	0.730	2
Hemoglobin \leq 10 g/dL	1.611	1.037	2.502	4.506	0.477	1
Multiple intravenous inotropes	3.197	1.851	5.524	17.355	1.162	2.5
INTERMACS class 1–3	2.903	1.723	4.893	16.014	1.066	2
Severe RV dysfunction*	2.055	1.183	3.57	6.534	0.720	2
Postoperative RHF model after adding CPB time						
RA/PCWP >0.54	2.151	1.412	3.278	12.699	0.766	1
Hemoglobin \leq 10 g/dL	2.609	1.544	4.409	12.839	0.959	1.5
Multiple intravenous inotropes	3.013	1.712	5.302	14.635	1.103	2
INTERMACS Class 1–3	3.393	1.946	5.915	18.561	1.222	2
Severe RV dysfunction*	2.099	1.193	3.694	6.618	0.742	1
CPB time >100 min	2.032	1.296	3.184	9.562	0.709	1



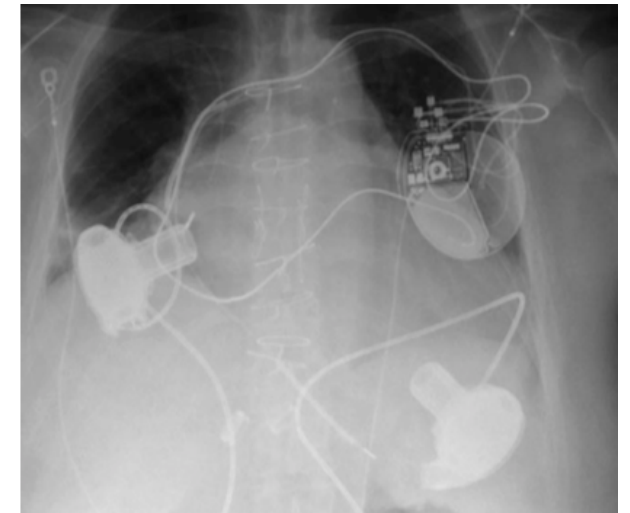
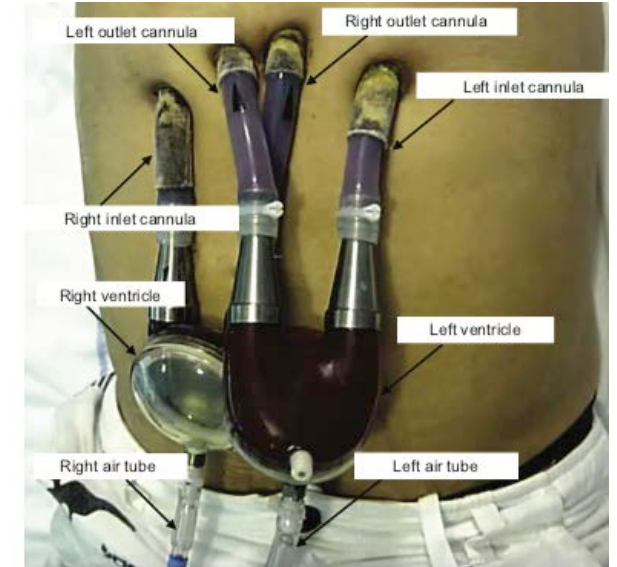
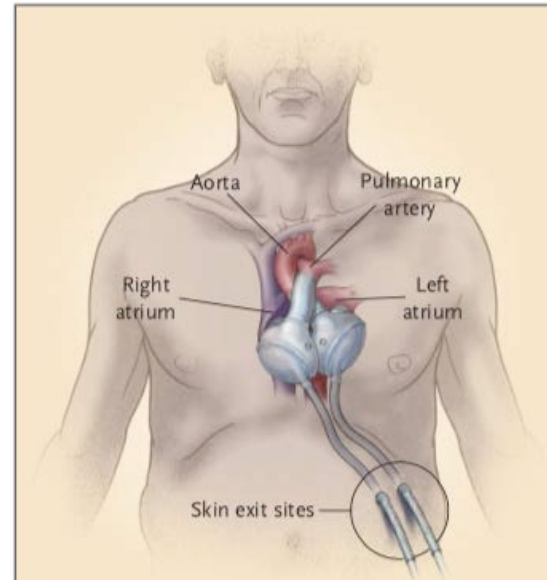


Dispositius d'Assistència Circulatòria Mecànica (BiV)

2019 EACTS Expert Consensus on long-term mechanical circulatory support

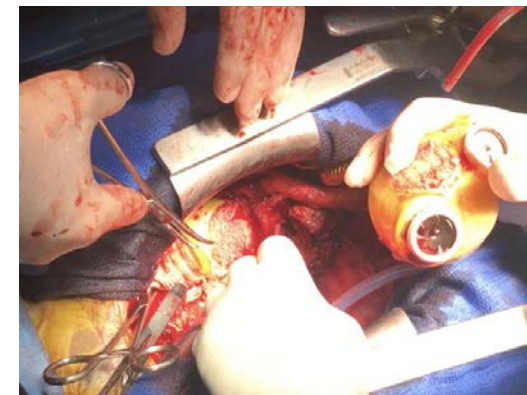
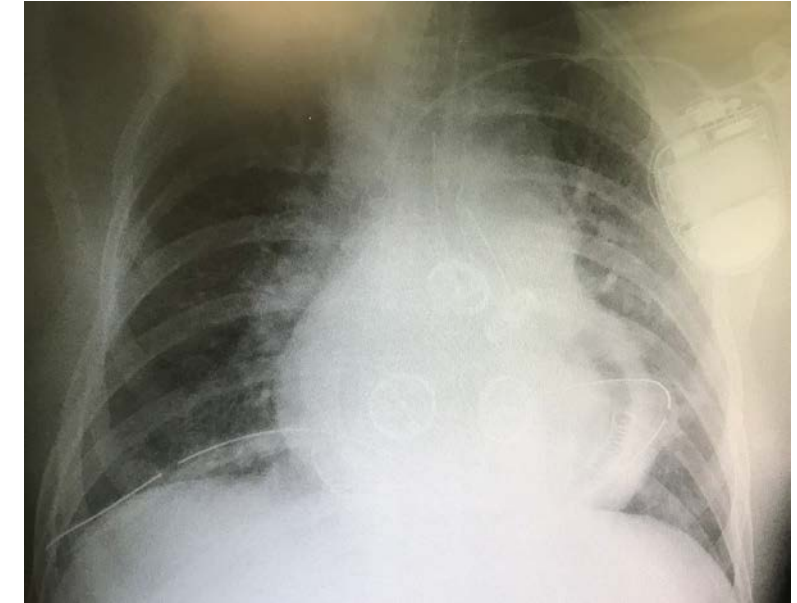
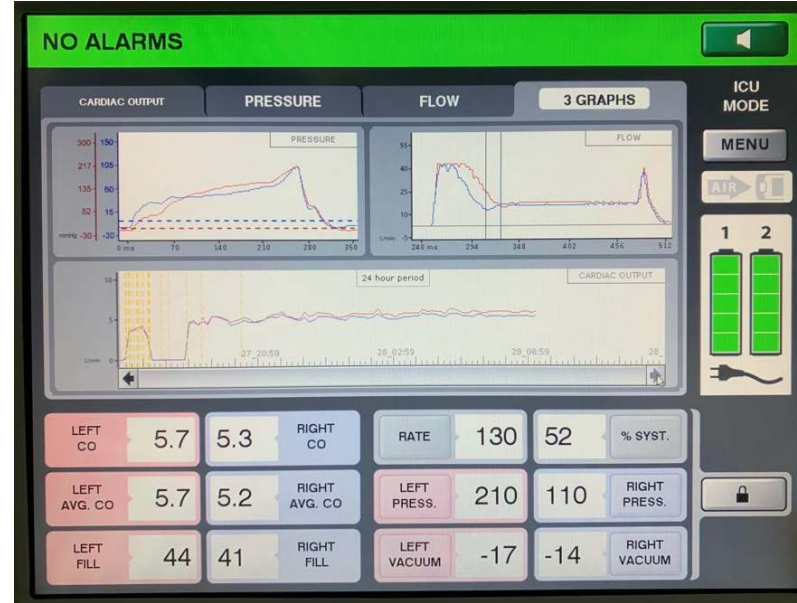
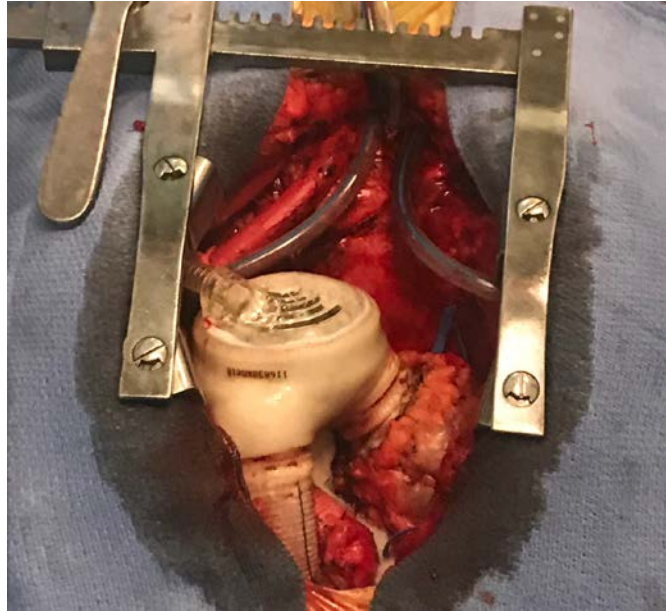
Evgenij V. Potapov^{a,*†} (EACTS Chairperson), Christiaan Antonides^{b,†},
 Maria G. Crespo-Leiro^c, Alain Combes^{d,e}, Gloria Färber^f, Margaret M. Hannan^g, Marian Kukucka^h,
 Nicolaas de Jongeⁱ, Antonio Loforte^j, Lars H. Lund^k, Paul Mohacsí^l, Michiel Morshuis^m, Ivan Netukaⁿ,
 Mustafa Özbaran^o, Federico Pappalardo^p, Anna Mara Scandroglio^q,
 Martin Schweiger^r, Steven Tsui^s, Daniel Zimpfer^t and Finn Gustafsson^{u,*} (EACTS Chairperson),
 The Task Force on Long-Term Mechanical Circulatory Support of the EACTS

Implantable BiVAD support may be considered in patients at high risk of right ventricular failure.	IIb	C	[81, 187-191]
Two CF-LVADs as an implantable BiVAD may be considered.	IIb	B	[192-196, 212, 213]
A TAH may be indicated in patients with biventricular failure, restrictive cardiomyopathy, cardiac tumours or large ventricular septal defects.	IIb	C	[187, 193, 197-201]
In patients with anatomical or other clinical conditions that are not well served with an LVAD or BiVAD, implantation of a TAH may be considered.	IIb	C	[203-208]





Suport Circulatori Mecànic Biventricular (TAH)





Situació actual: Teràpia combinada de SCM + VD pulmonars

Original Articles

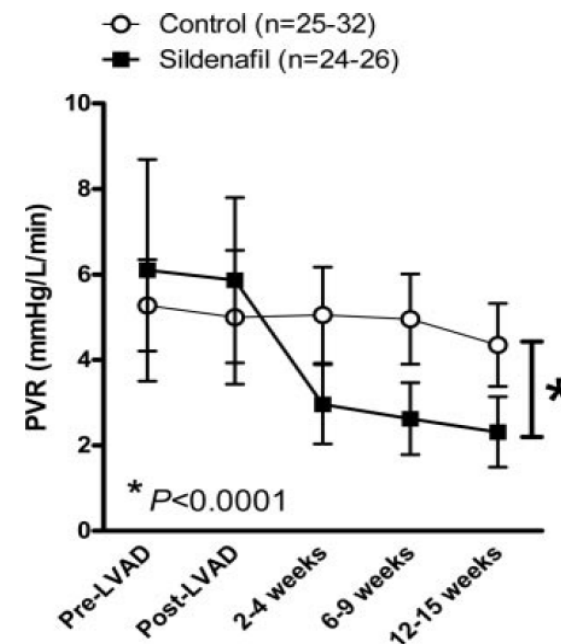
PDE5A Inhibitor Treatment of Persistent Pulmonary Hypertension After Mechanical Circulatory Support

Ryan J. Tedford, MD; Anna R. Hemnes, MD; Stuart D. Russell, MD; Ilan S. Wittstein, MD; Mobusher Mahmud, MD; Ari L. Zaiman, MD; Stephen C. Mathai, MD, MHS; David R. Thiemann, MD; Paul M. Hassoun, MD; Reda E. Girgis, MD; Jonathan B. Orens, MD; Ashish S. Shah, MD; David Yuh, MD; John V. Conte, MD; Hunter C. Champion, MD, PhD

58 pacients tractats amb LVAD pont a candidatura.
Persistència de RVP >3UW a los 7-14 dies tras LVAD

26 Sildenafil
32 Controles

Mayor reducción de RVP



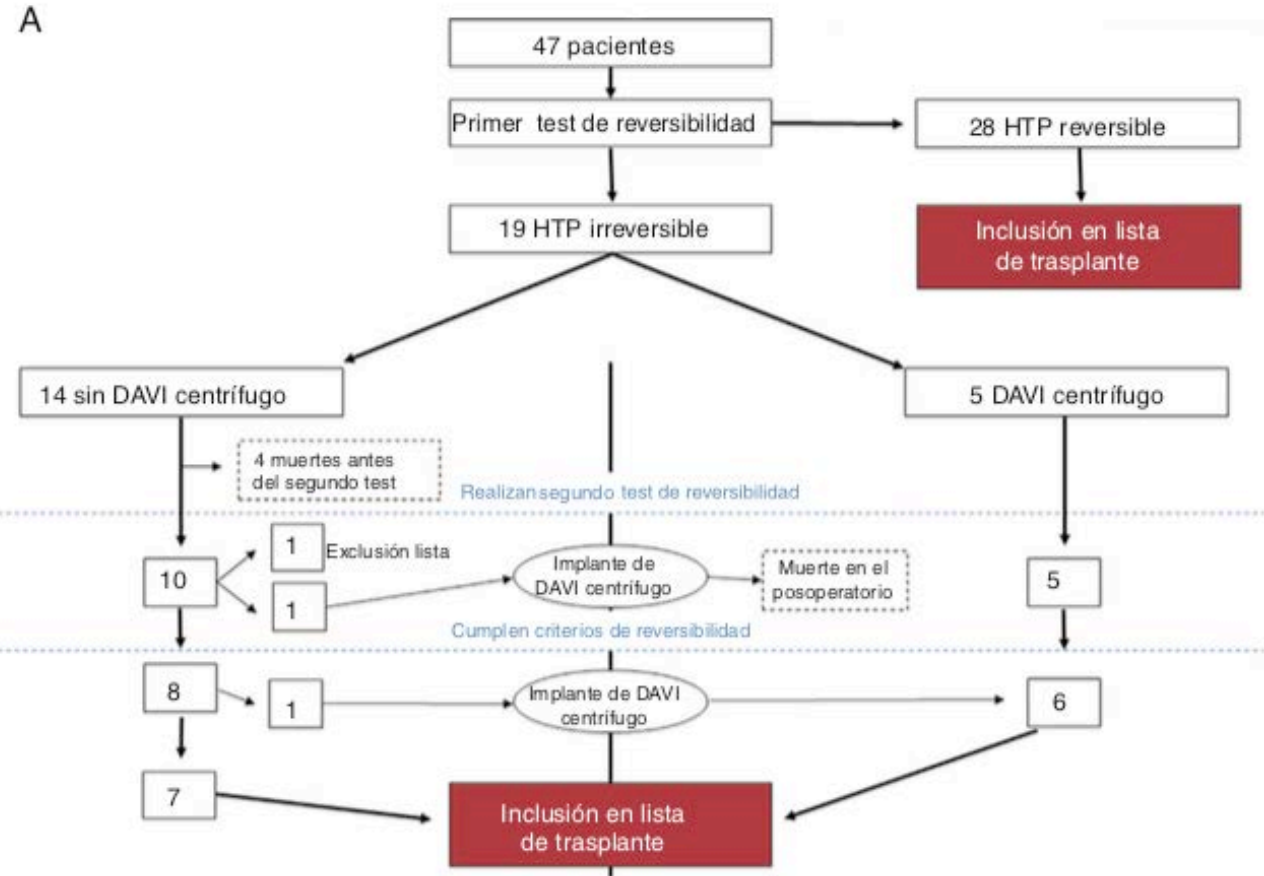
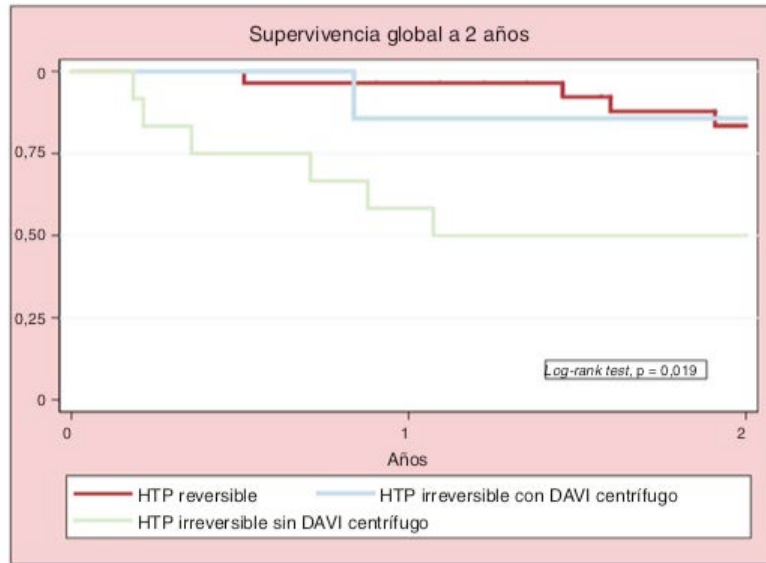


Experiència a l'Hospital de Bellvitge

Carta científica

Dispositivos de asistencia ventricular izquierda en pacientes candidatos a trasplante cardiaco con hipertensión pulmonar irreversible

Left ventricular assist devices in patients eligible for heart transplant with irreversible pulmonary hypertension



El subanálisis de pacientes que recibió un TxC no mostró diferencias significativas (p: 0,238)

De Frutos F, et al. REC. 2020. Ahead of pub

3

EL FUTUR INMEDIAT EN DISPOSITIUS



Situació actual: Teràpia combinada de SCM + VD pulmonars

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[Home](#) > Study Record Detail

Save this study

Clinical Study to Assess the Efficacy and Safety of Macitentan in Patients With Pulmonary Hypertension After Left Ventricular Assist Device Implantation (SOPRANO)



Pulmonary Artery Pressure-Guided Management of Patients With Heart Failure and Reduced Ejection Fraction



Michael M. Givertz, MD,^a Lynne W. Stevenson, MD,^a Maria R. Costanzo, MD,^b Robert C. Bourge, MD,^c Jordan G. Bauman, MS,^d Gregg Ginn, MS,^d William T. Abraham, MD,^e on behalf of the CHAMPION Trial Investigators

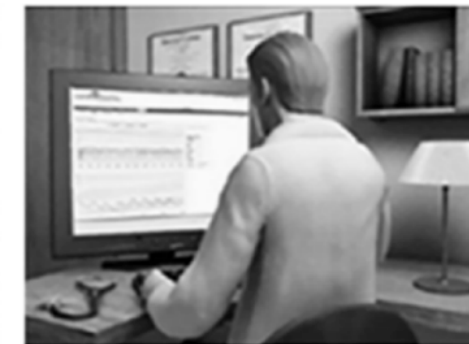
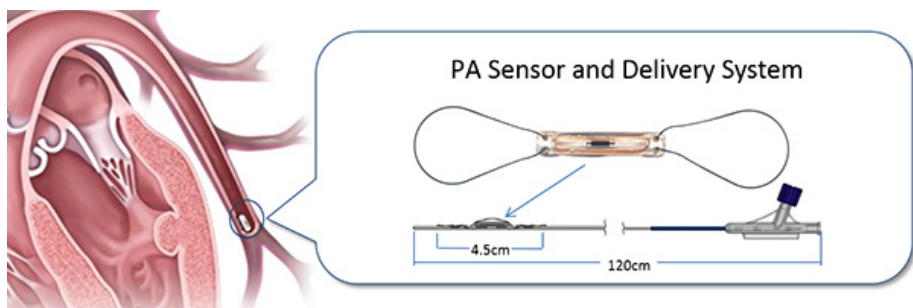


Figure 2. CardioMEMS delivery catheter. MEMS, Micro-Electro-Mechanical System.

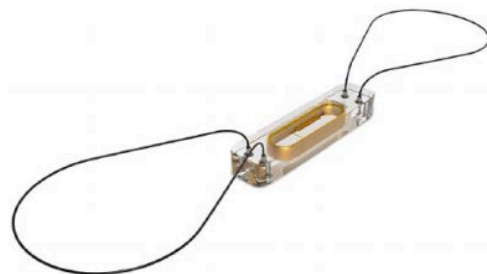
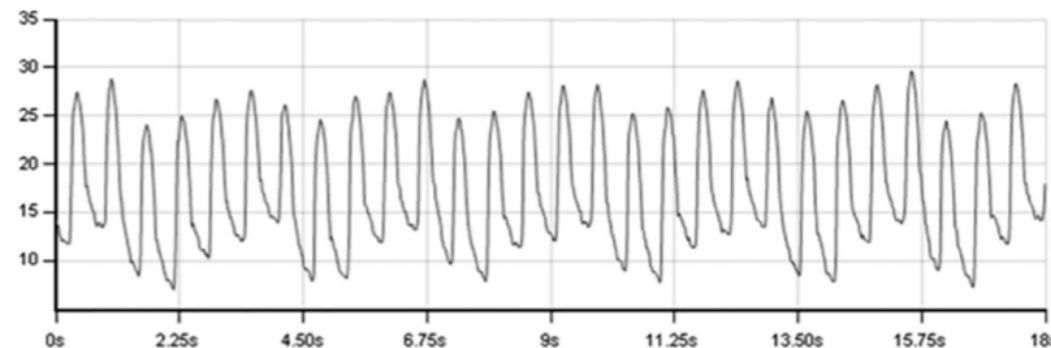


Figure 3. CardioMEMS PA sensor. MEMS, Micro-Electro-Mechanical System; PA, pulmonary artery.

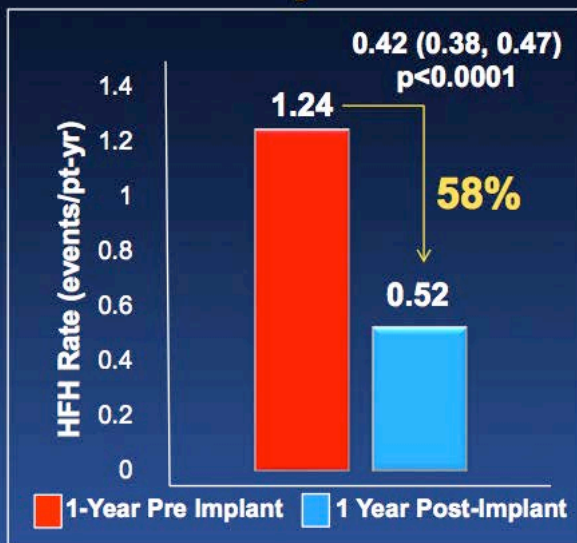




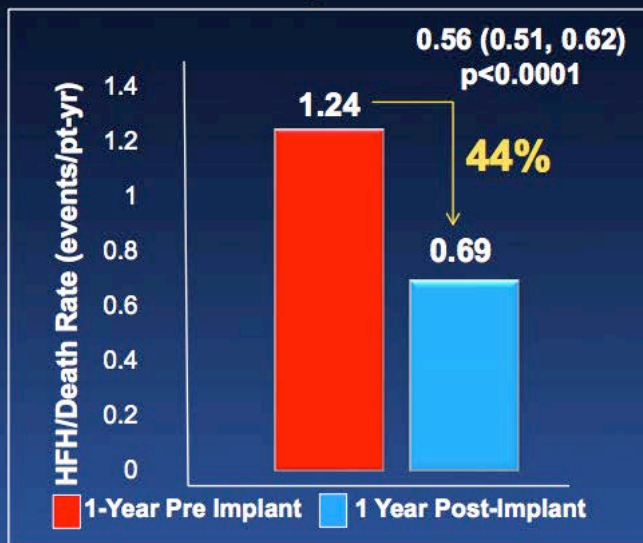
Dispositius de monitorització de la Pressió Pulmonar

Limitacions: Estudi en videa real però sense grup control
 Fortaleses: Seguretat del procediment <1% complicacions peri i post implant (desplaçament, corva aprenentatge).
 Sense complicacions greus del dispositiu a l'any.
 Resultats molt positius en quant a events en una població major i menys sel-leccionada

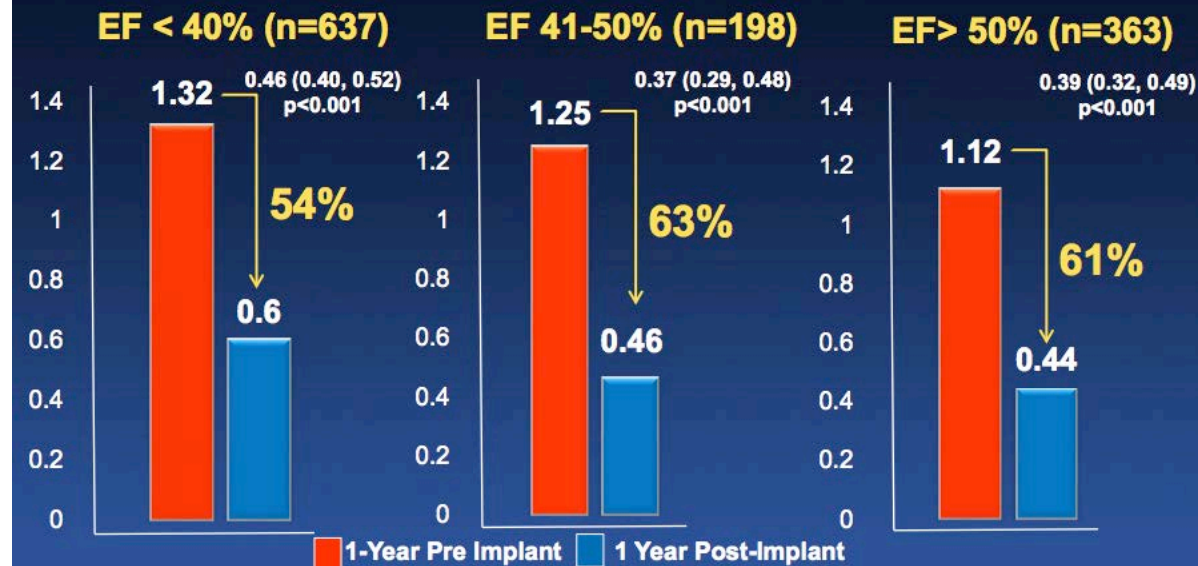
Hospitalizations for HF at 1 year



Hospitalizations for HF/Death at 1 year



Heart Failure Hospitalizations at 1 year Stratified by Ejection Fraction



Hazard Ratio, 95% Confidence Interval and p-value estimated from the Anderson-Gill model. All hospitalization events adjudicated by CEC.

PAS Guided therapy for ambulatory HF patients. Post-approval study. ACC. 2019 Presentation . Ahead of Pub

Abstract 19282: Safety and Utility of the CardioMEMs Device in Pulmonary Arterial Hypertension

Raymond Benza, Priscilla Correa-jaque, Veronica Franco, Mark Doyle, Jason A White, Greg Ginn, and Robert Biederman

Originally published 29 Mar 2018 | Circulation. 2016;134:A19282

Abstract

Introduction: Pulmonary arterial hypertension (PAH) remains fatal requiring better methods for outcome prediction. Although invasive hemodynamics are valuable prognostically, their routine use is impractical. The CardioMEMS™ HF System (CMHFS) is indicated for wireless monitoring of PA pressure in heart failure (HF) patients (pts).

Hypothesis: Use of CMHFS in PAH pts will be safe and result in more efficient and timely responses to therapy (Rx).

Methods: 17 PAH pts with NYHA class III/IV sx and a recent hospitalization (HOS) for HF were enrolled. 14 implants were performed and device mPAP, sPAP, dPAP, HR, and CO (sensor pressure based algorithm), total pulmonary resistance (TPR), stroke volume (SV) were collected daily. BNP levels, NYHA class (FC) and HF HOS events were collected at preimplant, implant, and 1, 4, 6, 12 months (mos). All pts were treated with FDA approved Rx and Rx changes were not mandated by the protocol. Pts were analyzed as a group and by predefined management profiles based on number of PAH specific drug changes: Highly (>8; n=9), Moderately/mildly (0-8; n=5).

Results: Pts consisted of 45% newly diagnosed pts. All pts were female, aged 57 ± 9 with IPAH (50%), scleroderma-related PAH (50%) with a mPAP 45 ± 14 mmHg and pulmonary vascular resistance of 7.5 ± 4 WU. There were no peri-procedural complications or device related SAE's post implant. Device related information was used to optimize PAH-specific Rx. Mean duration of follow-up was 14 ± 6 mos. Annualized HF HOS for the total cohort fell from ≥ 1 HFH/pt-yr prior to implant to 0.453 (CI 0.182 to 0.934) after implant. FC improved from baseline (3.13) after 1 mo (-0.83, $p=0.0004$) and through last follow-up (-1.01, $p=0.0004$). BNP levels <340 pg/ml were maintained or achieved in 75% of pts after 1 mo. mPAP and TPR improved significantly overtime ($p=0.04$; $p=0.01$, respectively) and as early as 1 mo (-6.5 mmHg, $p=0.0337$; -2.1 WU, $p=0.04$, respectively) and maximal by 12 mo (-10 mmHg, $p=0.002$; -2.9 WU, $p=0.006$). CO and SV improved overall at 4 mo (+ 1.2 l, $p=0.01$; + 10 cc, $p=0.02$, respectively), but the effect was isolated to those highly managed ($p<0.05$, all time points).

Conclusions: Use of CMHFS in PAH pts appears safe, may reduce HOS, and allows rapid optimization of hemodynamics and functional outcome.



Unidirectional left-to-right interatrial shunting for treatment of patients with heart failure with reduced ejection fraction: a safety and proof-of-principle cohort study

Maria Del Trigo, Sebastien Bergeron, Mathieu Bernier, Ignacio J Amat-Santos, Rishi Puri, Francisco Campelo-Parada, Omar Abdul-Jawad Altisent, Ander Regueiro, Neal Egler, Erez Rozenfeld, Philippe Pibarot, William T Abraham, Josep Rodés-Cabau

Millora la relació entre treball i PCP

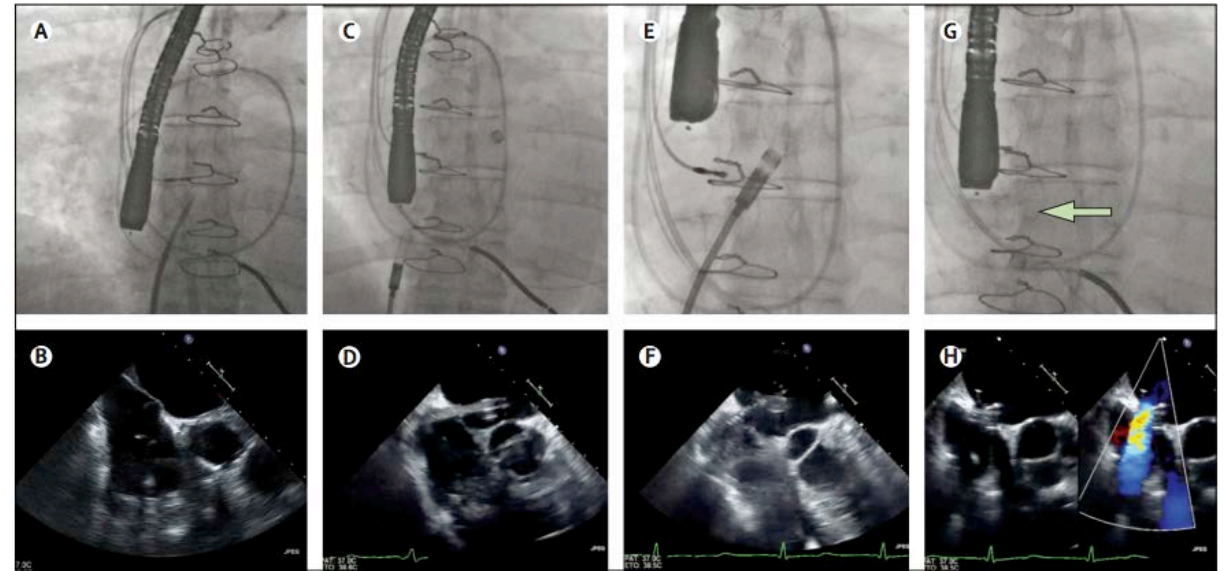
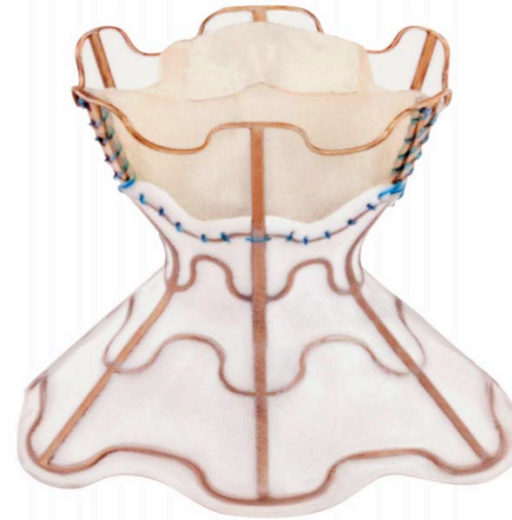
Lancet 2016; 387: 1290-97

See Editorial page 1252

See Comment page 1253

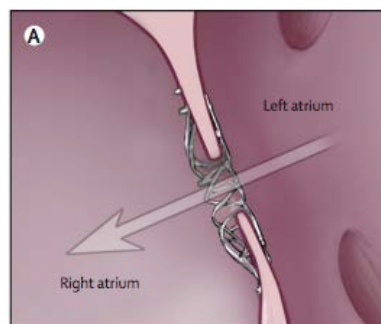
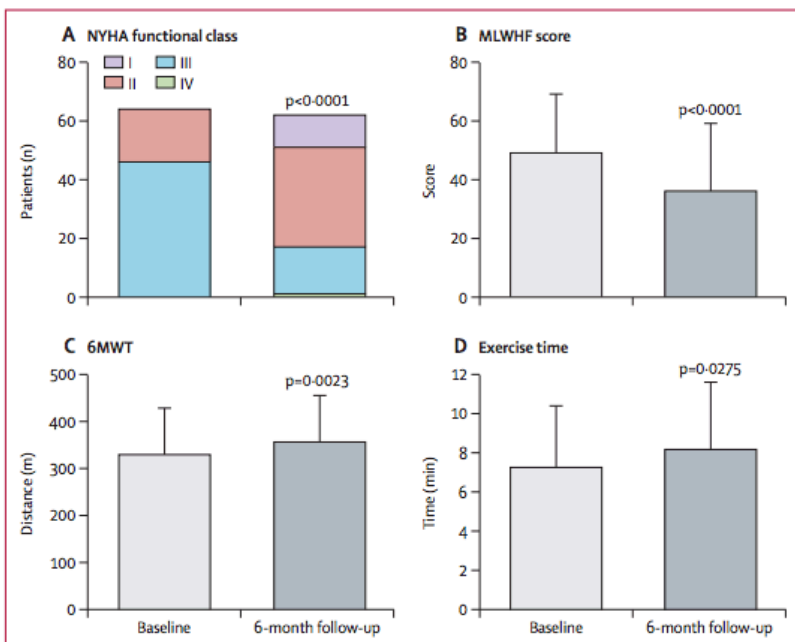
	Baseline (N=9)	3 months (N=9)	p value
Functional status and quality of life			
NYHA class*			0.0004
III-IV	9 (100%)	1 (11%)	..
I-II	0	8 (89%)	..
Duke Activity Status Index	13 (6-2)	24.8 (12.9)	0.016
Kansas City Cardiomyopathy Questionnaire	44.3 (9.8)	79.1 (13.0)	0.0001
6 min walk test (m)	244 (112)	319 (134)	0.016
Laboratory tests			
NT-pro BNP (pg/mL)	2485 (3318)	2473 (2984)	0.96
eGFR (mL/min)	55 (20)	49 (20)	0.27
Echocardiographic variables			
Left ventricular ejection fraction (%)	24.5 (8.3)	25.3 (8.8)	0.91
Stroke volume (mL)	56 (16)	51 (17)	0.082
Left ventricular end-diastolic volume (mL)	223 (65)	203 (49)	0.031
Left ventricular end-systolic volume (mL)	168 (58)	153 (51)	0.010
Tricuspid annular plane systolic excursion (mm)	16.1 (4.7)	18.7 (5.2)	0.10
Haemodynamics			
Heart rate (beats per min)	70 (7)	73 (7)	0.069
Mean arterial pressure (mm Hg)	81 (7)	90 (10)	0.027
Pulmonary capillary wedge pressure (mm Hg)	23 (5)	17 (8)	0.035
Right atrial pressure (mm Hg)	9 (4)	8 (5)	0.18
Mean pulmonary artery pressure (mm Hg)	29 (7)	26 (11)	0.37
Cardiac output (L/min)†	4.4 (1.0)	5.5 (0.9)‡	0.011
Cardiac index (L/min per m ²)§	2.1 (0.3)	2.6 (0.4)¶	0.020
Pulmonary vascular resistance (mm Hg × L ⁻¹ × min)	2.5 (1.1)	1.9 (0.7)	0.11
Pulmonary vascular resistance index (mm Hg × L ⁻¹ × min × m ²)	5.1 (1.8)	4.0 (1.2)	0.16
Ratio of pulmonary to systemic blood flow (Qp:Qs)	0.98 (0.05)	1.08 (0.10)	0.033

essure improve symptoms and cacy of therapeutic left-to-right



A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial

Gerd Hasenfuß, Chris Hayward, Dan Burkhoff, Frank E Silvestry, Scott McKenzie, Finn Gustafsson, Filip Malek, Jan Van der Heyden, Irene Lang, Mark C Petrie, John G F Cleland, Martin Leon, David M Kaye, on behalf of the REDUCE LAP-HF study investigators*



Lancet; 2016

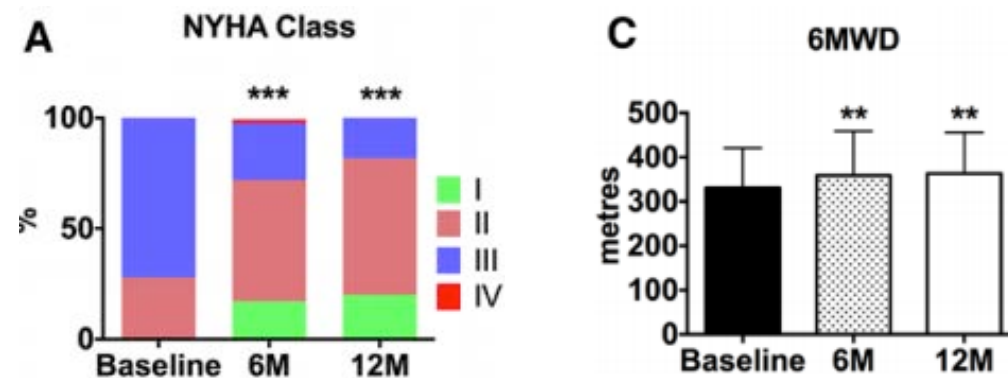
Original Article

OPEN

One-Year Outcomes After Transcatheter Insertion of an Interatrial Shunt Device for the Management of Heart Failure With Preserved Ejection Fraction

David M. Kaye, MD, PhD; Gerd Hasenfuß, MD; Petr Neuzil, MD; Martijn C. Post, MD;

Methods and Results—Patients (n=64) with left ventricular ejection fraction $\geq 40\%$, New York Heart Association class II–IV, elevated pulmonary capillary wedge pressure (≥ 15 mmHg at rest or ≥ 25 mmHg during supine bicycle exercise) participated in the open-label study of the interatrial septal shunt device. One year after interatrial septal shunt device implantation, there were sustained improvements in New York Heart Association class ($P < 0.001$), quality of life (Minnesota Living with Heart Failure score, $P < 0.001$), and 6-minute walk distance ($P < 0.01$). Echocardiography showed a small, stable reduction in left ventricular end-diastolic volume index ($P < 0.001$), with a concomitant small stable increase in the right ventricular end-diastolic volume index ($P < 0.001$). Invasive hemodynamic studies performed in a subset of patients demonstrated a sustained reduction in the workload corrected exercise pulmonary capillary wedge pressure ($P < 0.01$). Survival at 1 year was 95%, and there was no evidence of device-related complications.

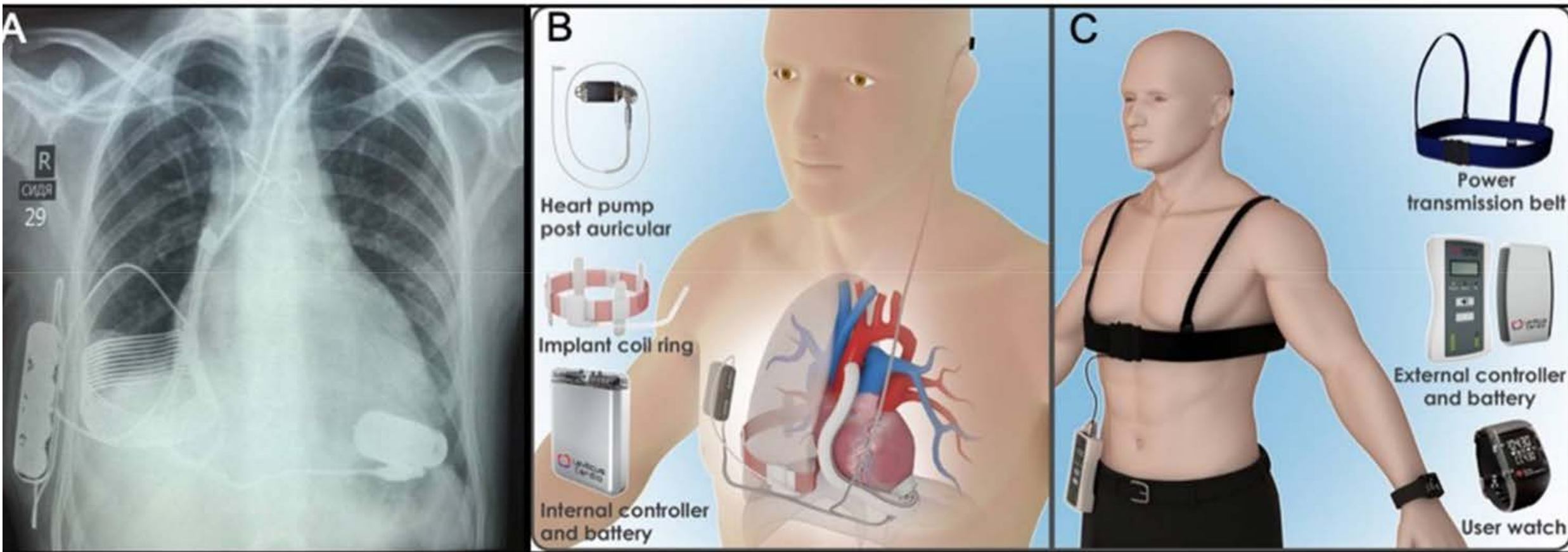


Circulation; 2015



Dispositius de Suport Circulatori Mecànic

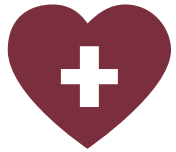
Leviticus Cardio's wireless power transfer technology, Coplanar Energy Transfer (CET)



Pyra Y et al. J Heart Lung Transp 2019. doi.org/10.1016/j.healun.2019.01.1316

4

CONCLUSIONS



Conclusions

- L'objectiu principal del tractament de la HTAP d'origen esquerre, és el d'optimitzar al màxim el tractament de base
- A nivell farmacològic, a data d'avui falta evidència per a recomanar el tractament amb fàrmacs vasodilatadors pulmonars en HTAP tipus 2
- Es possible que els estimuladors de la guanilat ciclasa siguin una opció per a determinats pacients amb IC i FE reduïda, independentment de les RVP.
- En el context de MCD amb IC reduïda, els dispositius de suport circulatori mecànic permeten una ràpida disminució de les resistències vasculares pulmonars, sobretot en combinació amb VD pulmonars.
- Cal fer un abordatge multidisciplinar en centres d'alta complexitat per al maneig d'aquests pacients (aprenentatge conjunt).



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HOSPITAL
EN XARXA

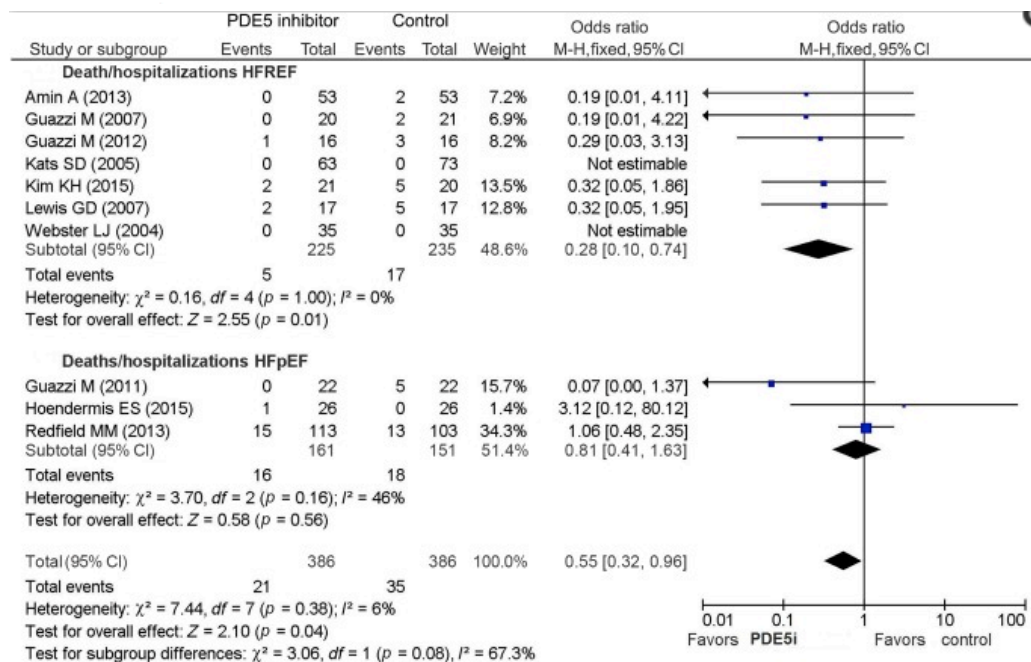
Gràcies per la vostra atenció!



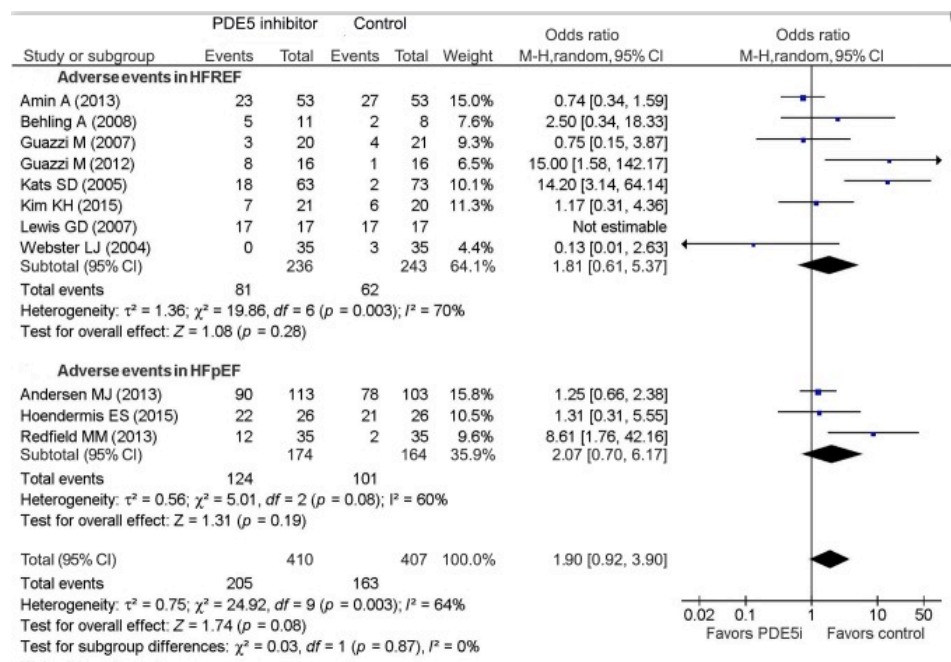
Inhibidors de la fosfodiesterasa 5: Sildenafil

Therapeutic benefits of phosphodiesterase-5 inhibition in chronic heart failure: A meta-analysis

RENATO DE VECCHIS^{1,*}, ARTURO CESARO², CARMELINA ARIANO¹



Respecte l'estudi anterior, divideix els resultats entre HFpEF i HFREF





Teràpia d'activació de Baroreceptors Carotidis