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CardioAdvancedForum

EXONERACIÓN DE RESPONSABILIDAD Y USO DE LA PRESENTACIÓN

Formación online en actualizaciones en Cardiología

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Principales estudios presentados en ESC22 que nos cambiarán nuestra práctica clínica

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SECURE Polypill Strategy in Secondary Cardiovascular Prevention

Study Overview

N=2500 Post MI >65

+ At Least One

- a. Documented DM
- b. Mild to moderate CKD
- c. Prior MI
- d. Prior coronary revascularization
- e. Prior stroke
- f. Age ≥ 75 years

ASPIRIN 100
ATORVASTATIN 20/40
RAMIPRIL 2.5/5/10

Median FU: 3 years

The primary composite endpoint
cardiovascular death, MI, stroke, or urgent revascularization.
The key secondary endpoint
cardiovascular death, MI, or stroke.

ESC Congress 2022. Castellano JM, et al. NEJM 2022 DOI: 10.1056/NEJMoa2208275

SECURE

Baseline Medical History, n (%)

	Polypill (n=1237)	Usual care (n=1229)
Age (years)		
Mean (SD)	75.8 (6.7)	76.1 (6.5)
<75	516 (41.7)	482 (39.2)
75+	721 (58.3)	747 (60.8)
Male	853 (69.0)	848 (69.0)
Female	384 (31.0)	381 (31.0)
Czech Republic	85 (6.9)	87 (7.1)
France	74 (6.0)	70 (5.7)
Germany	182 (14.7)	184 (15.0)
Hungary	45 (3.6)	45 (3.7)
Italy	366 (29.6)	365 (29.7)
Poland	63 (5.1)	60 (4.9)
Spain	422 (34.1)	418 (34.0)
Caucasian	1221 (99.2)	1211 (99.2)
Black	3 (0.2)	0 (0.0)
Other	7 (0.6)	10 (0.8)
Less than high school	580 (49.4)	576 (49.6)
Some high school	415 (35.3)	424 (36.5)
More than high school	179 (15.2)	162 (13.9)
Working full-time	37 (3.1)	27 (2.2)
Working part-time	17 (1.4)	13 (1.1)
Not working	39 (3.2)	34 (2.8)
Retired	1117 (92.3)	1132 (93.9)

	Polypill (n=1237)	Usual care (n=1229)
Smoking status,		
Current	175 (15.0)	161 (13.8)
Former	459 (39.4)	471 (40.4)
Never	532 (45.6)	534 (45.8)
Diabetes mellitus,	520 (42.0)	531 (43.2)
Not insulin-dependent	370 (29.9)	412 (33.5)
Insulin-dependent	149 (12.1)	119 (9.7)
Hypertension,	952 (77.0)	966 (78.8)
Hyperlipidemia,	702 (57.4)	724 (59.6)
Angina pectoris,	280 (22.6)	317 (25.8)
Angina class,		
I	66 (28.2)	82 (29.3)
II	84 (35.9)	106 (37.9)
III	49 (20.9)	49 (17.5)
IV	35 (15.0)	43 (15.4)
Missing (%)	46 (16.4)	38 (12.0)
Previous MI,	260 (21.0)	276 (22.5)
Coronary artery disease,	373 (30.2)	389 (31.7)
Previous PCI,	273 (22.1)	274 (22.3)
Previous CABG,	71 (5.7)	92 (7.5)
Previous stroke,	88 (7.1)	79 (6.4)
Prior vascular event,	406 (32.8)	417 (33.9)
Previous heart failure,	25 (2.0)	25 (2.0)
CKD,	465 (37.6)	435 (35.4)
Peripheral arterial disease,	104 (8.4)	106 (8.6)
History of COPD/asthma,	123 (10.0)	116 (9.5)
History of cancer,	140 (11.3)	150 (12.2)

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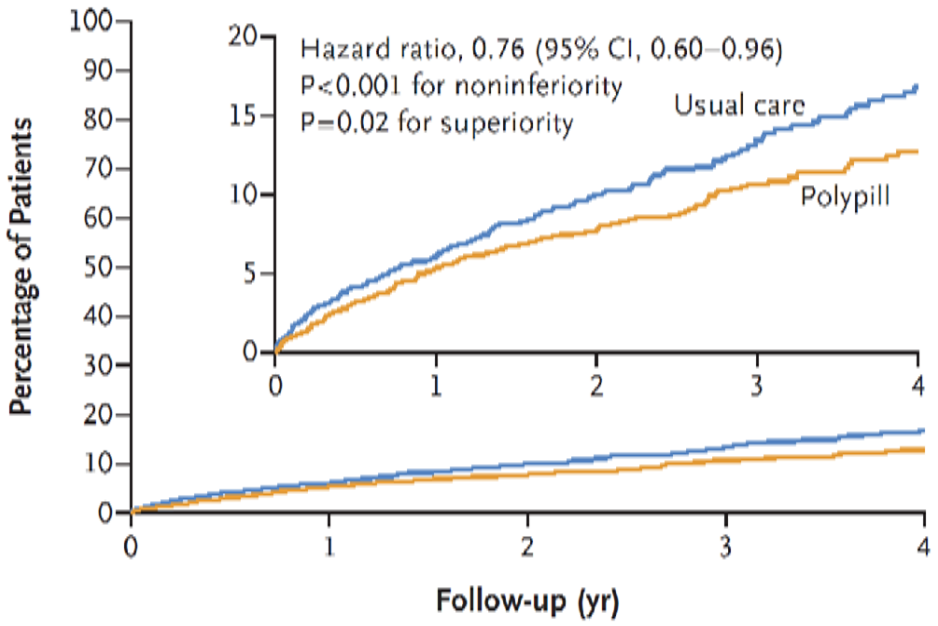
Primary outcome

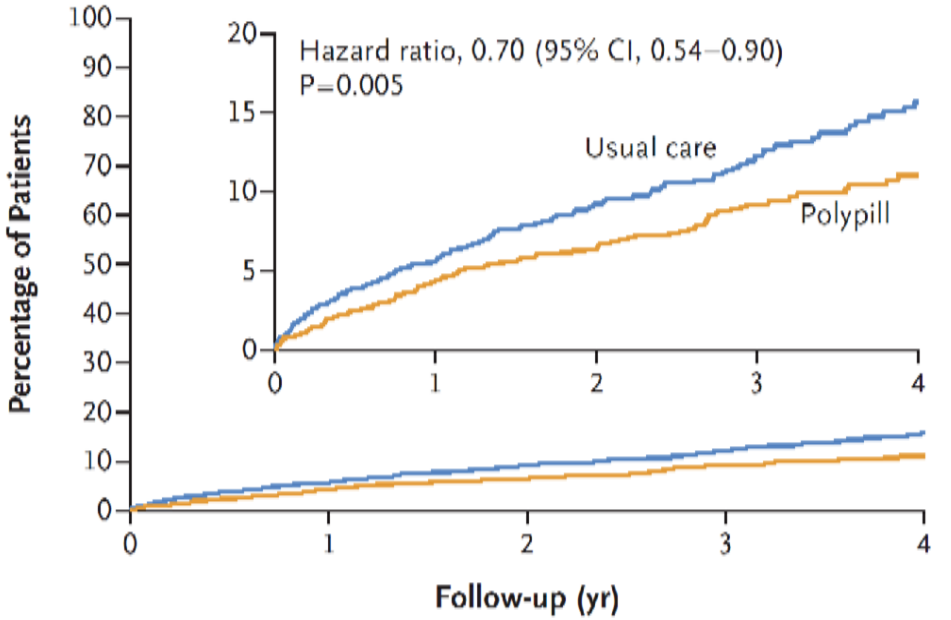
(CV death, nonfatal type 1 myocardial infarction, nonfatal ischemic stroke, or urgent revascularization)



No. at Risk					
Usual care	1229	1075	852	518	196
Polypill	1237	1064	848	511	192

Secondary outcome

(CV death, nonfatal type 1 MI, or nonfatal ischemic stroke).



No. at Risk					
Usual care	1229	1079	857	522	196
Polypill	1237	1074	859	521	201

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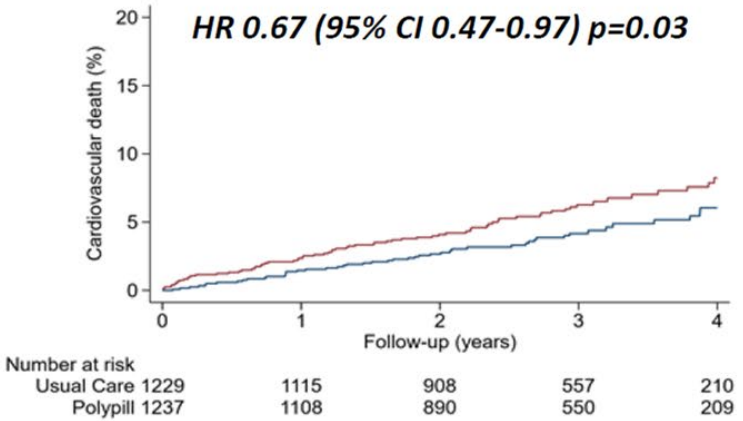
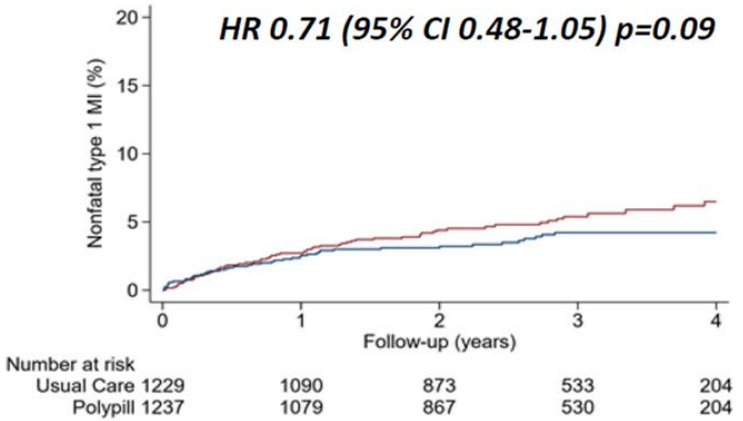
SECURE

Individual Components of the Primary Outcome

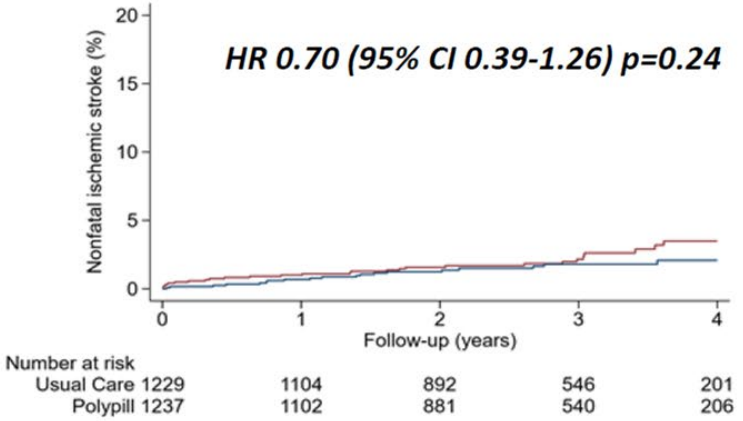
Cardiovascular Death



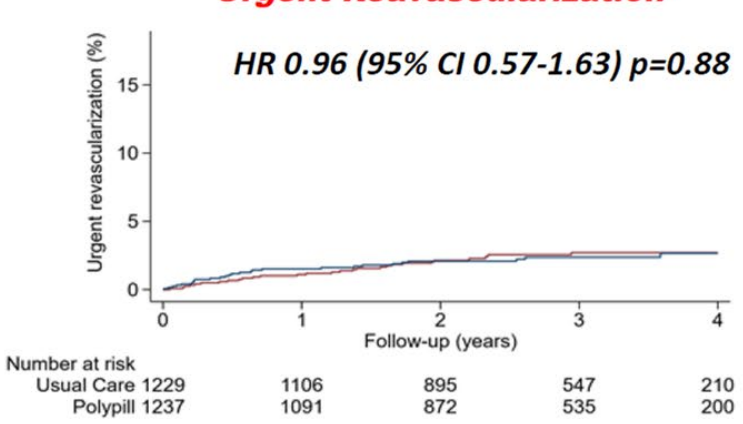
Nonfatal type 1 Myocardial Infarction



Non Fatal Ischemic Stroke



Urgent Reavascularization



Usual Care — Polypill

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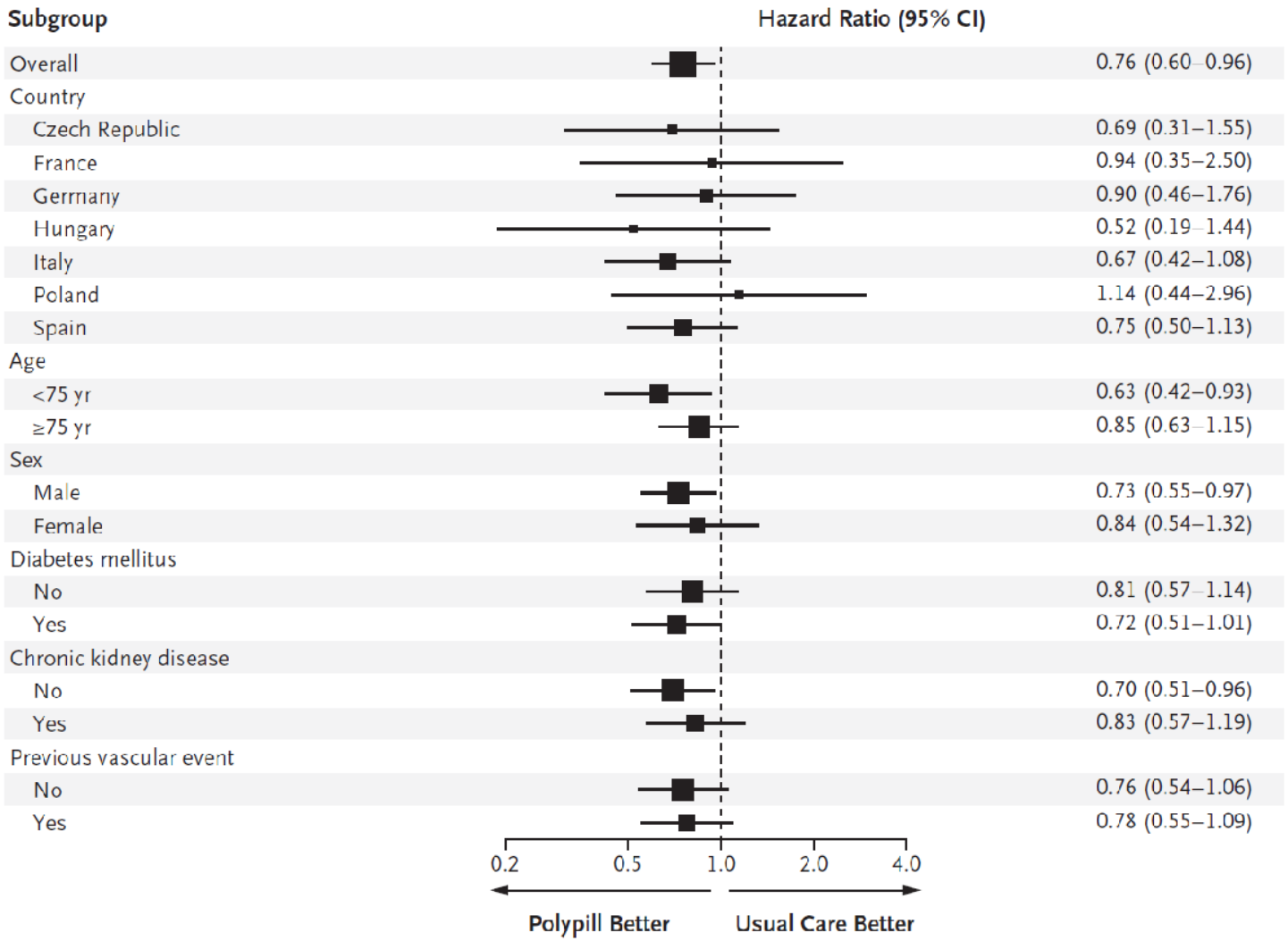
Primary Composite Outcome, According to Subgroup



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SECURE

	Polypill			Usual Care		
	N	Mean (SD)	Change from baseline, mean (SD)	N	Mean (SD)	Change from baseline, mean (SD)
SBP, mmHg						
Baseline	1235	129.1 (17.6)		1226	129.1 (17.9)	
6 months	1067		5.2 (21.3)	1053		5.7 (22.1)
12 months	986		7.5 (22.5)	972		5.7 (22.4)
24 months	882		6.3 (21.9)	830		6.3 (22.1)
DBP, mmHg						
Baseline	1235	71.1 (11.0)		1226	71.4 (11.4)	
6 months	1067		3.0 (12.7)	1052		2.7 (13.0)
12 months	986		3.5 (12.7)	972		2.3 (13.1)
24 months	882		3.6 (12.6)	829		3.1 (13.3)
LDL cholesterol, mg/dL						
Baseline	1144	90.3 (37.9)		1144	88.3 (36.3)	
12 months	874		-20.3 (35.6)	871		-20.5 (36.9)
24 months	781		-22.3 (36.7)	715		-20.7 (38.4)

No evidence of treatment differences over time

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SECURE

	Adherence At 6 Months			Adherence At 24 Months		
	Low (<6)	Medium (6 to <8)	High (8)	Low (<6)	Medium (6 to <8)	High (8)
Polypill	5.5	23.9	70.6	4.2	21.7	74.1
Usual Care	9.5	27.8	62.8	6.9	29.8	63.2
Common OR (95% CI)	1.46 (1.22, 1.74) p < 0.001			1.67 (1.36, 2.04) p < 0.001		

Adherence was measured using the Morisky Medication Adherence Scale which categorizes patients to low (< 6 points), medium (6-7 points), or high levels of adherence (8 points)

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Conclusiones

- El uso de una polipíldora cardiovascular como sustituto de varios fármacos cardiovasculares separados podría ser una parte integral de una estrategia eficaz de prevención secundaria.

- Estrategia segura, mejora la accesibilidad y la adherencia al tratamiento, disminuyendo así el riesgo de enfermedad recurrente y muerte cardiovascular.

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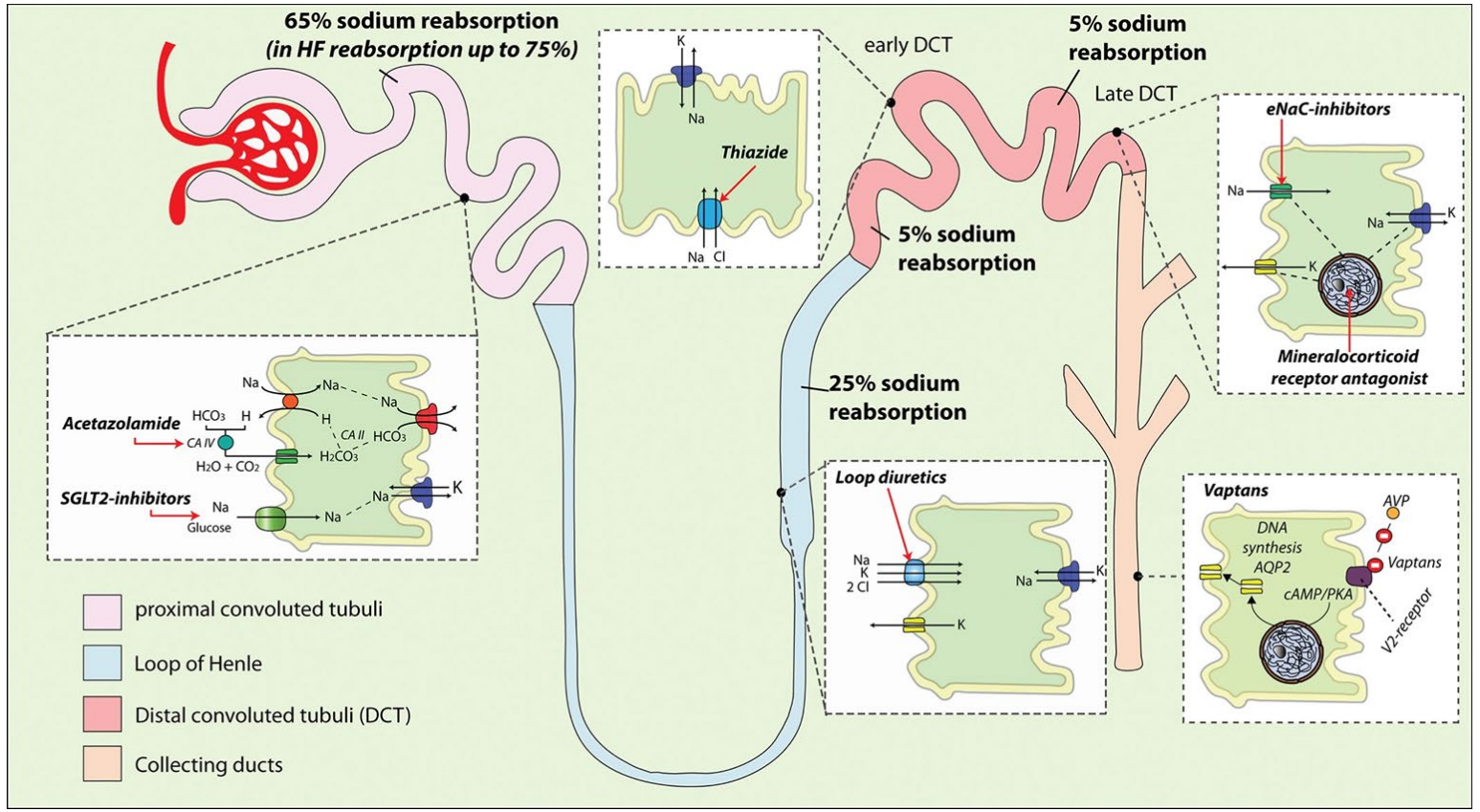
ADVOR Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

	Variable					
		EUVOLEMIA → CONGESTED				
Clinical congestion	Orthopnea	None		Mild	Moderate	Severe/worst
	JVP (cm)	<8 and no HJR	<8	8-10 or HJR+	11-15	>16
	Hepatomegaly		Absent	Liver edge	Moderate pulsatile enlargement	Massive enlargement and tender
	Edema		None	+1	+2	+3/+4
	6MWT	>400m	300-400m	200-300m	100-200m	<100m
Technical evaluation	NP (one of both): -BNP -NT-proBNP		<100 <400°	100-299 400-1500	300-500 1500-3000	>500 >3000
	Chest X-ray	clear	clear	cardiomegaly	- pulmonary venous congestion* - small pleural effusions*	- Interstitial or alveolar edema
	Vena Cava imaging [45]	none of two: - Max diameter >2.2 cm - collapsibility <50%		One of two: - Max diameter >2.2 cm - collapsibility <50%		Both: - Max diameter >2.2 cm - collapsibility <50%
	Lung Ultrasound [44]	<15 B-lines when scanning 28-sites		15-30 B-lines when scanning 28-sites		>30 B-lines when scanning 28-sites

Recommendations	Class[a]	Level[b]
It is recommended that patients hospitalized for HF be carefully evaluated to exclude persistent signs of congestion before discharge and to optimize oral treatment.[427,472]	I	C



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ADVOR Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

Main inclusion criteria

- Admitted with ADHF
- At least 1 sign of volume overload (oedema, pleural effusion*, ascites°)

  To be confirmed with radiography or ultrasonography of the chest or ultrasonography of the abdomen°*
- At least 1 month maintenance dose of oral loop diuretics (≥ 40 mg furosemide)
- NT-proBNP > 1000 pg/ml or BNP > 250 pg/ml

Main exclusion criteria

- Acetazolamide maintenance therapy
- Treatment with SGLT2i
- Systolic blood pressure < 90 mmHg
- eGFR < 20 ml/min

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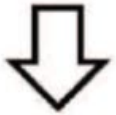
ADVOR Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

OEDEMA	No oedema (score 0)	Trace oedema (pitting disappear immediately) (score1)	Clear pitting oedema (score 2)	Visual deformation above ankle (score 3)	Visual deformation above knee (score 4)
PLEURAL EFFUSION (to be confirmed by chest X-ray or ultrasound on admission if suspected)	No pleural effusion (score 0)	Minor (non-amendable for punction) pleural effusion (score 2)		Major (amendable for punction) pleural effusion (score 3)	
ASCITES (to be confirmed by ultrasound on admission if suspected)	NO ascites (score 0)	Minor ascites, only detected by echography (score 2)		Significant ascites (score 3)	

Succesfull decongestion



Continue IV diurectic therapy

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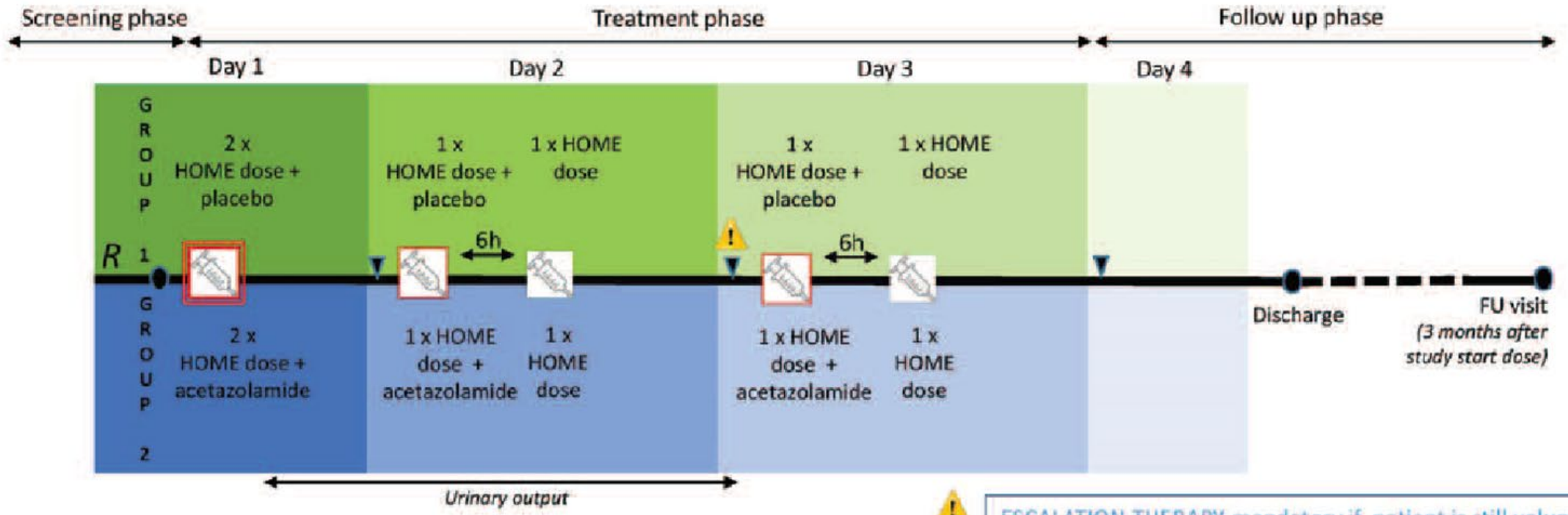
ADVOR Acetazolamide in Acute Decompensated Heart Failure with Volume Overload



R: randomization

Group 1: therapy with high-dose loop diuretics with placebo

Group 2: therapy with high-dose loop diuretics with azetazolamide

▼ *morning investigators Volume Assessment (oedema, pleural effusion or ascites) (figure 3)*

ESCALATION THERAPY mandatory if patient is still volume overloaded AND urinary output < 3.5l *(see section 8)* :

- Doubling IV loop diuretics dose
- Add oral chlorthalidone 50 mg daily
- Ultrafiltration or renal replacement therapy

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ADVOR Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

Primary end point:

Successful decongestion defined as congestion score ≤1 within 3 days after randomization without an indication for escalation of decongestive therapy

Secondary end points:

- Duration of the index hospital admission
- Death from any cause and rehospitalization for heart failure during 3 months follow-up

Safety end points: severe metabolic acidosis, renal events, hypokalemia, and hypotension

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ADVOR

Characteristics of the Patients at Baseline

Characteristic	Placebo (N=260)	Acetazolamide (N=259)	Total (N=519)
Age — yr	78.5±8.8	77.9 ±9.0	78.2±8.9
Male sex — no. (%)	155 (59.6)	170 (65.6)	325 (62.6)
White race — no. (%)†	256 (98.5)	258 (99.6)	514 (99.0)
Heart rate — beats/min	77±18	79±19	78±18
Blood pressure — mm Hg			
Systolic	127±22	126±20	127±21
Diastolic	73±13	72±13	72±13
Weight — kg	84.4±19.7	85.3±23.0	84.8±21.4
Median congestion score at baseline (IQR)‡	4 (3–6)	4 (3–5)	4 (3–6)
Components of congestion score — no. (%)			
Edema§	241 (92.7)	237 (91.5)	478 (92.1)
Pleural effusion	143 (55.0)	130 (50.2)	273 (52.6)
Ascites	25 (9.6)	21 (8.1)	46 (8.9)
Median home maintenance dose of furosemide equivalent (IQR) — mg	60 (40–100)	80 (40–120)	60 (40–100)
Left ventricular ejection fraction			
Mean — %	43±15	43±15	43±15
≤40% — no. (%)	111 (42.7)	113 (43.6)	224 (43.2)
Median NT-proBNP (IQR) — pg/ml	6483 (3262–11,839)	5600 (3034–10,100)	6173 (3068–10,896)
NYHA functional class — no. (%)			
II	35 (13.5)	31 (12.0)	66 (12.7)
III	148 (56.9)	148 (57.1)	296 (57.0)
IV	77 (29.6)	80 (30.9)	157 (30.3)
Ischemic cause — no. (%)	113 (43.5)	119 (45.9)	232 (44.7)
Serum hemoglobin — g/dl	11.9±2.0	11.9±2.0	11.9±2.0
Sodium — mmol/liter	140±4	139±4	139±4
Median serum creatinine (IQR) — mg/dl	1.5 (1.2–1.9)	1.5 (1.2–2.0)	1.5 (1.2–1.9)
Estimated GFR			
Median (IQR) — ml/min/1.73 m²	38 (29–51)	40 (30–52)	39 (29–52)
<60 ml/min/1.73 m² — no. (%)	215 (82.7)	209 (80.7)	424 (81.7)
Coexisting conditions — no. (%)			
History of atrial fibrillation	189 (72.7)	187 (72.2)	376 (72.4)
Diabetes	133 (51.2)	112 (43.2)	245 (47.2)
Hypertension	207 (79.6)	182 (70.3)	389 (75.0)

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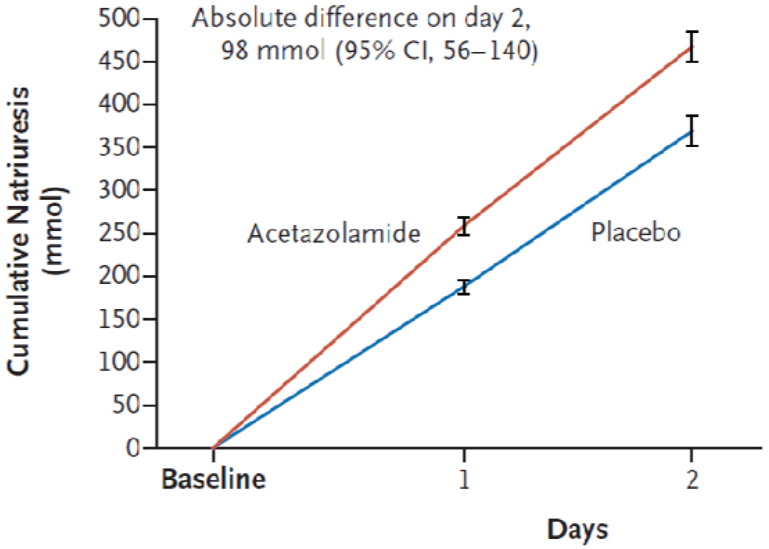
ADVOR

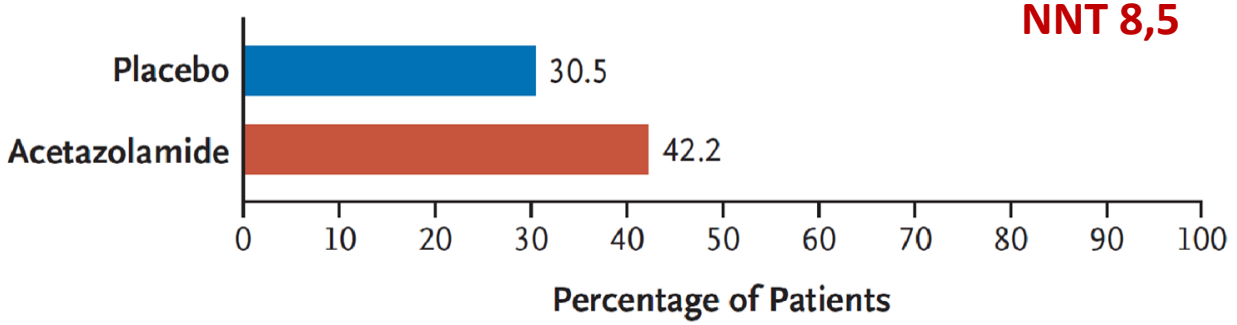
Natriuresis



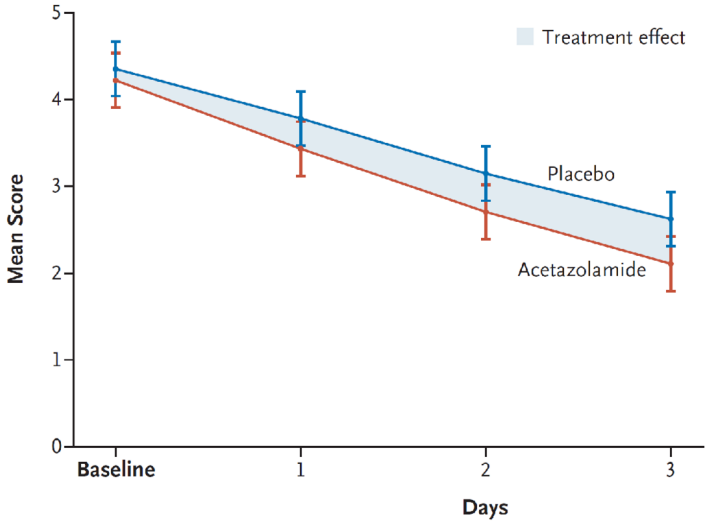
Successful Decongestion within 3 Days after Randomization (score ≤ 1)

Risk ratio, 1.46 (95% CI, 1.17–1.82)
P<0.001

NNT 8,5



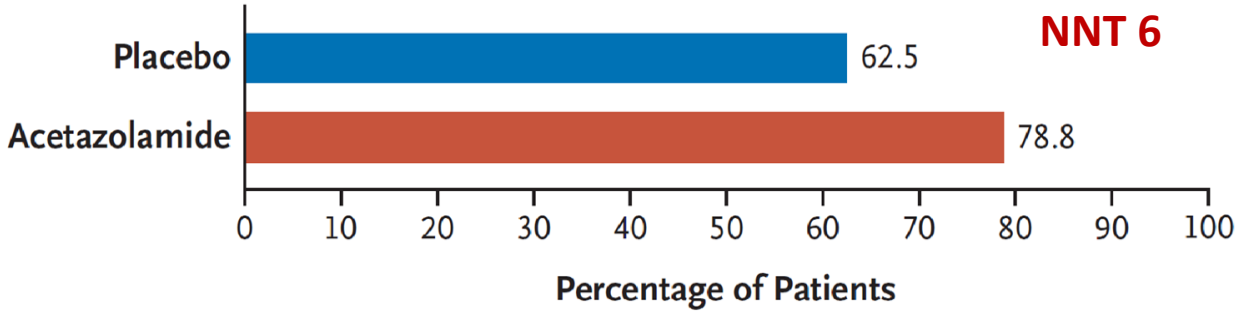
Congestion Score



Successful Decongestion at Discharge

Risk ratio, 1.27 (95% CI, 1.13–1.43)

NNT 6



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ADVOR

Results: Secondary end points

Outcomes	Placebo	Acetazolamide	Risk Ratio, Geometric Mean or Hazard Ratio [95%CI]	p-value
Secondary endpoint				
Length of stay (days)	9.9 (9.1-10.8)	8.8 (8.0-9.5)	GM 0.89 (0.81 to 0.98)	0.016
All-cause mortality and hospitalization for heart failure at 3months	72 (27.8%)	76 (29.7%)	HR 1.07 (0.78 to 1.48)	ns
All-cause mortality at 3 months	31 (12.0%)	39 (15.2%)	HR 1.28 (0.78 to 2.05)	ns
Hospitalization for heart failure at 3 months	45 (17.4%)	47 (18.4%)	HR 1.07 (0.71 to 1.59)	ns
Sensitivity analysis of primary endpoint				
Successful decongestion within 3 days, irrespective of escalation	86 (33.2%)	115 (44.9%)	RR 1.42 (1.15 to 1.76)	0.001

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Results: Safety end points

Outcome	Placebo	Acetazolamide	p-value
Adverse events during treatment phase			
Combined renal endpoint	2 (0.8%)	7 (2.8%)	0.10
Doubling of serum creatinine compared to baseline	0 (0%)	2 (0.8%)	0.24
≥50% sustained decrease in eGFR	1 (0.4%)	4 (1.6%)	0.21
Need for renal replacement therapy during index hospitalization	1 (0.4%)	4 (1.6%)	0.21
Severe metabolic acidosis bicarbonate <12 mmol/L	0 (0%)	0 (0%)	
Hypokalemia ≤3 mmol/L	10 (3.9%)	14 (5.5%)	0.39
Hypotension <85 mmHg	9 (3.5%)	17 (6.6%)	0.11
Adverse events during 3 months follow-up			
SAE overall	124 (47.9%)	123 (48.1%)	1.00
AE related to study drug	3 (1.2%)	8 (3.1%)	0.14
AE cardiovascular	122 (47.1%)	113 (44.1%)	0.53

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ADVOR

Conclusiones

- ADVOR es el ensayo clínico con tratamiento diurético más grande jamás realizado hasta la fecha en pacientes con IC descompensada aguda y teniendo un objetivo clínico muy importante de descongestión (Clase I)

- La adición de 500 mg de acetazolamida iv al tratamiento diurético de asa intravenoso se asoció a un 46% más de éxito en la resolución de los signos de congestión a los 3 días del ingreso

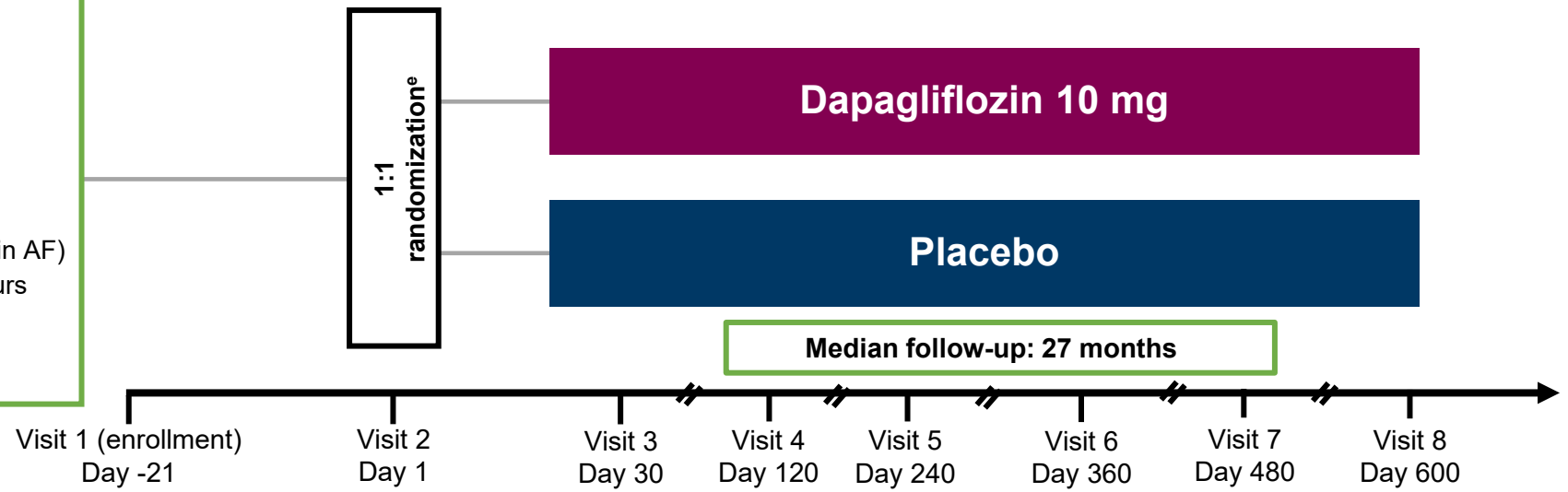
- Los pacientes tratados con terapia diurética combinada tuvieron mayor diuresis, mayor natriuresis, menor estancia hospitalaria y mayor probabilidad de ser dados de alta sin congestión residual.

ESC Congress 2022. Mullens W, et al NEJM 2022 DOI: 10.1056/NEJMoa2203094

DELIVER Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

6263 Patients

- Age ≥40 years with or without T2D
- LVEF >40% (including prior LVEF ≤ 40%)
- Symptomatic NYHA Class II-IV
- Structural heart disease (LVH or LA enlargement)
- Elevated Natriuretic Peptides (>300 pg/mL or 600 pg/ml in AF)
- Ambulatory or hospitalized off IV HF therapy[d] for ≥24 hours
- eGFR ≥25 mL/min/1.73 m^2



Primary Endpoint

- Time to first occurrence of any component of the composite of **CV death or worsening HF** events (hHF or urgent HF visit)
  - Full patient population
  - Patients with LVEF <60%

Secondary Endpoints

- Total number of HF events (first and recurrent) and CV deaths in the full patient population and in patients with LVEF <60%
- Change from baseline in KCCQ-TSS at 8 months
- Time to occurrence of CV death
- Time to occurrence of death from any cause

ESC Congress 2022. Solomon SD, et al NEJM 2022 DOI: 10.1056/NEJMoa2206286

DELIVER

Baseline characteristics

Older, Symptomatic Cohort

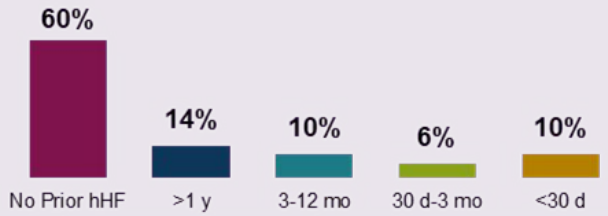
- **72 years** Mean Age
- **44%** Women
- **75%** NYHA Class II
- **25%** NYHA Class III
- **Moderate** Symptomatic Impairment[c]

High Rate of Comorbidities

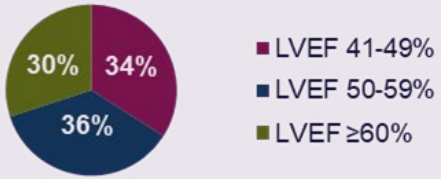
- **45%** T2D
- **45%** BMI ≥30 kg/m^2
- **89%** Hypertension
- **57%** History of AF/AFL
- **51%** Coronary artery disease
- **61 mL/min/1.73 m^2** Mean eGFR

Elevated Risk

- Median NT-proBNP: **1011 pg/mL**
- **16%** enrolled during or <90 days of hospitalization
- History of hospitalization for HF:

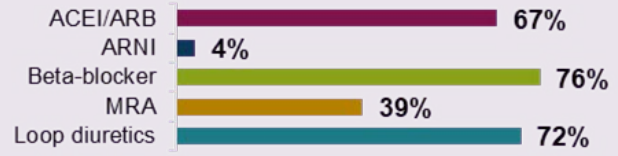


Well-represented LVEF Groups



- Mean LVEF: **54%**
- Patients with prior LVEF ≤40%[3]: **~18%**

High Use of HF Medical Therapies



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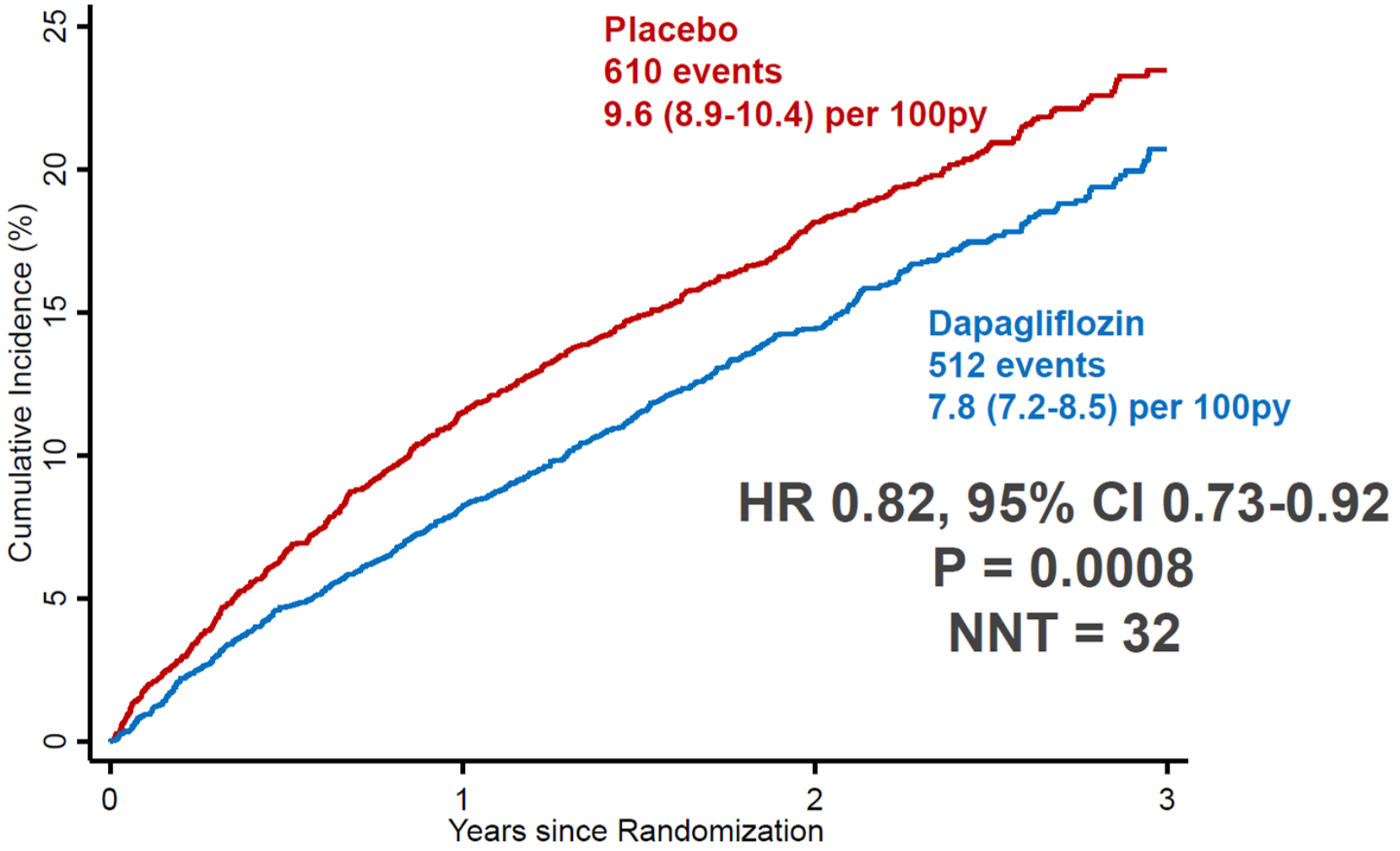
Primary Composite of CV Death or Worsening Heart Failure



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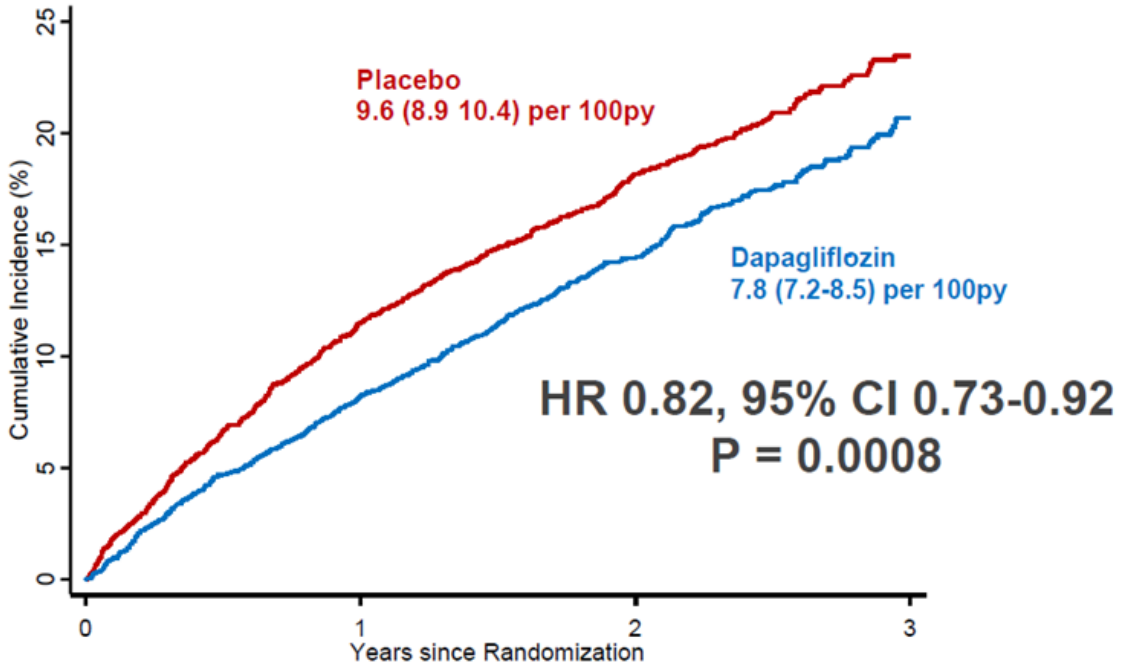
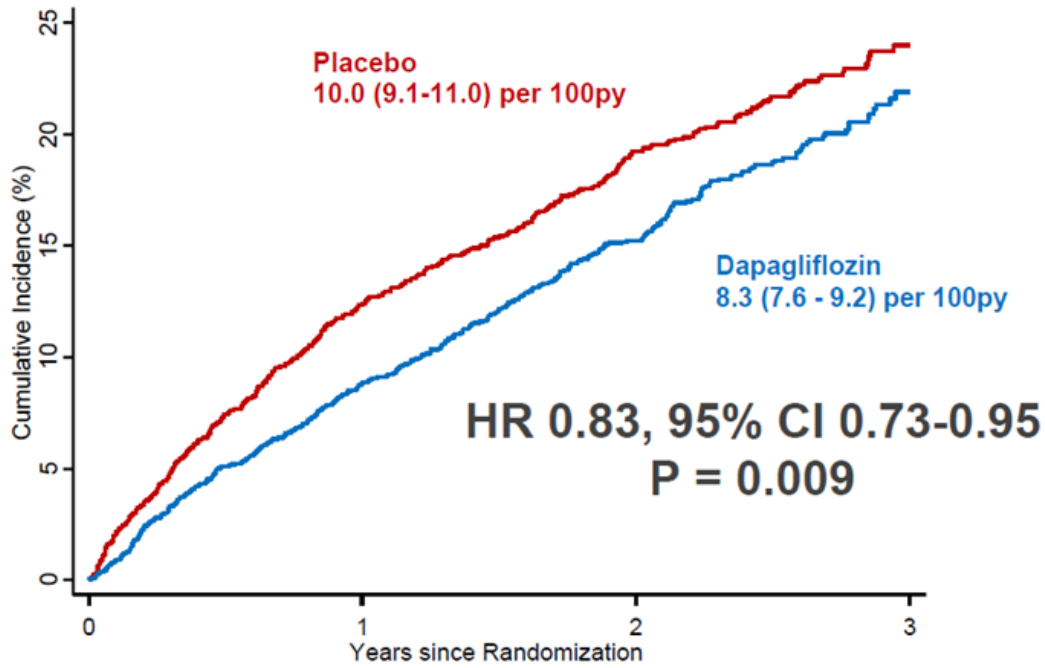
Primary Composite of CV Death or Worsening Heart Failure

Full Population
N = 6263



LVEF < 60%
N = 4372



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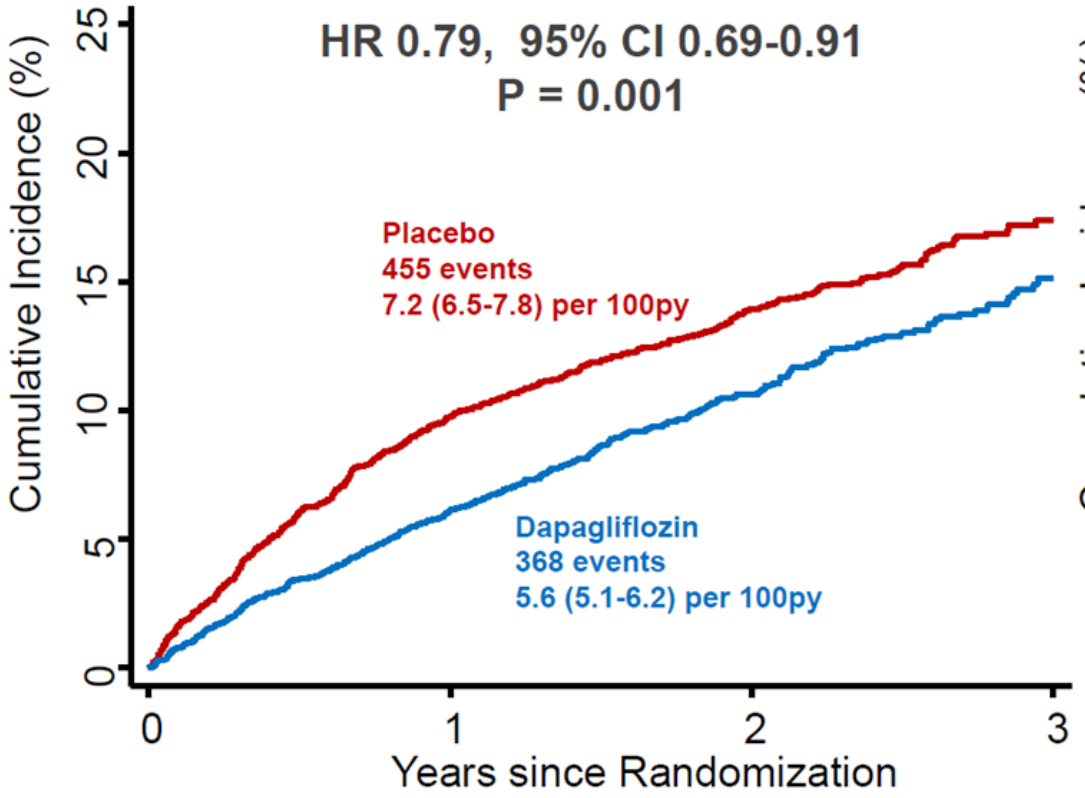
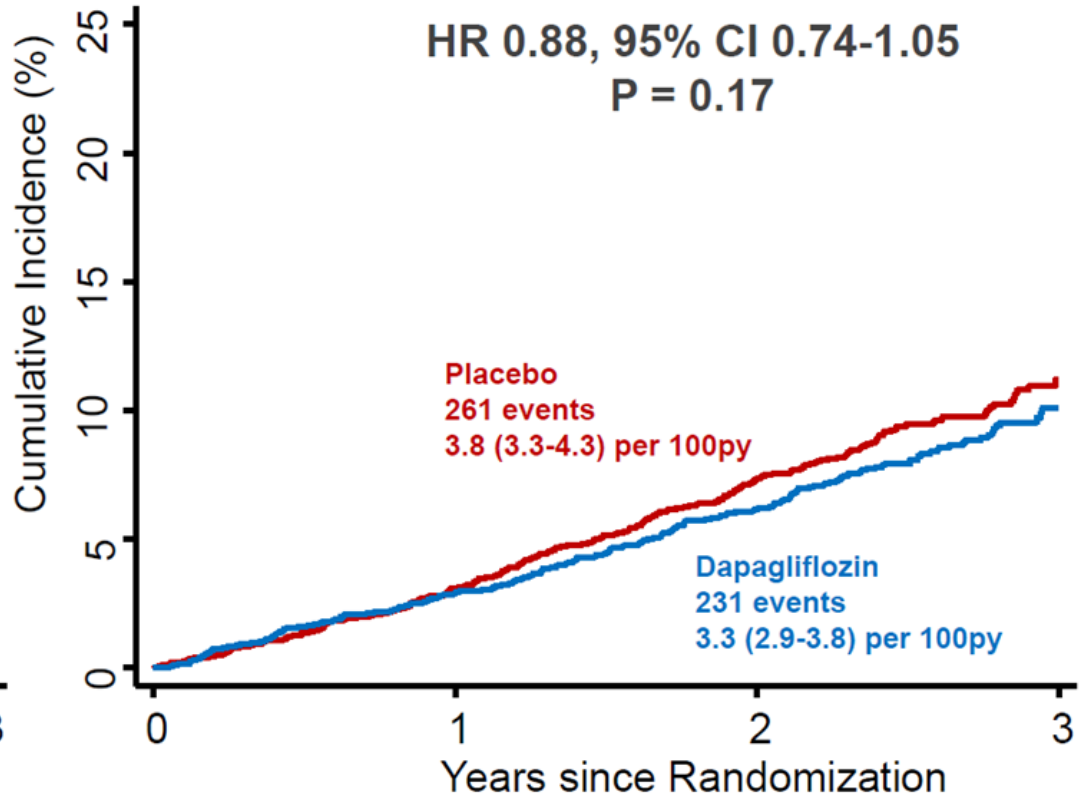
Components of Primary Endpoint (full population)

Worsening Heart Failure (HF Hospitalization + Urgent HF Visit)



Cardiovascular Death



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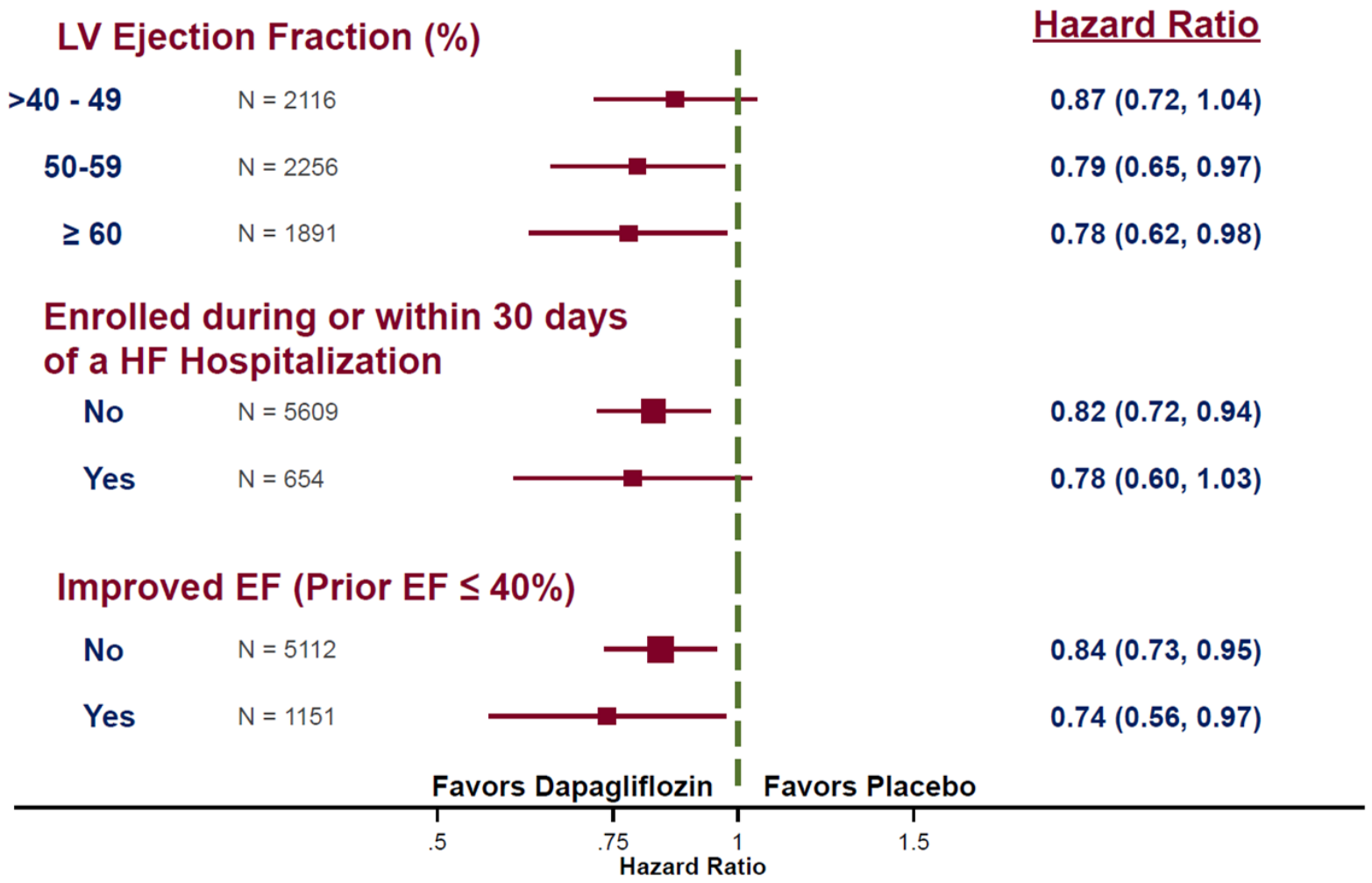
Primary Endpoint in prespecified subgroups



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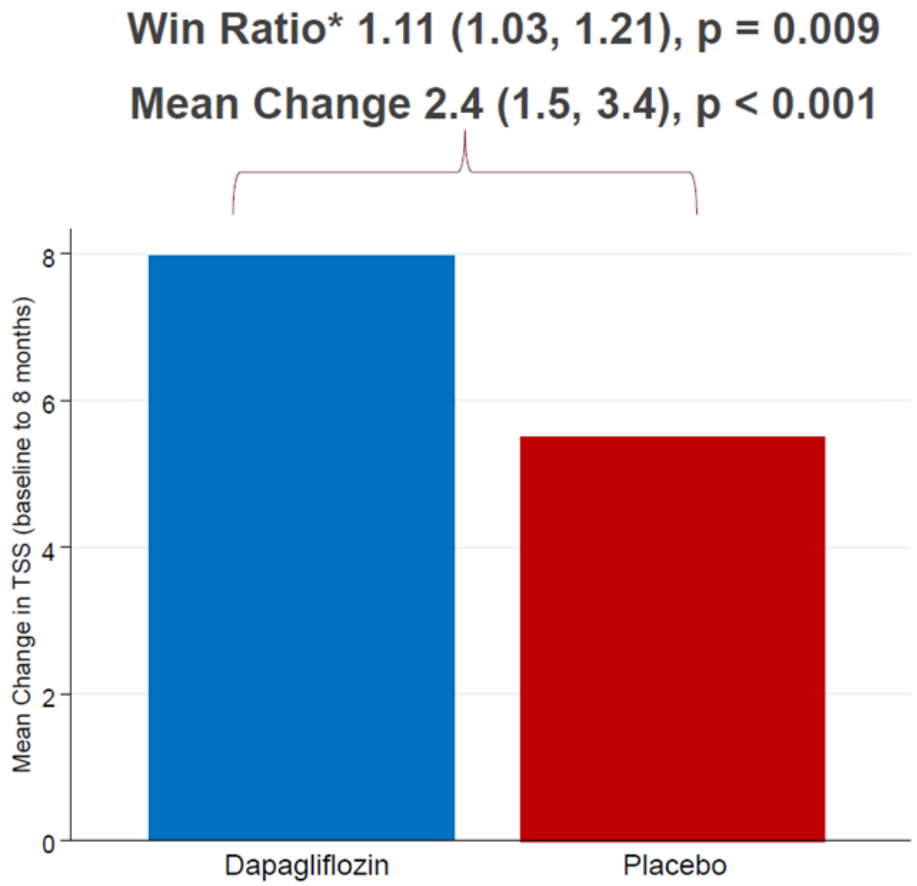
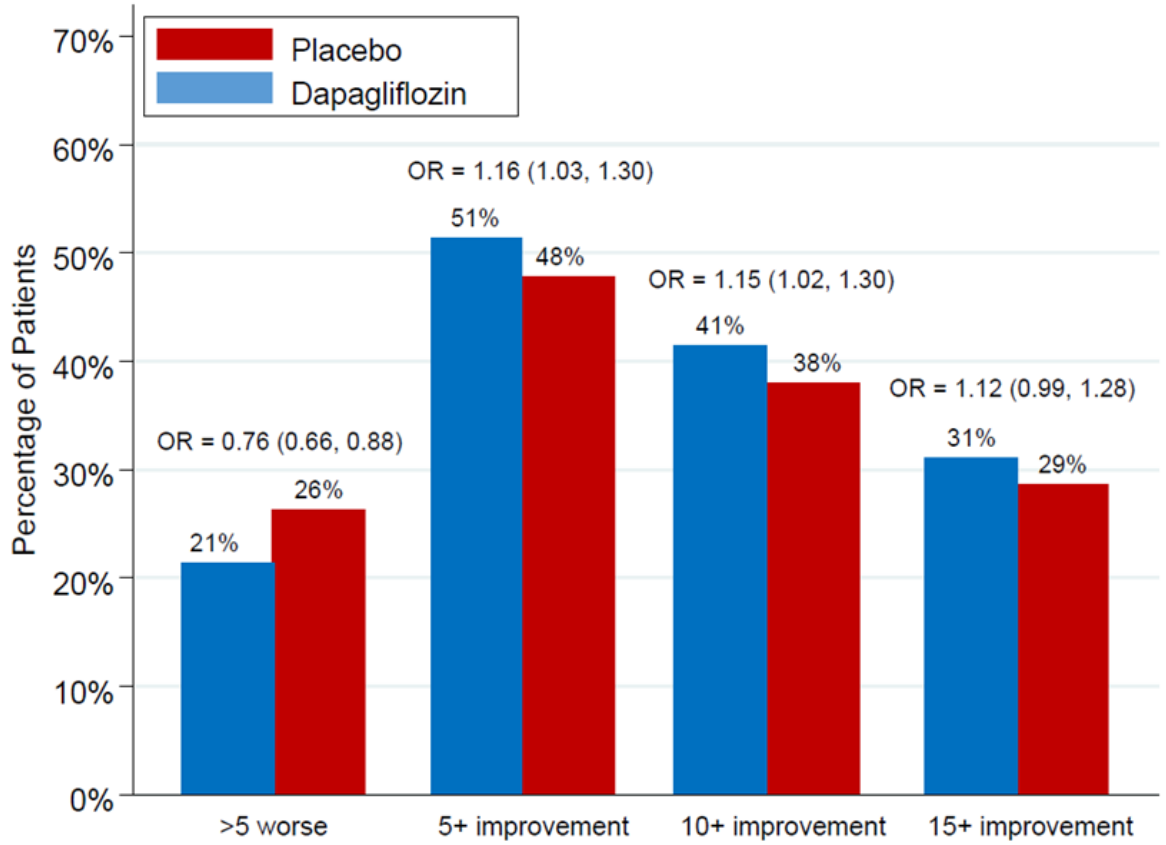
Secondary Endpoint: Improvement in KCCQ Total Symptom score





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Safety Outcomes

Event, n (%)	Dapagliflozin 10 mg n=3126[a]	Placebo n=3127[a]
Any serious AE[b]	1361 (43.5)	1423 (45.5)
AE leading to treatment discontinuation	182 (5.8)	181 (5.8)
AE leading to treatment interruption	436 (13.9)	494 (15.8)
AE of interest		
Amputation	19 (0.6)	25 (0.8)
Major hypoglycemic event	6 (0.2)	7 (0.2)
Diabetic ketoacidosis[c]	2 (0.1)	0 (0)
Volume depletion serious AE or treatment discontinuation AE	42 (1.3)	32 (1.0)
Renal serious AE or treatment discontinuation AE	73 (2.3)	79 (2.5)
Fournier's gangrene	0 (0.0)	0 (0.0)

AEs were similar between groups

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Conclusions

- En pacientes con ICFE ligeramente reducida e ICFE preservada, Dapaglifozina reduce el endpoint de muerte cardiovascular y hospitalización por IC en un 18%.

- Es efectivo en los subgrupos preespecificados, incluyendo a los pacientes con Hospitalización reciente por IC, en pacientes con IC recuperada y sin atenuación del efecto en pacientes con FEVI >60%

- Estos datos, conjuntamente con EMPEROR PRESERVED, apoyan en empleo de iSGLT2 como terapia fundamental en pacientes con Insuficiencia Cardiaca, independientemente de la FEVI

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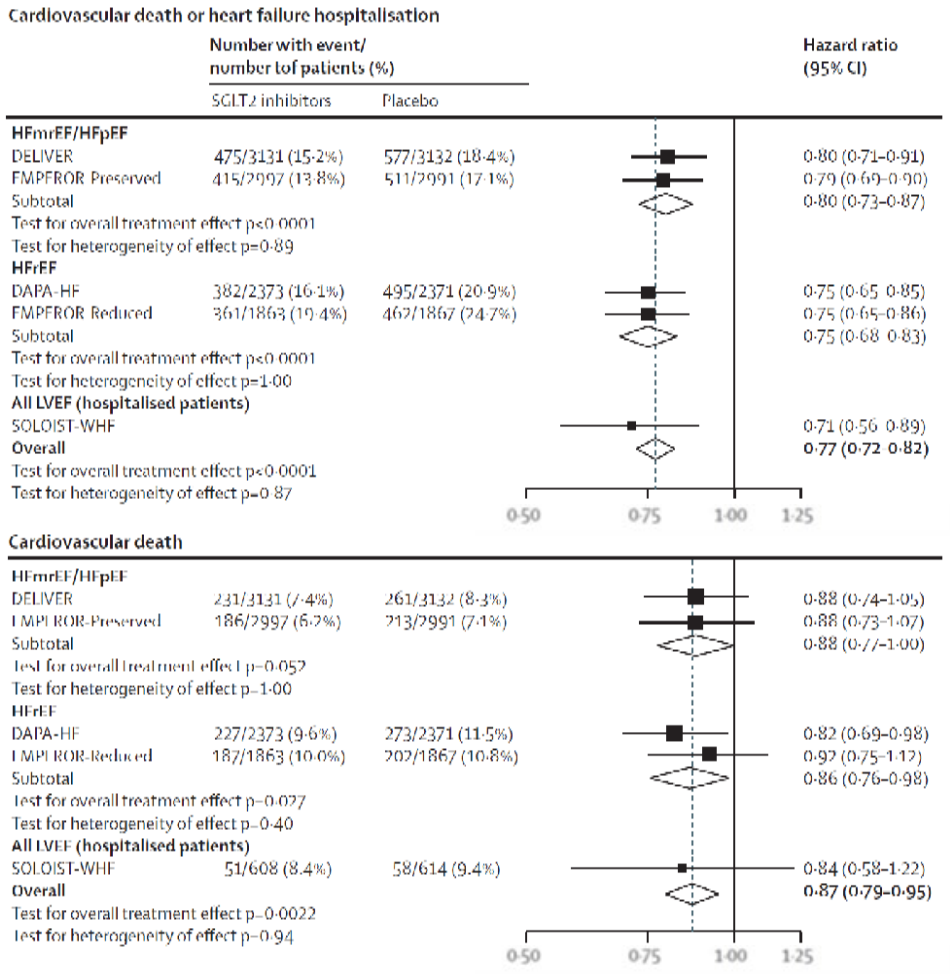
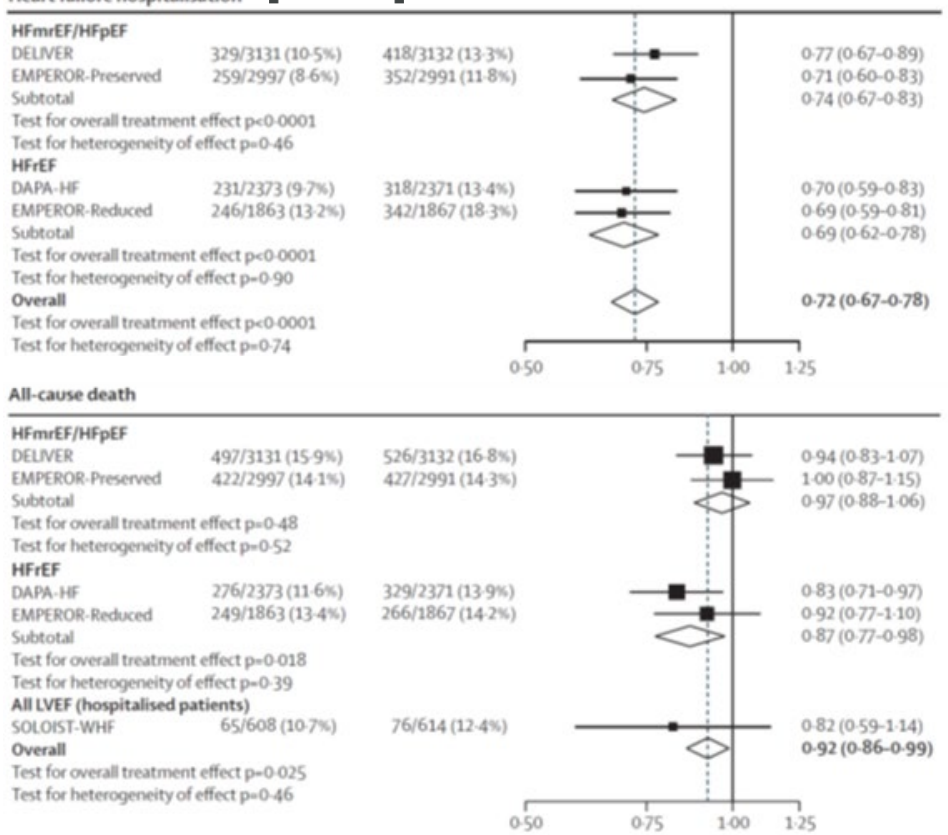
SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomized controlled trials





ESC Congress 2022. Vaduganathan M, et al. Lancet 2022 doi.org/10.1016/S0140-6736(22)01429-5

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