Sleep Apnea in Heart Failure with Mildly Reduced or Preserved Ejection Fraction: The FINEARTS-HF Trial

Sophia Rose Schneider, Henri Lu, Maria Pabòn, Henri Lu, Brian Claggett, Zi Miao, Akshay S. Desai, Pardeep S. Jhund, Carolyn S.P. Lam, Michele Senni, Sanjiv Jayendra Shah, Adriaan Voors, Faiez Zannad, Bertram Pitt, Flaviana Amarante, Katharina Mueller, Andrea Glasauer, Muthiah Vaduganathan, John J. V. McMurray, Scott Solomon

Brigham and Women's Hospital, Boston, MA, USA

BACKGROUND

- Sleep apnea is an underrecognized comorbidity in heart failure (HF) and is associated with increased cardiovascular morbidity and mortality through RAAS activation and adverse cardiac remodeling.
- Its clinical impact and effect on response to mineralocorticoid receptor antagonists (MRAs) remain unclear.
- We examined whether sleep apnea modifies clinical risk and treatment response to the nonsteroidal MRA finerenone in FINEARTS-HF.

METHODS

- FINEARTS-HF was a global, double-blind randomized trial of finerenone vs placebo in HF with LVEF ≥40%.
- This prespecified secondary analysis examined clinical outcomes and treatment responses to finerenone by sleep apnea status (investigator-reported).
- Primary outcome: Composite of cardiovascular death and total (first and recurrent) HF events. Additional outcomes included total HF events, cardiovascular death, and all-cause death.

RESULTS

- Of 6,001 participants, 401 (6.7%) reported history of sleep apnea. Those with sleep apnea had worse symptom burden at baseline **(Table 1)**.
- Over a 2.6-year median follow-up, sleep apnea was independently associated with higher risk of the primary outcome, primarily driven by recurrent HF events **(Table 2 and Figure 2).**

Finerenone:

- Consistently reduced risk of primary outcome irrespective of sleep apnea status with greater absolute rate reductions in those with sleep apnea **(Figure 1).**
- Was associated with a numerically greater improvement in KCCQ-TSS at 12 months among patients with sleep apnea (4.9 points; 95% CI 0.7–9.2) compared with those without sleep apnea (1.4 points; 95% CI 0.4–2.4); P_{int} = 0.07).
- Reduced systolic blood pressure at 12 months to a greater degree among patients with sleep apnea compared with those without sleep apnea **(Figure 3)**.

LIMITATIONS

- Sleep apnea history was investigator-reported.
- The type (obstructive vs central), severity, and treatment of sleep apnea were not captured.
- Variations in regional screening and diagnostic practices likely contributed to higher reported prevalence of sleep apnea in North America and Western Europe.

Among patients with HF in the FINEARTS-HF trial, comorbid sleep apnea was associated with excess cardiovascular risk and a higher burden of symptoms. Finerenone was associated with greater blood pressure reduction in patients with sleep apnea and consistently reduced clinical risk and improved symptoms irrespective of sleep apnea status.

Treatment effect of finerenone vs placebo by history of sleep apnea

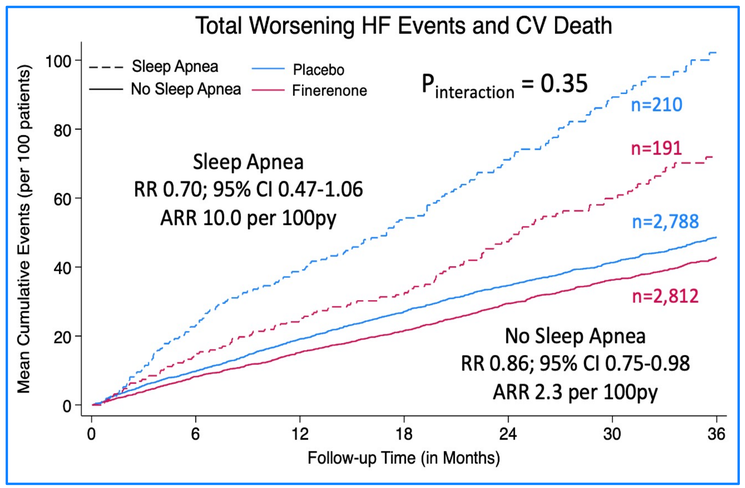


Figure 1

TABLE 1

Baseline Characteristics for History of Sleep Apnea

Parameters	No Sleep Apnea (N=5,600)	Sleep Apnea (N=401)	P-value
Age	72.0 ± 9.7	71.7 ± 9.5	0.60
Women	2,589 (46.2)	143 (35.7)	<0.001
Race			<0.001
Asian	957 (17.1)	39 (9.7)	
Black	70 (1.2)	18 (4.5)	
Other	170 (3.0)	12 (3.0)	
White	4,403 (78.6)	332 (82.8)	
Region			<0.001
Asia	944 (16.9)	39 (9.7)	
Eastern Europe	2,604 (46.5)	46 (11.5)	
Latin America	622 (11.1)	19 (4.7)	
North America	319 (5.7)	152 (37.9)	
Western Europe, Oceania and others	1,111 (19.8)	145 (36.2)	
Recency of HF event			<0.001
<= 7 days from randomization	1,164 (20.8)	55 (13.7)	
>7 days - <= 3 months	1,903 (34.0)	125 (31.2)	
>3 months or no index HF event	2,533 (45.2)	221 (55.1)	
SBP (mmHg)	129.3 ± 15.2	130.0 ± 16.8	0.42
BMI (kg/m^2)	29.6 ± 6.0	34.2 ± 6.6	<0.001
Creatinine (mg/dL)	1.1 ± 0.4	1.3 ± 0.4	<0.001
eGFR (mL/min/1.73m^2)	62.4 ± 19.7	57.4 ± 19.7	<0.001
LVEF (%)	52.5 ± 7.8	53.8 ± 8.1	<0.001
NT-proBNP (pg/mL)	1,046 [445, 1,963]	974 [476, 1,696]	0.31
NYHA class			0.003
NYHA Class II	3,896 (69.6)	250 (62.3)	
NYHA Class III + IV	1,703 (30.4)	151 (37.6)	
Hypertension	4,961 (88.6)	364 (90.8)	0.18
Diabetes mellitus	2,211 (39.5)	228 (56.9)	<0.001
Baseline KCCQ-TSS	67.5 ± 23.7	60.9 ± 25.7	<0.001

TABLE 2

Clinical Outcomes According to History of Sleep Apnea

	Events, n (%)	Event Rate per 100 py (95% CI)	Unadjusted	Adjusted (Model*)
Total heart failure events and CV death				
No Sleep Apnea (N=5,600)	2,088	15.4 (14.7 – 16.0)	1 (Reference)	1 (Reference)
Sleep Apnea (N=401)	278	29.6 (26.3 – 33.3)	1.52 (1.20-1.91)	1.43 (1.13-1.81)
Total heart failure events				
No Sleep Apnea (N=5,600)	1,627	12.0 (11.4 – 12.6)	1 (Reference)	1 (Reference)
Sleep Apnea (N=401)	239	25.5 (22.4 – 28.9)	1.57 (1.22-2.03)	1.46 (1.13-1.89)
CV death				
No Sleep Apnea (N=5,600)	462 (8.3)	3.4 (3.1 – 3.7)	1 (Reference)	1 (Reference)
Sleep Apnea (N=401)	40 (10.0)	4.3 (3.1 – 5.8)	1.28 (0.91-1.82)	1.27 (0.88-1.82)
All-cause death				
No Sleep Apnea (N=5,600)	932 (16.6)	6.8 (6.4 – 7.3)	1 (Reference)	1 (Reference)
Sleep Apnea (N=401)	81 (20.2)	8.5 (6.8 – 10.6)	1.09 (0.85-1.39)	1.14 (0.88-1.47)

Model* adjusted for: age, sex, systolic blood pressure, BMI, NYHA functional class, diabetes, atrial fibrillation, eGFR, LVEF, use of ACEi, ARB or ARNI, SGLT2i, loop diuretic, GLP-1 RA, log(NT-proBNP), treatment arm.
All models are additionally stratified by region.
Abbreviations: ACEi = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor–neprilysin inhibitor; BMI = body mass index; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; GLP1 RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; KCCQ-TSS = Kansas City Cardiomyopathy Questionnaire Total Symptom Score; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NT-proBNP = N-terminal pro–B-type Natriuretic Peptide; NYHA = New York Heart Association; SBP = systolic blood pressure; SGLT-2i = sodium–glucose cotransporter 2 inhibitor.

FIGURE 2

Prognostic impact of sleep apnea

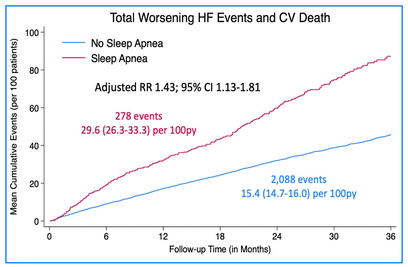
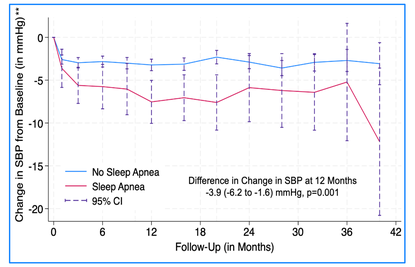


FIGURE 3

Placebo-corrected change in SBP with finerenone by history of sleep apnea



**Values represent placebo-corrected least squares mean change.

DISCLOSURES AND CONTACT

The FINEARTS-HF trial was funded by Bayer. S. Schneider reports a travel grant for this presentation. S Solomon reports reported receiving grants to institution from Alexion, Alnylam, Applied Therapeutics, AstraZeneca, Bellerophon, Bayer, BMS, Boston Scientific, Cardior, Cytokinetics, Edgewise, BridgeBio, Gossamer, GSK, Ionis, Lilly, NIH/NHLBI, Novartis, Novo Nordisk, Respicardia, Sanofi Pasteur, Tenaya, Theracos, US2.AI and consultant fees from Abbott, Action, Akros, Alexion, Alnylam, Amgen, Arena, Askbio, AstraZeneca, Bayer, BMS, Bridgebio, Cardior, Cardurion, Corvia, Cytokinetics, GSK, Intellia, Lilly, Novartis, Roche, Theracos, Quantum Genomics, Tenaya, Sanofi-Pasteur, Dinaqor, Tremeau, CellProThera, Moderna, American Regent, Sarepta, Lexicon, Anacardio, Akros, Valo, Synhale, and Recordati outside the submitted work.

Contact: sschneider5@mgb.org
@sofa_schneider

ACC.26