Table S2. ARNi administration compared to ARB or ACEi monotherapy in preclinical models of other cardiovascular diseases.

Model of	Paper by	Species	Gavage protocol	Drug dosage (mg/kg/d)*	Findings*
HFpEF due to pressure overload	Burke [1]	12-wk-old ♂ C57Bl6/J mice	Started a day before TAC, cont. for 4 wks	Vehicle ARB 26 ARNi 57	↑↑ LVEF in ARNi ↓↓ Interstitial fibrosis and fibroblast population in ARNi ↓↓ Cardiomyocyte CSA and heart weight/tibial weight ratio in ARNi
	Lu [2]	♂ SD rats	Started 4 wks after TAC, cont. for 32 days	Vehicle Enalapril 7 ARNi 30	↓↓ Sarcomere-length, LV fibrotic area, cardiomyocyte size and lung injury in ARNi ↓↓ Expressions of profibrotic, pro-oxidative, pro-apoptotic, DNA-damage, mitochondrial-damage and volume overload markers in LV in ARNi
	Norden [3]	♂ Sprague-Dawley rats	8 wks	Vehicle ARB 31 ARNi 68	↓↓ LV weight in ARNi ↓↓ Diastolic dysfunction in ARNi No differences in LVEF and myocardial fibrosis between groups
	Suo [4]	8-10-wk-old ♂ C57BL/6J mice	Started 8 wks after TAC, cont. for 4 wks	Vehicle ARB 48 ARNi 60	↑↑ LVEF in ARNi ↓↓ Fibrosis in ARNi
HT	Hamano [5]	10-wk-old ♂ SHRcp fed high-salt diet	I: 6 mos, with high-salt diet II: Started after 6 mos of high-salt diet, cont. for 6 mos	Vehicle ARB 3 ARNi 6	↓ LV/body weight ratio in ARNi in Plan I ↓↓ LV/body weight and pulmonary edema in ARB in Plan II No differences in cardiomyocyte CSA and fibrosis between groups
	Kusaka [6]	11-wk-old ♂ SHRcp fed high-salt diet	4 wks	Vehicle ARB 30 ARNi 60	↓ LV in ARNi ↓↓ Myocardial fibrosis in ARNi ↓↓ Impairment of Ach-induced vascular relaxation in ARNi
	Seki [7]	8-11-mo-old SHRs	12 wks	Vehicle ARB 20 ARNi 60	Endothelium-dependent hyperpolarization-mediated responses improved similarly in ARB and ARNi
	Sung [8]	18-wk-old ♀ SHRs	2 wks	Vehicle ARB 160 ARNi 300	↓↓ Diastolic dysfunction and ↓↓ ventricular hypertrophy in ARNi ↓↓ Incidence of ventricular arrhythmias in ARNi No differences in LVEF between groups
	Tashiro [9]	8-wk-old ♂ C57BL/6J mice	Started on the 7th day of Ang II infusion, cont. for 2 wks	Vehicle Enalapril 12 ARB 30 ARNi 60	↓↓ LV concentric hypertrophy in ARNi Myocyte CSA ↓ in ARB, ↓ in enalapril, and ↓↓ in ARNi No differences in fibrosis and TGFβ expression between groups
	Zhao [10]	12-wk-old ♀ SHRs	12 wks	Vehicle ARB 30 ARNi 60	LVEF ↑↑ in ARNi and ↑ in ARB ↓↓ LV mass in ARNi

					↓ Fibrosis, TGFβ expression and nNOS, eNOS protein expression in ARB and ARNi ↓↓ ACE, ATR1, and ↑↑ ACE2, MasR, ATR2 cardiac protein expression in ARNi
HF due to volume overload (by AVI)	Maslow [11]	♂ Sprague-Dawley rats	Started 4 wks after AVI, cont. for 4 wks.	Vehicle ARB 31 Sac 31 ARNi 68	Improved load-dependent indexes of left ventricle contractility and relaxation only in ARNi Improved load-independent index of contractility in ARB and ARNi ↑↑ Exercise tolerance in ARNi ↓↓ Myocardial fibrosis in ARNi
	Maslow [12]	♂ Sprague-Dawley rats	Started on the day of AVI, cont. for 8 wks.	Vehicle ARB 31 NEPi 31 ARNi 68	↑ LVEF in ARNi ↓ Myocardial fibrosis in ARB, NEPi, and ARNi ↑ Exercise tolerance in ARB and ARNi
HFpEF due to obesity	Aroor [13]	Zucker Obese rats	Started at 16 wks of age, cont. for 10 wks	Vehicle ARB 31 ARNi 68	↑ LVEF, ↓ fibrosis, and ↓ oxidative stress in ARB and ARNi ↑ Endothelial-dependent aortic relaxation in ARB and ARNi ↑↑ E'/a' ratio in ARNi
AF	Li [14]	♂ SPRD rats (200–250 g)	Started after AF induction, cont. for 4 wks	Vehicle ARB 48 ARNi 60	↑ LVEF in ARB and ARNi ↓↓ Atrial fibrosis and susceptibility to AF in ARNi
Myocarditis	Liang [15]	6-wk-old ♂ BALB/c mice	Started on the day of myocarditis, cont. for 3 wks	Vehicle ARB 10 ARNi 20	↓↓ Heart weight /body weight ratio, ↓↓ myocardial histopathologic scores, and ↓↓ cardiac troponin T levels in ARNi ↓↓ Serum hsCRP, IL6, and serum/myocardial IL17 levels in ARNi ↓↓ Th17 cells and their transcription factors in myocardial tissue in ARNi
CKD	Suematsu [16]	♂ SPRD rats (175–215 g)	Started 2 wks after nephrectomy, cont. for 8 wks.	Vehicle ARB 30 ARNi 60	Heart weight/body weight ratio, myocyte CSA, markers of oxidative stress, myocardial and aortic fibrosis ↓↓ in ARNi and ↓ in ARB ↓↓ expression of NF-κB and COX-2 in ARNi

Abbreviations: ACE – angiotensin-converting enzyme; ACE2 – angiotensin-converting enzyme 2; Ach – acetylcholine; AF – atrial fibrosis; ARNi – sacubitril/valsartan; ARB – valsartan; ATR1 – angiotensin II receptor type 1; ATR2 – angiotensin II receptor type 2; AVI – aortic valve insufficiency; COX-2 – cyclooxygenase 2; CKD – chronic kidney disease; cont. – continued; CSA – cross-sectional area; eNOS – endothelial nitric oxide synthase; HFpEF – heart failure with preserved ejection fraction; hs CRP – high-sensitivity C-reactive protein; HT – hypertension; IL – interleukin; LV – left ventricle; LVEF – left ventricle ejection fraction; MasR – Mas receptor; mo – month; NEPi – sacubitril; NF-κB – nuclear factor kappa-light-chain-enhancer of activated B cells; nNOS – neuronal nitric oxide synthase; TAC – transverse aortic constriction; TGFβ – transforming growth factor β; SHRs – spontaneously hypertensive rats; wk - week. Symbols: ↑/↓ – significantly increased/decreased compared to placebo; ↑↑/↓↓ – significantly increased/decreased compared to placebo and other treatments, ♂ – male, ♀ – female.

* Groups and results presented in the Table were chosen due to their importance for the review, they do not exhaust all of the results presented in selected papers.

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