A comparative *post hoc* analysis of finerenone and spironolactone in resistant hypertension in moderate-to-advanced CKD

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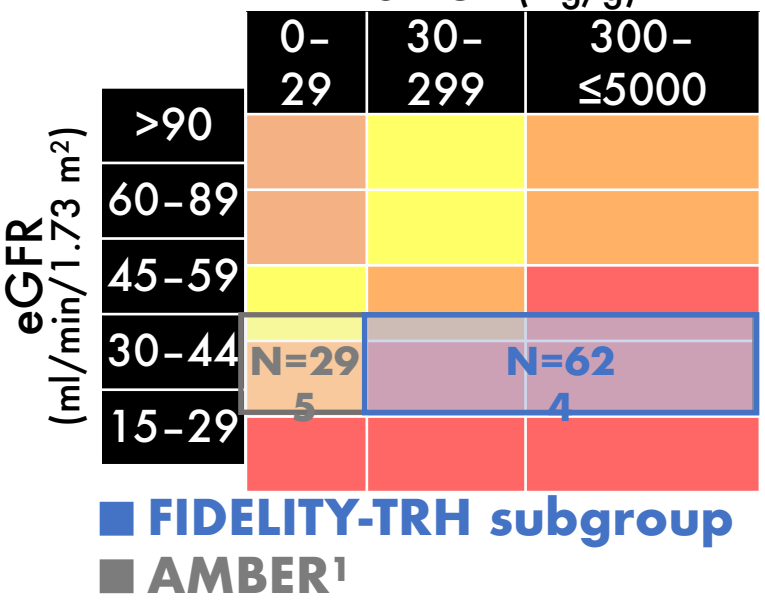
Aim and design: A *post hoc* analysis of TRH in FIDELITY with an indirect comparison to the AMBER study

- To determine the effect of finerenone on SBP and serum [K^+] in a population with TRH and moderate-to-advance CKD matched to AMBER entry criteria[1]
- To indirectly compare outcomes with spironolactone-treated patients

CKD eligibility criteria*



Other key TRH-subgroup eligibility criteria

TRH

- ✓ SBP 135–160 mmHg at baseline
- ✓ ≥3 antihypertensives including a diuretic and a RASi at baseline
- ✓ Serum [K^+] 4.3–5.1 mmol/l at baseline

Treated with an NSAID or [K^+]-affecting medication at baseline

Outcome assessment

- Change from baseline to month 4 in **SBP**
- Serum [K^+] ≥5.5 mmol/l)
- Hyperkalaemia leading to treatment discontinuation

FIDELITY-
At 4 months (~17 weeks)

AMBER[1]
At 12 weeks

*The FIDELITY-TRH population included those patients with an eGFR 25–45 mL/min/1.73 m² at screening. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NSAID, non-steroidal anti-inflammatory drug; RASi, renin angiotensin system inhibitor; SBP, systolic blood pressure; TRH, treatment-resistant hypertension; UACR, urine albumin-to-creatinine ratio

1. Agarwal R *et al. Lancet* 2019;394:1540

Baseline characteristics of patients from FIDELITY-TRH vs AMBER

	FIDELITY-TRH subgroup		AMBER[1]	
	Finerenone 10→20 mg od (n=316)	Placebo 10→20 mg od (n=308)	Spironolactone 25→50 mg and patiromer od (n=147)	Spironolactone 25→50 mg and placebo od (n=148)
Age, years, mean ± SD	68±8	68±9	68±12	69±11
Female, n (%)	110 (35)	109 (35)	71 (48)	71 (48)
Race/ethnicity, n (%)				
White/Black/other	240 (76)/17 (5)/59 (19)	236 (77)/17 (6)/55 (18)	145 (99)/2 (1)/0	145 (98)/2 (1)/1 (1)
SBP, mmHg, mean ± SD	146±7	146±7	143±7*	145±7*
Serum [K^+], mmol/l, mean ± SD	4.6±0.2	4.6±0.2	4.7±0.4	4.7±0.4
eGFR, ml/min/1.73 m^2, mean ± SD	37±8	36±7	35±7	36±8
UACR, mg/g, median (IQR)	647 (227–1424)	605 (186–1409)	87 (18–467)#	73 (19–400)#
Diabetes, n (%)	316 (100)	308 (100)	73 (50)	72 (49)
Heart failure, n (%)	36 (11)	35 (11)	63 (43)	69 (47)
Antihypertensive medications, n (%)			4 (3–4)	3 (3–4)
Beta blocker	205 (65)	214 (70)	87 (59)	86 (58)
Calcium channel blocker	229 (73)	211 (69)	107 (73)	106 (72)
Diuretic	316 (100)	308 (100)	146 (99)	145 (98)
RAAS inhibitor	316 (100)	308 (100)	147 (100)	147 (99)
Cumulative dose, mg,‡ mean	1444	1505	2942	2581

*Systolic automated office blood pressure; #24-hour UACR; ‡Cumulative dose over ~17 weeks in FIDELITY-TRH vs 12 weeks in AMBER. eGFR, estimated glomerular filtration rate; OD, once daily; RAAS, renin–angiotensin–aldosterone system; SBP, systolic blood pressure; TRH, treatment-resistant hypertension; UACR, urine albumin-to-creatinine ratio

1. Agarwal R *et al. Lancet* 2019;394:1540

In patients with TRH, finerenone was associated with a smaller reduction in BP and lower risk of hyperkalaemia* and discontinuation# vs spironolactone ± potassium-binding agent

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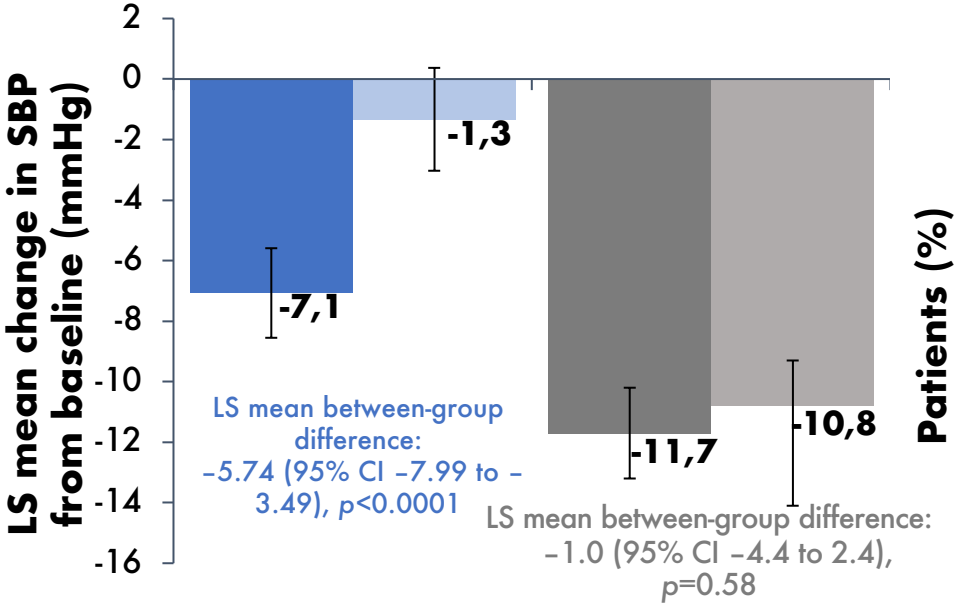
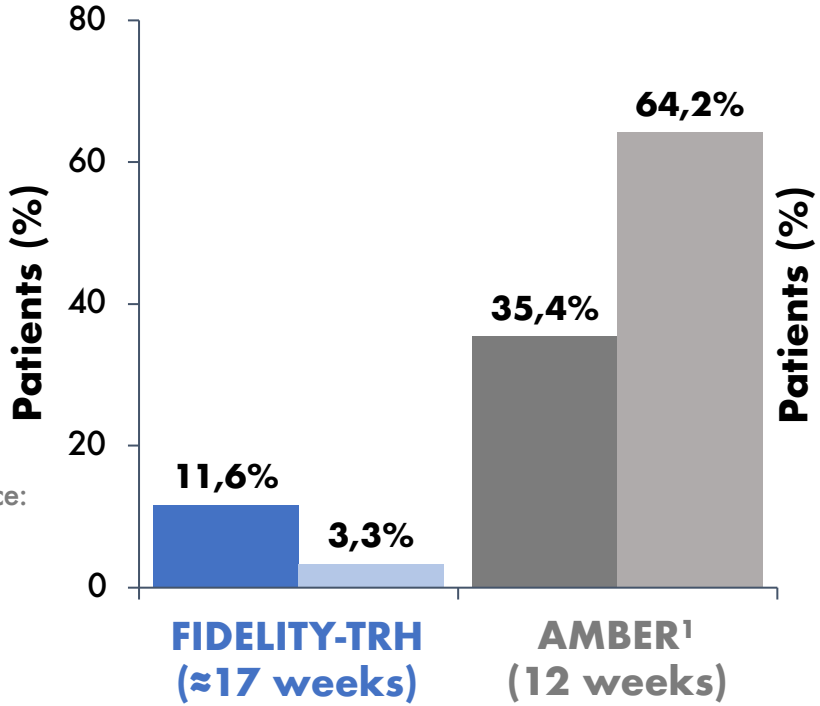
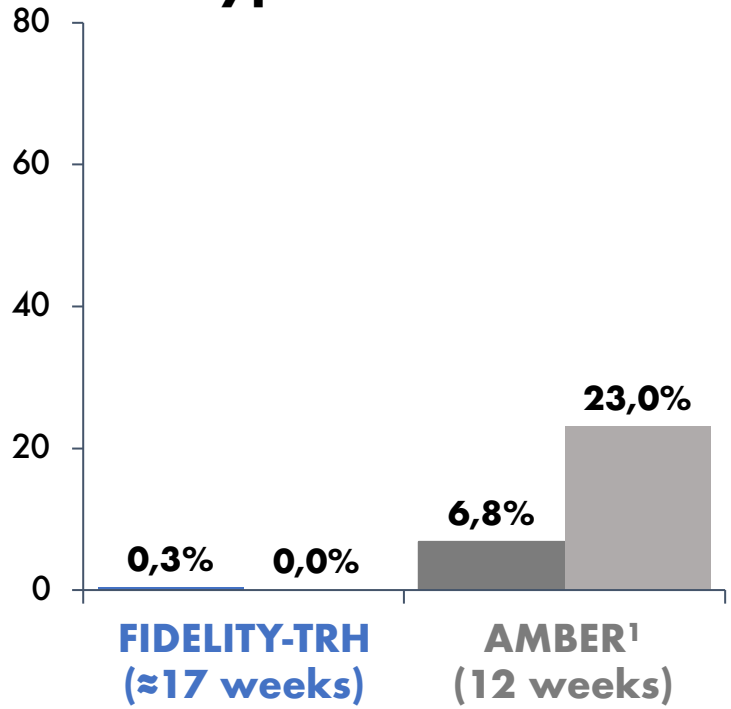
Change in SBP from baseline



Incidence of serum [K+] ≥5.5 mmol/l



Treatment discontinuation due to hyperkalaemia



Finerenone
Placebo
Spironolactone + patiromer
Spironolactone + placebo

*During the first 4 months of treatment; #due to hyperkalaemia. BL, baseline; LS, least squares; SBP, systolic blood pressure; TRH, treatment-resistant hypertension

1. Agarwal R *et al. Lancet* 2019;394:1540

Treatment-emergent AEs from baseline in FIDELITY-TRH and AMBER

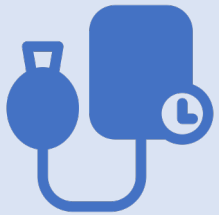
	FIDELITY-TRH subgroup (~17 weeks)		AMBER (12 weeks)[1]	
	Finerenone (n=316)	Placebo (n=308)	Spironolactone and patiromer (n=147)	Spironolactone and placebo (n=148)
Any AE, n(%)	144 (45.6)	162 (52.6)	82 (55.8)	79 (53.4)
Severe	12 (3.8)	14 (4.5)	2 (1.4)	3 (2.0)
Leading to discontinuation	7 (2.2)	3 (1.0)	10 (6.8)	21 (14.2)
Any SAE, n (%)	19 (6.0)	17 (5.5)	1 (0.7)	4 (2.7)
AE with outcome death, n (%)	1 (0.3)	0	0	1 (0.7)
Hypotension, n (%)	5 (1.6)	3 (1.0)	9 (6.1)	6 (4.1)
Leading to discontinuation	0	0	4 (2.7)	2 (1.4)
Worsening renal function, n (%)	19 (6.0)	6 (1.9)	17 (11.6)	14 (9.5)
Leading to discontinuation	3 (0.9)	0	2 (1.4)	3 (2.0)
eGFR decrease ≥30%, n/N (%)	22/314 (7.0)	20/304 (6.6)	28/147 (19.0)	26/148 (17.6)
eGFR decrease ≥50%, n/N (%)	3/314 (1.0)	2/304 (0.7)	1/147 (0.70)	4/148 (2.7)

AE, adverse event; eGFR, estimated glomerular filtration rate; SAE, serious adverse event; TRH, treatment-resistant hypertension

1. Agarwal R *et al. Lancet* 2019;394:1540

Post hoc analysis of the FIDELITY and AMBER studies: A summary

A subgroup of patients with TRH and moderate-to-advanced CKD from the FIDELITY study was matched to patients from the AMBER study[1] to indirectly compare efficacy, safety and tolerability of finerenone vs spironolactone ± a potassium-binding agent:



Finerenone lowered SBP in patients with TRH, although reductions were smaller than those achieved with spironolactone

Patients on **finerenone** had a **lower incidence of hyperkalaemia** and a **lower risk of discontinuation due to hyperkalaemia** than those on spironolactone ± patiromer

CKD, chronic kidney disease; [K^+], potassium concentration; SBP, systolic blood pressure; TRH, treatment-resistant hypertension

1. Agarwal R *et al. Lancet* 2019;394:1540