

**Table 1: Major heart failure clinical trials**

Clinical Trial	Year	Population and Intervention	n	Females	Age (Years)	Renal Function*	CKD	Renal Exclusion Criteria	Key Findings
CONSENSUS <sup>1</sup>	1988	Enalapril vs placebo in HF NYHA IV	253	30%	71	Cr 128 µmol/L	NA	Cr >300 µmol/L	Enalapril reduced mortality and improved symptoms
SOLVD <sup>2</sup>	1992	Enalapril vs placebo in HFrEF	4228	11.4%	59.1	Cr 106 µmol/L	21%	Cr >177 µmol/L	Enalapril reduced incidence and hospitalisations for HF
CIBIS-II <sup>3</sup>	1999	Bisoprolol vs placebo in HFrEF	2647	19.5%	61 (24-80)	NA	NA	Cr >300 µmol/L	Bisoprolol reduced mortality, hospitalisations, and sudden death
RALES <sup>4</sup>	1999	Spironolactone vs placebo in severe HF	1663	27%	65 ± 12	NA	48%	Cr >221 µmol/L	Along with usual therapy spironolactone reduced morbidity and mortality
I-PRESERVE <sup>5</sup>	2008	Irbesartan vs placebo in HFpEF	4128	60%	72.7 ± 7	eGFR 73 ± 23 ml/min/1.73 m <sup>2</sup>	31%	Cr >221 µmol/L	Irbesartan did not improve composite of death from

									any cause or CVD hospitalisations
EMPHASIS-HF <sup>6</sup>	2011	Eplerenone vs placebo in symptomatic HFrEF (EF<35%)	2737	22.3%	67.7 ± 7.7	eGFR 70.8 ml/min/1.73 m <sup>2</sup>	33%	eGFR <30 ml/min/1.73 m <sup>2</sup>	Eplerenone reduced risk of death and hospitalisations
TOPCAT <sup>7</sup>	2014	Spirolactone vs placebo in HFpEF	3445	51.6%	68.7	eGFR 65.4 ml/min/1.73 m <sup>2</sup>	39%	eGFR <30 ml/min/1.73 m <sup>2</sup> or serum Cr >221 µmol/L	Spirolactone non-statistically significantly reduced the composite outcome of CVD death, hospitalisation, or aborted cardiac arrest
PARADIGM-HF <sup>8</sup>	2014	Entresto vs enalapril in HFrEF	8399	21.8%	63.8 ± 11.4	Cr 99.9 ± 26.5 µmol/L	33%	eGFR <30 ml/min/1.73 m <sup>2</sup>	Entresto was superior to enalapril in reducing risk of death and hospitalisations for H
PARAGON-HF <sup>9</sup>	2019	Entresto vs valsartan in HFpEF	4796	51.7%	72.8 ± 8.4	eGFR 63 ± 19 ml/min/1.73 m <sup>2</sup>	NA	eGFR <30 ml/min/1.73 m <sup>2</sup>	Entresto non-statistically significantly reduced total and HF admissions

DAPA-HF <sup>10</sup>	2019	Dapagliflozin vs placebo in NYHA II-IV and EF <40%.	4744	23.4%	66.3 ± 10.9	eGFR 65.8 ± 19.4 ml/min/1.73 m <sup>2</sup>	41%	eGFR <30 ml/min/1.73 m <sup>2</sup>	Regardless of diabetes status dapagliflozin reduced the risk of worsening HF or cardiovascular death
EMPEROR-Reduced <sup>11</sup>	2020	Empagliflozin vs placebo in NYHA II-IV and EF <40%.	3730	23.9%	66.5 ± 11.2	eGFR 62.2 ± 21.5 ml/min/1.73 m <sup>2</sup>	53%	eGFR <20 ml/min/1.73 m <sup>2</sup>	Regardless of diabetes status, empagliflozin reduced the risk of cardiovascular death or HF hospitalisations. Empagliflozin also reduced the rate of decline in eGFR and lowered the risk of serious renal outcomes
EMPEROR-Preserved <sup>12</sup>	2021	Empagliflozin vs placebo in NYHA II-IV and EF >40%	5988	44.7%	71.9 ± 9.6	eGFR 60.6 ± 19.9 ml/min/1.73 m <sup>2</sup>	NA	eGFR <20 ml/min/1.73 m <sup>2</sup>	Regardless of diabetes status, empagliflozin reduced the risk of cardiovascular death or HF hospitalisations

SOLOIST- WHF <sup>13</sup>	2021	Sotagliflozin vs placebo in patients with diabetes mellitus admitted to hospital with worsening HF, regardless of EF	1222	33.7%	70 [64–76]	eGFR 49.7 [40.5–64.6] ml/min/1.73 m <sup>2</sup>	NA	eGFR <30 ml/min/1.73 m <sup>2</sup>	Sotagliflozin reduced the number of cardiovascular deaths and hospitalisations
DELIVER <sup>14</sup>	2022	Dapagliflozin vs placebo in HFpEF (EF >40%)	6263	43.9%	71.7 ± 9.6	eGFR 61.0 ± 19.9 ml/min/1.73 m <sup>2</sup>	NA	eGFR <25 ml/min/1.73 m <sup>2</sup>	Dapagliflozin reduced the combined risk of worsening HF or cardiovascular death

CKD = chronic kidney disease defined as eGFR <60 ml/min/1.73 m<sup>2</sup>; Cr = creatinine; CVD = cardiovascular disease; EF = ejection fraction; eGFR = estimated glomerular filtration rate; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; NA = not available; NYHA = New York Heart Association Functional Classification.

\*Age and kidney function are represented as a mean, mean ± standard deviation, mean (range), or median [interquartile range].

## References

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