

Supplementary Table 1: Clinical Events in Randomised Trials Enrolling HFpEF Patients with and without AF

| Trial, Reference | Number with HFpEF | Number with HFpEF and AF | Drug and Comparator | Ejection Fraction for HFpEF | Follow-Up (Years) | Outcome | Hazard Ratio in HFpEF | Hazard Ratio in HFpEF and AF |
|--------------------------------|-------------------|--------------------------|------------------------------|-----------------------------|-------------------|---|---------------------------------|--------------------------------|
| PEP-CHF ⁵⁸ | 850 | 172 | Perindopril versus placebo | >40% | 2.1 | Primary outcome: CV death or HF hospitalisation | 0.92, 95% CI 0.70–1.21; p=0.55 | |
| | | | | | | All-cause mortality | 1.09, 95% CI 0.75–1.58; p=0.67 | |
| | | | | | | HF hospitalisation | 0.86, 95% CI 0.61–1.20; p=0.38 | |
| I-PRESERVED ⁵⁹ | 4,128 | 1,209 | Irbesartan versus placebo | ≥45% | 4.2 | Primary outcome: Composite of death and hospitalisation | 0.95, 95% CI 0.86–1.05; p=0.35 | |
| | | | | | | All-cause mortality | 1.00, 95% CI 0.88–1.14; p=0.98 | |
| | | | | | | HF hospitalisation | 0.95, 95% CI 0.81–1.10; p=0.50 | |
| CHARM-preserved ⁶⁰ | 3,023 | 881 | Candesartan versus placebo | >40% | 3.1 | Primary outcome: CV death or HF hospitalisation | 0.86, 95% CI 0.74–1.00; p=0.051 | |
| | | | | | | CV death | 0.95, 95% CI 0.76–1.18; p=0.64 | |
| | | | | | | HF hospitalisation | 0.84, 95% CI 0.70–1.00; p=0.047 | |
| Beta-blockers in Heart Failure | 317 | 73 | Beta blockers versus placebo | ≥50% | 1.3 | All-cause mortality | 1.79, 95% CI 0.78–4.10; p=0.17 | 0.86, 95% CI 0.19–3.94; p=0.85 |

| | | | | | | | | |
|-----------------------------------|-------|-------|---|------|-----|--|--------------------------------------|--------------------------------------|
| Collaborative Group ⁵¹ | | | | | | CV hospitalisation | 0.66, 95% CI 0.37–1.18; p=0.16 | 1.33, 95% CI 0.56–3.16; p=0.52 |
| J-DHF ⁶¹ | 245 | 83 | Carvedilol versus placebo | >40 | 3.2 | Primary outcome: Composite of CV death and HF hospitalisation | 0.90, 95% CI 0.55–1.49; p=0.69 | 1.12, 95% CI 0.57–2.20; p=0.33 |
| TOPCAT ²⁵ | 3,445 | n/s | Spirolactone versus placebo | ≥45% | 3.3 | All-cause mortality | 0.99, 95% CI 0.53–1.87; p=0.98 | |
| | | | | | | Primary outcome: Composite of CV death, aborted cardiac arrest, or HF hospitalisation | 0.89, 95% CI 0.77–1.04; p=0.14 | |
| | | | | | | HF hospitalisation | 0.83, 95% CI 0.69–0.99; p=0.04 | |
| | | | | | | All-cause mortality | 0.91, 95% CI 0.77–1.08; p=0.29 | |
| TOPCAT America ⁶² | 1,765 | 760 | Spirolactone versus placebo | ≥45% | 2.9 | All-cause mortality | | 1.09, 95% CI 0.88–1.35; p=0.42 |
| | | | | | | HF hospitalisation | | 1.22, 95% CI 0.99–1.50; p=0.06 |
| PARAGON-HF trial ²³ | 4,822 | 1,552 | Sacubitril– valsartan versus Valsartan | ≥45% | 2.9 | Primary outcome: composite of HF hospitalisations and CV death | 0.87, 95% CI 0.75–1.01; p=0.06 | 0.83, 95% CI 0.69–1.00 |
| | | | | | | All-cause mortality | 0.97, 95% CI 0.84–1.13 | |
| | | | | | | HF hospitalisation | 0.85, 95% CI 0.72–1.00 | |

| | | | | | | | | |
|-------------------------------------|-------|-------|--------------------------------|------|-----|--|---------------------------------------|---------------------------|
| EMPORER- PRESERVED ²⁴ | 5,988 | 3,057 | Empaglifozin versus placebo | >40% | 2.1 | Primary outcome: composite of CV death and HF hospitalisation | 0.79, 95% CI 0.69–0.90; p<0.001 | 0.78, 95% 0.66–0.93 |
| | | | | | | | All-cause mortality | 1.00, 95% CI 0.87–1.15 |
| | | | | | | | HF hospitalisation | 0.71, 95% CI 0.60–0.83 |

Glossary: PEP-CHF=perindopril in elderly people with chronic heart failure.