

Efficacy and Safety of Finerenone in Type 2 Diabetes: A Pooled Analysis of Trials of Heart Failure and Chronic Kidney Disease – FINE-HEART

Pardeep S Jhund

**BHF Cardiovascular Research Centre, University of Glasgow & Queen
Elizabeth University Hospital, Glasgow, Scotland, UK on behalf of the
FINE- HEART committees and investigators**

Disclosures

- **Presenter Disclosure:** Speakers Fees –AstraZeneca, Novartis, Alkem Metabolics, ProAdWise Communications, Sun Pharmaceuticals, Intas pharma; Advisory Board – AstraZeneca, Boehringer Ingelheim, Novartis; Research Funding – AstraZeneca, Boehringer Ingelheim, Analog Devices Inc, Roche Diagnostics; My employer, the University of Glasgow, has been remunerated for my time working on clinical trials by AstraZeneca, Novartis, NovoNordisk and Bayer AG

FINE-HEART: Background & introduction

- The increasing overlap between type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD) and heart failure (HF) is well recognised
- Recently treatment SGLT2 inhibitors have been shown to benefit each of these growing populations alone, and, when found together
- Another common pathway in the pathogenesis of these conditions is mineralocorticoid receptor activation
- Finerenone, a non-steroidal mineralocorticoid receptor antagonist (MRA), has been shown to reduce the risk of cardiovascular events and kidney failure in patients with T2DM and CKD and more recently in patients with HF with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF) without T2DM and CKD
- We evaluated the efficacy and safety of finerenone versus placebo on cardiovascular-kidney outcomes in participants with T2DM according to baseline glycemic control and background glucose-lowering therapy (GLT)

Design of FINE-HEART Umbrella Program



(n=18,991 Participants)

Prospectively Registered:
PROSPERO CRD42024570467

Prespecified in Dedicated
Statistical Analysis Plans



Pooling data in the FINE-HEART program increased precision to robustly assess the efficacy and safety of the non-steroidal MRA finerenone on important cardio-kidney outcomes and is enriched for participants with a high burden of CKM multimorbidity.

Study design of the included trials

| | FINEARTS-HF | FIDELIO-DKD and FIGARO-DKD |
|-----------------------------|--|---|
| Validly Randomized | 6,001 | 12,990 |
| Countries | 37 | 48 |
| Patient population | HFmrEF or HFpEF | CKD and T2D |
| Inclusion criteria | <ul style="list-style-type: none"> • Adults (≥40 years) • Symptomatic HF • LVEF ≥40% • Elevation natriuretic peptides • Structural heart disease • Recent diuretic use | <ul style="list-style-type: none"> • Adults (≥18 years old) • T2D • UACR ≥ 30 mg/g • Maximally tolerated RASi |
| Exclusion criteria | Potassium ≥5.0 mmol/L | Potassium ≥4.8 mmol/L |
| Dosage and titration | eGFR ≤60: 10 up to 20 mg eGFR >60: 20 up to 40 mg (potentially down to 10 mg) | eGFR <60: 10 up to 20 mg eGFR ≥60: 20 mg (potentially down to 10 mg) |
| Study duration | 2.6 years | 2.6 years (FIDELIO-DKD) 3.4 years (FIGARO-DKD) |

FINE-HEART: Pre-specified Efficacy Endpoints

| Outcome | | HR (95% CI) | P-value |
|--|--|------------------|---------|
| Primary Endpoint | | | |
| CV death (excluding undetermined death) | | 0.89 (0.78–1.01) | 0.076 |
| <i>Prespecified sensitivity analysis:</i> CV death (including undetermined death) | | 0.88 (0.79–0.98) | 0.025 |
| Secondary Endpoints | | | |
| Kidney Composite Endpoint | | 0.80 (0.72–0.90) | <0.001 |
| HF Hospitalization | | 0.83 (0.75–0.92) | <0.001 |
| CV Death or HF Hospitalization | | 0.85 (0.78–0.93) | <0.001 |
| New-onset Atrial Fibrillation | | 0.83 (0.71–0.97) | 0.018 |
| Major Adverse Cardiovascular Events | | 0.91 (0.85–0.98) | 0.010 |
| All-cause Death | | 0.91 (0.84–0.99) | 0.027 |
| All-cause Hospitalization | | 0.95 (0.91–0.99) | 0.025 |
| All-cause Death or All-cause Hospitalization | | 0.94 (0.91–0.98) | 0.007 |



FINE-HEART: Methods

- Individual patient level data from all three trials were combined
- Patients with T2DM (as defined by investigator report) were included in this analysis
- Subgroups were defined according to baseline glycated hemoglobin (HbA1c) category
 - $\leq 6.9\%$
 - ≥ 7.0 to $\leq 8.0\%$
 - $\geq 8.1\%$
- Glucose lowering therapy (GLT) regimens were defined according to the following categories:
 - insulin monotherapy
 - insulin plus metformin
 - metformin monotherapy
 - metformin plus sulfonylurea
 - other (any regimen used by <1000 patients)
- Additional groups by SGLT2 inhibitor or GLP-1RA use as well as number of GLT at baseline (0-1, 2, or ≥ 3)
- Safety according to baseline HbA1c

FINE-HEART: Baseline characteristics by HbA_{1c}

| | Baseline HbA _{1c} Category | | | |
|---|-------------------------------------|------------|----------------|------------|
| | Overall | ≤6.9% | ≥7.0% to ≤8.0% | ≥8.1% |
| | (n=15365) | (n=5564) | (n=4780) | (n=5021) |
| Age, y | 65.8 ± 9.8 | 67.4 ± 9.8 | 66.2 ± 9.6 | 63.7 ± 9.6 |
| Female | 4938 (32%) | 1662 (30%) | 1410 (30%) | 1866 (37%) |
| Race | | | | |
| Asian | 3237 (21%) | 1254 (23%) | 1088 (23%) | 895 (18%) |
| Black | 559 (4%) | 163 (3%) | 179 (4%) | 217 (4%) |
| Other | 801 (5%) | 226 (4%) | 237 (5%) | 338 (7%) |
| White | 10768 (70%) | 3921 (71%) | 3276 (69%) | 3571 (71%) |
| Region | | | | |
| Asia | 3013 (20%) | 1178 (21%) | 1008 (21%) | 827 (17%) |
| Eastern Europe | 4336 (28%) | 1618 (29%) | 1192 (25%) | 1526 (30%) |
| Latin America | 1698 (11%) | 477 (9%) | 480 (10%) | 741 (15%) |
| North America | 2268 (15%) | 782 (14%) | 719 (15%) | 767 (15%) |
| Western Europe, Oceania and Others | 4050 (26%) | 1509 (27%) | 1381 (29%) | 1160 (23%) |

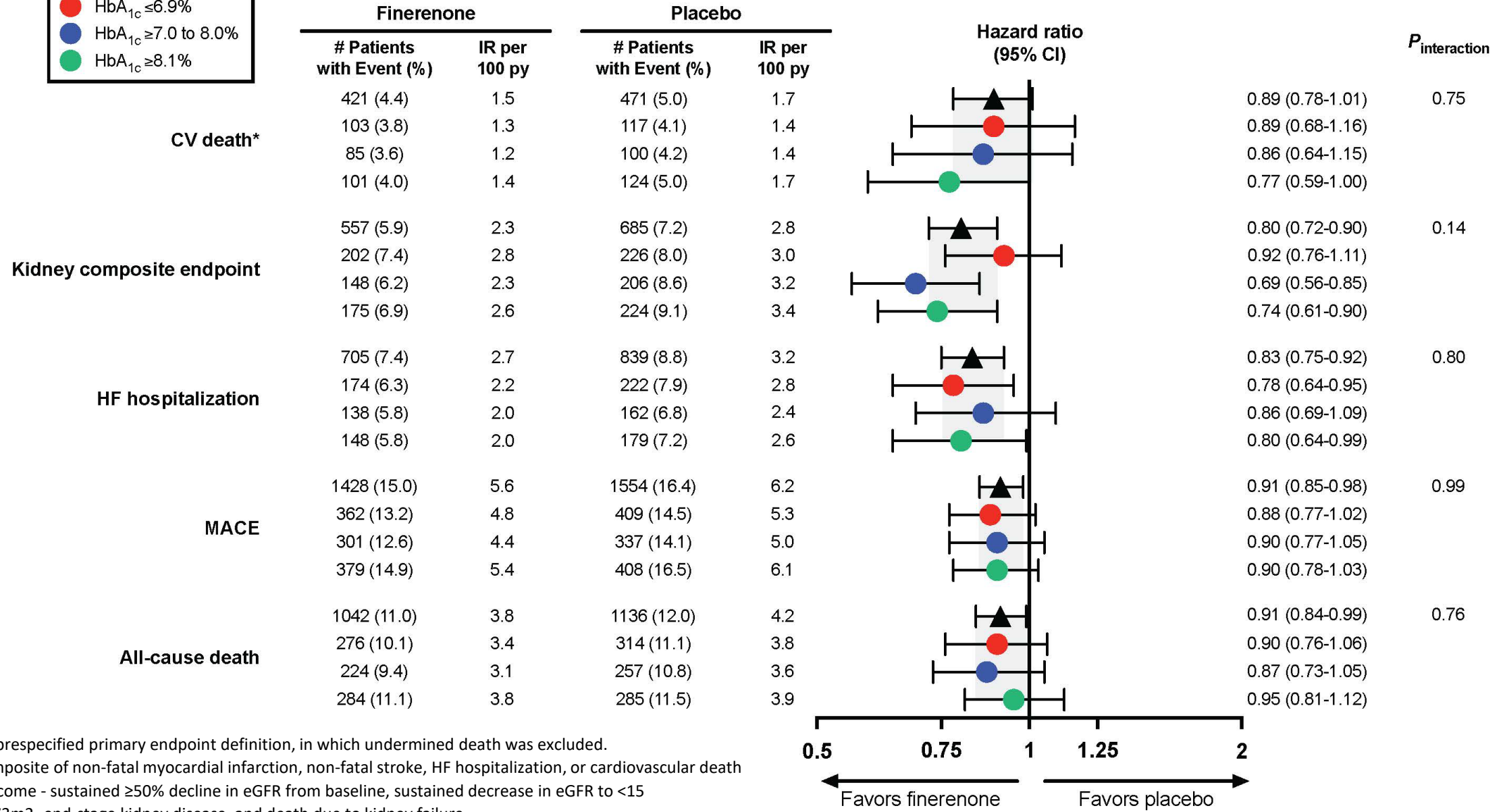
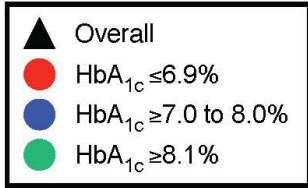
FINE-HEART: Baseline characteristics by HbA_{1c}

| | Baseline HbA _{1c} Category | | | |
|---|-------------------------------------|-------------------|----------------------------|-------------------|
| | Overall (n=15365) | ≤6.9% (n=5564) | ≥7.0% to ≤8.0% (n=4780) | ≥8.1% (n=5021) |
| Baseline body mass index, kg/m² | 31.3 ± 6.0 | 30.6 ± 6.0 | 31.1 ± 5.9 | 32.2 ± 6.1 |
| Baseline systolic blood pressure, mm Hg | 135.8 ± 14.5 | 134.6 ± 14.5 | 136.2 ± 14.8 | 136.6 ± 14.2 |
| Baseline potassium, mmol/L | 4.4 ± 0.4 | 4.3 ± 0.4 | 4.4 ± 0.4 | 4.4 ± 0.5 |
| Baseline HbA_{1c}, % | 7.6 ± 1.4 | 6.3 ± 0.5 | 7.5 ± 0.3 | 9.2 ± 1.0 |
| Baseline eGFR, mL/min/1.73 m² | 57.9 ± 21.5 | 56.6 ± 20.4 | 57.3 ± 21.2 | 60.0 ± 22.6 |
| eGFR category, mL/min/1.73 m² | | | | |
| <25 | 183 (1%) | 60 (1%) | 66 (1%) | 57 (1%) |
| 25 to <45 | 4844 (32%) | 1820 (33%) | 1552 (33%) | 1472 (29%) |
| 45 to <60 | 4050 (26%) | 1530 (28%) | 1267 (27%) | 1253 (25%) |
| ≥60 | 6288 (41%) | 2154 (39%) | 1895 (40%) | 2239 (45%) |
| Baseline UACR, mg/g | 423 [114, 1030] | 340 [75, 884] | 426 [125, 1033] | 515 [174, 1176] |
| Baseline UACR category, mg/g | | | | |
| <30 | 1344 (9%) | 742 (13%) | 332 (7%) | 270 (5%) |
| 30 to <300 | 4895 (32%) | 1867 (34%) | 1579 (33%) | 1449 (29%) |
| ≥300 | 9054 (59%) | 2920 (53%) | 2855 (60%) | 3279 (66%) |

FINE-HEART: Baseline characteristics by HbA_{1c}

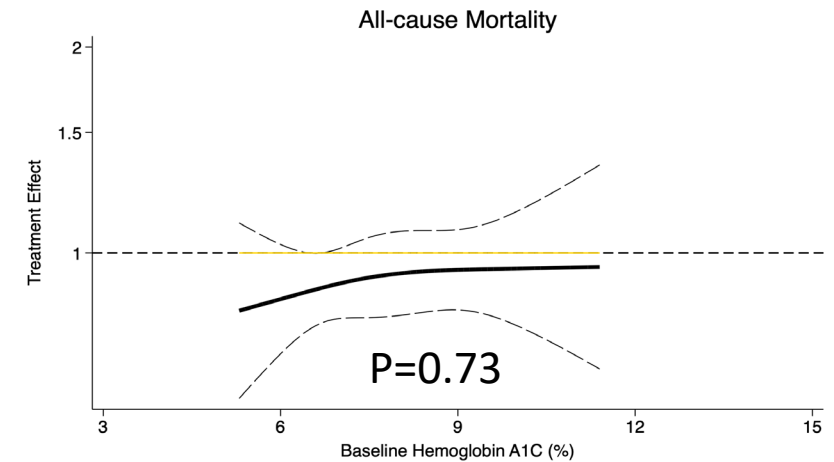
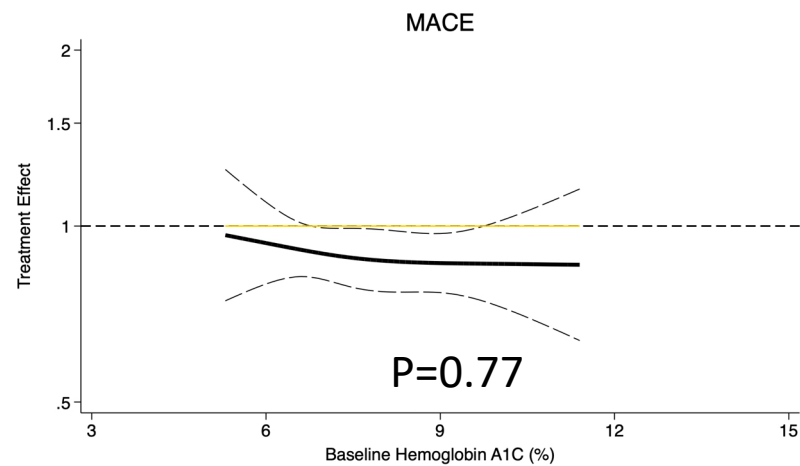
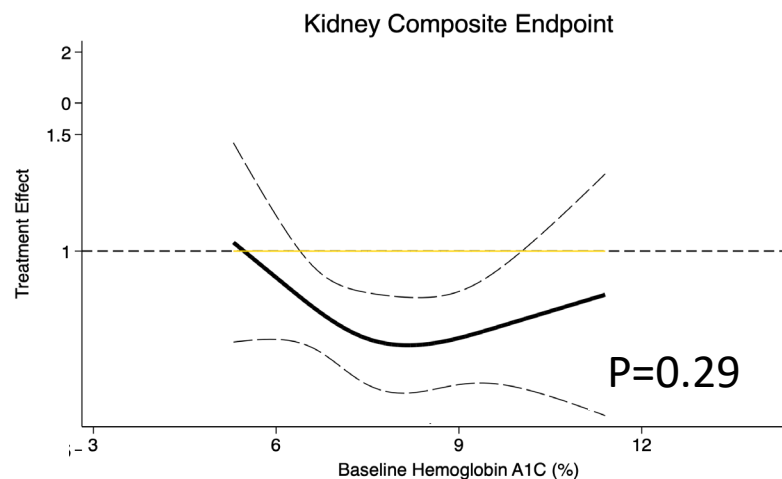
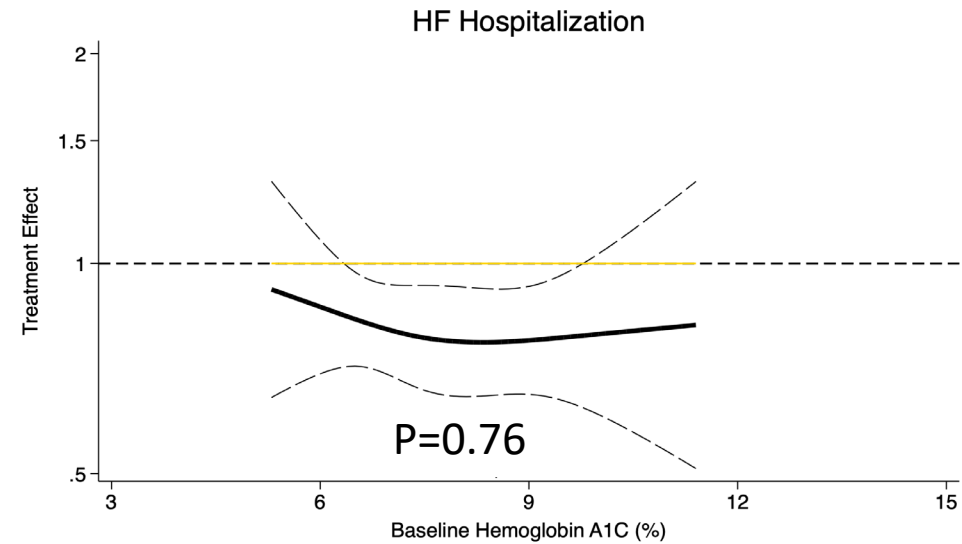
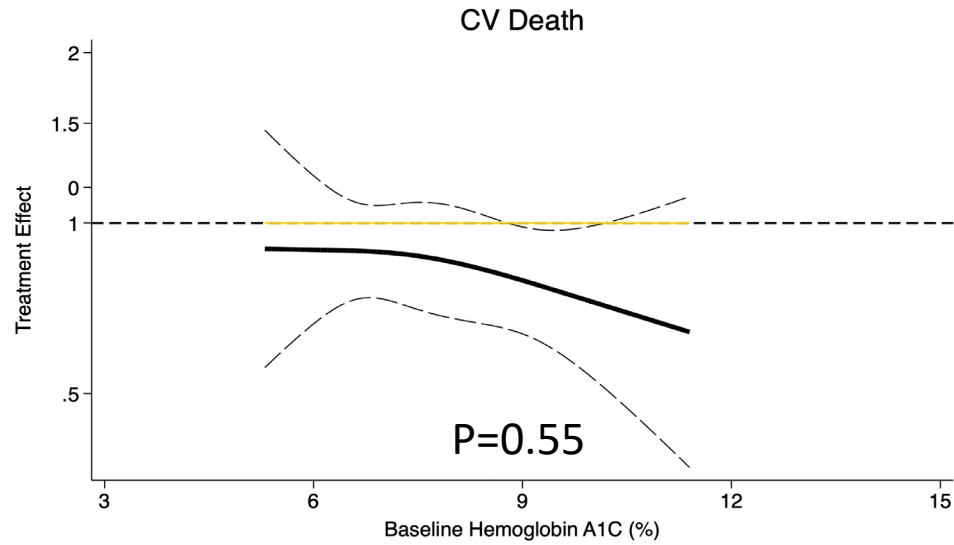
| | Baseline HbA _{1c} Category | | | |
|-------------------------------------|-------------------------------------|-------------------|----------------------------|-------------------|
| | Overall (n=15365) | ≤6.9% (n=5564) | ≥7.0% to ≤8.0% (n=4780) | ≥8.1% (n=5021) |
| Background medication use | | | | |
| Diuretics | 9058 (59%) | 3395 (61%) | 2775 (5%) | 2888 (58%) |
| ACEi/ARB/ARNI | 14902 (97%) | 5336 (96%) | 4657 (97%) | 4909 (98%) |
| Aspirin | 7276 (47%) | 2415 (43%) | 2316 (49%) | 2545 (51%) |
| Statin | 11175 (73%) | 3958 (71%) | 3569 (75%) | 3648 (73%) |
| SGLT2i | 1476 (10%) | 462 (8%) | 517 (11%) | 497 (10%) |
| GLP-1RA | 1101 (7%) | 292 (5%) | 399 (8%) | 410 (8%) |
| Potassium lowering therapies | 190 (1%) | 73 (1%) | 66 (1%) | 51 (1%) |

FINE-HEART: Efficacy by Baseline HbA1c categories



*: Reflects prespecified primary endpoint definition, in which undermined death was excluded.
MACE - composite of non-fatal myocardial infarction, non-fatal stroke, HF hospitalization, or cardiovascular death
Kidney Outcome - sustained ≥50% decline in eGFR from baseline, sustained decrease in eGFR to <15 mL/min/1.73m², end-stage kidney disease, and death due to kidney failure

FINE-HEART: Efficacy by Baseline HbA1c (continuous)



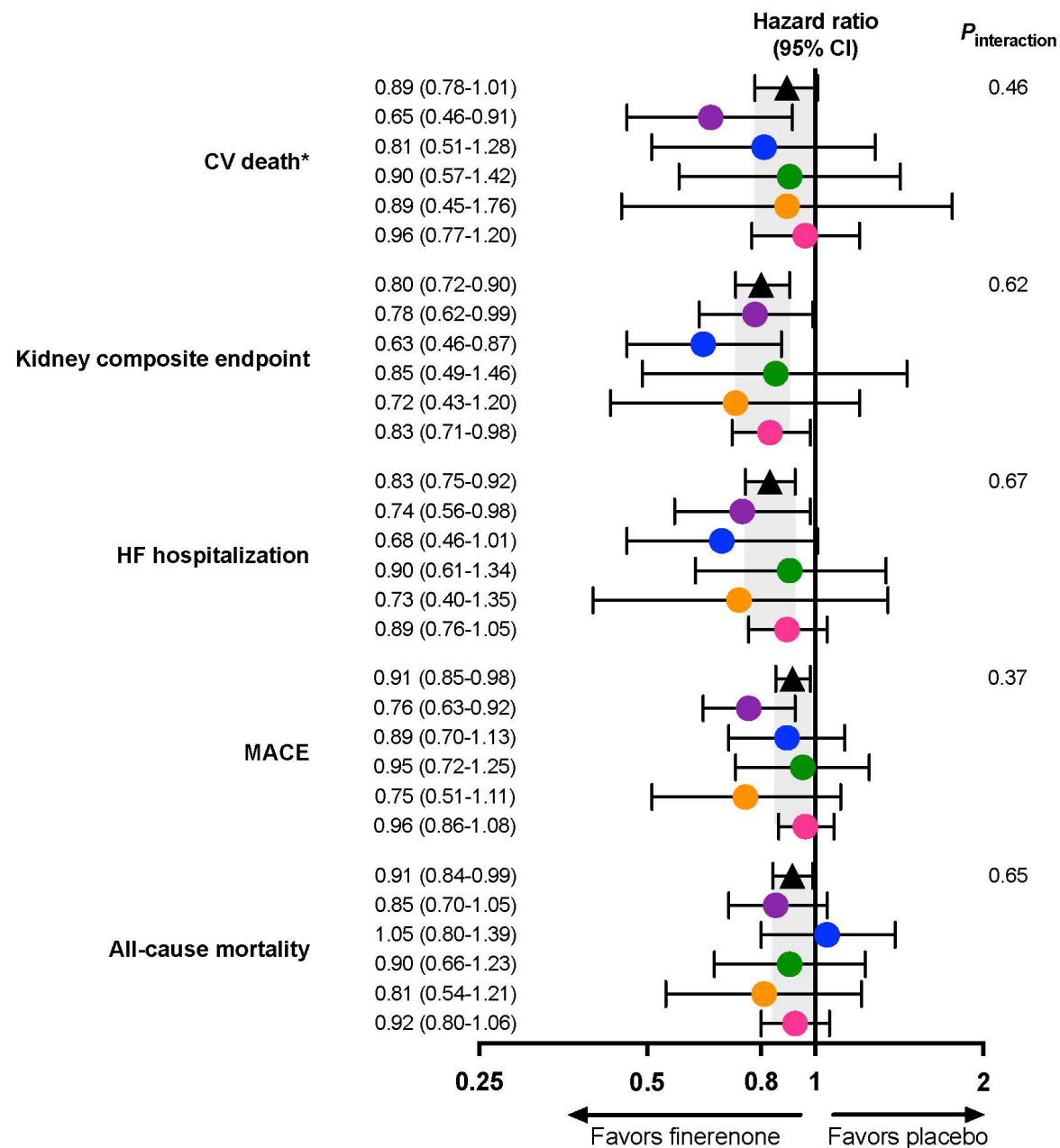
*: Reflects prespecified primary endpoint definition, in which undermined death was excluded.

MACE - composite of non-fatal myocardial infarction, non-fatal stroke, HF hospitalization, or cardiovascular death

Kidney Outcome - sustained $\geq 50\%$ decline in eGFR from baseline, sustained decrease in eGFR to < 15

mL/min/1.73m², end-stage kidney disease, and death due to kidney failure

FINE-HEART: Baseline Diabetes Therapy Regimen



*: Reflects prespecified primary endpoint definition, in which undermined death was excluded.

MACE - composite of non-fatal myocardial infarction, non-fatal stroke, HF hospitalization, or cardiovascular death

Kidney Outcome - sustained $\geq 50\%$ decline in eGFR from baseline, sustained decrease in eGFR to < 15 mL/min/1.73m², end-stage kidney disease, and death due to kidney failure

FINE-HEART: Number of Baseline Diabetes Therapies

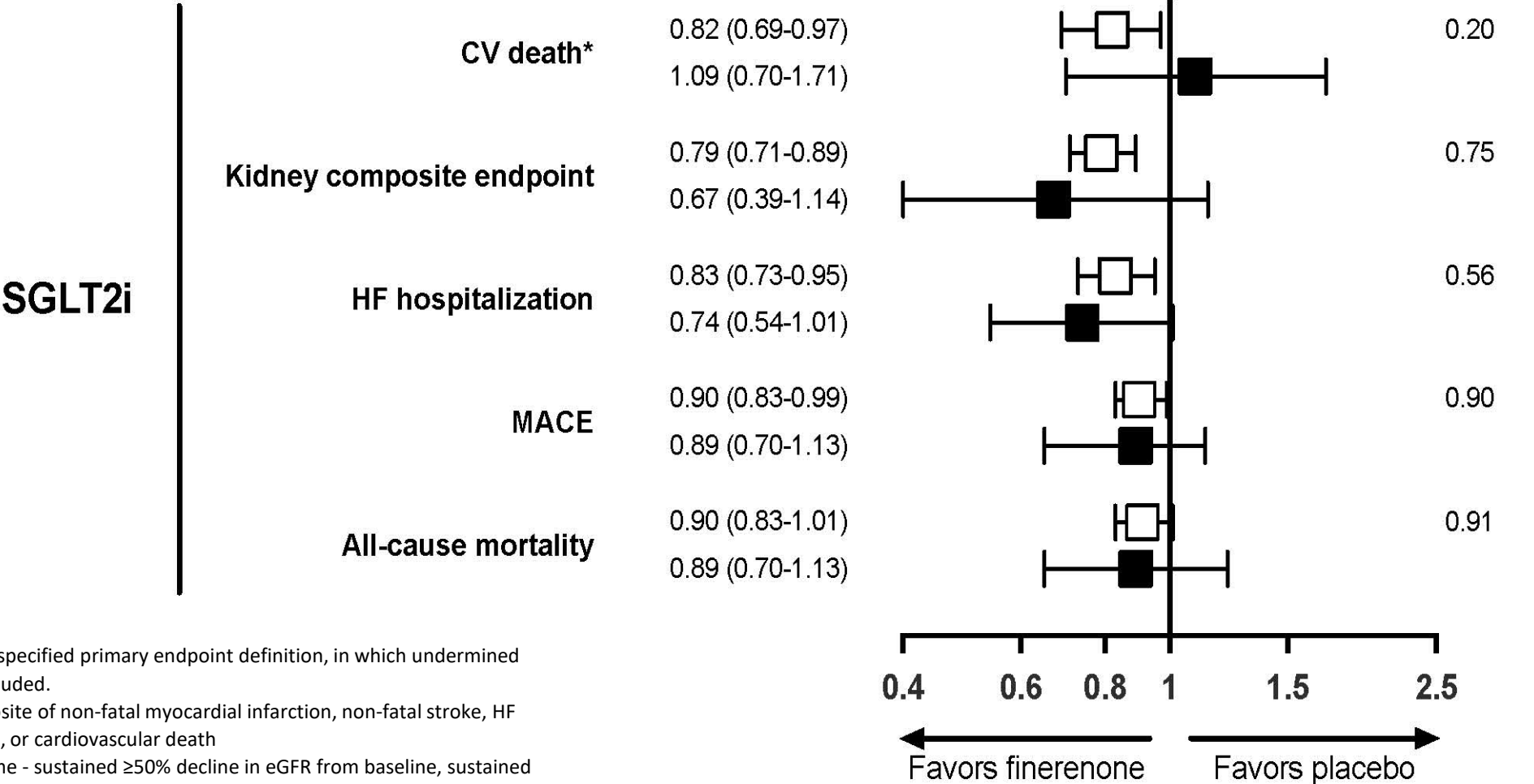
*: Reflects prespecified primary endpoint definition, in which undermined death was excluded.

MACE - composite of non-fatal myocardial infarction, non-fatal stroke, HF hospitalization, or cardiovascular death

Kidney Outcome - sustained $\geq 50\%$ decline in eGFR from baseline, sustained decrease in eGFR to < 15 mL/min/1.73m², end-stage kidney disease, and death due to kidney failure

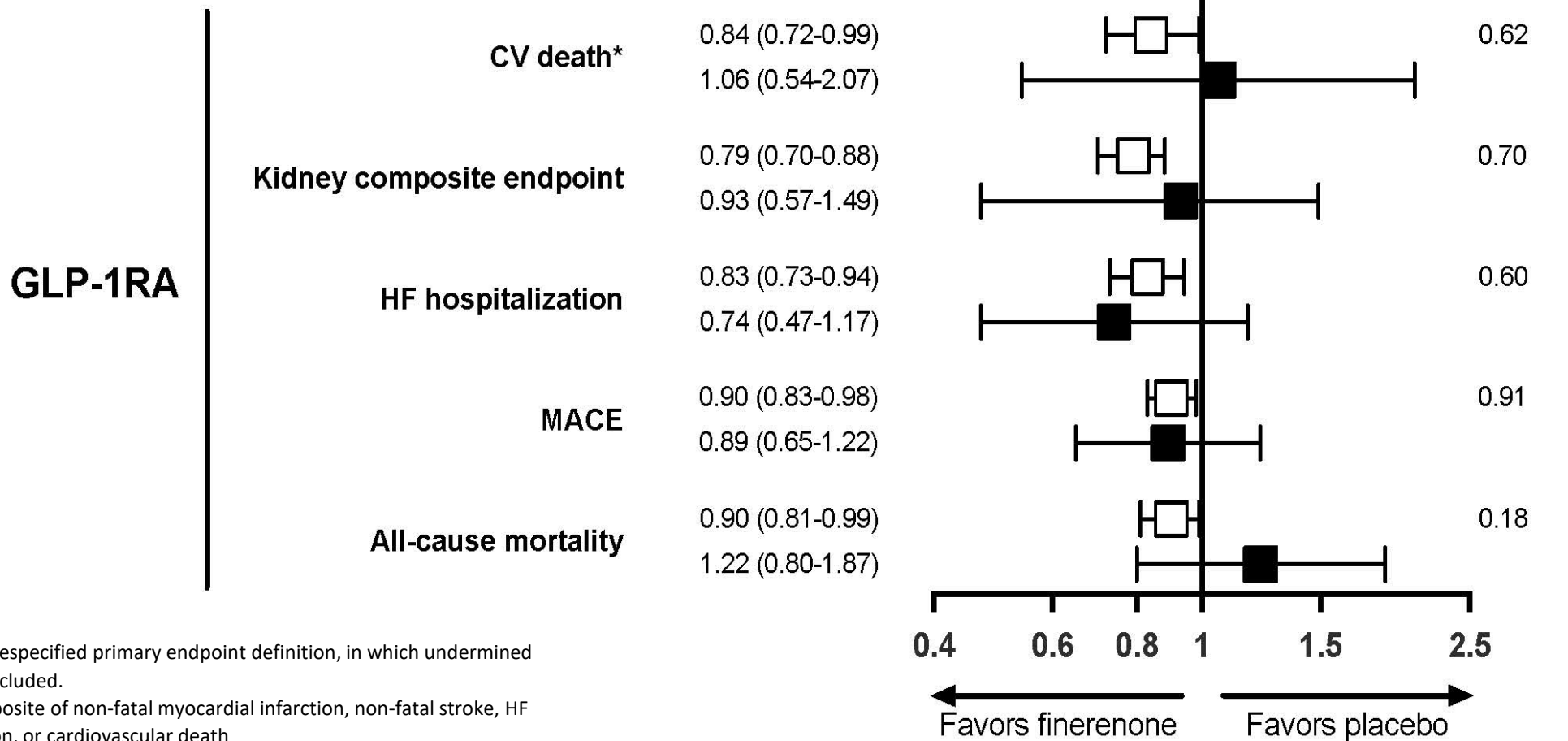
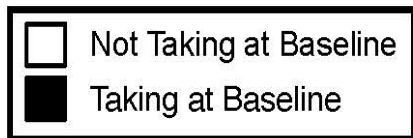
FINE-HEART: Baseline SGLT2 inhibitor use

Not Taking at Baseline
 Taking at Baseline



*: Reflects prespecified primary endpoint definition, in which undermined death was excluded.
 MACE - composite of non-fatal myocardial infarction, non-fatal stroke, HF hospitalization, or cardiovascular death
 Kidney Outcome - sustained $\geq 50\%$ decline in eGFR from baseline, sustained decrease in eGFR to < 15 mL/min/1.73m², end-stage kidney disease, and death due to kidney failure

FINE-HEART: Baseline GLP-1RA use



*: Reflects prespecified primary endpoint definition, in which undermined death was excluded.

MACE - composite of non-fatal myocardial infarction, non-fatal stroke, HF hospitalization, or cardiovascular death

Kidney Outcome - sustained $\geq 50\%$ decline in eGFR from baseline, sustained decrease in eGFR to < 15 mL/min/1.73m², end-stage kidney disease, and death due to kidney failure

FINE-HEART: Safety by baseline HbA_{1c} – Kidney and blood pressure outcomes

| | Baseline HbA _{1c} Category | | | | | |
|---|-------------------------------------|---------------------|------------------------|---------------------|------------------------|---------------------|
| | ≤6.9% | | ≥7.0% to ≤8.0% | | ≥8.1% | |
| | Finerenone (n=2739) | Placebo (n=2816) | Finerenone (n=2388) | Placebo (n=2385) | Finerenone (n=2545) | Placebo (n=2462) |
| Acute kidney injury^b | 94 (3.4 %) | 96 (3.4 %) | 90 (3.8 %) | 101 (4.2 %) | 107 (4.2 %) | 91 (3.7 %) |
| Acute kidney injury leading to treatment discontinuation | 5 (0.2 %) | 5 (0.2 %) | 4 (0.2 %) | 3 (0.1 %) | 5 (0.2 %) | 4 (0.2 %) |
| Acute kidney injury leading to hospitalization | 41 (1.5 %) | 42 (1.5 %) | 29 (1.2 %) | 41 (1.7 %) | 51 (2.0 %) | 26 (1.1 %) |
| Any systolic blood pressure <100 mm Hg | 286 (10.6%) | 147 (5.3 %) | 199 (8.4 %) | 136 (5.8 %) | 205 (8.1 %) | 133 (5.5 %) |
| Gynecomastia | 2 (0.1 %) | 1 (0.0 %) | 6 (0.3 %) | 9 (0.4 %) | 4 (0.2 %) | 6 (0.2 %) |

^b: Based on investigator-reported adverse events

1 patient with baseline HbA_{1c} ≥8.1% who was randomized to placebo but who actually received finerenone. There were no instances of death due to hyperkalemia.

FINE-HEART: Safety by baseline HbA_{1c} - Potassium

| | Baseline HbA _{1c} Category | | | | | |
|--|-------------------------------------|---------------------|------------------------|---------------------|------------------------|---------------------|
| | ≤6.9% | | ≥7.0% to ≤8.0% | | ≥8.1% | |
| | Finerenone (n=2739) | Placebo (n=2816) | Finerenone (n=2388) | Placebo (n=2385) | Finerenone (n=2545) | Placebo (n=2462) |
| Any potassium >5.5 mmol/L^a | 468 (17.3%) | 187 (6.7 %) | 407 (17.3%) | 190 (8.1 %) | 454 (18.1%) | 230 (9.5 %) |
| Any potassium >6.0 mmol/L^a | 103 (3.8 %) | 32 (1.2 %) | 76 (3.2 %) | 33 (1.4 %) | 92 (3.7 %) | 44 (1.8 %) |
| Any potassium <3.5 mmol/L^a | 129 (4.8 %) | 303 (10.9%) | 107 (4.5 %) | 238 (10.1%) | 121 (4.8 %) | 224 (9.2 %) |
| Hyperkalemia^b | 382 (13.9%) | 193 (6.9 %) | 334 (14.0%) | 162 (6.8 %) | 357 (14.0%) | 177 (7.2 %) |
| Hyperkalemia leading to treatment discontinuation^b | 48 (1.8 %) | 18 (0.6 %) | 27 (1.1 %) | 13 (0.5 %) | 43 (1.7 %) | 10 (0.4 %) |
| Hyperkalemia leading to hospitalization^b | 30 (1.1 %) | 4 (0.1 %) | 16 (0.7 %) | 4 (0.2 %) | 24 (0.9 %) | 8 (0.3 %) |

^a: Based on central laboratory measurements of potassium levels, ^b: Based on investigator-reported adverse events

1 patient with baseline HbA_{1c} ≥8.1% who was randomized to placebo but who actually received finerenone. There were no instances of death due to hyperkalemia.

FINE-HEART: Summary and conclusions

- In the FINE-HEART trials, including participants with investigator-reported T2DM and either CKD or HFmrEF/HFpEF, finerenone reduced kidney disease progression, HF hospitalisation, major adverse cardiovascular events, and all-cause mortality in patients with T2D
- The benefits were consistent across baseline HbA1c levels, number and categories of baseline glucose lowering therapies and regardless of SGLT2 inhibitor or GLP-1RA use
- Hyperkalaemia was more common, and hypokalaemia less common, in those randomised to finerenone (compared to placebo) but this was not different in any of the subgroups above
- Finerenone reduces the risk of a broad range of outcomes in patients with type 2 diabetes mellitus who also have chronic kidney disease or HFmrEF/HFpEF