

Table 1. Frequency of primary outcome, composite safety outcome and their components by treatment group

| Outcome | Standard (n=4683) | | Intensive (n=4678) | | % difference in annual event rate (95% CI) | Hazard ratio (95% CI) | P-value |
|---------------------------------|----------------------|-----------------------------|-----------------------|-----------------------------|---|-----------------------|---------|
| | N event | Annual event rate (%) | N event | Annual event rate (%) | | | |
| Primary outcome | 319 | 2.2% | 243 | 1.7% | -0.5 (-0.9 to -0.2) | 0.75 (0.64 to 0.89) | 0.0009 |
| Myocardial infarction | 116 | 0.8% | 97 | 0.7% | -0.1 (-0.3 to 0.1) | 0.83 (0.63 to 1.09) | 0.18 |
| Acute coronary syndrome | 40 | 0.3% | 40 | 0.3% | -0.0 (-0.1 to 0.1) | 1.00 (0.64 to 1.55) | 0.99 |
| Stroke | 69 | 0.5% | 60 | 0.4% | -0.1 (-0.2 to 0.1) | 0.87 (0.61 to 1.22) | 0.41 |
| Heart Failure | 98 | 0.7% | 61 | 0.4% | -0.3 (-0.4 to -0.1) | 0.62 (0.45 to 0.85) | 0.0032 |
| Cardiovascular death | 58 | 0.4% | 35 | 0.2% | -0.2 (-0.3 to -0.0) | 0.60 (0.40 to 0.92) | 0.018 |
| Composite safety outcome | 406 | 2.9% | 521 | 3.8% | 0.9 (0.4 to 1.3) | 1.30 (1.14 to 1.48) | 0.0001 |
| Hypotension | 66 | 0.5% | 110 | 0.8% | 0.3 (0.1 to 0.5) | 1.67 (1.23 to 2.26) | 0.0010 |
| Syncope | 80 | 0.6% | 107 | 0.7% | 0.2 (0.0 to 0.4) | 1.34 (1.00 to 1.79) | 0.050 |
| Bradycardia | 73 | 0.5% | 87 | 0.6% | 0.1 (-0.1 to 0.3) | 1.19 (0.87 to 1.62) | 0.28 |
| Electrolyte abnormality | 107 | 0.7% | 144 | 1.0% | 0.3 (0.0 to 0.5) | 1.35 (1.05 to 1.73) | 0.020 |
| Injurious fall | 110 | 0.8% | 105 | 0.7% | -0.0 (-0.2 to 0.2) | 0.95 (0.73 to 1.24) | 0.71 |
| Acute kidney injury or failure | 117 | 0.8% | 193 | 1.3% | 0.5 (0.3 to 0.8) | 1.66 (1.32 to 2.08) | <0.0001 |

Legend: Acute kidney injury or failure is defined by and estimated glomerular filtration rate (eGFR) drop superior to 30% relative to the baseline value or eGFR below 60 ml/min/1.73m² if the patient did not have chronic kidney disease or eGFR drop superior to 50% relative to the baseline value or end-stage renal disease if the patient had chronic kidney disease defined as baseline eGFR below 60 ml/min/1.73m².

Table 2. Risk ratios for covariates selected for the risk prediction models

| Characteristic | Primary outcome | | Composite safety outcome | |
|--|---------------------|---------|--------------------------|---------|
| | Risk ratio (95% CI) | P-value | Risk ratio (95% CI) | P-value |
| Intensive therapy | 0.74 (0.62 to 0.88) | 0.0005 | 1.29 (1.13 to 1.47) | 0.0002 |
| Age (per 5 years higher) | 1.24 (1.18 to 1.31) | <0.0001 | 1.25 (1.20 to 1.30) | <0.0001 |
| <i>Log</i> albumin creatinine ratio (per doubling) | 1.19 (1.14 to 1.24) | <0.0001 | 1.15 (1.11 to 1.19) | <0.0001 |
| Sub-clinical cardiovascular disease | 2.16 (1.81 to 2.59) | <0.0001 | 1.42 (1.21 to 1.66) | <0.0001 |
| Number of anti-hypertensive agents | 1.12 (1.03 to 1.21) | 0.0099 | 1.14 (1.07 to 1.22) | 0.0001 |
| Current smoker | 1.81 (1.41 to 2.31) | <0.0001 | 1.59 (1.30 to 1.95) | <0.0001 |
| <i>Log</i> serum creatinine (per doubling) | 1.29 (1.05 to 1.57) | 0.013 | 1.28 (1.01 to 1.64) | 0.041 |
| <i>Log</i> triglycerides (per doubling) | 1.25 (1.11 to 1.41) | 0.0002 | | |
| Chronic kidney disease | | | 1.30 (1.05 to 1.60) | 0.014 |
| Female sex | | | 1.17 (1.00 to 1.36) | 0.055 |