Appendix 4. Simulated clinical events by study arm.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Arm1 | | Arm2 | | Arm3 | | Arm4 | | Arm5 | | Arm6 | | Arm7 | | Arm8 | |
| Treatment | MET | | MET | | MET | | MET | | MET | | MET | | MET | | MET | |
| 2nd line | +SGLT-2-i | | +SGLT-2-i | | +DPP-4-i | | +DPP-4-i | | +GLP-1-RA | | +SU | | +SU | | +INS | |
| 3rd line | +SU | | +DPP-4-i | | +SU | | +SGLT-2-i | | +SU | | +DPP-4-i | | +SGLT-2-i | | +SU | |
| INS line | MET+INS | | MET+INS | | MET+INS | | MET+INS | | MET+INS | | MET+INS | | MET+INS | | MET+INS | |
| Macrovascular | Non-Fatal | Fatal | Non-Fatal | Fatal | Non-Fatal | Fatal | Non-Fatal | Fatal | Non-Fatal | Fatal | Non-Fatal | Fatal | Non-Fatal | Fatal | Non-Fatal | Fatal |
| IHD | 103.20 | 0.00 | 103.43 | 0.00 | 103.93 | 0.00 | 103.90 | 0.00 | 102.85 | 0.00 | 103.90 | 0.00 | 103.71 | 0.00 | 103.25 | 0.00 |
| MI | 112.38 | 144.67 | 112.39 | 145.33 | 113.07 | 145.95 | 113.07 | 145.93 | 112.34 | 143.77 | 113.32 | 145.83 | 113.31 | 145.16 | 113.07 | 144.20 |
| CHF | 75.32 | 7.84 | 75.58 | 7.88 | 76.09 | 7.89 | 76.07 | 7.89 | 75.06 | 7.78 | 75.95 | 7.88 | 75.64 | 7.85 | 75.28 | 7.79 |
| Stroke | 61.79 | 17.31 | 61.82 | 17.39 | 62.61 | 17.56 | 62.58 | 17.55 | 61.77 | 17.25 | 62.79 | 17.53 | 62.74 | 17.43 | 62.60 | 17.37 |
| Microvascular |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Blindness | 54.94 | 0.00 | 55.30 | 0.00 | 55.41 | 0.00 | 55.39 | 0.00 | 54.34 | 0.00 | 55.11 | 0.00 | 54.78 | 0.00 | 54.18 | 0.00 |
| Nephropathy | 22.15 | 2.36 | 22.12 | 2.35 | 22.40 | 2.38 | 22.40 | 2.38 | 22.26 | 2.35 | 22.51 | 2.38 | 22.53 | 2.38 | 22.56 | 2.36 |
| Amputation | 30.94 | 3.32 | 31.24 | 3.38 | 31.67 | 3.41 | 31.65 | 3.40 | 30.50 | 3.27 | 31.46 | 3.39 | 31.15 | 3.32 | 30.66 | 3.29 |
| Fatal Events |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Macrovascular |  | 169.82 |  | 170.59 |  | 171.40 |  | 171.37 |  | 168.80 |  | 171.23 |  | 170.43 |  | 169.36 |
| Microvascular |  | 5.67 |  | 5.73 |  | 5.79 |  | 5.78 |  | 5.62 |  | 5.77 |  | 5.69 |  | 5.65 |
| Other |  | 824.50 |  | 823.68 |  | 822.81 |  | 822.85 |  | 825.58 |  | 823.00 |  | 823.87 |  | 824.99 |

IHD: ischaemic heart disease; MI: myocardial infarction; CHF: congestive heart failure