SUPPLEMENTARY DATA

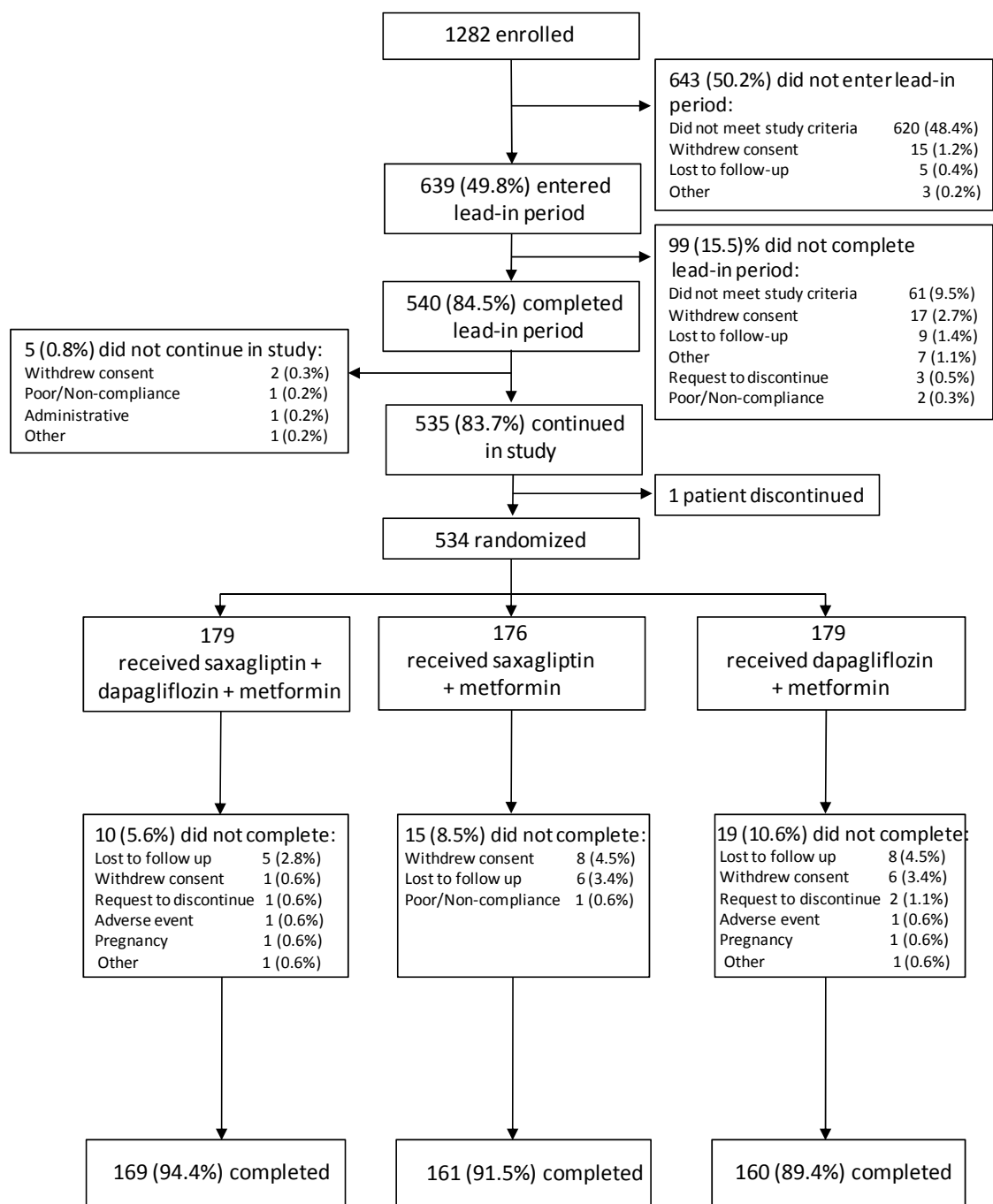**Supplementary Text.**

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**Supplementary Figure 1.** Patient disposition

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**Supplementary Table 1.** Adjusted Mean Change From Baseline at 24 Weeks in HbA1c Stratified by Baseline HbA1c Subgroup

| Baseline HbA1c subgroup | SAXA+DAPA+MET n=179 | SAXA+MET n=176 | DAPA+MET n=179 |
|---|---|---|---|
| <8% (<64 mmol/mol) | | | |
| Baseline mean (SD), % [mmol/mol] | 7.50 (0.40) [58 (4.4)] | 7.61 (0.31) [60 (3.4)] | 7.41 (0.44) [57 (4.8)] |
| n* | 37 | 29 | 37 |
| Adjusted mean change from baseline (95% CI), % [mmol/mol] | −0.80 (−1.12, −0.47) [−9 (−12.2, −5.1)] | −0.69 (−1.06, −0.33) [−8 (−11.6, −3.6)] | −0.45 (−0.77, −0.13) [−5 (−8.4, −1.4)] |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | −0.10 (−0.60, 0.39) [−1 (−6.6, 4.3] | −0.35 (−0.81, 0.11) [−4 (−8.9, 1.2)] |
| ≥8% to <9% (≥64 to <75 mmol/mol) | | | |
| Baseline mean (SD), % [mmol/mol] | 8.44 (0.26) [69 (2.8)] | 8.54 (0.29) [70 (3.2)] | 8.49 (0.28) [69 (3.1)] |
| n* | 56 | 51 | 52 |
| Adjusted mean change from baseline (95% CI), % [mmol/mol] | −1.17 (−1.44, −0.90) [−13 (−15.7, −9.8)] | −0.51 (−0.78, −0.25) [−6 (−8.5, −2.7)] | −0.84 (−1.11, −0.57) [−9 (−12.1, −6.2)] |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | −0.66 (−1.03, −0.28) [−7 (−11.3, −3.1)] | −0.33 (−0.71, 0.05) [−4 (−7.8, 0.5)] |
| ≥9% (≥75 mmol/mol) | | | |
| Baseline mean (SD), % [mmol/mol] | 10.02 (0.78) [86 (8.5)] | 9.90 (0.75) [85 (8.2)] | 9.95 (0.78) [85 (8.5)] |
| n* | 65 | 63 | 62 |
| Adjusted mean change from baseline (95% CI), % [mmol/mol] | −2.03 (−2.27, −1.80) [−22 (−24.8, −19.7)] | −1.32 (−1.56, −1.09) [−14 (−17.1, −11.9)] | −1.87 (−2.11, −1.63) [−20 (−23.1, −17.8)] |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | −0.71 (−1.04, −0.38) [−8 (−11.4, −4.2)] | −0.16 (−0.50, 0.17) [−2 (−5.5, 1.9)] |

*Number of randomized patients with non-missing baseline values and week 24 value.

**Supplementary Table 2.** Adjusted Mean Change From Baseline at 24 Weeks in HbA1c Stratified by Age

| Age subgroup, y | SAXA+DAPA+MET n=179 | SAXA+MET n=176 | DAPA+MET n=179 |
|---|---|---|---|
| <65 | | | |
| Baseline mean (SD), % [mmol/mol] | 8.98 (1.21) [75 (13.2)] | 9.04 (1.10) [75 (12.0)] | 8.90 (1.18) [74 (12.9)] |
| n* | 140 | 118 | 133 |
| Adjusted mean change from baseline (95% CI), % [mmol/mol] | −1.47 (−1.64, −1.31) [−16 (−17.9, −14.3)] | −0.85 (−1.02, −0.67) [−9 (−11.1, −7.3)] | −1.22 (−1.38, −1.05) [−13 (−15.1, −11.5)] |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | −0.63 (−0.86, −0.39) [−7 (−9.4, −4.3)] | −0.26 (−0.49, −0.02) [−3 (−5.4, −0.2)] |
| ≥65 | | | |
| Baseline mean (SD), % [mmol/mol] | 8.50 (0.88) [69 (9.6)] | 8.99 (0.79) [75 (8.6)] | 8.64 (1.09) [71 (11.9)] |
| n* | 18 | 25 | 18 |
| Adjusted mean change from baseline (95% CI), % [mmol/mol] | −1.40 (−1.87, −0.94) [−15 (−20.4, −10.3)] | −1.04 (−1.42, −0.66) [−11 (−15.5, −7.2)] | −1.05 (−1.51, −0.60) [−12 (−16.5, −6.6)] |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | −0.37 (−0.97, 0.24) [−4 (−10.6, 2.6)] | −0.35 (−1.00, 0.30) [−4 (−10.9, 3.3)] |

*Number of randomized patients with non-missing baseline values and week 24 value.

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**Supplementary Table 3.** Proportion of Patients Achieving HbA1c <7% at Week 24 by Baseline HbA1c Subgroup

| Baseline HbA1c subgroup | SAXA+DAPA+MET n=179 | SAXA+MET n=176 | DAPA+MET n=179 |
|---|---|---|---|
| <8% (64 mmol/mol) | | | |
| Baseline mean (SD), % [mmol/mol] | 7.50 (0.40) [58 (4.4)] | 7.61 (0.31) [60 (3.4)] | 7.41 (0.44) [57 (4.8)] |
| X/n* | 26/40 | 16/30 | 18/40 |
| Proportion (95% CI) adjusted for baseline HbA1c , % | 65 (50.6, 79.7) | 58 (40.4, 75.5) | 42 (27.1, 57.0) |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | 7 (–15.3, 29.4) | 23 (2.4, 43.7) |
| ≥8% to <9% (≥64 to 5 mmol/mol) | | | |
| Baseline mean (SD), % [mmol/mol] | 8.44 (0.26) [69 (2.8)] | 8.54 (0.29) [70 (3.2)] | 8.49 (0.28) [69 (3.1)] |
| X/n* | 30/58 | 6/61 | 11/58 |
| Proportion (95% CI) adjusted for baseline HbA1c , % | 50 (37.0, 62.4) | 11 (3.0, 17.9) | 19 (8.9, 29.1) |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | 39 (24.5, 53.9) | 31 (14.5, 46.9) |
| ≥9% (≥75 mmol/mol) | | | |
| Baseline mean (SD), % [mmol/mol] | 10.02 (0.78) [86 (8.5)] | 9.90 (0.75) [85 (8.2)] | 9.95 (0.78) [85 (8.5)] |
| X/n* | 18/79 | 7/84 | 11/75 |
| Proportion (95% CI) adjusted for baseline HbA1c , % | 24 (14.3, 32.6) | 9 (2.6, 14.4) | 15 (6.6, 22.6) |
| Mean (95% CI) difference vs SAXA+DAPA+MET | | 15 (4.1, 25.8) | 9 (–3.2, 21.0) |

*X=number of responders, n= number of randomized patients with non-missing baseline and week 24 last observation carried forward values.

**Supplementary Table 4.** Change from baseline at 24 weeks for seated blood pressure and serum fasting lipids.

| | SAXA+DAPA+MET n=179 | SAXA+MET n=176 | DAPA+MET n=179 |
|---|---|---|---|
| **Systolic blood pressure, mm Hg** | | | |
| n[a] | 179 | 176 | 179 |
| Baseline mean±SD | 129±12.2 | 128±12.5 | 130±14.1 |
| n[b] | 167 | 160 | 157 |
| Change from baseline mean±SD | −1.9±12.0 | 0.3±10.2 | −3.5±12.9 |
| **Diastolic blood pressure, mm Hg** | | | |
| n[a] | 179 | 176 | 179 |
| Baseline mean±SD | 78±8.5 | 78±7.8 | 79±8.1 |
| n[b] | 167 | 160 | 157 |
| Change from baseline mean±SD | −1.0±8.0 | −0.4±7.0 | −1.4±8.4 |
| **Total cholesterol, mg/dL** | | | |
| n[b] | 164 | 159 | 155 |
| Baseline mean±SD | 188±41 | 193±47 | 182±36 |
| Adjusted mean percent change from baseline (95% CI), % | 0.4 (−1.8, 2.7) | −1.9 (−4.2, 0.3) | 3.8 (1.5, 6.3) |
| Difference (95% CI) vs saxagliptin + metformin,% | 2.4 (−0.8, 5.7) $P$=0.15 | | |
| Difference (95% CI) vs dapagliflozin + metformin,% | −3.3 (−6.4, −0.2) $P$=0.04 | | |
| **LDL cholesterol, mg/dL** | | | |
| n[b] | 161 | 158 | 153 |
| Baseline mean±SD | 102±36 | 103±35 | 98±30 |
| Adjusted mean percent change from baseline (95% CI),% | 3.7 (−0.9, 8.6) | −0.6 (−5.1, 4.1) | 1.5 (−3.1, 6.4) |
| Difference (95% CI) vs saxagliptin + metformin,% | 4.3 (−2.2, 11.4) $P$=0.20 | | |
| Difference (95% CI) vs dapagliflozin + metformin,% | 2.2 (−4.3, 9.1) $P$=0.52 | | |
| **HDL cholesterol, mg/dL** | | | |
| n[b] | 164 | 159 | 155 |
| Baseline mean±SD | 45±11 | 45±11 | 43±10 |

| | | | |
|---|---|---|---|
| Adjusted mean percent change from baseline (95% CI) ,% | 5.4 (3.0, 7.8) | 0.9 (–1.4, 3.3) | 7.7 (5.2, 10.2) |
| Difference (95% CI) vs saxagliptin + metformin,% | 4.4 (1.1, 7.8)<br>$P$=0.009 | | |
| Difference (95% CI) vs dapagliflozin + metformin,% | –2.1 (–5.3, 1.1)<br>$P$=0.19 | | |
| Triglycerides, mg/dL<br>n[b]<br>Baseline mean±SD<br>Adjusted mean percent change from baseline (95% CI),% | 163<br>221±194<br>–10.8 (–16.0, –5.4) | 159<br>248±302<br>–3.7 (–9.4, 2.2) | 155<br>216±166<br>–2.5 (–8.3, 3.6) |
| Difference (95% CI) vs saxagliptin + metformin,% | –7.4 (–14.9, 0.8)<br>$P$=0.08 | | |
| Difference (95% CI) vs dapagliflozin + metformin,% | –8.5 (–15.9, –0.4)<br>$P$=0.04 | | |

[a]Number of randomized patients with non-missing baseline values and at least one post-baseline value.

[b]Number of randomized patients with non-missing baseline values and week 24 values.

DAPA=dapagliflozin; HDL=high density lipoprotein; LDL=low density lipoprotein. MET=metformin; SAXA=saxagliptin.