

SUPPLEMENTARY DATA

**Supplementary Table S1. Mean Percent Changes in Clinical Laboratory Parameters at Week 26**

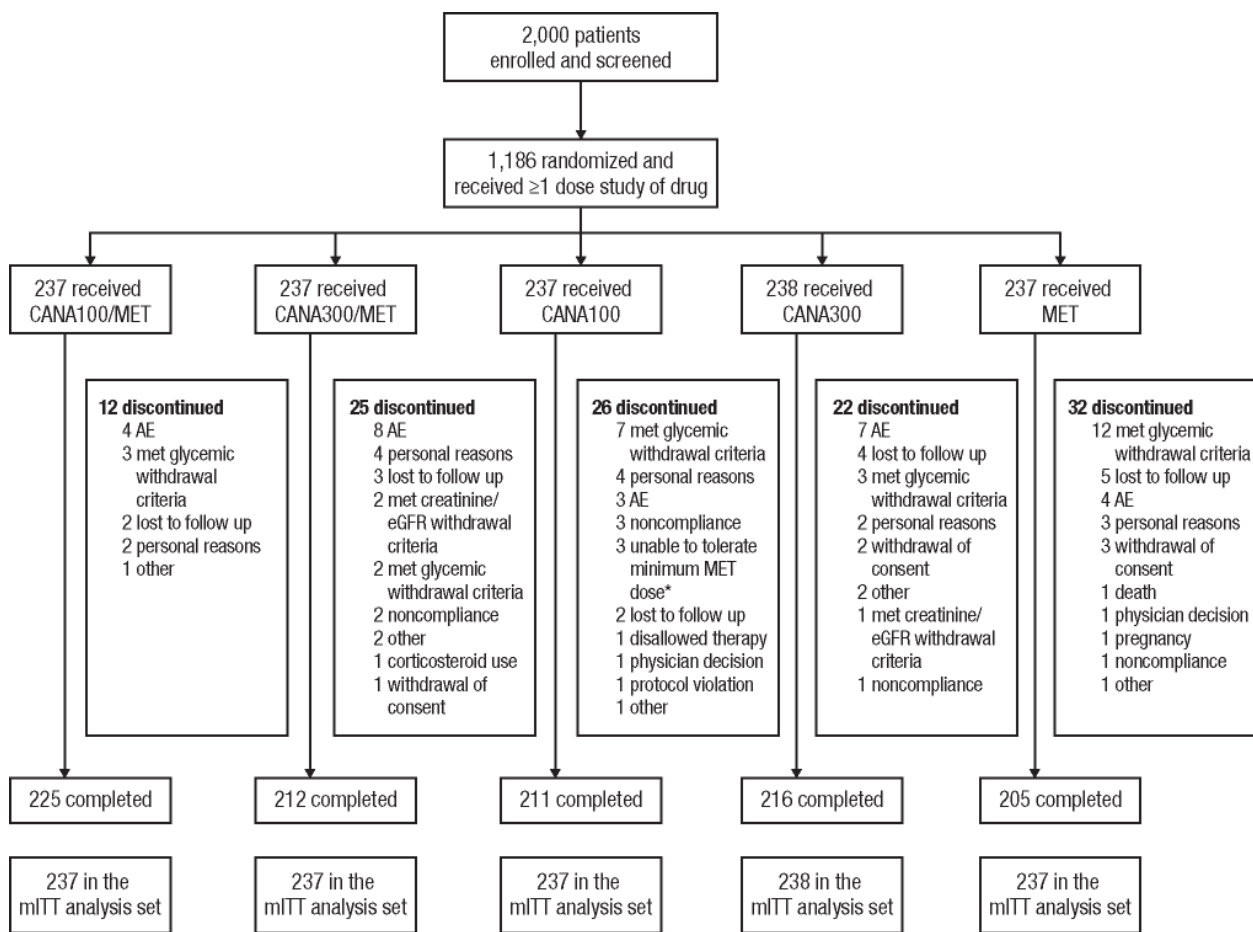
| <b>Parameter</b>                          | <b>CANA100/MET</b> | <b>CANA300/MET</b> | <b>CANA100</b>   | <b>CANA300</b>   | <b>MET</b>      |
|---|--------------------|--------------------|------------------|------------------|-----------------|
| ALT, n                                    | 214                | 205                | 196              | 204              | 195             |
| Mean baseline, U/L                        | 30.0               | 29.5               | 31.9             | 28.0             | 27.1            |
| Mean $\pm$ SD percent change              | $-16.9 \pm 33.8$   | $-13.5 \pm 52.7$   | $-16.1 \pm 40.5$ | $-12.9 \pm 49.0$ | $-0.4 \pm 57.8$ |
| Bilirubin, n                              | 215                | 204                | 196              | 204              | 195             |
| Mean baseline, $\mu\text{mol/L}$          | 9.4                | 9.9                | 10.0             | 9.6              | 9.6             |
| Mean $\pm$ SD percent change              | $0.1 \pm 36.4$     | $1.4 \pm 35.8$     | $8.4 \pm 48.9$   | $9.4 \pm 45.1$   | $4.2 \pm 45.3$  |
| BUN, n                                    | 217                | 205                | 197              | 205              | 197             |
| Mean baseline, mmol/L                     | 5.2                | 5.3                | 5.2              | 5.5              | 5.4             |
| Mean $\pm$ SD percent change              | $16.0 \pm 42.5$    | $12.2 \pm 30.3$    | $13.0 \pm 30.9$  | $12.1 \pm 35.8$  | $0.7 \pm 26.3$  |
| Creatinine, n                             | 217                | 204                | 197              | 206              | 197             |
| Mean baseline, $\mu\text{mol/L}$          | 72.9               | 73.2               | 70.9             | 75.2             | 73.1            |
| Mean $\pm$ SD percent change              | $0.4 \pm 28.7$     | $-0.4 \pm 12.5$    | $1.0 \pm 12.9$   | $1.5 \pm 12.6$   | $-1.2 \pm 18.0$ |
| eGFR, n                                   | 217                | 204                | 197              | 206              | 197             |
| Mean baseline, mL/min/1.73 m <sup>2</sup> | 88                 | 87                 | 90               | 85               | 86              |

SUPPLEMENTARY DATA

|                          |             |             |             |             |             |
|--------------------------|-------------|-------------|-------------|-------------|-------------|
| Mean ± SD percent change | 4.0 ± 20.3  | 2.4 ± 15.7  | 0.5 ± 13.8  | 0.0 ± 14.2  | 4.6 ± 19.7  |
| Urate, n                 | 217         | 205         | 197         | 206         | 197         |
| Mean baseline, μmol/L    | 303.4       | 300.5       | 296.6       | 312.7       | 304.8       |
| Mean ± SD percent change | -2.2 ± 22.9 | -3.1 ± 31.4 | -4.2 ± 27.7 | -6.7 ± 19.8 | 12.0 ± 24.4 |
| Hemoglobin, n            | 215         | 206         | 192         | 201         | 194         |
| Mean baseline, g/L       | 144.7       | 144.8       | 144.4       | 144.6       | 144.7       |
| Mean ± SD percent change | 1.6 ± 7.3   | 2.9 ± 6.9   | 4.4 ± 7.1   | 4.2 ± 11.2  | -1.5 ± 6.3  |

ALT, alanine aminotransferase; BUN, blood urea nitrogen; CANA100, canagliflozin 100 mg; CANA300, canagliflozin 300 mg; eGFR, estimated glomerular filtration rate; MET, metformin extended-release; PBO, placebo; SD, standard deviation.

**Supplementary Figure S1. Study flow diagram.**

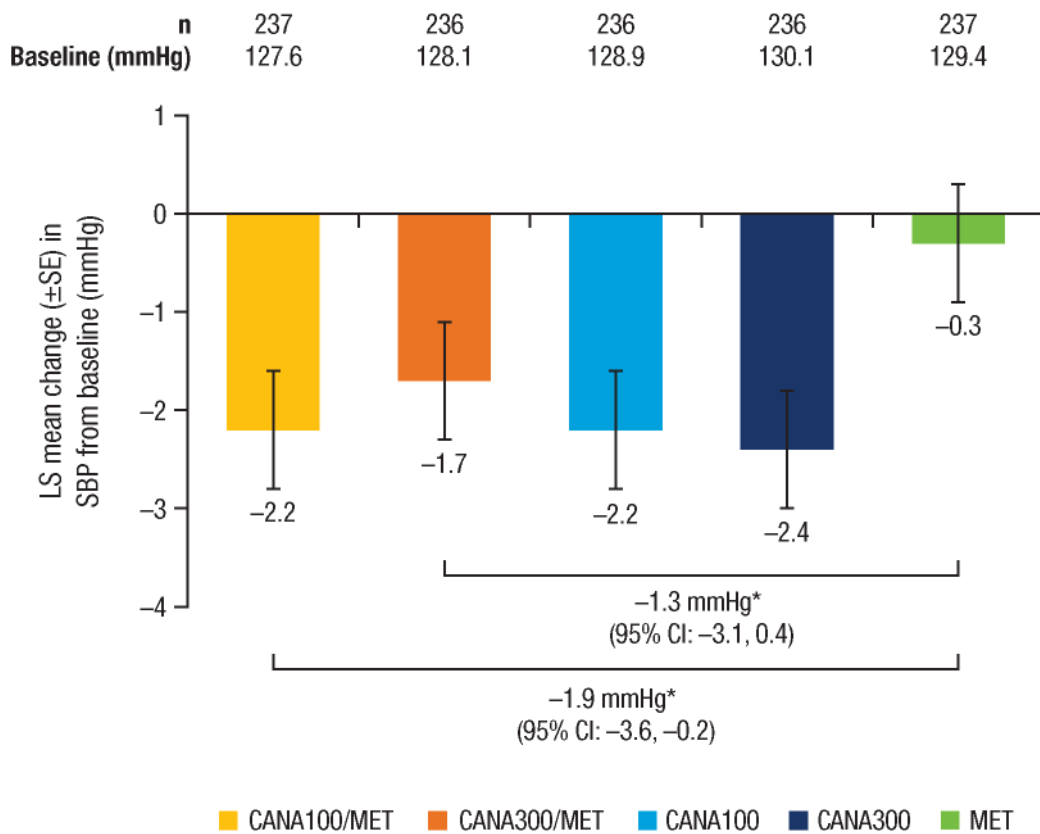


AE, adverse event; CANA100, canagliflozin 100 mg; CANA300, canagliflozin 300 mg; eGFR, estimated glomerular filtration rate; mITT, modified intent-to-treat; MET, metformin extended-release; PBO, placebo.

\*A double-dummy design was used in this study such that patients assigned to the CANA monotherapy groups received PBO matching MET, and patients assigned to MET monotherapy received PBO matching CANA.

SUPPLEMENTARY DATA

**Supplementary Figure S2. Change from baseline in SBP at week 26.**

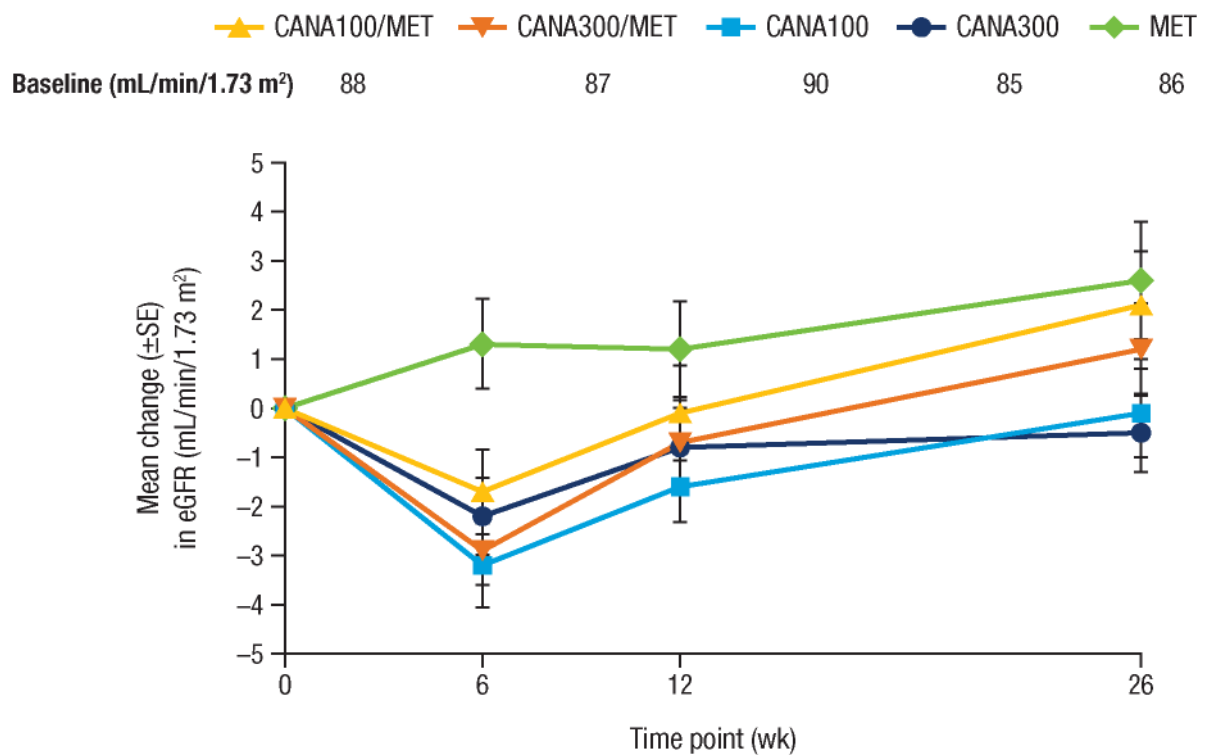


CANA100, canagliflozin 100 mg; CANA300, canagliflozin 300 mg; CI, confidence interval; LS, least squares; MET, metformin extended-release; NS, not significant; SBP, systolic blood pressure; SE, standard error.

\**P* = NS vs. MET.

SUPPLEMENTARY DATA

Supplementary Figure S3. Mean eGFR over time.



CANA100, canagliflozin 100 mg; CANA300, canagliflozin 300 mg; eGFR, estimated glomerular filtration rate; MET, metformin extended-release; SE, standard error.