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SUPPLEMENTARY INFORMATION

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# Verapamil and beta cell function in adults with recent-onset type 1 diabetes

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**Supplemental Table 1:**

**Baseline Participant Characteristics***

| | | **Verapamil** (*n* = 11) | **Placebo** (*n* = 13) |
|---|---|---|---|
| **Sex** | Male | 6 (55) | 8 (62) |
| | Female | 5 (45) | 5 (38) |
| **Race** | White | 10 (91) | 13 (100) |
| | African American | 1 (9) | |
| **Age** (years) | | 32.3 ±2.3 | 28.3 ±2.1 |
| **Weight** (kg) | | 74.3 ±4.1 | 70.2 ±3.6 |
| **Body Mass Index** (kg/m$^2$) | | 24.4 ±0.8 | 22.1 ±0.7 |
| **Fasting Plasma Glucose** (mmol/L) | | 6.4 ±1.0 | 6.9 ±1.0 |
| **HbA1C** (%) | | 6.6 ±0.4 | 6.8 ±0.3 |
| **Blood Pressure** | (systolic, mmHg) | 114 ±3 | 110 ±2 |
| | (diastolic, mmHg) | 74 ±3 | 71 ±1 |
| **Heart Rate** (beats/min) | | 75 ±5 | 70 ±2 |
| **Creatinine** (µmol/L) | | 72 ±4 | 72 ±4 |
| **eGFR** (mL/min/1.73m$^2$) | | 116 ±5 | 110 ±4 |
| **ALT** (units/L) | | 29 ±8 | 21 ±1 |
| **AST** (units/L) | | 23 ±4 | 21 ±1 |

** Values represent number of patients (percent) or means ±SE; none were significantly different between the treatment groups. eGFR: glomerular filtration rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase*

**Supplemental Table 2:**

**Sensitivity Analysis: Estimated treatment differences in stimulated C-peptide AUC (verapamil vs placebo)**

| Outcome | Complete case analysis (non-missing values only)* | | | Analysis after multiple imputation# | | |
|---|---|---|---|---|---|---|
| | Treatment difference | 95% CI | *P* | Treatment difference | 95% CI | *P* |
| AUC 3 months (nmol/L) | 0.31 | 0.04-0.58 | 0.0270 | 0.32 | 0.07-0.57 | 0.0120 |
| AUC 12 months (nmol/L) | 0.28 | 0.05-0.51 | 0.0186 | 0.30 | 0.08-0.53 | 0.0088 |
| Change in AUC 3 months (%) | 29.0 | 0.1-57.9 | 0.0491 | 28.5 | 0.6-56.5 | 0.0457 |
| Change in AUC 12 months (%) | 35.4 | 0.8-69.9 | 0.0451 | 37.9 | 4.4-71.4 | 0.0267 |

***** *Verapamil n = 11, Placebo n = 13, two-sided Student's t-tests.* # *Verapamil n = 13, Placebo n = 13; overall estimate of treatment effect and 95%CI were obtained by combining the treatment effect and standard error from each imputed dataset with Rubin's combining rules; and the P values were calculated from two-sided Student's t-tests using overall estimate of treatment effect and combined standard error. (Rubin DB. Multiple imputation for nonresponse in surveys. New York: Wiley, 1987).*

**Supplemental Table 3:**

**Summary of Adverse Events**

| **Event** | **Verapamil** (*n* = 11) | **Placebo** (*n* = 13) |
|---|---|---|
| | *Number of patients (percent)* | |
| **Adverse event leading to treatment discontinuation** | 0 | 0 |
| **Adverse event leading to dose interruption** | 0 | 0 |
| **Adverse event leading to dose reduction** | 0 | 0 |
| **Severe hypoglycemia** (requiring assistance of another person) | 0 | 0 |
| **Constipation** | 5 (45) | 1 (8) |
| **Dizziness** | 1 (9) | 0 |
| **Nausea** | 1 (9) | 0 |
| **Headache** | 0 | 1 (8) |
| **ALT increased** | 0 | 0 |
| **AST increased** | 0 | 0 |

*ALT: alanine aminotransferase; AST: aspartate aminotransferase*

**Supplemental Table 4:**

**Individual Diagnostic Factors**

| Subject | Symptoms | | | | HG* (>11.1mmol/L) | HbA1C* (>6.5%) | C-peptide (nmol/L) | GAD65 (& other autoantibodies) |
|---|---|---|---|---|---|---|---|---|
| | F | PU | PD | WL | | | | |
| **1** | + | | | | 13.7 | 14.0 | 0.2 | + |
| **2** | | + | + | + | 19.7 | 14.0 | 0.2 | + |
| **3** | + | + | + | + | 14.4 | 10.2 | 0.2 | + |
| **4** | + | + | + | + | 21.6 | 7.1 | 0.2 | + |
| **5** | + | | | | 16.9 | 7.9 | 0.4 | + (ICA) |
| **6** | + | | | | 15.9 | 12.9 | 0.6 | + (IA-2) |
| **7** | + | | | | 14.4 | 7.4 | 0.3 | ICA, MIAA |
| **8** | + | + | + | + | 14.2 | 15.0 | 0.2 | + (IA-2) |
| **9** | + | | | + | 17.0 | 7.1 | 0.6 | + |
| **10** | + | | | | 16.1 | 13.1 | 0.2 | + |
| **11** | + | | | | 15.6 | 6.8 | 0.5 | + (ICA) |
| **12** | + | + | + | + | 10.8 | 12.7 | 0.3 | + |
| **13** | + | + | + | | 14.9 | 7.3 | 0.4 | + (ICA) |
| **14** | | | | + | 19.0 | 14.0 | 0.3 | + (ICA, ZnT8) |
| **15** | + | + | + | + | 20.3 | 8.1 | 0.2 | + |
| **16** | | + | | + | 16.3 | 10.4 | 0.2 | + |
| **17** | + | + | + | + | 16.8 | 12.8 | 0.3 | + |
| **18** | + | + | + | + | 14.4 | 6.7 | 0.2 | + (ICA) |
| **19** | + | + | + | + | 16.1 | 7.2 | 0.2 | + |
| **20** | + | | | | 17.7 | 10.2 | 0.2 | + |
| **21** | | + | + | + | 16.8 | 12.3 | 0.4 | + |
| **22** | | + | + | | 20.9 | 11.6 | 0.2 | + |
| **23** | + | | | | 25.1 | 14.0 | 0.4 | + (ICA, ZnT8) |
| **24** | | | | + | 28.7 | 12.9 | 0.2 | + |

*F: Fatigue; PU: polyuria; PD: polydipsia; WL: weight loss; HG: documented hyperglycemia; GAD65: glutamic acid decarboxylase, ICA: islet cell, IA-2: insulinoma-associated, MIAA: microinsulin, ZnT8: zinc transporter autoantibodies*
** Either one represents criteria for diabetes diagnosis*