**# jc.2017-00822**: ATTENUATION OF INSULIN ACTION BY AN ALLOSTERIC INSULIN RECEPTOR ANTIBODY IN HEALTHY VOLUNTEERS. KW Johnson, et al.

**SUPPLEMENTAL TABLES**

**Supplemental Table 1: PK Parameters for Intravenous X358** (Mean + SEM)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Dose** (mg/kg) | **N** | **Cmax**  (g/ml) | **Tmax**  (days) | **AUC0-inf** (g/ml\*day) | **t1/2**  (days) | **Vss**  (ml/kg) | **CL** (ml/day/kg) |
| 0.1 | 4 | 3.3 (0.4) | 0.04 (0.03) | 29 (2) | 17 (2) | 73 (10) | 3.5 (0.3) |
| 0.3 | 3 | 9.0 (0.6) | 0.04 (0.03) | 118 (38) | 22 (5) | 72 (7) | 2.9 (0.9) |
| 1 | 3 | 29.4 (5.3) | 0.05 (0.02) | 324 (35) | 20 (5) | 77 (13) | 3.1 (0.4) |
| 3 | 4 | 100.0 (7.1) | 0.06 (0.02) | 1150 (117) | 25 (4) | 79 (6) | 2.7 (0.3) |
| 6 | 4 | 184 (10) | 0.05 (0.02) | 2050 (107) | 17 (1) | 65 (6) | 2.9 (0.2) |
| 9 | 3 | 242 (31) | 0.06 (0.02) | 2700 (85) | 22 (2) | 88 (3) | 3.3 (0.1) |

**Supplemental Table 2: Fasting Ketone (beta hydroxybutyrate) Levels (mmol/L)** (Mean + SEM)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Group** | **Day -1** | **Day 1** | **Day 2** | **Day 3** | **Day 6** |
| Placebo  N=5 | 0.23  (0.05) | 0.21  (0.02) | 0.23  (0.03) | 0.23  (0.03) | 0.18  (0.03) |
| 0.1 mg/kg  N=4 | 0.3  (0.08) | 0.25  (0.05) | 0.23  (0.03) | 0.20  (0.02) | 0.23  (0.03) |
| 0.3 mg/kg  N=3 | 0.23  (0.04) | 0.27  (0.07) | 0.23  (0.04) | 0.43  (0.18) | 0.27  (0.04) |
| 1 mg/kg  N=3 | 0.27  (0.04) | 0.20  (0.02) | 0.30  (0.07) | 0.3  (0.07) | 0.2  (0.02) |
| 3 mg/kg  N=4 | 0.23  (0.04) | 0.24  (0.03) | 0.60\*  (0.05) | 0.44  (0.07) | 0.25  (0.07) |
| 6 mg/kg  N=5 | ND | ND | ND | ND | ND |
| 9 mg/kg  N=3 | ND | ND | ND | ND | ND |

\*p<0.05 vs Day -1 and placebo

ND = not determined

**Supplemental Table 3: Postprandial Glucose and Insulin Changes** (Mean + SEM)

| **Treatment Group (mg/kg)** | **Day 3 Postprandial\*** | |
| --- | --- | --- |
| **Glucose (mg/dL)** | **Insulin (μIU/ml)** |
| Placebo | 114 + 4 | 47 + 5 |
| 0.1 | 115 + 4 | ND |
| 0.3 | 145 + 3 | ND |
| 1 | 153 + 20 | 181 + 47 |
| 3 | 171 + 25\* | 369 + 59\* |
| 6 | 158 + 14\* | 503 + 92\* |
| 9 | 171 + 5\* | 676 + 86\* |

\* 2 hr post-dinner (9-10pm)

Mean + SEM values

ND = not determined

**Supplemental Table 4: HOMA-IR (**Mean + SEM)

| **Dose Group (mg/kg)** | **N** | **Morning Fasting HOMA-IR‡ (mean [SD])** | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Baseline**  **(Day -1)** | **Day 1** | **Day 2** | **Day 3** | **Day 6** |
| **0.1** | 4 | 0.8  (0.3) | **3.2 (0.6)** | 1.7 (0.2) | 1.9  (0.2) | 1.5  (0.3) |
| **0.3** | 3 | 1.4  (0.7) | ***5.8 (1.9)*** | 1.8 (0.4) | **3.7**  **(1.5)** | 2.7  (0.9) |
| **1** | 3 | 2.0  (0.7) | ***10.2 (6.5)*** | **3.3 (1.1)** | ***5.7***  ***(0.1)*** | 2.9  (0.7) |
| **3** | 4 | 1.4  (0.2) | ***7.2 (1.3)*** | ND | ND | ***5.3 (0.9)*** |
| **6** | 5 | 1.2(0.2) | ***15.1 (3.6)*** | ***5.0 (1.1)*** | ***16.8***  ***(3.1)*** | ***14.1 (1.9)*** |
| **9** | 3 | 2.5  (0.8) | ***26.9 (5.0)*** | ***11.4 (2.3)*** | ***25.1 (2.7)*** | ***14.9 (3.1)*** |

‡ Fasting HOMA-IR = fasting glucose (mg/dL) \* fasting insulin (uIU/mL)/405

ND = not determined (ITT days)

**bold:** HOMA-IR value 3 – 5 = moderate insulin resistance

**bold *italic***: HOMA-IR value ≥ 5 = severe insulin resistance

**Supplemental Table 5: Insulin Tolerance Test KITT Values in X358-dosed Healthy Volunteers**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **KITT** | | | | | | | |
| **X358 Group** | **Day of ITT** | | | | | | |
| **Baseline**  **(Day -1)** | **2** | **3** | **5** | **11** | **22** | **29** |
| **3.0 mg/kg Mean (± SEM)** | 2.9 ± 0.9 | 1.1 ± 0.5 | 0.7 ± 0.01 | 1.0 ± 0.3 | ND | ND | ND |
| **6.0 mg/kg Mean (± SEM)** | 1.9 ± 0.4 | ND | 1.4 ± 0.4 | 1.2 ± 0.3 | 0.8\* | ND | 2.0\* |
| **9.0 mg/kg Mean (± SEM)** | 4.0 ± 1.1 | ND | ND | 0.9 ± 0.2 | 0.7 ± 0.2 | 1.7 ± 0.4 | ND |

\* N = 1

ND = not determined