**Supplementary table 1. Baseline, end-of-treatment, and median percent change values for secondary lipid, apolipoprotein (apo), and inflammatory marker endpoints according to treatment group (12-week completer population).**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable**  **(mg/dL)** | **Treatment** | **N** | **Baseline**  **Median**  **(Q1, Q3)** | **Week 12**  **Median**  **(Q1, Q3)** | **Change (%) from Baseline Median**  **(Q1, Q3)** | **Icosabutate vs. Placebo** | |
| **Median (%) change from baseline (Asymptotic 95% Hodges-Lehmann CI)** | **Wilcoxon  rank-sum  p-value** |
| **TG** | Placebo | 42 | 261.3  (215.0, 378.0) | 243.3  (205.0, 307.0) | -11.3  (-23.4, 7.8) | -29.1  (-38.4, -20.8) | <0.001 |
| Icosabutate | 36 | 270.5  (226.0, 326.0) | 155.8  (134.5, 198.3) | -43.4  (-47.5, -32.1) |
| **VLDL-C** | Placebo | 42 | 42.0  (34.0, 69.0) | 40.3  (31.0, 55.0) | -11.6  (-27.5, 9.8) | -27.0 (-38.9, -12.2) | <0.001 |
| Icosabutate | 36 | 42.5  (31.5, 55.0) | 25.3  (19.3, 33.5) | -38.6  (-57.1, -14.4) |
| **HDL-C** | Placebo | 42 | 40.0  (34.5, 47.5) | 40.8  (35.5, 45.5) | -1.7  (-6.4, 5.0) | 10.2  (4.8, 16.0) | <0.001 |
| Icosabutate | 36 | 45.0  (37.8, 49.3) | 48.8  (41.3, 54.8) | 9.6  (1.1, 17.3) |
| **Total-C** | Placebo | 42 | 200.0  (188.0, 218.5) | 202.8  (185.5, 217.0) | -3.1  (-9.0, 7.2) | -4.1 (-10.0, 2.6) | 0.191 |
| Icosabutate | 36 | 203.3  (190.5, 221.8) | 194.0  (177.8, 210.3) | -4.4  (-15.5, 3.5) |
| **LDL-C** | Placebo | 42 | 111.0  (93.0, 134.0) | 113.8  (99.0, 132.5) | 1.8  (-11.3, 14.5) | -0.5  (-10.5, 9.4) | 0.936 |
| Icosabutate | 36 | 123.0  (97.5, 130.5) | 117.3  (105.5, 131.8) | 0.0  (-12.4, 17.0) |
| **Apo B** | Placebo | 42 | 108.0  (99.0, 120.0) | 111.0  (96.0, 120.0) | 3.8  (-9.2, 11.5) | -7.6  (-15.1, 0.4) | 0.067 |
| Icosabutate | 36 | 109.0  (101.0, 121.0) | 100.0  (88.0, 115.5) | -5.8  (-15.3, 6.0) |
| **Apo C-III** | Placebo | 40 | 17.6  (14.0, 20.2) | 15.0  (12.3, 17.9) | -13.9  (-26.2, 0.8) | -21.1  (-29.4, -12.4) | <0.001 |
| Icosabutate | 36 | 17.3  (14.2, 19.4) | 11.3  (9.2, 12.9) | -35.5  (-43.3, -24.2) |

CI = confidence interval; Q1 = first quartile; Q3 = third quartile.

**Supplementary table 2. Effect on Glucose Metabolism (intention-to-treat population)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Treatment** | **N** | **Baseline**  **Mean (SD)** | **Week 12 Endpoint**  **Mean (SD)** | **Change from Baseline**  **Least-squares Mean (SE)**  **P-value** | **Icosabutate vs. Control**  **Least-squares Mean (95% CI)**  **P-value** |
| **Fasting plasma glucose (mg/dL)** | Control | 47 | 114.1 (35.10) | 111.5 (26.64) | -3.0 (2.42)  P=0.23 | -1.1  (-8.0, 5.7)  P=0.75 |
| Icosabutate | 42 | 121.2 (44.94) | 115.8 (37.46) | -4.1 (2.48)  P=0.10 |
| **HbA1c** | Control | 46 | 6.02 (0.749) | 6.05 (0.951) | 0.02 (0.058)  P=0.71 | 0.00  (-0.16, 0.17)  P=097 |
| Icosabutate | 42 | 6.37 (1.228) | 6.39 (1.161) | 0.02 (0.059)  P=0.68 |
| **Fasting plasma**  **insulin (mIU/L)** | Control | 47 | 23.17 (20.115) | 20.94 (12.852) | -0.62 (1.348)  P=0.65 | -2.38  (-6.23, 1.47)  P=0.22 |
| Icosabutate | 42 | 16.37 (7.739) | 15.56 (8.187) | -3.00 (1.387)  P=0.34 |
| CI = confidence interval, SD = standard deviation, SE = standard error | | | | | | |

**Ophthalmological examination**

After eligibility had been confirmed, and at the last study visit or at Early Termination, subjects underwent an ophthalmological examination completed by an off-site licensed optometrist or ophthalmologist. The optometrist or ophthalmologist performed the following assessments in the order given at to minimize the risk of 1 test interfering with another:

* Administration of a structured ocular surface disease index questionnaire;
* Best corrected visual acuity (Snellen);
* Schirmer I test of reflex tear flow without anesthesia;
* Simple grading scale of Meibomian gland function (Pflugfelder scale
* 1998);
* Tear film stability using the tear film break-up test;
* Intraocular pressure; and
* Slit lamp examination of the anterior segment.