**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.