**SUPPLEMENTAL DATA**

**SUPPLEMENTAL TABLES**

**Table e-1. Exploratory endpoints at Week 48**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Laquinimod 0.6 mg vs. placebo** | **N** | **Output** | **Estimate** | **Standard error** | **95% CI** | ***P* value** |
| BICAMS, adjusted mean (95% CI) |
| CVLT-II – Verbal memoryBVMT – Nonverbal memorySDMT – Processing speedLCVA (chart type 100%)aMSWS-129HPT | 224199232218232235 | Treatment effectTreatment effectTreatment effectTreatment effectTreatment effectTreatment effect | 0.3400.3821.9870.785-2.045-0.525 | 1.03230.79570.97160.77081.19720.5102 | –1.6945, 2.3750–1.1876, 1.95100.0812, 3.8934–0.7295, 2.3002–4.3936, 0.3036–1.5250, 0.4750 | 0.7420.6320.410.3090.0880.412 |
| CDP alternatives, n (%)12-week EDSS CDP24-week EDSS CDP12-week CDP (EDSS or T25FW)12-week T25FW CDP12-week CDP (EDSS, T25FW, 9HPT, or SDMT) | 276279276276276 | Hazard ratioHazard ratioHazard ratioHazard ratioHazard ratio | 0.90.71.00.91.0 |  | 0.52, 1.410.39, 1.240.69, 1.520.56, 1.480.68, 1.45 | 0.5410.2150.9060.7110.989 |

Abbreviations: 9HPT = 9-Hole Peg test; BICAMS = Brief International Cognitive Assessment for Multiple Sclerosis; BVMT = Brief Visuospatial Memory Test; CDP = confirmed disability progression; CI = confidence interval; CVLT-II = California Verbal Learning Test–II; EDSS = Expanded Disability Status Scale; N = number of patients included in the analysis; LCVA = low-contrast visual acuity; MSWS-12 = 12-Item Multiple Sclerosis Walking Scale; SDMT = Symbol Digit Modalities Test; T25FW = timed 25-foot walk.

a Estimated mean.

**Table e-2. Patients with prior use of MS disease-modifying treatment (ITT population)**

|  | **Placebo(n = 140)** | **Laquinimod 0.6 mg(n = 139)** | **Laquinimod 1.5 mg(n = 95)** | **Total(n = 374)** |
| --- | --- | --- | --- | --- |
| **Patients with prior DMT use, n (%)** | 31 (22) | 28 (20) | 30 (32) | 89 (24) |
|  Investigational drug | 4 (3) | 10 (7) | 12 (13) | 26 (7) |
| Antineoplastic agents | 0 | 1 (<1) | 2 (2) | 3 (<1) |
| Mitoxantrone | 0 | 0 | 2 (2) | 2 (<1) |
| Rituximab | 0 | 1 (<1) | 0 | 1 (<1) |
| Corticosteroids for systemic use | 1 (<1) | 0 | 0 | 1 (<1) |
| Methylprednisolone | 1 (<1) | 0 | 0 | 1 (<1) |
| Immune sera and immunoglobulins | 0 | 1 (<1) | 1 (1) | 2 (<1) |
| Immunoglobulins NOS | 0 | 1 (<1) | 1 (1) | 2 (<1) |
| Immunostimulants | 17 (12) | 10 (7) | 12 (13) | 39 (10) |
| Glatiramer acetate | 8 (6) | 3 (2) | 7 (7) | 18 (5) |
| Interferon beta-1a | 8 (6) | 6 (4) | 3 (3) | 17 (5) |
| Interferon beta-1b | 5 (4) | 2 (1) | 2 (2) | 9 (2) |
| Interferon beta | 0 | 0 | 1 (1) | 1 (<1) |
| Immunosuppressants | 8 (6) | 10 (7) | 13 (14) | 31 (8) |
| Fingolimod | 3 (2) | 5 (4) | 10 (11) | 18 (5) |
| Azathioprine | 1 (<1) | 2 (1) | 2 (2) | 5 (1) |
| Fingolimod hydrochloride | 3 (2) | 1 (<1) | 1 (1) | 5 (1) |
| Methotrexate | 1 (<1) | 0 | 0 | 1 (<1) |
| Methotrexate sodium | 0 | 1 (<1) | 0 | 1 (<1) |
| Ocrelizumab | 0 | 1 (<1) | 0 | 1 (<1) |
| Teriflunomide | 1 (<1) | 0 | 0 | 1 (<1) |
| Muscle relaxants | 1 (<1) | 0 | 0 | 1 (<1) |
| Baclofen | 1 (<1) | 0 | 0 | 1 (<1) |
| Tizanidine hydrochloride | 1 (<1) | 0 | 0 | 1 (<1) |
| Other nervous system drugs | 2 (1) | 4 (3) | 2 (2) | 8 (2) |
| Fampridine | 2 (1) | 4 (3) | 0 | 6 (2) |
| Dimethyl fumarate | 0 | 0 | 2 (2) | 2 (<1) |
| Unspecified herbal and traditional medicine | 1 (<1) | 0 | 0 | 1 (<1) |
| *Camellia sinensis* | 1 (<1) | 0 | 0 | 1 (<1) |
| Urologicals | 1 (<1) | 0 | 0 | 1 (<1) |
| Fesoterodine fumarate | 1 (<1) | 0 | 0 | 1 (<1) |
| Uncoded | 4 (3) | 1 (<1) | 1 (1) | 6 (2) |
| Blood and blood-forming organs | 4 (3) | 1 (<1) | 1 (1) | 6 (2) |

 Abbreviations: DMT = disease-modifying treatment; ITT = intention-to-treat; MS = multiple sclerosis; NOS = not otherwise specified.

**Table e-3. Trial comparison**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **INFORMS17** | **ORATORIO19, 26** | **PROMISE27** | **OLYMPUS21** | **SPRINT22** | **ARPEGGIO** |
| **Study characteristics** |  |  |  |  |  |  |
| Study drug | Fingolimod | Ocrelizumab | Glatiramer acetate | Rituximab | Ibudilast | Laquinimod |
| Study period | 36 months | 120 weeks | 36 months | 96 weeks | 96 weeks | 48 weeks |
| N | 823 | 732 | 943 | 439 | 255 | 374 |
| **Baseline characteristics** |
| Age, mean years (SD) | 48.5 (8.4) | 44.6 | 50.4 (8.3) | 49.9 (8.9) | 56 | 46.3 (7.0) |
| Male, n (%) | 425 (52) | 371 (50.7) | 460 (48.8) | 218 (49.7) | 133 (66.5) | 205 (55.0) |
| White, n (%) | 791 (96) | 94.1 | 747 (89.8) | 402 (91.6) | 236 (92.5) | 362 (97) |
| Time since symptom onset, mean years (SD) | 5.8 (2.4) | 6.5 (3.89) | 10.9 (7.5) | 9.1 (6.6) | Median 9 years placebo, 11 years treatment arm | 8.0 (5.8) |
| EDSS score, mean (SD) | 4.67 (1.03) | 4.70 (1.7) | 4.9 (1.2) | 4.8 (1.4) | Median 6 both arms | 4.5 (0.9) |
| Prior use of DMT, n (%) | 179 (22) | 85 (12.0) | NR | 154 (35.1) | NR | 89 (24) |
| **Study endpoint baseline values** |
| T25FW score (seconds), mean (SD) | 9.08 (6.87) | NR | 12.4 (13.8) | 8.08 median | Median 9.93 placebo, median 9.35 treatment arm | 9.7 (8.4) |
| 9-HPT dominant hand score (s), mean (SD) | 28.65 (14.62) | NR | 29.1 (19.3) | NR | Median 30.31 placebo, median 28.68 treatment arm | 32.4 (22.4) |
| Gd-enhancing lesions count, mean (SD) | 0.3 (1.06) | 1.0 (4.31) | 0.45 (2.7) | NR | NR | 0.3 (1.3) |
| Free of Gd+, n (%) | 260 (87.0) | 534 (73.0) | 85.9 | 75.5 | NR | 84.2 |
| Total volume of T2 lesions (mm3), mean (SD) | 9794.5 (11943.5) | 12, 100 | NR | 9173.3 (13114.0) | 10000 | 6129.0 (8885.1) |
| Normalized brain volume (cm3), mean (SD) | 1491.4 (85.5) | 1465.0 (86.0) | NR | 1205.8 (123.3) | NR | 1458.5 (102.7) |

Abbreviations: 9-HPT = 9-Hole Peg Test; DMT = disease-modifying treatment; EDSS = Expanded Disability Status Scale; Gd = gadolinium; NR = not reported; SD = standard deviation; T25FW = timed 25-foot walk.