**Supplemental Digital Content 1**

Oral betahistine reference group (open label)

1. **Patient characteristics**

The TRAVERS trial enrolled 16 patients into an open label oral treatment group (betahistine 16 mg t.i.d. for four weeks). All of them underwent vestibular schwannoma resection.

**TABLE 1.** *Patient demographics and vestibular schwannoma characteristics*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gender, n (%)** |  |  | **Canal paresis (calorics), %** |  |
| Male | 5 (31) |  | Mean (SD) | 26.5 (15.9) |
| Female | 11 (69) |  | Median  | 22.9 |
| **Age, years**  |  |  | Range | 0-55 |
| Mean (SD) | 53.0 (10.8) |  | **Koos grade, n (%)** |  |
| Range, years | 30 to 68 |  | Grade I | 4 (25) |
| **Surgery indication, n (%)** |  |  | Grade II | 9 (56) |
| Vestibular schwannoma  | 16 (100) |  | Grade III | 3 (19) |
| Endolymphatic sac carcinoma | 0 (0) |  | **Operated side, n (%)** |  |
| Vestibular neurectomy  | 0 (0) |  | Right | 10 (63) |
| Facial nerve schwannoma | 0 (0) |  | Left | 6 (37) |
| **Vestibular schwannoma size, mm**  |  |  | **Surgical approach, n (%)** |  |
| Mean (SD) | 12.1 (9.8) |  | Middle fossa craniotomy | 3 (19) |
| Median  | 12.5 |  | Translabyrinthine craniotomy | 10 (62)  |
| Range | 0-30 |  | Retrosigmoid craniotomy |  3 (19) |

SD: standard deviation. Canal paresis: Jongkee’s formula (absolute values). “Intention-to-treat” analysis set (n=16).

**TABLE 2.** *Baseline vestibular characteristics (Day 3)*

| **Spontaneous nystagmus, beats/30 sec.**  |  |  | **Tandem Romberg test, sec.**  |  |
| --- | --- | --- | --- | --- |
| Mean (SD)  | 45.4 (20.2) |  | Mean (SD) | 1.3 (3.3) |
| Median  | 44 |  | Median  | 0.0 |
| Range  | 9-90 |  | Range |  0-13 |
| **Subjective visual vertical, degrees** |  |  | **Standing on Foam test, sec.**  |  |
| Mean (SD) | 8.7 (4.4) |  | Mean (SD) | 2.6 (7.6) |
| Median  | 9.0 |  | Median  | 0.0  |
| Range | 2.6-19.1 |  | Range |  0-30 |
| **European Evaluation of Vertigo scale**  |  |  | **Tandem Gait test, steps**  |  |
| Mean (SD) | 12.6 (3.8) |  | Mean (SD) | 0.3 (1.0) |
| Median  | 13.5 |  | Median  | 0.0  |
| Range | 4-17 |  | Range | 0-4 |

SD: standard deviation. “Intention-to-treat” analysis set (n=16).

1. **Efficacy outcomes**

Patients in the oral betahistine group improved their TRT time to failure on average by 8.8 sec. (median: 5 sec.) by Day 28 and by 10.3 sec. (median: 8 sec.) by Day 42. At these time points, their mean spontaneous horizontal nystagmus decreased by 20.9 and 24.9 beats / 30 sec., respectively. Fewer than 10% of them experienced full resolution.

**TABLE 3.** *Change in efficacy endpoints from baseline*

|  | **Mean Δ (SD)** | **Median Δ** |  |  | **Mean Δ (SD)** | **Median Δ** |
| --- | --- | --- | --- | --- | --- | --- |
| **Tandem Romberg test, sec.**  |  | **Tandem Gait test, steps**  |
| Δ Day 7 | 2.3 (4.55) | 3.5 |  | Δ Day 7 | 7.4 (5.85) | 7.5 |
| Δ Day 14 | 6.9 (8.28) | 5.0 |  | Δ Day 14 | 12.1 (5.77) | 13.0 |
| Δ Day 28 | 8.8 (7.99) | 5.0 |  | Δ Day 28 | 19.2 (1.52) | 20.0 |
| Δ Day 42 | 10.3 (10.25) | 8.0 |  | Δ Day 42 | 16.9 (5.33) | 20.0 |
| **Standing on Foam test, sec.**  |  | **Subjective visual vertical, degrees** |
| Δ Day 7 | 10.1 (11.51) | 6.5 |  | Δ Day 7 | -2.09 (3.18) | -1.00 |
| Δ Day 14 | 15.3 (10.95) | 13.0 |  | Δ Day 14 | -4.41 (4.37) | -3.80 |
| Δ Day 28 | 21.2 (7.53) | 20.0 |  | Δ Day 28 | -5.80 (4.59) | -3.60 |
| Δ Day 42 | 22.9 (11.06) | 30.0 |  | Δ Day 42 | -6.21 (4.57) | -4.90 |
| **Spontaneous nystagmus, beats/30 sec.**  |  |  |
| Δ Day 7 | -11.2 (14.31) | -9.5 |  |  |  |  |
| Δ Day 14 | -17.7 (29.84) | -21.0 |  |  |  |  |
| Δ Day 28 | -20.9 (24.05) | -27.0 |  |  |  |  |
| Δ Day 42 | -24.9 (24.67) | -23.0 |  |  |  |  |

SD: standard deviation. “Intention-to-treat” analysis set (n=16).

1. **Safety outcomes**

Among the patients in the oral betahistine group, 63% had TEAEs; 19% experienced treatment-related TEAEs (dermatitis, chest pain, elevated alkaline phosphatase). There was one SAE (unknown infection, unrelated), and one patient discontinued the study due to TEAE (aphthous ulcer).