BASELINE CHARACTERISTICS OF IDIOPATHIC HYPERSOMNIA SUBJECTS ENROLLED IN A CLINICAL TRIAL (ARISE^2)

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Introduction: Idiopathic hypersomnia (IH) is a rare neurological sleep disorder recognized under the International Classification of Sleep Disorders (ICSD) as a central disorder of hypersomnolence. However, the nature of IH is not well defined. Here we report the baseline characteristics of patients enrolled in (ARISE^2), a Phase 2 study evaluating a pharmacological intervention for IH.

Methods: Subjects were screened by a committee of 3 independent sleep researchers/clinicians with experience with IH (authors, AA. LR, TR). Although the final decision regarding eligibility was determined by a consensus of the committee, they were working with the following pre-specified guidelines: 1. Historical sleep history consistent with a diagnosis of IH and inconsistent with other causes of hypersomnolence (e.g. SRBD, narcolepsy, insufficient sleep, other psychological disorders); 2. Historical PSG adequately documenting Total Sleep Time(TST), SE, sleep stage distribution, an AHI $\leq$15 and PLMAI$\leq$10/hr; 3. Historical MSLT showing a mean sleep latency $\leq$8.0m and < 2 REM onsets (including a SOREM on the PSG); 4. Historical and current medication use focusing on potential REM suppressing medications; 5. Current sleep diary demonstrating an average of at least 7 hours in bed nightly over a 7 day period; 6. Current ESS$\geq$11 and 7. Current Mental fog score from Idiopathic Hypersomnia Symptom Diary (IHSD) of $\geq$6 over the preceding week.

Results: 134 subjects were screened and 39 (27%) were enrolled. In terms of demographics, 33 were women (85%), mean age was 37.2, sd 12.2. The age of onset was 17.6, sd 4.4. All subjects reported at least one medical or psychiatric comorbidity. On the historic PSG mean TST was 417.2, sd 19.9, sleep latency was 17.3, sd 19.9, WASO 27.3, sd 18.9 REM latency 116.1, sd 74.0 mean PLMAI 1.2, sd 2.5 and mean AHI 1.6, sd 1.7. On study entry PSG, the subjects showed a mean TST 421.7, sd 33.4 with a sleep efficiency of 91%, sd 6.0% The mean sleep latency on the historic MSLT was 4.6, sd 2.1 with an average of 0.1 REM onsets. Interestingly on the MWT performed at enrollment, the mean sleep latency was 19.6, sd 12.4. On the current sleep diary subjects reported a mean bed time of 19:40, sd 3h44m, TIB of 8h39m, sd 1h17m, and a sleep efficiency of 91.1%, sd 7.3%. In terms of daytime symptoms the ESS mean was 16.8, sd 2.9 and on the IHSD completed for one week (11-point scale) showed a mental fog score of 7.2, sd 1.6, exhaustion 7.9, sd 1.2 difficulty remembering 6.9, sd1.8 and difficulty completing tasks 7.1, sd 1.6.

Discussion: On the pre-treatment MWT, the mean sleep latency was 19.6 minutes (median was 18.1). Despite the requirement for historical MSLT of sleep latency < 8 minutes, subjects showed an essentially normal MWT. This relatively normal MWT contrasts with the high ESS. This suggests that the subjective perception of sleepiness might relate better to daytime impairment as documented on the symptom diary rather than objective measures of alertness.

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