

CHARACTERISTICS OF SUBJECTS EXCLUDED FROM AN IDIOPATHIC HYPERSOMNIA RANDOMIZED CLINICAL TRIAL (ARISE²)

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Introduction: Research of the safety and efficacy of new treatments is conducted via randomized controlled trials (RCTs). Rigorous inclusion and exclusion criteria are standard practice in high-quality RCTs. Inclusion criteria define the target population investigated while exclusion criteria identify participants with characteristics that could increase risk for a negative outcome. To establish a diagnosis of Idiopathic Hypersomnia (IH), patients must have daytime sleepiness, impairment in daytime function, normal or extended sleep and exclusion of other hypersomnolence causes. The present report sought to identify the frequency and primary reasons subjects were excluded from ARISE², a Phase 2 RCT in IH.

Methods: Potential study participants with a preliminary diagnosis of IH were screened by a committee of 3 independent sleep diseases experts (authors, AA, LR, TR). The final decision regarding eligibility was determined by a consensus of the committee 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), 2. Historical PSG adequately documenting, TST, SE, sleep stage distribution and an AHI and PLMAI < 15, 3. Historical MSLT showing a mean sleep latency < 8.0m and < 2 REM onsets, 4. Historical and current medication use focusing on potential REM suppressing medications, 5. Current sleep diary demonstrating average > 7 hours in bed nightly over the past week, 6. Current ESS >10, 7. Current Mental fog score from Idiopathic Hypersomnia Symptom Diary (0 to 10 scale) of >6 over the preceding week.

Results: Thus far, 134 subjects were reviewed by the committee. Of these, 94 (68%) were excluded. The major reasons were: historic MSLT>8 (22), discontinued interest (20), failed to show mental fog score> 5 (12), failed to demonstrate >7 hours mean nocturnal sleep time (10), unable to comply with study restrictions (prohibited concomitant medication washout, alcohol, nicotine, caffeine) (12), ESS< 10 (6), other diagnosed causes of hypersomnolence (5), habitual bedtime after midnight (2), abnormal clinical labs (2), BMI>35 (1), CPAP use (1), and elevated suicidality score (1).

Conclusion: A majority of patients with a preliminary diagnosis of IH failed study screening. Most of the screen failures were due to inability to meet inclusion criteria necessary for the IH diagnosis. Other major reasons include patients withdrawing consent due to inability or unwillingness to commit for the duration of the study as well as inability to comply with protocol (i.e., use of alcohol, nicotine, caffeine or concomitant medications). It is possible that the subjects enrolled are not fully representative of the general IH population. Alternative methods such as all-comer studies and open label clinical case series may be needed to contextualize the results of the more rigorous clinical studies.

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