Sublingual Flumazenil Treatment for Recurring Stupor

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Background

• Long history of stupor
  • Quote – patient “would go home and go straight to sleep, to the exclusion of everything else, like seeing friends, eating or exercising. It really affected my work and my life”.

• Initial treatments with standard therapy only provided transient relief
  • At one point, patient slept 57 hours straight
  • Round the clock monitoring required
  • Quote – patient "I could go to bed one night and wake up more than a day later, sleeping through the phone or even someone shaking me"

• Spinal tap revealed that patient overproduces endozepine

• Flumazenil IV administration
  • Had been developed for benzodiazepines overdoses
  • Quote – patient "I will never forget it. I felt incredible. I was animated, could focus and simply felt alive for the first time in 12 years".
Current Patient Status

- Patient has been on flumazenil approx 9 months at this time
  - No issues from chronic dosing have been identified

- Patient takes up to six fumazenil tablets a day
  - Gaining strength is able to get by on 10 or 11 hours sleep.
  - Back to work 75% time

- For the first time in many years, patient can go to the movies or join friends for dinner

- Attempting to classify this condition classified as a sleep disorder calling it Endogenous Hypersomnia (EH).

- 13 other probable EH patients at Emory (including patient's younger brother)
Unmet Medical Need

• Recurring Stupor/ Hypersomnia
  – Excessive sleepiness
  – Elevated CSF endozepine levels
    • 6,000,000 patients (2% of the population)

• Other indications
  – "non-narcoleptic" "central" (i.e., brain) causes of hypersomnia
    • 60,000 patients (0.02% of the population)

• "secondary" causes of hypersomnia/excessive sleepiness
  – 12M – 30M patients (4% – 10%, dependent on mechanism)
Opportunity

• Repurposed therapeutic for new indication

• Novel formulations of flumazenil
  – Sublingual
  – Topical

• Novel therapeutic uses of flumazenil

• Define new indications based on endozapine levels
IP Status

- Emory has filed provisional applications on the method of using both sublingual and topical formulations of flumazenil to treat recurrent stupor

- Work is planned to identify additional patient populations with increased endozepine levels
Development Plan

- Develop blood test

- File for FDA Orphan Status?

- Phase II dosing study
  - Formulation is worked out
    - Sublingual
    - Topical
  - Patient population is identified

- Phase III efficacy study
  - Multicenter trial