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CLINICAL MANIFESTATIONS

POSTER PRESENTATION

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# Pilot trial of dronabinol adjunctive treatment of agitation in Alzheimer's disease (THC-AD)

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## Abstract

**Background:** Although agitation in Alzheimer's Disease (Agit-AD) is a common and troubling neuropsychiatric syndrome, behavioral interventions lack consistent efficacy and there are no FDA-approved medications. Neurobiological mechanisms that contribute to Agit-AD include brain atrophy, degradation of neurotransmission, neuroinflammation, disrupted circadian rhythms, comorbidities and frailty. Agit-AD is a major source of disease progression, patient disability, financial burden, and caregiver stress. Dronabinol is synthetic tetrahydrocannabinol (THC, one of the predominant biochemical constituents of cannabis). Cannabinoids may improve Agit-AD by providing protection against neuroinflammation and excitotoxicity, regulating neurotransmitters, improving comorbidities, stabilizing circadian rhythms, and increasing cerebral blood flow.

**Method:** THC-AD is a three-week placebo-controlled, double-blind, RCT of dronabinol (10 mg QD) in 80 patients with severe Agit-AD. Twice daily administration maximizes daytime coverage for agitation and minimizes sundowning. Inclusionary criteria include a diagnosis of AD, severe agitation, and being 60-95 years old, while exclusionary criteria include serious or unstable medical illness, seizure disorder, delirium, current use of lithium, and inability to swallow a pill. Primary outcomes include a change in the Pittsburgh Agitation Scale and NPI-C Agitation/Aggression subscales.

**Result:** We have enrolled 37 out of 80 participants (Table 1: mean age 78.2 years, 78.4% female, 83.8% Caucasian, mean education 13.2 years, 48.6% family history). Study participants are significantly cognitively impaired (Table 2: mean baseline MMSE of 7.1), agitated (mean NPI-C Agitation 14.8, mean NPI-C Aggression 6.4) and in reasonable overall health (Figure 1: General Medical Health Rating, 10.8% "excellent," 48.6% "good" and 40.5% "fair"). Recorded AEs have been tolerable (Figure 2). Due to the COVID-19 pandemic, we expanded our inpatient trial to include outpatient enrollments and implemented hybrid visits with telemedicine to limit in-person interactions. To bolster our recruitment, we are collaborating with additional clinical sites, increasing dementia bed capacity, and deploying recruitment strategies for

outpatients, including referrals from providers and other research trials, social media ads, and virtual community outreach. Updated results will be presented at AAIC (estimated 6-10 additional participants).

**Conclusion:** Safe and effective interventions for severe agitation are greatly needed. This pilot trial will help to examine the safety and efficacy of dronabinol for Agit-AD.

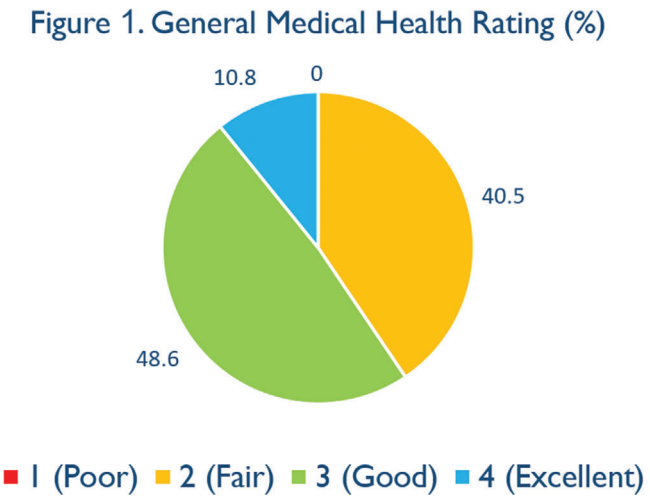


**FIGURE 1**

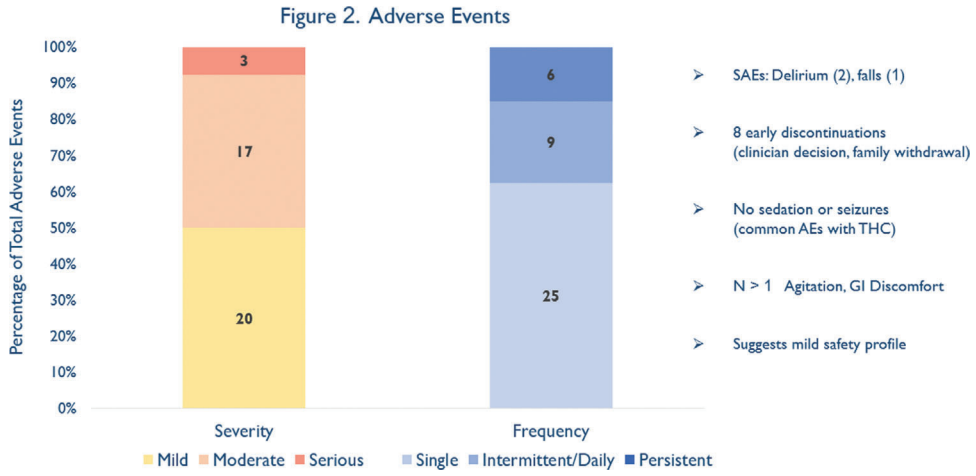


**FIGURE 2**

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**TABLE 1**

**Table 1. Participant Demographics**

| Demographic | *n* (%) | *mean, SD [min-max]* |
|---|---|---|
| Total | 37 | |
| Age | | 78.2, 7.4 [65 – 94] |
| Female | 29 (78.4) | |
| Education (years) | | 13.2, 3.5 [3 – 19] |
| White | 31 (83.8) | |
| Family History | 18 (48.6) | |

*Family history of known memory impairment due dementia.*

**TABLE 2**

**Table 2. Baseline Clinical Status**

| Assessment | *n* (%) | *mean, SD [min-max]* |
|---|---|---|
| NPI-C | | |
| Agitation subtotal | | 14.8, 6.8 [0-30] |
| Aggression subtotal | | 6.4, 5.8 [0-21] |
| PAS | | 6.8, 4.1 [0-15] |
| CMAI-SF | | 28.6, 8.6 [16-50] |
| Short CAM | | |
| Alert | 31 (83.3) | |
| Vigilant | 3 (8.3) | |
| Lethargic | 3 (8.3) | |
| Cognitive Scores | | |
| MMSE | | 7.1, 5.9 [0-20] |
| SIB-8 | | 11.4, 6.8 [0-21] |

*NPI-C = Neuropsychiatric Inventory Clinician-Rating Scale. PAS = Pittsburgh Agitation Scale. CMAI-SF = Cohen-Mansfield Agitation Inventory – Short Form. CAM = Confusion Assessment Method. MMSE = Mini-Mental State Examination. SIB-8 = Severe Impairment Battery (8-item).*