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CLINICAL MANIFESTATIONS



POSTER PRESENTATION

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

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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. General Medical Health Rating (%)



FIGURE 1

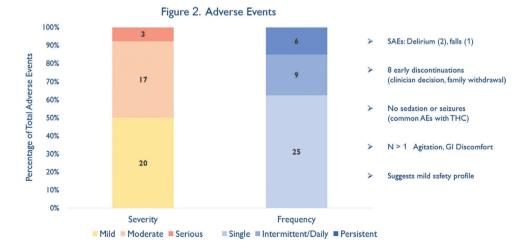


FIGURE 2

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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).