INTRODUCTION

• Cannabidiol (CBD) is the primary non-psychoactive cannabinoid found in Cannabis.
• Evidence suggests that CBD can reduce seizures in patients with epilepsy.
• Humans have a high natural oral delivery of CBD for children with refractory epilepsy.

OBJECTIVE

• Evaluate the safety and efficacy of ZYN002, a permeation-enhanced, pharmaceutically-produced synthetic CBD gel for transdermal delivery, as adjunctive therapy for the treatment of focal epilepsy in adults.

METHODS

Study Conduct

• Synthetic Transdermal Cannabidiol for the Treatment of Focal Epilepsy in Adults (STAR 1) was a phase 2a, randomized, double-blind, placebo-controlled study of the efficacy and safety of ZYN002 in adults with focal seizures (Figure 1).
• After an 8-week baseline period that assessed seizure frequency and type, patients were randomized to receive 195 mg CBD daily (given as 97.5 mg CBD BID) or placebo in a 1:1 ratio.

RESULTS

• In total, 188 patients were randomized, 186 were analyzed for efficacy, and 174 completed STAR 1 (Figure 2).
• Of the 14 patients who discontinued, 13 received ZYN002; 5 patients discontinued due to AEs (4 in the ZYN002 groups and 1 in the placebo group).
• Part of their seizure history and diagnosis reviewed and confirmed by the epilepsy Study Consortium prior to enrollment.

Exclusion Criteria:

- Use of...

Inclusion Criteria:

- Aged 18 to 70 years and in generally good health.

Following the 12-week treatment period, patients who completed STAR 1 could elect to participate in an 18-month open-label extension study (STAR 2); the dose could be reduced to 195 mg CBD daily as needed.

METHODS cont.

• STAR 1 primary efficacy analysis: log-transformed seizure frequency per 28-day period (SF28) during the 12-week treatment period, controlling for the baseline period.
• Post-hoc analysis: Percent reduction from STAR 1 baseline at Months 3 and 6 of STAR 2; the efficacy is calculated in patients with at least 24 days of data.

SAFETY

• Assessments: Adverse events (AEs); physical and neurological examinations; 12-lead ECG; laboratory assessments, pregnancy test, Columbia Suicide Severity Rating Scale (C-SSRS); and skin irritation examinations.

CONCLUSIONS

• After 12 weeks of blinded treatment, the change in seizure frequency did not statistically differ between placebo and both doses of ZYN002.
• A 50% response among 24% of placebo-treated patients contributed to the lack of separation.

Efficacy

• ZYN002 was very well tolerated with an incidence of AEs similar to placebo and no significant differences between the active treatment groups (Table 3).
• The failure of ZYN002 to separate from placebo was likely due in part to 15 placebo-treated patients (24%) who achieved at least a 50% reduction in focal seizures (73% were female); 13 of these 15 patients (87%) had a relatively low baseline seizure frequency (SF28 >50).

RESULTS cont.

• Patients taking 195 mg or 390 mg CBD daily for 6 months (3 patients in STAR 1 and 3 patients in STAR 2) had greater seizure reductions compared with patients who took placebo.
• At Month 6 of STAR 2, seizure rates continued to improve compared to baseline (Figure 3).

Demographics and Baseline Characteristics

• Most patients were female (54.8%) and white (88.3%), with a mean age of 39.2 years (Table 1). The safety profile of ZYN002 was consistent with previously released data from the Phase 1 trials.

REFERENCES