Interim Long-term Safety and Efficacy of XEN1101, a Potent, Selective Potassium Channel Opener: Update From an Ongoing, Open-label Extension of a Phase 2b Study (X-TOLE) in Adults With Focal Epilepsy

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RESULTS

- **Patients**: A total of 320 patients were randomized (patients naïve to 10 mg group: n=80, 10 mg group: n=80, 25 mg group: n=80, 50 mg group: n=80). At baseline, 253 patients (79.1%) received the DBP (75%±23% failure rate in the DBP.

- **Efficacy in the OLE**: Efficacy was evaluated by median percentage change (MPC) in monthly FOS frequency from DBP baseline and percentage of patients with ≥50% reduction from DBP baseline in monthly FOS frequency.

- **Safety**: Safety was assessed as severity and frequency of treatment-emergent AEs (TEAEs) and serious AEs, change in seizure presentation, and weekly changes in seizure onset.

- **Conclusion**: XEN1101 20 mg (n=275) was generally well tolerated, and the safety profile observed was similar to that of the DBP.

METHODS

- The study design for the 2b trial (ClinicalTrials.gov Identifier: NCT03756241) is shown in Figure 1.

- **Inclusion criteria**: Age at epilepsy onset, mean (SD), y; BMI, mean (SD), kg/m²; Age at study entry, mean (SD), y; Number of prestudy ASMs failed, mean (SD); Number of AMs at Baseline; CYP3A4 inducer use, n (%); Antiseizure medications (ASMs) at entry, n (%); Number of ASMs at entry, n (%); Number of ASMs at entry, n (%). The key eligibility criteria for the DBP were as follows: Age at epilepsy onset, mean (SD), y; Number of prestudy ASMs failed, mean (SD); Number of ASMs at entry, n (%); Number of ASMs at entry, n (%).

- **Exclusion criteria**: Patients who were receiving 1 to 2 ASMs were treated in the OLE for 24 months (32.4% for ≥6 months and 23.6% for ≥12 months.

- **Consecutive Months of Seizure Reduction in the OLE**: Seizure reduction was defined as a ≥75% reduction in seizure frequency.

- **Change in Ziprasidone Plasma Levels**: Plasma levels were not significantly different from DBP baseline. Ziprasidone levels were lower in the OLE than in the DBP.

- **Conclusion**: In addition to the TEAEs summarized in Table 1, 2 patients required a dose reduction, 1 reported as mild and the 2 other as moderate; no dose changes were made in any case.

- **DISCUSSIONS**: The key findings of the study were:

  - **Efficacy**: In the OLE study, OLE patients separated by prior DBP treatment groups showed higher reductions in seizure frequency.

  - **Safety**: Safety was assessed as severity and frequency of treatment-emergent AEs (TEAEs) and serious AEs.

  - **Conclusion**: XEN1101 20 mg (n=275) was generally well tolerated, and the safety profile observed was similar to that of the DBP.

- **CONCLUSIONS**: XEN1101 continues to be generally well tolerated in the OLE with AEs consistent with prior results and other AEs; no new safety signals were identified.

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