Electronic Seizure Diary Compliance In An Adult Focal Epilepsy Clinical Trial

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**BACKGROUND**
- Clinical trials in epilepsy typically measure seizure frequency and type as the primary outcome to assess efficacy of a therapy.
- Paper diaries have typically been used for seizure documentation. Handheld electronic devices are increasingly more accessible and offer several advantages in terms of ease of use in recording and tracking of seizures, timeliness of data and ability to provide immediate feedback.
- We are developing XEN1101, a novel voltage-gated potassium (Kv7.2/3) channel opener, for the treatment of epilepsy. In the recently completed X-TOLE phase 2 clinical study (Fig 1) in adults with focal onset seizures (FOS) (NCT03796962), median percent reductions in monthly FO5 frequency were 32.8% in the XEN1101 25 mg group (p=0.01), 46.4% in the XEN1101 50 mg group (p=0.001) compared to the placebo group.

**METHODS**
- A custom eDiary (Fig 2) was developed and used in X-TOLE, a randomized, double-blind, placebo-controlled, multicenter study of XEN1001 as adjunctive therapy in adult patients with focal onset epilepsy. The eDiary stored daily seizure and treatment compliance information which was transmitted to the database by wifi or cellular networks.
- Data were analyzed from the baseline period and the subsequent randomized DBP (156 days).
- Central surveillance of eDiary functionality and compliance was utilized to inform participating sites of their subjects’ status, enabling them to provide feedback in real time.
- UP counts could only be entered in the eDiary on the day after their occurrence, in the event of documented technical issues encountered with the eDiary.
- Central surveillance of eDiary functionality and compliance was utilized to inform participating sites of their subjects’ status, enabling them to provide feedback in real time.

**RESULTS**
- OF 530 potential participants, 129 were treated, 323 subjects were treated and provided seizure data (mITT population). Table 2, and 285 completed the study (N = 109 placebo; N = 45 at 10 mg XEN1101; N = 43 at 20 mg XEN1101; N = 88 at 25 mg XEN1101).
- The median (range) duration of the baseline period was 58.0 (32.9-139.0) days in the mITT population. During baseline 18997 daily seizure counts were reported. eDiary compliance was 95.1 ± 1.7% (mean ± SD) and median compliance was 98.4%. No significant differences were found in compliance between males and females during the baseline period, with a mean compliance of 95.2 and 95.3% respectively (Fig 3).
- An unexpected opportunity to explore the flexibility and utility of an eDiary was presented by the occurrence of the global COVID pandemic during baseline, resulting in a break period of up to 140 days in case of COVID-related site access restrictions. Three subjects thus had an extended baseline period of 67-73 days.
- No significant differences were found in the DBP compliance between regions, or by number of AEDs (taken at baseline) (Fig 4 and 5).
- At least one paper back-up daily entry was used by 26 subjects that completed the DBP:
- The data show that good eDiary compliance can be achieved in randomized clinical trials in adult focal epilepsy.

**CONCLUSIONS**
- Over the conduct of the study, there were over 42000 daily seizure recordings entered in the eDiary.
- We learned that high eDiary compliance could be maintained in adults with focal onset epilepsy, aided by central monitoring and ability to provide feedback in real time.
- The eDiary was used as the primary source for seizure related efficacy data.
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- We learned that high eDiary compliance could be maintained in adults with focal onset epilepsy, aided by central monitoring in real time. The eDiary helped to maintain a strong connection to the subject’s clinical status and enabled rigorous assessment of compliance for eligibility to randomize to evade progression through the study with inaccurate data.

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