Long term safety and tolerability of Eslicarbazepine acetate (ESL): results from BIA-2093-311/EXT study - the 2 year open label extension of the ESL monotherapy study (BIA-2093-311)

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Introduction Eslicarbazepine acetate (ESL) was approved by the European Medicines Agency as monotherapy treatment for newly diagnosed adults with focal seizures based on a phase III, randomized, double-blind (DB), active-controlled (controlled-release carbamazepine, CBZ-CR), non-inferiority study (BIA-2093-311) (Trinka et. al., Epilepsia:59;479-491,2018). The patients concluding the DB study were allowed to continue to 2-year open-label (OL) extension study (BIA-2093-311/EXT). Here, it is presented the safety/tolerability of ESL in long-term use. Material and methods Patients previously treated with CBZ-CR (N=97) in the DB study switched to ESL in the OL (CBZ-ESL group), whilst those treated with ESL (N=109) continued with their last evaluated dose in the DB study, 800mg, 1200mg or 1600mg QD (ESL-ESL group). Safety/tolerability was analyzed through treatment emergent adverse events (TEAEs), serious TEAEs, and TEAEs leading to treatment discontinuation. Results 172 (83.5%) of 206 patients who entered the OL study completed the 2-year extension study. Median treatment duration was 734 for ESL-ESL and 731 days for CBZ-ESL groups, whilst median daily dose was 800.0mg and 796.2mg, respectively. At least one TEAE occurred in 57.8% (63/109) patients of ESL-ESL and in 67.0% (65/97) of CBZ-ESL, with 20.2% and 20.6% reported as at least possibly-related TEAEs respectively. The majority of TEAEs were of mild-moderate intensity (80.7% ESL-ESL vs 88.7% CBZ-ESL), with blood creatine phosphokinase increased (3.7%), gamma-glutamyltransferase increased (3.7%) and somnolence (2.8%) the most frequently reported TEAEs considered at least possibly-related. Overall, 17.4% (ESL-ESL group) and 15.5% (CBZ-ESL group) of patients discontinued treatment prematurely, 2.8% and 6.2% due to TEAEs, respectively. Serious TEAEs reported were similar in ESL-ESL group (9.2%,10/109) and in CBZ-ESL group (7.2%,7/97), nevertheless only one serious TEAE (preferred-term, seizure) in CBZ-ESL group was considered at least possibly-related (1.0%,1/97). Conclusions Long-term safety data obtained supported the use of ESL as monotherapy, including in those patients previously treated with CBZ-CR.

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