

## ECTRIMS 2016 ABSTRACT

### **Efficacy of SFX-01, a sulforaphane-based drug, in experimental autoimmune encephalomyelitis**

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**Background.** Oxidative stress secondary to cell-mediated inflammation plays an important role in the pathology of multiple sclerosis (MS). Sulforaphane, a naturally occurring isothiocyanate, has dual therapeutic potential in MS by upregulating Nrf2-mediated anti-oxidant cytoprotective mechanisms and inhibiting NF-kB-mediated inflammatory responses. Activation of Nrf2 by sulforaphane is an order of magnitude higher compared to dimethyl fumarate (BG-12). SFX-01 is a proprietary, synthetic and stabilized form of sulforaphane, developed as a pharmaceutical product. First-in-man trials have documented safety and the product is in Phase II clinical trials for other indications. Here the efficacy of SFX-01 is tested in experimental autoimmune encephalomyelitis (EAE), a mouse model recapitulating some features of MS.

**Methods.** EAE was induced in 72 female SJL mice using PLP139-151 and pertussis toxin. Groups of 12 mice received vehicle, SFX-01 at 10, 50 or 300 mg/kg or BG-12 15mg/kg. The experiment was performed with two different dosing schedules: prophylactic (Day 0 to Day 19) and therapeutic (after recovery and before relapse, ie Day 19 to Day 41). Clinical scores and weights were measured, and tissue prepared for histological analysis.

**Results.** With prophylactic dosing: (1) SFX-01 caused a dose-dependent reduction in EAE scores but this did not reach significance even at 300mg/kg; (2) 300mg/kg of SFX-01 was equivalent to BG-12. With therapeutic dosing: (1) neither SFX-01 nor BG-12 affected relapse rate; (2) SFX-01 caused a dose-dependent reduction in relapse severity and end score, which achieved significance at the 300 mg/kg dose; (3) BG-12 did not significantly affect EAE relapse measures. Histological examination of the lumbar, thoracic, and cervical spinal cord were consistent with the clinical findings. In SFX-01 treated animals, all histological readouts including demyelination and the number of apoptotic cells were significantly improved compared to the vehicle group. In BG-12 treated animals, only demyelination was statistically improved.

**Conclusions.** SFX-01 appears to be superior to BG-12 in the therapeutic EAE model. SFX-01 appears to exert maximum effects later in the course of the disease by enabling superior neurological recovery in the chronic stage after relapse. SFX-01 is a promising drug candidate in MS, and warrants further investigation.