Evobrutinib significantly reduces relapses and magnetic resonance imaging outcomes in patients with multiple sclerosis: association with baseline neurofilament light chain levels

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Abstract

Introduction: Evobrutinib, a highly selective Bruton's tyrosine kinase (BTK) inhibitor, was shown to be effective and well tolerated in a phase II trial (NCT02975349) in patients with MS.

Objective: Evaluate the effect of evobrutinib on serum neurofilament light chain (sNfL), a biomarker of neuro-axonal damage, and analyze the prognostic value of sNfL on clinical relapse and MRI lesion activities.

Methods: Data were included from patients receiving placebo, evobrutinib 25mg once-daily (QD), 75mg QD, or 75mg twice-daily (BID). In patients with sNfL values at baseline and ≥1 post-baseline (n=166), measured blinded to treatment (SimoaNF-light™), the effect of evobrutinib on sNfL at Weeks 4, 12, and 24 was evaluated through mixed model repeated measures modelling, controlling for significant baseline covariates. To evaluate the effect of evobrutinib, stratified by baseline sNfL levels (high sNfL: ≥11.36pg/ml; low sNfL: <11.36pg/ml), on qualified relapses over 24 weeks and on T1 Gd+ lesions and T2 lesions over Weeks 12, 16, 20 and 24, patients with baseline sNfL values (n=162; modified intent-to-treat population) were grouped by high doses (evobrutinib 75mg QD/BID) or placebo/low dose (placebo/evobrutinib 25mg QD).

Results: Baseline covariates that affected sNfL over time were age, T2 lesion volume and Expanded Disability Status Scale score. Evobrutinib 75mg BID significantly reduced sNfL levels at Weeks 12 (p=0.010) and 24 (p=0.040) vs placebo. High evobrutinib doses vs placebo/low dose reduced the odds of qualified relapse (p=0.0028) when stratified by baseline sNfL, and both the number of Gd+ T1 lesions (high sNfL, p=0.0018; low sNfL, p=0.0102), and T2 lesions (high sNfL, p=0.0458; low sNfL, p=0.0012).

Conclusions: These results indicate a beneficial effect for evobrutinib 75mg BID on reducing neuro-axonal damage in MS. Higher evobrutinib doses reduced qualified relapses and MRI activity when stratifying for baseline sNfL levels. This further supports sNfL as a prognostic marker of MS disease activity.

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