Abstract 1395

High plasma glial fibrillary acidic protein levels predict disability milestone EDSS 7 in non-active secondary progressive multiple sclerosis

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Background

Glial fibrillary acidic protein (GFAP) is released into the cerebrospinal fluid and blood upon astroglial injury and activation, one of the hallmarks of progressive multiple sclerosis (PMS). It is unclear whether blood GFAP levels are associated with disability accumulation in secondary progressive MS (SPMS).

Objectives

To explore GFAP as a prognostic biomarker of disability worsening in patients with active and/or non-active SPMS (aSPMS and/or naSPMS) in the Phase 3 EXPAND study.

Methods

In this post-hoc analysis from the EXPAND study, baseline (BL) GFAP was quantified in EDTA plasma samples using Single Molecule Array technology. GFAP was categorized as high/low based on the gender stratified 80 percentile. The effect of GFAP on time to Expanded Disability Status Scale [EDSS] 7 (wheelchair restricted) was assessed using a Cox regression model adjusted for age, gender, disease duration, treatment, relapses in the 24 months prior to study start, and BL EDSS. Subgroup analyses were conducted in patients with aSPMS/naSPMS (with/without relapses ≤24 months prior to study entry, and/or gadolinium-enhancing T1 lesions at BL) and were also stratified by gender.

Results

Samples were available for 1405 of the 1651 patients randomized in the EXPAND study; median GFAP levels (pg/mL) were 119.6 (male) and 141.4 (female). Overall, the risk of reaching EDSS 7 was higher in patients with high BL GFAP (96%: high vs low GFAP, [34/281, 12.1%] vs [54/1117, 4.8%]; HR 1.96 [1.27; 3.03]; p=0.0024). Interestingly, the increased risk of reaching EDSS 7 was mainly seen in females (23/169; 13.6%] vs [34/673; 5.1%]; HR 2.22 [1.30; 3.80]; p=0.0035), and not significant in males ([11/112, 9.8%] vs [20/444, 4.5%]; HR 1.45 [0.67; 3.12]; p=0.3457). Increase in risk of reaching EDSS 7 was mainly observed in naSPMS patients (high GFAP [14/133; 10.5%] vs low GFAP [22/570; 3.9%]; HR 3.40 [1.71; 6.75]; p=0.0005) and was not significant in aSPMS patients (high GFAP [20/144; 13.9%] vs low GFAP [30/521; 5.8%]; HR 1.58 [0.88; 2.82]; p=0.1250). However, associations between BL GFAP levels and time to 6-months confirmed disability progression showed similar trends, but were less pronounced.

Conclusions

Blood GFAP appears to be a prognostic biomarker of disability worsening. The relevance of the gender difference and the stronger correlations found in SPMS patients with non-active versus active disease needs further investigation.

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