

# Cognitive Processing Speed Predicts Disease Progression in Secondary Progressive Multiple Sclerosis: Post Hoc Analysis from the EXPAND Study

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## Objective:

Assess the predictive value of cognitive processing speed (CPS), using the Symbol Digit Modalities Test (SDMT) score, on disability progression in secondary progressive multiple sclerosis (SPMS).

## Background:

CPS may be indicative of functional brain reserve and network efficiency, reflecting the ability of the brain to compensate for neuro-axonal damage/loss that accumulates with disease progression. Studies suggest cognitive impairment in MS can predict long-term physical disability progression.

## Design/Methods:

SPMS patients from the Phase 3 EXPAND study (core part [CP] and core+extension part [CP+EP]) were categorized into quartiles of baseline SDMT score (worst-WQ [Q1], intermediate [Q2-Q3], and best-BQ [Q4] quartile). The predictive value of baseline SDMT quartiles for time-to-wheelchair (T2W; i.e., Expanded Disability Status Scale [EDSS] score  $\geq 7$ ) sustained until end of follow-up, or 6-month confirmed disability progression (6mCDP) by EDSS, were assessed at the end of the CP (up to 37-months) and CP+EP (up to 5-years) by Cox regression (adjusted for treatment, age, gender, baseline EDSS, baseline SDMT quartile, and treatment-by-baseline SDMT quartile interaction).

## Results:

Analyses included 1628/1651 patients (98.6%) randomized in EXPAND (baseline SDMT: WQ, n=435; intermediate, n=808; BQ, n=385). Risk of T2W in the CP was higher for WQ vs BQ ( $HR_{WQ/BQ}=1.31$ , 95% CI:0.72–2.38;  $p=0.37$ ) and increased with long-term follow-up ( $HR_{WQ/BQ}=1.81$ ; 1.17–2.78;  $p=0.01$ ). Baseline SDMT was not predictive of 6mCDP. The predictive value of baseline SDMT for T2W in the CP was weaker with siponimod (n=1088;  $HR_{WQ/BQ}=1.12$ , 0.55–2.29;  $p=0.75$ ) vs placebo (n=540;  $HR_{WQ/BQ}=1.86$ , 0.73–4.78;  $p=0.19$ ), possibly due to siponimod preventing relatively more T2W events in the WQ. Predictive value of on-study changes will be presented at the congress.

## Conclusions:

The results support the predictive value of CPS for long-term (up to 5-years) physical disability progression in SPMS and highlight the relevance of monitoring CPS in daily practice to help identify patients at risk of progressing.

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