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Stage

Submitted

Type

Oral

Status

Pending

Abstract Topic

MS and related disorders

Date Submitted

12/1/2022 7:39 PM

**Body**

Title

Does Cognitive Impairment Predict Physical Disability Progression? Evidence from EXPAND, a Phase 3 Long-Term SPMS Study

Introduction

Assess the predictive value of cognitive processing speed (CPS), using the Symbol Digit Modalities Test (SDMT) score, on the time-to-wheelchair (T2W) disability progression milestone in secondary progressive multiple sclerosis (SPMS) patients from the Phase 3 EXPAND study.

Methods

Patients from the core and core+extension parts (core+EP) of EXPAND were categorized into quartiles by baseline SDMT score and on-study (Month 0–24) SDMT change (worst–WQ [Q1], intermediate [Q2–Q3], best–BQ [Q4]). The predictive value of these baseline and on-study change categories for time-to-wheelchair (T2W: Expanded Disability Status Scale [EDSS] score  $\geq 7$ ) after up to 5-years of the core+EP was assessed for the total study population. The predictive value of on-study change was also assessed separately in the siponimod-group (patients received consistent treatment during the core and the subsequent EP).

Results

Risk of T2W was significantly higher in the WQ vs BQ by baseline SDMT (HRWQ/BQ=1.81,  $p=0.007$ ). On-study SDMT change was predictive of subsequent T2W in both the total study population (HRWQ/BQ=1.73,  $p=0.046$ ) and in the siponimod arm (HRWQ/BQ=1.93,  $p=0.047$ ).

Conclusion

In line with previous smaller studies, these findings from the EXPAND study confirm that CPS, considered an indirect measure of thalamic network efficiency and functional brain reserve, may have predictive value for long-term physical disability progression. Monitoring CPS in daily practice might therefore help identify patients at increased risk of progressing.

Disclosure

This study was funded by Novartis Pharma AG, Basel, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

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