2014]. Additionally, interim 2-year results support the maintenance of benefit and the significantly greater efficacy of the Q2W dose regime (vs the Q4W regime) [Deykin A et al. *Neurology* 2014].

The objective of the post hoc analysis presented by Dr. Arnold was to assess FMDA in patients treated with peginterferon beta-1a during Year 1 of ADVANCE. Results of the analysis showed that significantly more subjects receiving Q2W dosing achieved overall FMDA from baseline to Week 48 (33.9%) compared with those receiving placebo (15.1%; p<0.0001) or Q4W dosing (21.5%; p<0.0001). Between Week 24 and Week 48, 60.2% of subjects receiving Q2W dosing achieved FMDS compared with 28.9% receiving placebo (p<0.0001) or Q4W dosing (36.6%; p<0.0001) Subjects on the Q4W dosing were more like to achieve overall FMDA than were those receiving placebo.

Among subjects achieving MRI FMDA only, significantly (p<0.0001) higher proportions were from the group receiving Q2W dosing compared with those receiving placebo or Q4W dosing at both time points. Subjects in the Q4W dosing group were significantly (p<0.05) more likely to achieve MRI FMDA compared with those receiving placebo.

At both time points (baseline to Week 48 or Week 24 to Week 48), subjects in the Q2W dosing group were significantly (p<0.001) more likely to achieve clinical FMDA than were those receiving placebo or Q4W dosing. However, the proportion of patients achieving clinical FMDA was not significantly different between the 2 peginterferon beta-1a dosing regimens.

The robustness of these findings was confirmed with sensitivity analyses allowing for minimal MRI activity. Peginterferon beta-1a Q2W values were significantly (p<0.0001) greater than placebo and Q4W values. Q4W values were significantly (p<0.02) greater than placebo values.

These data, along with previous findings, support the use of peginterferon beta-1a as an effective treatment for patients with RRMS, with the benefit of less frequent subcutaneous administration.

Asymptomatic Carotid Stenosis Is Associated With Cognitive Dysfunction

Written by Maria Vinall

Moira C. Dux, PhD, University of Maryland School of Medicine and Baltimore VA Medical Center, Baltimore, Maryland, USA, presented results from a cross-sectional study that demonstrated significantly worse cognition in patients with asymptomatic carotid stenosis compared with patients with vascular risk factors but no stenosis. The difference was driven primarily by poor motor and processing speed and learning and memory in patients with asymptomatic carotid disease, with deficits ranging from mild to moderate.

Several published studies have identified evidence of cognitive impairment in patients with asymptomatic carotid disease. However, methodologic issues, such as the use of healthy controls, the use of differing cognitive testing, and inadequate standardization of scores, have raised questions regarding the validity of these findings.

The Asymptomatic Carotid Stenosis: Cognitive Function and Plaque Correlates study (ClinicalTrials.gov identifier NCT01353196) was designed to provide a comprehensive assessment of neuropsychological function in patients with asymptomatic carotid stenosis compared with patients with similar vascular risk factors but no evidence of carotid stenosis. A total of 67 consecutive patients with ≥50% carotid stenosis and no prior transient ischemic attack or stroke as well as 60 control patients with risk factors for vascular disease but no evidence of carotid stenosis underwent comprehensive cognitive testing (Table 1). The presence and degree of stenosis were confirmed by duplex ultrasonography, while asymptomatic status was determined by neurologic and National Institutes of Health Stroke Scale testing.

Table 1. Neuropsychological Battery

Focus of Test	Test
Learning and memory	Hopkins Verbal Learning Test–Revised
	Brief Visuospatial Memory Test–Revised
Motor/processing speed	Trail Making Test Part A
	Grooved Pegboard Test
Executive function	Trail Making Test Part B
	Rey Complex Figure Test–Copy
Attention/working memory	Wechsler Adult Intelligence Scale–III: Digit Span Forward
	Wechsler Adult Intelligence Scale–III: Digit Span Backward
Language	Verbal Fluency (phonemic and semantic)
	Boston Naming Test (2nd edition)

Test scores were adjusted for age, sex, education, and race using standardized normative data. An overall index of cognitive function and 5 domain-specific composite scores were calculated. Independent-sample t tests were used to compare groups, and Cohen's d was calculated to determine effect sizes.

The proportion of vascular risk factors was similar in both groups (Table 2).

Table 2. Vascular Risk Factors[a]

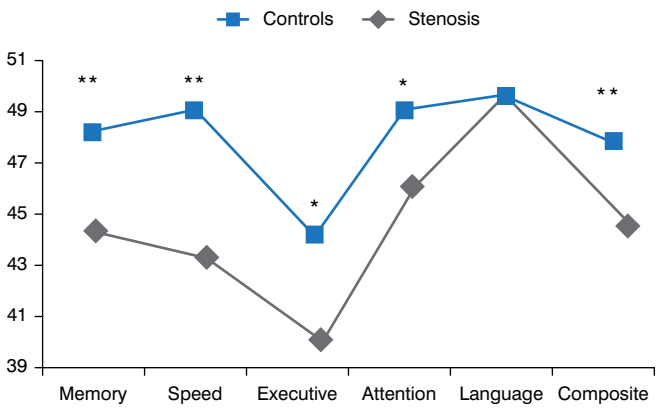
Risk Factor	ACS Group (% of Sample)	Controls (% of Sample)
Diabetes	54	53
Hypertension	85	89
Dyslipidemia	71	73
Peripheral vascular disease	49	41
Symptomatic coronary artery disease	11	14
Smoking	73	78

ACS=asymptomatic carotid stenosis.

[a]There was no significant difference between the ACS and control groups for any risk factor.

Patients with asymptomatic carotid stenosis performed worse on the overall neurocognitive composite score (t=2.8, p<0.01, d=0.52), the motor and processing speed domain score (t=3.5, p<0.01, d=0.69), and the learning and memory domain score (t=2.6, p<0.05, d=0.48) compared with the control group. There was a trend toward worse performance for executive function, attention, and working memory (d=0.35 and d=0.26, respectively). The groups did not differ on the language domain; both performed in the normal range. Full results are illustrated in Figure 1.

Figure 1. Outcomes for Neurocognitive Measures



*p≤0.15; **p≤0.05.

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These findings showed that patients with asymptomatic carotid stenosis do have increased evidence of neurocognitive impairment. This study did not explore why patients with >50% carotid stenosis have an increase in cognitive dysfunction compared with matched controls (eg, increased silent strokes on magnetic resonance imaging). Moving forward, further studies are needed to explore these issues, as well as to determine whether modified diagnostic approaches (eg, increased screening for stenosis) and new treatment approaches (eg, cognitive rehabilitation, aggressive medical management, revascularization) or targets (eg, cognitive symptoms) can improve outcomes in patients with asymptomatic carotid stenosis.

Fampridine Prolonged Release Improves Walking Ability and Balance in Patients With Multiple Sclerosis

Written by Phil Vinall

Treatment with prolonged-release (PR) fampridine results in sustained, clinically meaningful improvement in walking ability and balance in patients with multiple sclerosis (MS), said Jan Lycke, MD, University of Gothenburg, Gothenborg, Sweden, who presented the results of Exploratory Study to Assess the Effect of Fampridine on Walking Ability and Balance in Patients With Multiple Sclerosis (MOBILE; ClinicalTrials.gov identifier NCT01597297), an exploratory, phase 2, randomized, double-blinded, placebo-controlled trial.

Among patients with MS, difficulty walking is a commonly reported disability that negatively affects quality of life. PR fampridine (also known as sustained- or modified-release fampridine and dalfampridine extended release) is the only drug currently approved to improve walking in patients with MS. The objective of the MOBILE study was to evaluate the effect of PR fampridine on self-assessed walking ability, dynamic and static balance, and quality of life for patients with MS.

Patients in the MOBILE study had primary or secondary progressive MS, progressive-relapsing MS, or relapsing-remitting MS and Expanded Disability Status Scale scores of 4 to 7. Walking ability was assessed using the 12-item Multiple Sclerosis Walking Scale (MSWS-12) and the Patient Global Impression of Change scale. Mobility and balance (dynamic and static) were assessed using the Timed Up and Go (TUG) test and the Berg Balance Scale. The physical subscale of the 29-item Multiple Sclerosis Impact Scale and the EuroQol 5-Dimension 5-Level instrument were used to evaluate quality of life. Clinically meaningful improvement was defines as ≥8-point mean improvement on the MSWS-12 and ³15% mean improvement on the TUG test.

A total of 132 patients from 24 sites were randomized to treatment with PR fampridine (10-mg tablets; n=68) or placebo (n=64) twice daily for 24 weeks. Subjects' mean age was 49.8 years, and their mean Expanded Disability