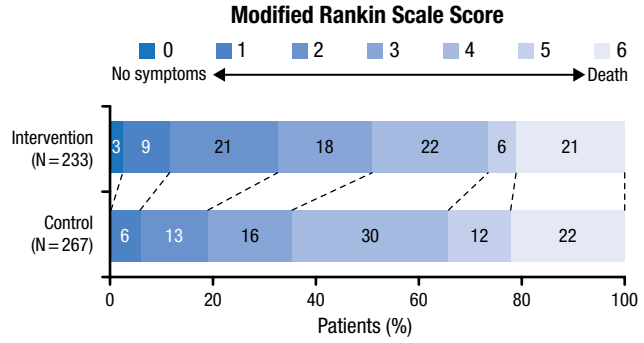
Figure 1. Effect of Endovascular Intervention on Functional Outcome at 90 Days



From *N Engl J Med*, Berkhemer OA et al., A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke, Volume No. 372, 11-20. Copyright © (2015) Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

effect of intra-arterial treatment on functional outcome in AIS, on a background of best medical management.

The open-label trial [Berkhemer OA et al. *N Engl J Med*. 2015] included 500 patients (≥ 18 years) with AIS with cranial arterial anterior circulation occlusion that was confirmed on imaging and could be treated intra-arterially within 6 hours of symptom onset. NIH Stroke Scale (NIHSS) scores were ≥ 2. The primary outcome was the score on the modified Rankin Scale (mRS) at 90 days.

Participants received usual care (which could include IV alteplase) and were randomized to also receive either intra-arterial intervention (n = 233) or no additional treatment (n = 267). The time from onset to groin puncture in the intervention group was 260 minutes.

Patients in the intervention group had lower mRS categories, consistent with improved function, at 90 days (adjusted OR, 1.67; 95% CI, 1.21 to 2.30; Figure 1).

Prof Dippel also highlighted unpublished subanalyses from MR CLEAN. Intra-arterial intervention was superior to no additional treatment for all age groups in the study, in particular, for those aged ≥ 80 years (adjusted OR, 3.24; 95% CI, 1.22 to 8.62), and for those with the most severe strokes (NIHSS score ≥ 20; adjusted OR, 1.85; 95% CI, 1.06 to 2.31).

Compared with controls, intra-arterial intervention with local anesthesia (adjusted OR, 2.79; 95% CI, 1.70 to 4.59) was more likely to result in a good outcome than general anesthesia (adjusted OR, 1.09; 95% CI, 0.56 to 2.12), which showed no benefit over usual care.

Prof Dippel concluded that intra-arterial intervention on a background of usual best stroke care is effective and safe in many patients if provided within 6 hours of stroke onset.

AVP-825 Produces Effective, Well-Tolerated Migraine Relief

Written by Maria Vinall

High-dose (100 mg) sumatriptan tablets are commonly used to treat migraines; however, they have a relatively slow onset of action and may be poorly absorbed because of impaired gastrointestinal impairment occurring during migraine. This has led to the development of a low-dose (22 mg) sumatriptan powder delivered intranasally through a breath-powered delivery system (AVP-825). In a pharmacokinetic study, AVP-825 was shown to have fewer triptan-associated adverse events and have a faster onset of action compared with tablets [Obaidi M et al. *Headache*. 2013]. Results of pooled analysis of data from a phase 2 [Djupesland PG et al. *Cephalalgia*. 2010] and a phase 3 [TARGET; Cady RK et al. *Headache*. 2015] trial of AVP-825 were presented in a poster by Roger K. Cady, MD, Headache Care Center, Springfield, Missouri, USA, and showed that AVP-825 conferred rapid headache relief that was sustained over placebo out to 48 hours and was well tolerated.

Both studies were randomized, multicenter, double-blind, placebo-controlled, parallel-group trials that included patients with migraines, with headache severity scores of grade 2 or 3 for at least 1 year, and with no known resistance to sumatriptan. The objective was to evaluate the efficacy and safety of AVP-825 using a larger, uniform pool of patients. Outcomes included:

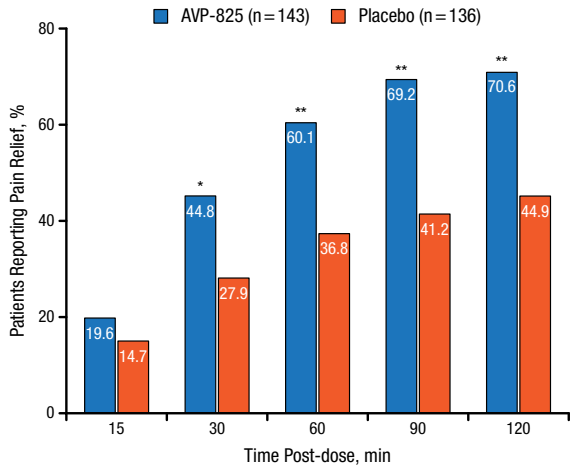
1. the proportion of patients with pain relief, freedom from pain, no clinical disability, and no migraine-associated symptoms (eg, nausea, vomiting, photophobia, and phonophobia); and
2. meaningful relief (subject-reported interpretation) within 120 minutes of treatment.

The percentage of patients requiring rescue medication over the first 48 hours after treatment, and the frequency and severity of treatment-emergent adverse events (TEAEs), were also recorded.

The pooled study included 279 patients randomized to either AVP-825 (n = 143) or placebo (n = 136). Significantly more patients receiving AVP-825 experienced pain relief (defined as reduction of their headache severity score from moderate or severe to mild or none) 30 to 120 minutes after treatment compared with those receiving placebo ($P < .01$; Figure 1).

Similarly, a higher percentage of patients experienced relief from pain (defined as reduction of their headache severity score from mild, moderate, or severe to none) than those receiving placebo, significantly ($P < .05$) at 60, 90, and 120 minutes post-administration (Figure 2).

Figure 1. Comparison of Pain Relief With AVP-825 and Placebo



*P<.01; **P<.001.
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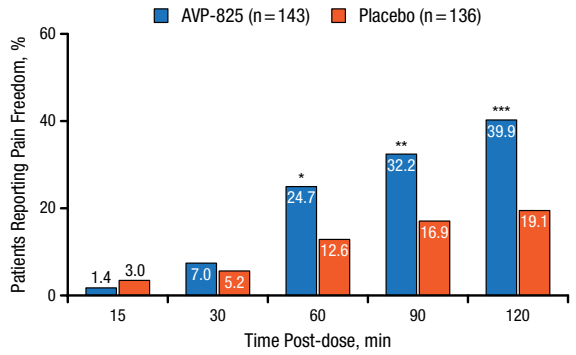
Figure 2. Comparison of Pain Freedom With AVP-825 and Placebo



*P<.05; **P<.01; ***P<.001.
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At 120 minutes, significantly more AVP-825–treated patients reported no clinical disability (P<.01), no migraine-associated symptoms (P<.05), and meaningful pain relief (P<.001). Additional rescue medication was less likely to be used during the first 48 hours by patients in the AVP-825 group. More AVP-825–treated patients reported TEAEs: 36% vs 11% for placebo. The most common TEAEs were abnormal taste, nasal discomfort, rhinorrhea, and rhinitis. There was a very low incidence of triptan sensations associated with AVP-825.

AVP-825 is a drug–device combination product containing low-dose (22 mg) sumatriptan delivered intranasally via a breath-powered device. As a treatment for migraines, it is well tolerated and delivers rapid headache relief that is sustained over placebo out to 48 hours.

MODERATO Study to Assess the Effect of Rasagiline on Patients With Parkinson Disease and Mild Cognitive Impairment

Written by Maria Vinall

Parkinson disease with mild cognitive impairment (PD-MCI) is thought to affect as many as one-third of nondemented PD patients. However, it is rarely diagnosed, and currently there are no approved treatments. The MODERATO study [NCT01723228] is designed to evaluate the effect of rasagiline on cognitive function in adult PD patients with MCI. Daniel Weintraub, MD, University of Pennsylvania and the Parkinson's Disease Center at the Philadelphia VA Medical Center, Philadelphia, Pennsylvania, USA, and one of the study investigators, presented the MODERATO study design and the baseline data for the enrolled patients.

Rasagiline is a selective irreversible MAO-B inhibitor indicated for the treatment of signs and symptoms of PD. Results of a small randomized, double-blind, placebo-controlled study indicated that it might exert beneficial effects on attention and executive abilities in PD patients with MCI [Hanagasi HA et al. *Mov Disord.* 2011].

MODERATO, the largest trial to date to evaluate a treatment for PD-MCI, is a 24-week, double-blind, placebo-controlled, phase 4 add-on study in men and women aged 45 through 80 years with idiopathic PD (based on the UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria) and PD-MCI as defined by the Movement Disorder Society Task Force Diagnostic Criteria and a Montreal Cognitive Assessment (MoCA) rating scale score of 20 to 25. Patients were required to be Hoehn and Yahr stage ≥1 and ≤3 and on a stable dopaminergic medication regimen for ≥30 days before entering the study. Patients with dementia were excluded. Eligible participants were randomized to 24 weeks of treatment with rasagiline 1 mg/d or placebo in addition to their current medications.

The purpose of the study is to measure the effectiveness of rasagiline on cognition in PD-MCI individuals with mild cognitive impairment. The primary study outcome measure is the mean change from baseline to week 24 in the Scales for Outcomes in Parkinson's Disease-Cognition summary score. Key secondary measures include the Unified Parkinson's Disease Rating Scale motor and activities of daily living scores, MoCA scores, and Functional Independence Index. A total of 170 patients have been enrolled from 40 study centers.