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The American Academy of Neurology (AAN) 68th Annual Meeting was held in Vancouver, BC, Canada, April 15th-21st, 2016. In this article, we summarize new developments and promising future studies that were presented during the congress. One of the most exciting studies presented at the congress was a study that reported the results of gene therapy in childhood cerebral adrenoleukodystrophy. The study was designed to improve the production of functional ALDP by autologous hematopoietic stem cells transduced with the lentiviral vector Lenti-D encoding ABCD1 cDNA. Seventeen patients had been included in this ongoing phase 2/3 trial so far, and 94% of the patients had stable neurologic function scores and imaging at 6 months with 2-year follow-up in three of these patients. It was stated that a serious drug-related adverse event (grade 3 viral cystitis) was observed in one patient and a probable drug-related adverse event (grade 2 tachycardia) had occurred in another, but these findings were reported to regress in both patients with standard treatments.

Trials on 'Calcitonin Gene-Related Peptide' in the treatment of episodic migraine were at the forefront. Three monoclonal antibody trials related to the peptide adrenoleukodystrophy (ALD) (LY2951743, ALD403, TEV-48125) and one monoclonal antibody trial related to the receptor (AMG 334) were discussed. The mean decrease in the duration of headaches in these studies was as follows: 4.2 days in a phase 2 LY2951743 trial that evaluated a subcutaneous injection every 2 weeks for 12 weeks (3 days in the placebo group), 5.6 days in the active headache group in a phase 2 ALD403 trial (4.6 days in the placebo group), and 3.4 days in a phase 2 AMG 334 trial that evaluated monthly subcutaneous injections (2.3 days in the placebo group).

It was shown that the combination of idalopirdine, an antagonist of the serotonin 5-HT6 receptor, and donepezil was more potent than donepezil monotherapy in patients with moderate Alzheimer's disease. In this 24-week-long phase 2 double-blind study, 278 patients were randomly allocated to combination therapy (30 mg idalopirdine/3 times a day), and the change-from-baseline in the Alzheimer's Disease Assessment Scale-cog total score was +1.38 in the monotherapy group and -0.77 in the idalopirdine group.

Another interesting study presented at the congress was about sports with obvious head trauma. In a study in 40 retired National Football League players, a decline in connections between brain regions was reported in 17 players and traumatic axonal injury in 12 players on diffusion tensor imaging, which is a technique based on the movement of water molecules.

Everolimus, which acts as an inhibitor of the mammalian target of rapamycin, was reported to reduce the frequency of seizures in patients with refractory tuberous sclerosis. In this phase 3 trial that evaluated higher doses (9 to 15 ng/mL) or lower doses (3 to 7 ng/mL) of everolimus in 366 patients, the findings indicated the superiority of both treatments versus placebo; approximately 40% and 15% vs. 29%, respectively, were reported.

Antipsychotic drug-related involuntary movements of the face and limbs were reported to improve greatly with valbenazine. In this randomized, phase 3 trial, the change-from-baseline in the Abnormal Involuntary Movement Scale was +0.1 in the placebo group and +3.2 in the 80mg valbenazine group ($p<0.0001$). In the same study, 40mg valbenazine showed less effect than 80 mg; however, with a statistically significantly greater effect compared with placebo ($p=0.0021$).

The results of ocrelizumab, which is an Anti-CD20+ monoclonal antibody, in patients with relapsing-remitting multiple sclerosis (MS) were presented within the scope of the OPERA I and OPERA II trials. It was specified that 48% of ocrelizumab-treated patients fulfilled the No Evidence of Disease

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Activity criteria and that this percentage was almost twice as much as in interferon-1βtreated patients. Other than this, the results of 732 patients with primary progressive MS included in the ORATORIO trial were presented as a poster. The results did not differ from the results of the 2015 European Committee for Treatment and Research in Multiple Sclerosis Congress, and the drug was shown to provide a 24% reduction in a 12-week clinical disability progression (hazard ratio=0.76, p=0.0321).

An abstract was presented on clemastine fumarate, a widely-used antihistamine, on the restoration of demyelination in the optic nerve. The effect of the drug on remyelination and its potential effect in progressive MS, which has no treatment, was discussed. However, it was stated that somnolence and fatigue-causing effects of the drug, as with all antihistamines, might limit its use in patients with MS.

The updated AAN guidelines were presented, which take into account all publications on the use of botulinum neurotoxin in blepharospasm, cervical dystonia, adult spasticity, and headache since 2008. According to the new guidelines, 4 types of botulinum neurotoxin (onabotulinum toxin A, abobotulinum toxin A, incobotulinum toxin A and rimabotulinum toxin B) were reported to act in these 4 different diseases at different levels. It was emphasized that three botulinum toxin A preparations were effective in upper limb spasticity (level of evidence I), and that abobotulinum toxin A and onabotulinum toxin A also had significant effects in lower limb spasticity (level of evidence I). Unlike the 2008 guidelines, information on the use of botulinum toxin in headache features in this guideline.

A presentation was made on dichlorphenamide, which was recently approved in the treatment of periodic paralysis. It was reported that the drug reduces relapse duration and frequency by 80% to 90% in this rare genetic disease with a prevalence of 1/100 000. Paresthesia and cognitive impairment were stated as adverse events.

Ethics

Peer-review: Internal peer-reviewed.