Increased frequency of anti-Ma2 encephalitis associated with immune checkpoint inhibitors

**Objective** To report the induction of anti–Ma2 antibody–associated paraneoplastic neurologic syndrome (Ma2-PNS) in 6 patients after treatment with immune checkpoint inhibitors (ICIs). We also analyzed (1) patient clinical features compared with a cohort of 44 patients who developed Ma2-PNS without receiving ICI treatment and (2) the frequency of neuronal antibody detection before and after ICI implementation.

**Methods** Retrospective nationwide study of all patients with Ma2-PNS developed during ICI treatment between 2017 and 2018.

**Results** Our series of patients included 5 men and 1 woman (median age, 63 years). The patients were receiving nivolumab (n = 3), pembrolizumab (n = 2), or a combination of nivolumab and ipilimumab (n = 1) for treatment of neoplasms that included lung (n = 4) and kidney (n = 1) cancers and pleural mesothelioma (n = 1). Clinical syndromes comprised a combination of limbic encephalitis and diencephalitis (n = 3), isolated limbic encephalitis (n = 2), and a syndrome characterized by ophthalmoplegia and head drop (n = 1). No significant clinical difference was observed between our 6 patients and the overall cohort of Ma2-PNS cases. Post-ICI Ma2-PNS accounted for 35% of the total 17 Ma2-PNS diagnosed in our center over the 2017–2018 biennium. Eight cases had been detected in the preceding biennium 2015–2016, corresponding to a 112% increase of Ma2-PNS frequency since the implementation of ICIs in France. Despite ICI withdrawal and immunotherapy, 4/6 patients died, and the remaining 2 showed a moderate to severe disability.

**Conclusion** We show a clear association between ICI use and increased diagnosis of Ma2-PNS. Physicians need to be aware that ICIs can trigger Ma2-PNS because clinical presentation can be challenging.

Late-onset neuromyelitis optica spectrum disorder: The importance of autoantibody serostatus

**Objective** To describe the clinical features of late-onset (≥50 years) neuromyelitis optica spectrum disorder (LO-NMOSD), to compare the outcome with that of early-onset (EO-NMOSD), and to identify predictors of disability.

**Methods** A retrospective, multicenter study of 238 patients with NMOSD identified by the 2015 criteria. Clinical and immunologic features of patients with LO-NMOSD were compared with those with EO-NMOSD. All patients were evaluated for aquaporin-4 (AQP4-IgG) and myelin oligodendrocyte glycoprotein (MOG-IgG) antibodies.

**Results** Sixty-nine (29%) patients had LO-NMOSD. Demographic features, initial disease presentation, annualized relapse rate, and frequency of AQP4-IgG and MOG-IgG did not differ between patients with LO-NMOSD and EO-NMOSD. Among patients with AQP4-IgG or double seronegativity, those with LO-NMOSD had a higher risk to require a cane to walk (hazard ratio [HR], 2.10, 95% CI 1.3–3.54, p = 0.003 for AQP4-IgG, and HR, 13.0, 95% CI 2.8–59.7, p = 0.001, for double seronegative). No differences in outcome were observed between patients with MOG-IgG and LO-NMOSD or EO-NMOSD. Older age at onset (for every 10-year increase, HR 1.63, 95% CI 1.35–1.92 p < 0.001) in NMOSD, and higher disability after the first attack (HR 1.68, 95% CI 1.32–2.14, p < 0.001), and double seronegativity (HR 3.74, 95% CI 1.03–13.6, p = 0.045) in LO-NMOSD were the main independent predictors of worse outcome.

**Conclusion** Patients with LO-NMOSD have similar clinical presentation but worse outcome than EO-NMOSD when they are double seronegative or AQP4-IgG positive. Serostatus and residual disability after first attack are the main predictors of LO-NMOSD outcome.