

Alemtuzumab following natalizumab in pediatric- and adult-onset multiple sclerosis.

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Background. Pediatric Onset Multiple Sclerosis (POMS) is characterized by an aggressive course and requires an effective therapeutic strategy. However, current protocols derive from the application of Adult-Onset MS (AOMS) therapeutic algorithms and are mainly based on first-line drugs. **Objectives.** To evaluate in a common clinical scenario (i.e., switching from natalizumab, NTZ, due to safety concern) the efficacy and safety of alemtuzumab (ALZ) in both POMS and AOMS. **Methods.** All patients switching from NTZ to ALZ for safety concerns (i.e., high anti-JCV Index value) from September 2015 to August 2020 were enrolled in this retrospective, case-control open label study. Based on age at onset, patients were divided into POMS (10 patients) and AOMS (17 patients). Patients were followed up for 48.5 ± 36.5 months. **Results.** Between baseline and month 24, 2 POMS and 1 AOMS had a clinical relapse (20% vs 5.9%, $p=0.54$), while 3 POMS and 2 AOMS had radiological disease activity (30.0% vs 17.7%, $p=0.64$). Survival analysis revealed an increased risk of disease reactivation in POMS compared with AOMS after the second ALZ infusion ($p=0.0430$). This association was partially confirmed by Cox regression analysis ($p=0.066$), which disclosed age at ALZ (H.R.: 0.86, 95%CI: 0.70-0.96, $p=0.035$), further confirmed by survival analysis (Log Rank p -value = 0.0004). No POMS developed autoimmune adverse events, while 4 AOMS developed an autoimmune thyroiditis and 1 AOMS developed an autoimmune encephalitis. **Conclusion.** ALZ seems more effective in AOMS than in POMS following NTZ. Additional studies are needed to clarify whether ALZ (or more broadly, induction therapies) might be an effective therapeutic approach for POMS, especially when shifting from NTZ, and if an additional ALZ course should be always considered in younger patients, especially in POMS.