***The efficacy of Natalizumab on inflammatory parameters of disease activity in Pediatric-Onset Multiple Sclerosis patients***

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**Introduction.** Pediatric-onset multiple sclerosis (POMS) is characterized by an aggressive disease course and development of physical and cognitive disability early.

**Objectives.** To evaluate the efficacy of natalizumab (NTZ) in POMS on clinical, radiological, and cognitive outcomes.

**Methods.** All POMS starting NTZ between and June 2015 and October 2021 were enrolled in this single-centre, prospective study. Patient were evaluated every 6 months both clinically and radiologically and followed up for 31.0±17.6 months (6-71 months). No radiological (i.e., no evidence of new/enlarging white matter lesions nor gadolinium-enhancing lesion) or clinical (i.e., no evidence of clinical relapse or EDSS worsening) evidence of disease activity (rNEDA and cNEDA respectively) were evaluated at 12 and 24 months. In addition, survival analysis for overall NEDA condition (i.e., radiological and clinical) was also analyzed. As control, an EDSS-, disease duration, and gender- matched cohort of adult-onset MS starting natalizumab during the same period was enrolled.

**Results.** Thirty-seven POMS were enrolled in our study. None of POMS and 2 adult-onset patients experience a clinical relapse (p=0.5) during the first 2 years of treatment. 29 POMS (78.4%) and 33 (76.7%, p=0.80) adult-onset MS fulfilled the rNEDA condition at 12 months, while between 12 and 24 months, 1 out of 26 POMS (3.8%) and 13 (30.2%) experienced a radiological disease reactivation (p=0.001). After 24 months of NTZ therapy, 80.8% of POMS and 60.5% of adult-onset MS fulfilled the NEDA condition (p=0.054). After month 24, no POMS experience any radiological disease reactivation. Median EDSS value was 1.0 at month 12 and 24, and it did not change significantly during the follow-up (p=0. 86). Indeed, only 2 patients had 0.5 increase confirmed after 6 months. NEDA condition was not associated to any clinical or demographic baseline variable. However, survival analysis revealed a trend for the risk of NEDA based on naïve- or switching-baseline status (Log rank p-value: 0.19).

**Conclusions.** NTZ is a highly effective treatment for POMS. While in adult-onset MS disease reactivation may occur during the first year of NTZ therapy, in POMS the effect of NTZ is rapid and stable. Our data further support the use of NTZ as first treatment choice in POMS.