Natalizumab Evaluation of Safety and Efficacy in the transition from intravenous and subcutaneous administration: a retrospective study (NEST-sc study)

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INTRODUCTION

In 2021 the European Medicines Agency (EMA) authorized the subcutaneous (SC) formulation of Natalizumab (NTZ) for multiple sclerosis (MS) treatment [1] based on the evidence provided by two studies, the DELIVER[2] and REFINE[3] studies, which compared the intravenous (IV) and subcutaneous administrations of Natalizumab. Thereafter some authors [4,5] described lower drug concentrations with NTZ-SC compared to IV administration, suggesting a possible reduced efficacy of NTZ-SC.

AIM

To evaluate the efficacy and safety of NTZ-SC in patients who have switched from NTZ-IV in a large real-world setting, considering both clinical and radiological features. We also searched for any potential factors associated to NTZ-SC failure in maintaining the NEDA-3 (No Evidence of Disease Activity) status. Finally we wanted to compare adverse events (AE) incidence between the two NTZ formulations.

METHOD

We retrospectively included adult patients diagnosed with Multiple Sclerosis according to the McDonald 2017 criteria who have been treated for 6 months or more with NTZ-SC after at least 2 years of NTZ-IV treatment. We collected demographic, clinical and radiological data and we searched for any difference in clinical and/or radiological reactivations rate between the NTZ-IV period and the subsequent NTZ-SC follow-up. Extended-dosing regimen (EID) during NTZ-IV period or after NTZ-SC switching was recorded when the interval between infusions exceeded 5 weeks.

RESULTS

620 patients, 71% female, mean age 42.4 years old

No statistically significant difference in ARR → during NTZ-IV vs NTZ-SC period → 0.017 vs 0.008

% of patients without new or Gd+ lesions
NTZ-IV = 93% NTZ-SC = 98.7%

NEDA-3 during NTZ-SC treatment → 94% of patients

No association between NEDA-3 loss and age, disease duration, patients' weight, dosing regimen, ARR in NTZ-EV.

	n = 620
MS center, n	28
Female, n (%)	443 (71)
Age, mean ± SD (years)	42.4 (11.1)
Weight, mean ± SD (kg)	67.2 (13.5)
Disease duration, mean ± SD (years)	12.3 (7.7)
Follow-up NTZ-SC, mean ± SD (months)	11.8 (3.2)
EDSS, median (range)	2.0 (0 – 7.0)
Dosing regimen, n (%) • Every 4-5 weeks (SID) • Every 6 weeks (EID)	 286 (46%) 332 (54%)
Dosing regimen change at switch, n (%)	136 (22%)
AE during NTZ-EV, n (%) AE during NTZ-SC, n (%)	31 (5%) 30 (4.8%)

CONCLUSION

In our large, real-world, Italian multicenter setting, subcutaneous Natalizumab showed a similar efficacy and safety profile compared to the intravenous route of administration, independently to demographic data, ARR during IV-NTZ treatment, dosing regimen and other potential risk factors. Weight, extended dosing regimen or changes to the dosing regimen after switch do not appear to lead to reduced efficacy of subcutaneous Natalizumab formulation.

***1. European Medicines Agency**. Summary of product characteristics. Tysabri. **2. Plavina** T et al. J Clin Pharmacol. 2016 **3. Trojano** M et al. Mult Scler. 2021 **4. Toorop** AA et al. NEXT-MS study group. J Neurol Neurosurg Psychiatry. 2023 5. **Gelissen** LMY et al. Mult Scler Relat Disord. 2024*