Results

Filename	Confidence	Paper Title	Conclusion	Type of Study	Population	Intervention	comparison	outcome	Results
1-s2.0-S0022510X21003166-main.pdf	0.9	Wearing-off symptoms during standard and extended natalizumab dosing intervals: Experiences from the COVID-19 pandemic	Our observations support the need to study the effect of EID on wearing-off symptoms in randomized controlled trials.	Observational study	RRMS patients over 18 years of age receiving natalizumab	Extended interval dosing (EID) from 4 to 6 weeks	Standard interval dosing (SID) vs extended interval dosing (EID)	Wearing-off symptoms	New or increased wearing-off symptoms during EID were reported by 50%. Symptom increase was more frequent among patients with pre-existing wearing-off symptoms during standard dosing compared to patients without such pre-existing symptoms [p = 0.0005]. None had decreased symptoms. Median natalizumab RO at SID was lower in 9 of 11 leukocyte subtypes in patients who later reported symptom increase during EID compared to patients with unchanged symptoms during EID, but the difference was not

									statistically significant.
1-s2.0-S221103482100612X-main.pdf	0.9	Safety of Natalizumab infusion in multiple sclerosis patients during active SARS-CoV-2 infection	Our data supports the safety of NTZ redosing in pwMS during active SARS-CoV-2 infection.	Retrospective study	18 relapsing-remitting multiple sclerosis patients	Natalizumab (NTZ) infusion	Not Found	Safety of NTZ infusion during active SARS-CoV-2 infection (no worsening of infection or recovery delay observed)	No worsening of SARS-CoV-2 infection or recovery delay was observed in 18 pwMS receiving NTZ retreatment during confirmed SARS-CoV-2 infection.
1-s2.0-S1878747924000370-main.pdf	0.9	Commentary Extended interval dosing of natalizumab: More evidence in support	The main findings support extended interval dosing (EID) of natalizumab without compromising benefits, potentially reducing PML risk, though further data needed for first-line use and in more active disease; EID shows similar outcomes to standard interval dosing (SID) at 6-week intervals, with benefits like cost reduction and convenience.	Commentary	Adults with multiple sclerosis receiving natalizumab (clinically stable, on natalizumab for at least 12 months, predominantly female with average disease duration of 8.5 years, many with prior disease-modifying therapy)	Extended interval dosing of natalizumab (EID)	Standard interval dosing (SID) vs. Extended interval dosing (EID)	Evidence of disease activity (EDA), defined as clinical relapses, MRI activity, or disability worsening per the Expanded Disability Status Scale (EDSS)	In primary analysis, no differences between SID and EID (5–7 weeks) for specified outcomes; similar for 7–8 weeks with trend toward greater clinical relapse hazard in EID (HR 1.74, p=0.054); BMI analysis showed interaction with treatment regimen for EDA; no differences in EDA between groups after inverse probability weighting.
10.1007@s00415-014-7574-6.pdf	0.9	Intense immunosuppression for the treatment of an immune	In the meantime, IRIS can be a serious manifestation related to NTZ	Case report	43-year-old woman with relapsing–remitting multiple	Intense immunosuppression (1 g IV cyclophosphamide followed by	Standard therapy (IVMP, plasma exchange) vs intense	Clinical and radiological improvement (EDSS improved from	Patient's condition improved clinically (EDSS 5.0) and

		reconstitution inflammatory syndrome-like exacerbation after natalizumab withdrawal: a case report	treatment interruption and the administration of intense immunosuppression, once PML is ruled out, a therapeutic option for such rapidly worsening condition. The information provided may be useful because controlled trials for this rare complication are unlikely.		sclerosis (RRMS)	rituximab)	immunosuppression	9.0 to 3.0 over time)	radiologically (lesion reduction) after intense immunosuppression; eventually EDSS 3.0 and disease activity free for 16 months.
A real world multi center study on efficacy and safety of natalizumab in Indian patients with multiple sclerosis_Author links open overlay panel_Thomas Mathew a_, _Vikram Kamath b_, _Saji K John a_, _M Netravat.pdf	0.9	A real world multi center study on efficacy and safety of natalizumab in Indian patients with multiple sclerosis	Natalizumab is highly effective and safe in Indian MS patients, with no cases of PML identified at last follow up.	Multicentre ambispective study	Indian patients with multiple sclerosis (age ≥18 years treated with natalizumab)	Natalizumab (NTZ)	Before and after natalizumab treatment	Relapse rate, EDSS score, occurrence of PML	During the study period of 9 years, 116 patients were treated with NTZ. Mean age of the cohort was 35.6 ± 9.7 years; 83/116 (71.6%) were females. Relapse rate for the entire cohort in the year before NTZ was 3.1 ± 1.51 while one year after was 0.20±0.57 (p = 0.001; CI 2.45 -3.35). EDSS of the entire cohort in the year before NTZ was 4.5 ± 1.94 and one

									year after was 3.8 ± 2.7 (p = 0.013; CI 0.16–1.36). At last follow up (38.3 ± 22.78 months) there were no cases of PML identified.
Balduzzi et al. - 2019 - How to perform a meta-analysis with R a practical tutorial.pdf	0.9	How to perform a meta-analysis with R: a practical tutorial	R represents a powerful and flexible tool to conduct meta-analyses. This publication gives a brief glimpse into the topic and provides directions to more advanced meta-analysis methods available in R.	Meta-analysis tutorial (practical guide using R software)	Patients with symptoms of schizophrenia	Haloperidol	Placebo	Clinical improvement (binary outcome: response to treatment)	Fixed effect and random effects meta-analysis showed haloperidol significantly more effective than placebo (RRs not crossing null line), but prediction interval suggests future studies may favor placebo; heterogeneity moderate (I2=54%). Subgroup analysis by missing data showed studies without missing data had larger haloperidol effect. Sensitivity analyses for missing data yielded similar results. Small-study effects detected (Harbord test p<0.001); trim-and-fill adjusted

									RR=1.40 (non-significant), limit meta-analysis adjusted RR=1.29 (non-significant).
Bernardes et al. - 2024 - Natalizumab extended interval dosing what about wearing-off effect.pdf	0.9	Natalizumab extended interval dosing: what about wearing-off effect?	WO affects a significant proportion of MS patients under natalizumab. Despite clinical effectiveness maintenance, its prevalence, severity, and duration increase on EID, and therefore, we recommend that this posology should be individualized. Further investigation to elucidate the cause of WO and possible association with disease activity, namely on EID, is needed to ultimately guide dosing decisions.	Observational retrospective study	Patients with multiple sclerosis (MS) receiving natalizumab therapy (clinically stable patients on natalizumab for more than one year, switched to extended interval dosing)	Extended interval dosing (EID) with every six weeks infusions	Standard interval dosing (SID) vs. Extended interval dosing (EID)	Wearing-off (WO) effect (prevalence, severity, duration) and annual relapse rate (ARR)	Seventy-six patients were included. No significant differences were found in the annual relapse rate after the switch to EID (p = 0.083). However, there was a significant increase in the proportion of patients complaining of WO from 38.2% to 56.6% (p = 0.001). Moreover, patients with WO on SID, referred a significant increase in severity (p = 0.019) and duration of WO symptoms (p = 0.029), due to an anticipation of the symptoms relative to the day of natalizumab infusion (p = 0.019), when switching to EID.
Bigaut et al. -	0.9	Long-term effect	In our cohort of	observational	Patients with	natalizumab	Not Found	Time to onset of	770 patients

2021 - Long-term effect of natalizumab in patients with RRMS TYSTEN cohort.pdf		of natalizumab in patients with RRMS: TYSTEN cohort	patients treated with NTZ, poor outcomes were infrequent and are driven by disease activity. Not reaching NEDA-3, MRI worsening, increased EDSS score, and to a lesser extent the occurrence of relapse were identified as predictive of disability at the long-term.	study	relapsing-remitting multiple sclerosis (RRMS) who started natalizumab treatment between 2007 and 2012	(NTZ)		secondary progressive multiple sclerosis (SPMS), time to reach Expanded Disability Status Scale (EDSS) worsening, EDSS 4.0, EDSS 6.0, and treatment failure	were included. The mean follow-up duration was 97 months and the mean time exposure to NTZ was 66 months. At 10 years, the cumulative probability of SPMS was 27.7%. Predictive factors for poor outcomes were a ≥1-point increase in EDSS score from baseline, new T2 lesion or T1 gadolinium-enhancing lesion, the occurrence of relapse at 1 or 2 years and No Evidence of Disease Activity (NEDA-3) was a protective factor.
Bomprezzi and Pawate - 2014 - Extended interval dosing of natalizumab a two-center, 7-year experience.pdf	0.9	Extended interval dosing of natalizumab: a two-center, 7-year experience	Natalizumab is effective in controlling MS as very few clinical relapses were observed in our dataset. We found that EID did not compromise the treatment effect as measured by relapse rate and	Retrospective review (chart review)	Patients with multiple sclerosis (MS) treated with natalizumab at two MS centers	Extended interval dosing (EID) of natalizumab (administered every 6 or 8 weeks instead of every 4 weeks)	Monthly dosing (standard every 4 weeks) of natalizumab vs extended interval dosing (EID)	Clinical relapse rate and MRI activity (number of new T2, fluid-attenuated inversion recovery or contrast enhancing lesions)	A total of 361 patients received natalizumab for 22 ± 13 months... Over the study period, there was no significant difference between the relapse rate in

			no significant breakthrough disease activity was observed. EID is an optional regimen for maintenance natalizumab therapy, but prospective studies are warranted to determine its efficacy.						the monthly dosing (13%) and the EID (13%) groups... The number of new MRI lesions was 36/340 (11%) in monthly dosing and 8/87 (9%) in EID.
Brandstadter et al. - 2017 - The use of natalizumab for multiple sclerosis.pdf	1.0	The use of natalizumab for multiple sclerosis	Natalizumab remains an important part of the treatment arsenal for patients with RRMS. It has proven to be highly efficacious in the reduction of clinical relapses and prevention of new MRI activity. Though generally well-tolerated, natalizumab does carry a risk for the life-threatening condition PML. Risk mitigation awareness and development of a formal monitoring program have encouraged careful prescribing of	Review	Multiple sclerosis patients (including relapsing-remitting and secondary progressive subtypes)	Natalizumab	Placebo, interferon beta-1a, and other treatments	Clinical relapse rate, MRI lesion activity, disability progression	Natalizumab demonstrated high efficacy in Phase III trials by reducing the annualized relapse rate, preventing multiple sclerosis (MS) lesion accumulation on magnetic resonance imaging, and decreasing the probability of sustained progression of disability.

			natalizumab, though the risk of PML has not been fully eliminated. Future work continues into the development of new biomarkers that may better predict an individual's risk of PML and further improve upon natalizumab's safety.						