Supplement

Real-World Effectiveness of Natalizumab Extended Interval Dosing in a French Cohort

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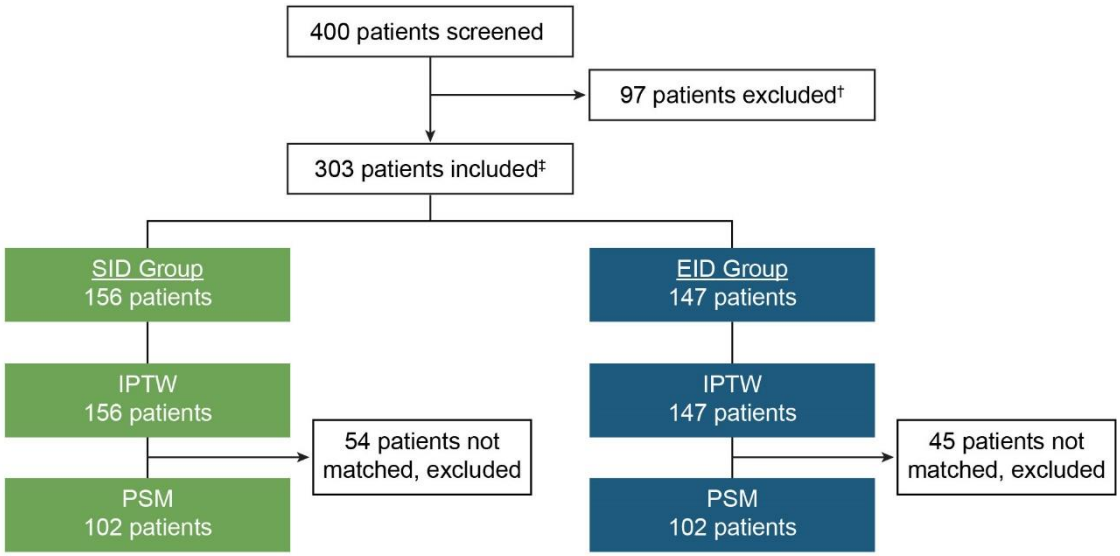
Supplemental Figure 1. Flowchart.



†Fifteen patients (3.7%) presented at least one of the exclusion criteria; 61 patients (15%) did not meet inclusion criteria; and 21 patients (5.2%) were excluded because of missing data.
‡One recruiting center provided patients for the SID group only (Strasbourg), and one center provided patients for the EID group only (Toulouse).
EID extended interval dosing, *IPTW* inverse probability treatment weighting, *PSM* propensity score weighting, *SID* standard interval dosing

Supplemental Table 1. Baseline characteristics in raw and shrinkage IPTW populations

Baseline characteristics	Raw data			IPTW (shrinkage)		
	SID group (N = 156)	**EID group (N =147)**	***p* value[a]**	**SID group (wN = 129.9)**	**EID group (wN = 142.3)**	***p* value[b]**
Age (y), mean (SD)	40.2 (10.6)	39.3 (9.7)	0.467	39.3 (9.8)	39.8 (9.5)	0.694
Female, n (%)	123 (79)	110 (75)	0.408	102.0 (78)	109.8 (77)	0.794
BMI (kg/m²), median (IQR)[c]	24.6 (23.0–25.0)	24.6 (21.7–25.9)	0.192	24.6 (22.8–25.1)	24.6 (21.7–26.2)	0.420
Weight (kg), mean (SD)[d]	70.2 (15.7)	68.3(15.5)	0.374	70.4 (15.3)	68.7 (15.7)	0.427
≤ 80 kg, n (%)[d]	132 (85)	117 (80)	0.254	60.8 (73)	105.0 (77)	0.495
Any disease-modifying therapy before natalizumab, n (%)	132 (85)	121 (82)	0.590	106.3 (82)	116.4 (82)	0.989
RRMS disease duration at baseline (months), median (IQR)	132.5 (72.0–205.0)	139.0 (83.0–199.0)	0.915	128.0 (63.0–202.0)	139 (84.0–199.0)	0.557
ARR at baseline, median (IQR)	0.50 (0.23–0.70)	0.40 (0.21–0.67)	0.214	0.50 (0.20–0.70)	0.43 (0.22–0.67)	0.417
Duration of natalizumab exposure at baseline (months), median (IQR)	28.5 (12.0–73.5)	27.0 (21.0–54.0)	0.259	26.0 (12.0–67.0)	27.0 (21.0–56.0)	0.053
Number of relapses at baseline, median (IQR)	5.0 (3.0–9.0)	4.0 (3.0–7.0)	0.127	5.0 (3.0–8.0)	5.0 (3.0–7.0)	0.673
EDSS score at baseline, median (IQR)[d]	2.0 (1.0–4.0)	2.0 (1.0–4.0)	0.617	2.0 (1.0–4.0)	2.5 (1.0–4.0)	0.931
Positive JCV serology at baseline, n (%)[d]	39 (26)	37 (29)	0.588	32.8 (26)	35.2 (28)	0.813

Variables included in the propensity score model are in boldface type.

ARR annualized relapse rate, *BMI* body mass index, *EDSS* Expanded Disability Status Scale, *EID* extended interval dosing, *IPTW* inverse probability treatment weighting, *IQR* interquartile range, *JCV* JC virus, *RRMS* relapsing-remitting multiple sclerosis, *SD* standard deviation, *SID* standard interval dosing, *wN* weighted number

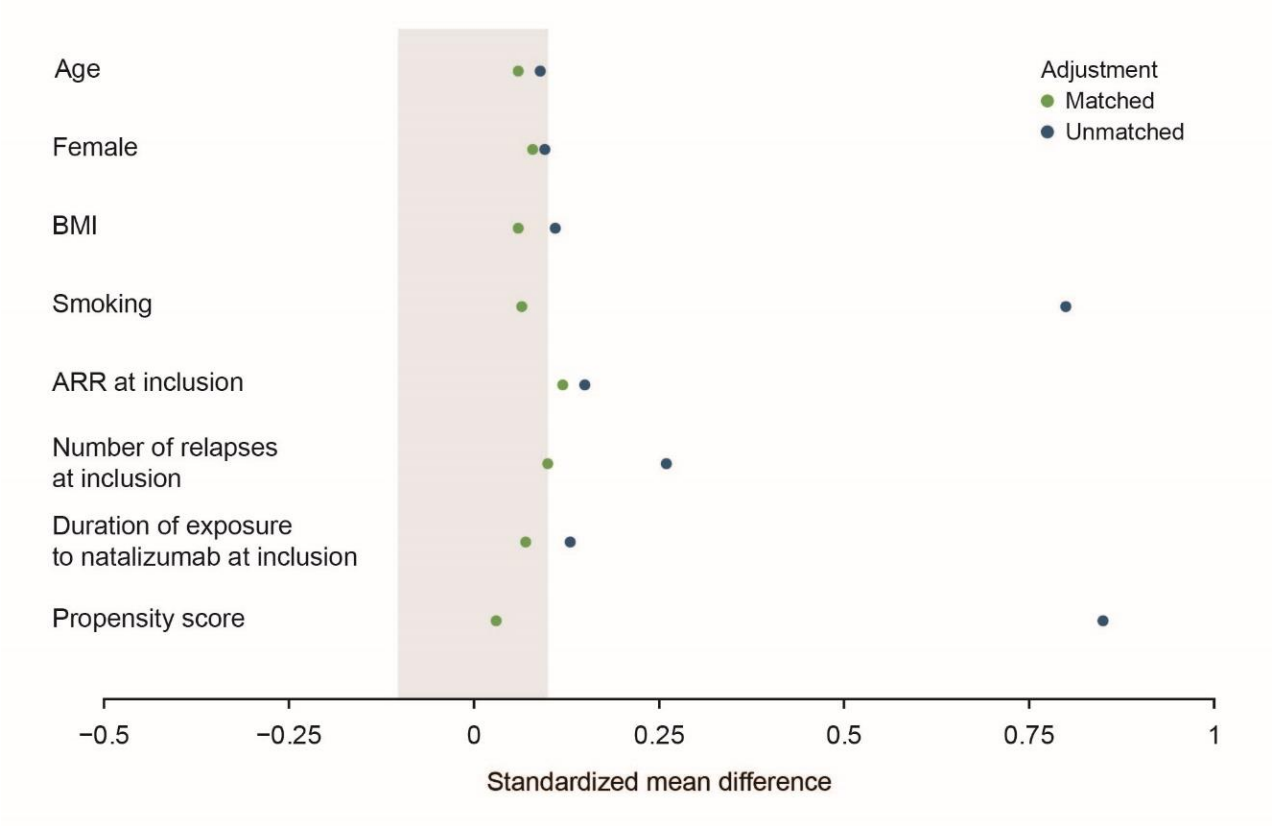
[a]*p* value of Student *t* test or Mann-Whitney U test for continuous variables and chi-square test or Fisher exact test for qualitative variables.

[b]*p* value of Student *t* test or Mann-Whitney U test for continuous variables and chi-square test or Fisher exact test for qualitative variables, weighted on stabilized weights.

[c]Imputation by the mean.

[d]Body weight was missing for 70 patients (23%), EDSS score for 10 patients (3%), and anti-JCV serostatus for 25 patients (8%), respectively.

Supplemental Fig. 2 Standardized mean differences



ARR annualized relapse rate, *BMI* body mass index

Supplemental Table 2. Sensitivity analyses of primary endpoint and ARR at 12 months adjusted on therapy groups and ARR at baseline in matched model

Sensitivity analysis	**Matched model (N = 204)**		
Potential factors associated with at least one relapse for 12 months	**OR**	**95% CI**	***p*[a]**
Therapy group			
SID	**1**		
EID	0.63	0.21–1.90	0.410
ARR at baseline	1.57	0.63–3.94	0.333
Potential factors associated with ARR at 12 months	**RR**	**95% CI**	***p*[b]**
Therapy group			
SID	1		
EID	0.67	0.22–2.02	0.543
ARR at baseline	1.71	0.82–3.54	0.152

ARR annualized relapse rate, *CI* confidence interval, *EID* extended interval dosing, *OR* odds ratio, *RR* relative risk, *SID* standard interval dosing

[a]*p* value obtained by univariate generalized linear model with a binomial distribution taking into account matched data.

[b]*p* value obtained by univariate generalized linear model with a Poisson distribution taking into account matched data.

Supplemental Table 3. Change in lesion volume

	Raw data		
MRI endpoint	**SID group (n = 44)**	**EID group (n = 48)**	***p*[a]**
Change of lesion volume from baseline to 12 months, median (IQR)[b]	−0.28 (−1.14 to 0.42)	−0.38 (−1.38 to 1.02)	0.852

EID extended interval dosing, *IQR* interquartile range, *MRI* magnetic resonance imaging, *SID* standard interval dosing

[a]*p* value obtained by the Wilcoxon signed rank test.

[b]For lesion volume overall, 211 (70%) patients with missing data, with 112/156 patients (72%) missing data in the SID group and 99/147 patients (67%) missing data in the EID group.

Supplemental Table 4. JCV index values

	Baseline		12-month	
	SID	**EID**	**SID**	**EID**
Number of patients with anti–JCV index value (n)	64	73	141	117
Mean (SD)	0.62 (0.82)	0.78 (1.10)	0.35 (0.71)	0.48 (0.95)
Median (IQR)	0.32 (0.00–0.84)	0.23 (0.00–0.95)	0.00 (0.00–0.52)	0.00 (0.00–0.47)
Min–max	0.00–3.48	0.00–4.55	0.00–3.65	0.00–3.85
Anti–JCV index (n)				
≤ 0.9	50	54	120	96
> 0.9 to ≤ 1.5	9	2	14	3
> 1.5	5	17	7	18
Missing	92	74	15	30

EID extended interval dosing, *IQR* interquartile range, *JCV* JC virus, *max* maximum, *min* minimum, *SD* standard deviation, *SID* standard interval dosing