

Rebound Disease Activity Reduction in Relapsing Multiple Sclerosis Patients Transitioned From Natalizumab to Teriflunomide

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BACKGROUND

Prolonged natalizumab (NTZ) treatment for relapsing multiple sclerosis (MS) is associated with increased risk of progressive multifocal leukoencephalopathy (PML) in JC virus (JCV) positive patients. Discontinuation of NTZ in JCV-positive patients has been associated with a high risk of relapse in the ensuing 6-12 months, the risk of relapse increasing with duration of post-NTZ "washout". To date, no known prospective study has demonstrated a therapeutic strategy which reduces the risk of relapse following the discontinuation of NTZ.

OBJECTIVES

To determine if early introduction of teriflunomide (TFM) will be safe and effective in reducing the risk of disease activity after withdrawing NTZ treatment.

METHODS

- Adult patients with relapsing MS, who had at least 12 consecutive relapse-free months of NTZ treatment, and the presence of serum anti-JCV antibodies, were switched to TFM within 28 ± 7 days after their last NTZ infusion.
- Full physical and neurological exam, 3T brain MRI, and labs were performed at baseline, monthly for 6 months, and 12, 18, and 24 months after initiating TFM.
- A total of 62 subjects have been screened, 55 of them completed baseline, and 40 of them, the subjects of this presentation, have completed at least 6 months of TFM therapy as of June 30th, 2016.

RESULTS

- 40 subjects, 75% female, age 48.46 ± 8.87 years, with a mean baseline EDSS of 3.06 ± 1.30 were included in the analysis (Table 1).
- Mean duration of prior NTZ treatment was 44.53 ± 25.68 months and mean duration of TFM treatment was 16.28 ± 5.80 months (Table 1).
- 14 patients (35%) have had new T2, enlarging T2, or enhancing brain lesions (Table 2).
- 7 patients had mild and transient hepatic enzyme elevation but no one was dropped from the study as a result (Table 2).
- 17 patients had mild to moderate hair loss (Table 2).
- 6 patients had clinical relapses, only one of which occurred in the first 6 months. Annualized relapse rate while receiving TFM was 0.11. No cases of PML have occurred (Table 2).
- We have observed no significant EDSS change from baseline (3.2 ± 1.3) to month 12 (3.1 ± 1.5) among the 35 patients who have completed 12 months of TFM therapy.

Table 1 Demographic and Clinical Information

Variable	n	% or Mean (SD)	Range
Female, %	40	75	n/a
Age, years	40	48.46 (8.87)	19-63
EDSS at Baseline	40	3.06 (1.30)	1.0-6.0
EDSS at Month 12	35	3.13 (1.54)	1.0-6.5
Months of NTZ infusion	40	44.53 (25.68)	12-114
Months of TFM treatment	40	16.28 (5.80)	6-24

CONCLUSIONS

Our results demonstrate that early initiation of TFM was associated with a 2.5% (1/40) relapse rate in the first 6 months, and 5.7% (2/35) in the first 12 months following NTZ withdrawal, compared to previously reported rate of 30% or higher, which may be related, in part, to elimination of NTZ washout before initiating TFM therapy, and should inform decisions regarding the washout strategies to employ after NTZ termination.

Table 2 Observed Clinical Relapses, MRI Changes, and Adverse Events

Subject	Age at Baseline	Gender	Months of TFM	Months of NTZ	EDSS at Baseline	EDSS at Month 12	Had Clinical Relapse	Had MRI Change	Reported Hair Thinning	Had Elevated Liver Enzymes
1	41	Female	24	64	2.0	2.0		month 24	Yes	Yes
2	25	Female	18	69	2.5	2.5		months 6 & 12		
3	52	Male	18	27	2.5	2				
4	48	Female	18	52	2.0	2.5			Yes	
5	45	Female	18	12	5.0	4.5				Yes
6	58	Female	18	72	6.0	6.0			Yes	Yes
7	57	Female	18	13	1.5	2.0		month 2	Yes	Yes
8	60	Female	18	114	2.0	2.0			Yes	
9	56	Female	9	49	3.0	*			Yes	
10	58	Male	12	75	2.0	1.5		month 6		Yes
11	50	Female	12	52	3.5	3.5			Yes	
12	63	Female	12	12	4.5	4.5			Yes	
13	44	Female	18	23	3.0	4.0	month 18	month 12		
14	42	Female	20	65	3.5	2.0				
15	42	Male	22	34	2.0	2.0	month 22	months 6 & 12		
16	57	Female	24	45	6.0	6.0	month 6		Yes	Yes
17	40	Female	12	34	4.5	6.0	month 15	month 12		
18	42	Female	24	75	3.0	2.5		month 24		
19	54	Female	12	60	6.0	6.5				
20	43	Female	24	54	3.5	1.5		months 3 & 4		
21	49	Female	18	48	2.0	1.5				Yes
22	57	Male	24	63	2.0	2.0				
23	52	Female	24	29	4.0	4.0		month 12	Yes	
24	57	Female	12	34	4.0	5.5			Yes	
25	40	Female	24	13	2.5	2.5			Yes	
26	48	Female	12	77	3.0	4.0		month 12	Yes	
27	51	Female	12	94	2.5	2.0		month 12	Yes	
28	59	Female	24	65	3.5	3.5				
29	58	Male	24	52	4.0	4.0		month 6		
30	40	Female	18	58	2.5	1.0			Yes	
31	42	Female	12	13	4.0	3.5			Yes	
32	37	Male	18	18	1.0	1.0	month 15	months 5 & 12		
33	54	Female	18	20	3.5	2.5				
34	31	Male	12	24	4.0	3.0				
35	62	Male	12	30	1.0	2.0				
36	56	Male	12	68	2.5	4.0	month 11			
37	37	Female	6	18	3.5	*				
38	46	Female	6	12	1.5	*			Yes	
39	47	Male	6	32	1.5	*				
40	59	Female	6	12	2.0	*				

*not yet due for month 12 EDSS

Disclosures:

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