

An Interim Analysis of Monthly Surveillance 3T MRI in MS patients switching from long term natalizumab to teriflunomide in a prospective study

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BACKGROUND

Natalizumab (NTZ) has the risk of causing progressive multifocal leukoencephalopathy (PML) after extended use by patients testing positive for serum anti-JCV-antibody. There is a need to have an alternative disease modifying treatment (DMT) that would be safe and effective to prevent recurrence of MS exacerbations upon discontinuation of NTZ.

OBJECTIVES

To determine if teriflunomide will be safe and effective in reducing breakthrough MS disease activity in patients switching from NTZ.

METHODS

Patients must have received 12 or more consecutive NTZ treatments, be anti-JCV-ab positive, not have received prior immunosuppressive therapy, and been free of clinical relapses during prior 12 months of NTZ treatment. Patients began teriflunomide 14 mg daily, within 4 weeks after their last dose of NTZ. Monthly 3T brain MRI, EDSS, laboratory tests, interim history and complete neurological and physical examinations were performed for 6 months.

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Table 1: Patient demographics

Patients switched from natalizumab to teriflunomide, n=28	Percentage	Mean (SD)	Range
Female (n=22)	79%	n/a	n/a
Age (n=28)	n/a	47 (8.55)	26-59
Total No of years of MS	n/a	15 (7.99)	3.27-38.22
Baseline EDSS	n/a	3.30 (1.33)	1.0-6.0
EDSS at month 6	n/a	3.09 (1.37)	1.0 - 6
Number of natalizumab infusions (SD)	n/a	47 (23.08)	12 - 94
Number of months on natalizumab (SD)	n/a	45 (22.79)	11 - 86

RESULTS

To date, 28 patients have had at least 6 months of teriflunomide after NTZ withdrawal. Mean age was 47 (SD=8.55). 79 percent were female. The mean number of NTZ treatments prior to treatment with teriflunomide was 47. The mean EDSS at baseline was 3.30 (SD=1.33); and after 6 months of teriflunomide treatment mean EDSS was 3.09 (SD=1.37). Results showed 22 of the 28 patients stable in all MRI parameters from baseline to month 6. 4 patients had both Gd+ and new T2 hyperintensities. 1 patient had Gd+ activity only and 1 had T2 only. Of these patients, only 2 had clinically apparent relapses. Teriflunomide was discontinued in only one patient due to relapse with Gd+ at month 5.

There was no emergence of PML. There were 10 patients with mild hair thinning. There were 3 patients experienced transient mild elevation of LFTs, twice ULN or less with spontaneous resolution without discontinuation of teriflunomide.

CONCLUSION

There is a need for a DMT that can reduce the high risk of breakthrough MS disease activity commonly seen in patients, particularly in the first 6 months, after discontinuing NTZ due to PML risk. Our results demonstrate that teriflunomide may be a safe and effective therapy for the transition from NTZ.

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Table 2: Baseline data

#	Patient #	Age	Gender	Baseline EDSS	# of Exacerbations 1 year prior to NAT start	# of GAD Enhancing Lesions on MRI 1 year prior to NAT start
1	101	44	Female	3	2	0
2	102	42	Female	3.5	2	0
3	103	42	Male	2	2	1
4	104	57	Female	6	3	0
5	105	40	Female	4.5	1	0
6	106	42	Female	3	2	3
7	107	54	Female	6	2	4
8	108	43	Female	3.5	3	0
9	109	49	Female	2	1	0
10	110	57	Male	2	4	0
11	111	52	Female	4	5	1
12	113	57	Female	4	0	0
13	114	40	Female	2.5	2	1
14	115	48	Female	3	2	0
15	117	51	Female	2.5	0	0
16	118	59	Female	3.5	0	0
17	119	58	Male	4	1	0
18	120	40	Female	2.5	3	1
19	121	42	Female	4	2	0
20	122	37	Male	1	2	0
21	123	54	Female	4	2	8
22	201	41	Female	2	2	0
23	204	26	Female	2.5	1	0
24	205	52	Male	2.5	1	0
25	206	31	Male	2	7	10
26	207	49	Female	2	0	0
27	208	45	Female	5	0	0
28	209	58	Female	6	0	0
	Mean	47		3.3		

Table 3: Data at 6 months on teriflunomide

#	Patient #	Age	Gender	EDSS at Month 6	EDSS Status	# of New Gd+ on MRI	# of New T2 on MRI	Lesions occurring at Month #	MRI Activity only	Clinical Relapse
1	101	44	Female	2.5	Improved by 0.5	0	0	-	-	No
2	102	42	Female	2.5	Improved by 1.0	0	0	-	-	No
3	103	42	Male	2	No change	2	2	Month 6	Yes	No
4	104	57	Female	6	No change	0	0	-	-	Yes, Relapse at Month 6
5	105	40	Female	4.5	No change	0	0	-	-	No
6	106	42	Female	3	No change	0	0	-	-	No
7	107	54	Female	6	No change	0	0	-	-	No
8	108	43	Female	2.5	Improved by 1.0	1	1	Months 3 and 4	Yes	No
9	109	49	Female	1.5	Improved by 0.5	0	0	-	-	No
10	110	57	Male	2	No change	0	0	-	-	No
11	111	52	Female	2.5	Improved by 1.5	0	0	-	-	No
12	113	57	Female	3.5	Improved by 0.5	0	0	-	-	No
13	114	40	Female	3	Worse by 0.5	0	0	-	-	No
14	115	48	Female	4	Worse by 1.0	0	0	-	-	No
15	117	51	Female	2	Improved by 0.5	0	0	-	-	No
16	118	59	Female	4	Worse by 0.5	0	0	-	-	No
17	119	58	Male	3	Improved by 1.0	0	1	Month 6	Yes	No
18	120	40	Female	2.5	No change	0	0	-	-	No
19	121	42	Female	2	Improved by 2.0	1	1	-	-	No
20	122	37	Male	1	No change	1	0	Month 5	Yes	No
21	123	54	Female	4	No change	0	0	-	-	No
22	201	41	Female	2	No change	0	0	-	-	No
23	204	26	Female	2.5	No change	1	0	Month 6	Yes	No
24	205	52	Male	2	Improved by 0.5	0	0	-	-	No
25	206	31	Male	3	Worsened by 1.0	5	3	Months 3 and 5	Yes	Yes
26	207	49	Female	2	No change	0	0	-	-	No
27	208	45	Female	5	No change	0	0	-	-	No
28	209	58	Female	6	No change	0	0	-	-	No
	Mean	47		3.09						

1 patient discontinued Teriflunomide after 5 months