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Evaluation of switching to teriflunomide in high risk natalizumab patients

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INTRODUCTION

Natalizumab (NTZ) may cause progressive multifocal leukoencephalopathy (PML) in patients with detected anti-JCV-antibody after extended use. Prior use of immunosuppressive agents further increases risk of PML. There are no guidelines for switching from NTZ to another disease modifying therapy (DMT). Significant reactivation of the patient's MS disease activity may occur after NTZ withdrawal.

PURPOSE

To determine if teriflunomide is safe and effective in patients switching from NTZ to teriflunomide.

METHODS

Twenty-five consecutive RMS patients, ages 28 to 60, who had received 12 or more NTZ treatments and who were anti-JCV antibody detected, were switched to teriflunomide and were analyzed using retrospective data collection. Teriflunomide treatment was started as soon as medication was available upon stopping NTZ. Prior use of an immunosuppressant was recorded. Clinical status was measured by tolerance and safety, clinical relapses and EDSS at 6 and 12 months. MRI findings were analyzed.

RESULTS

Mean age was 47.5 (SD 6.8); 80% were female. Mean number of NTZ treatments was 39 (SD 12). Mean months of teriflunomide treatment was 21 (SD 12). Nine patients had prior immunosuppression (36%) with a mean treatment duration with NTZ of 48 months (SD 11). Mean time between last NTZ dose and first teriflunomide dose was 6 weeks (SD 4). Mean EDSS at baseline was 3.5 (SD 1.5). After 6 months, the mean EDSS of remaining 23 patients was 3.3 (SD 1.5) and there were no clinical exacerbations. Two of the 25 patients discontinued due to gastrointestinal issues in the first few weeks of treatment. Five patients (20%) had temporary hair thinning with full recovery. There were no laboratory abnormalities. Between 6 and 12 months, four patients had mild exacerbations and switched to other therapies. There were no serious exacerbations (greater that 1 EDSS score). Of the 23 patients who had MRIs performed at 12 months, 12 patients had stable MRIs. One patient had new T2 lesions and one other patient had GD+ lesions. No cases of PML occurred.

CONCLUSION

There is a need for a DMT for patients who are discontinuing NTZ due to risk of PML. Teriflunomide may be a safe and effective therapy for transition from NTZ. A shortened "washout" interval appears to be effective with a low relapse rate.

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Table 1: Patient demographics

Patients switched from natalizumab to teriflunomide, n=25	Percentage	Mean (SD)	Range
Female (n=20)	80 %	n/a	n/a
Age (n= 25)	n/a	47.5 (6.8)	28-60
Baseline EDSS	n/a	3.5 (1.5)	1.5 - 6.5
EDSS at month 6 (n=23)	n/a	3.3 (1.5)	1.5 - 6.5
Number of natalizumab infusions (SD)	n/a	39 (12.0)	17 - 67
Washout period in weeks (SD)	n/a	6 (4.0)	0 - 11
Duration of teriflunomide treatment in months (SD)	n/a	21 (12.0)	0 - 43

Table 2: Baseline data

#	Age	Gender	Baseline EDSS	JCV status	Baseline MRI impression	NAT infusion #	Washout period in weeks
1	60	Female	3.5	JCV+ ; no IS	unchanged	49	5
2	42	Female	2	JCV+ ; no IS	stable	31	11
3	47	Female	2	JCV+ ; no IS	stable	26	8
4	57	Female	5.5	Triple +ve	stable	50	11
5	46	Female	4	Triple +ve	stable	44	5
6	51	Female	2	JCV+ ; no IS	unchanged	21	11
7	53	Male	3.5	JCV+ ; no IS	stable	17	2
8	44	Female	2.5	Triple +ve	stable	58	3
9	48	Female	3.5	JCV+ ; no IS	stable	43	8
10	28	Male	3.5	Triple +ve	unchanged	47	11
11	52	Female	6	Triple +ve	stable	29	6
12	55	Female	6.5	Triple +ve	unchanged	48	4
13	49	Female	4	JCV+ ; no IS	unchanged	36	5
14	60	Female	1.5	JCV+ ; no IS	unchanged	40	8
15	45	Female	2	JCV+ ; no IS	unchanged	49	11
16	57	Male	3	Triple +ve	unchanged	55	2
17	43	Female	6.5	Triple +ve	unchanged	67	1
18	42	Female	4	JCV+ ; no IS	unchanged	36	0
19	53	Male	3.5	Triple +ve	unchanged	37	3
20	44	Female	3	JCV+ ; no IS	stable	24	2
21	52	Female	2	JCV+ ; no IS	stable	35	3
22	41	Male	2	JCV+ ; no IS	2 new plaques, no enhancement	34	1
23	40	Female	4.5	JCV+ ; no IS	unchanged	34	8
24	44	Female	-	JCV+ ; no IS	stable	30	8
25	49	Female	-	JCV+ ; no IS	unchanged	38	7
Mean	**47.5**		**3.5**			**39**	**6**

Table 3: Data at 6 & 12 months on teriflunomide

#	Age	Gender	EDSS at 6 Months	EDSS Status	MRI Impressions at 6 Months	MRI Impressions at 12 Months	Total Months on Teriflunomide	Mild Clinical Exacerbation
1	60	Female	3.5	No change	n/a	No abnormal enhancement	43	-
2	42	Female	1.5	Improved by 0.5	stable	stable	12	-
3	47	Female	3.5	Worsened by 1.5	stable	No abnormal enhancement	14	-
4	57	Female	5	Improved by 0.5	n/a	No abnormal enhancement	17	-
5	46	Female	2	Improved by 2.0	stable	stable	39	-
6	51	Female	2	No change	stable	stable	17	-
7	53	Male	3.5	No change	unchanged	stable	8	Yes
8	44	Female	2	Improved by 0.5	New T2 and Gd+ lesions	unchanged	38	-
9	48	Female	3.5	No change	stable	unchanged	22	-
10	28	Male	4	Worsened by 0.5	unchanged	unchanged	22	-
11	52	Female	6	No change	stable	stable	12	-
12	55	Female	6.5	No change	New T2 and Gd+ lesions	stable	7	Yes
13	49	Female	2	Improved by 2.0	unchanged	unchanged	8	Yes
14	60	Female	1.5	No change	n/a	unchanged	43	-
15	45	Female	2	No change	stable	No abnormal enhancement	32	-
16	57	Male	3	No change	n/a	stable	31	-
17	43	Female	6.5	No change	unchanged	n/a	31	-
18	42	Female	4	No change	unchanged	n/a	11	Yes
19	53	Male	3.5	No change	unchanged	Gd+ lesion	29	-
20	44	Female	3	No change	stable	unchanged	23	-
21	52	Female	2	No change	unchanged	unchanged	23	-
22	41	Male	2	No change	New T2 lesions	New T2 lesion	21	-
23	40	Female	4.5	No change	unchanged	unchanged	23	-
24	44	Female	DCD within first few week of starting Teriflunomide due to severe gastrointestinal issues				2	-
25	49	Female	DCD within first few week of starting Teriflunomide due to severe gastrointestinal issues				0	-
Mean	**47.5**		**3.3**				**21**	

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