Changes in JC Virus Antibody Index in JC Positive MS Patients Treated with Natalizumab

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OBJECTIVE

Determine if Natalizumab treatment of JC pos MS patients causes an increased JC antibody index.

BACKGROUND

Natalizumab (NAT) rarely alters the JC virus so that it causes PML (Progressive Multifocal Leukoencephalopathy). PML risk factors are duration of NAT treatment, prior immunosuppression (IS) and a positive (pos) JC IgG index. There is a theoretical concern that NAT can cause dissemination and reproduction of the JC virus . Presumably, viral reproduction causes an increased JC index.

METHODS

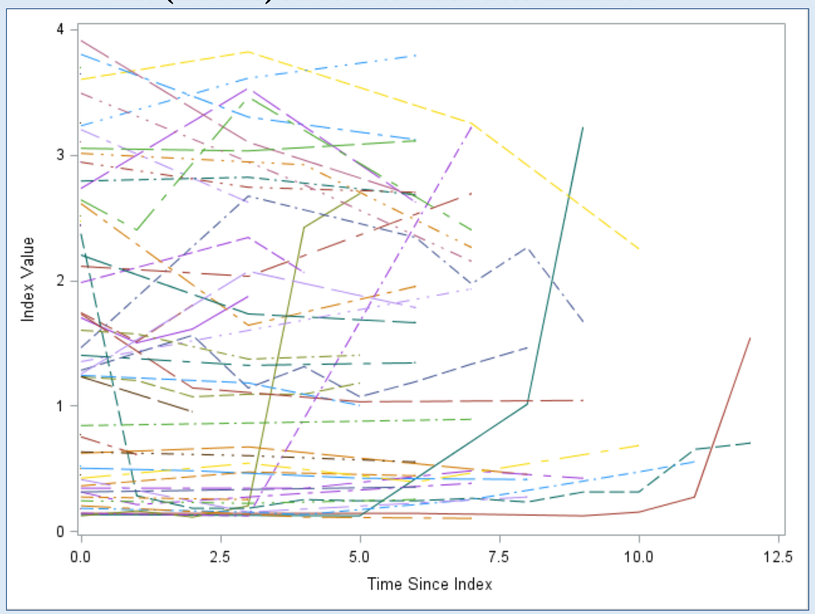
Index values from JC pos MS pts treated with NAT at 2 clinical sites were analyzed. Initial values were obtained when the test became available, some patients had received multiple infusions before initial determination. 25% had index values determined at treatment onset. 75% had initial determination during the course of treatment. Baseline variables included age, gender, race/ethnicity, and prior IS use. Treatment variables included IV steroid use, exacerbations and infections during NAT therapy. A generalized linear mixed effect model was used to adjust for time and JC index value, steroid use, infections and exacerbations.

RESULTS

Results: Patients: n = 81, (48 F, 33 M), Mean age 41.8 years, prior IS use 3. During NAT treatment: 30 infections, 14 pts had IV Steroid, 10 exacerbations. The number of index values per patient ranged from 1-13.

For each month of NAT treatment, the JC index increased by 1.89% (p = 0.129). This result was not statistically significant. Exacerbations, steroid use and infections had no effect on the index titers

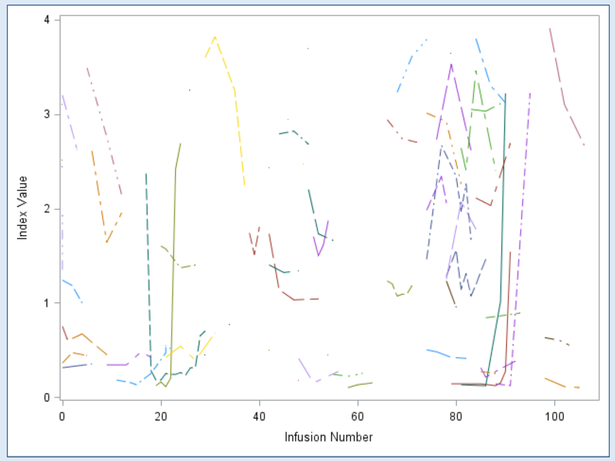
Time (months) since first index determination



Patient Population	
Variable of Interest	**All Patients†**
Number of Patients	89 (100.0)
Age at first infusion (years)	42 ± 11.3
Female	56 (62.9)
Non-Hispanic White	68 (76.4)
History of Immunosuppressant	5 (5.6)
Prior Treatment before Tysabri	20 (22.5)
IV Steroid during Tysabri	14 (15.7)
Exacerbation during Tysabri	10 (11.2)
Infection During Tysabri	34 (38.2)
†Data presented as mean ± standard deviation or count (percent).	

Time effect on JC titer		
Time Effect	Percent Change	P-value
Unadjusted	1.94	0.117
Adjusted	1.93	0.120

Index value and infusion #.



Many patients started treatment before titers were available.

CONCLUSIONS

A non-statistically significant increase in JC index occurred in our sample of JC pos MS patients treated with NAT. Steroids, infection and exacerbations did not affect the index. Assuming the biological correlate of JC viral proliferation is an increased JC titer, it would appear that NAT treatment does not cause viral proliferation at a level detected by this study. However, it is possible that viral proliferation does occur and that NAT prevented antibody production.

The dramatic increases that occurred in a few patients may be secondary to re-infection rather than reactivation of JC virus. Further studies with a direct measure of viral load and a larger patient population may prove beneficial.

Disclosure

Dr Gottesman and Dr. Newman have received honoraria from Biogen, Teva, Sanofi and Novartis.