

T-cell count with Natalizumab in MS: predictor of non-CNS opportunistic infections?

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Background and Rationale

- It is known that based on its mechanism of action, Natalizumab (marketed as Tysabri) reduces T-cell counts in the CSF of patients as observed by Stuve *et al.*¹ As such, much concern has been placed over PML (progressive multifocal leukoencephalopathy) resulting from JCV (John Cunningham virus) infection, but no other infections. In theory, the T-cell count of peripheral blood should remain constant.
- It was our belief that the peripheral T-cell count varies enough over a given time period for other opportunistic infections to be of concern. Our findings would potentially allow physicians to place greater concern for patients under Natalizumab treatment with regards to other opportunistic infections.

Goal

The purpose of our study was to track the changes in T-cell count of peripheral blood in MS patients undergoing treatment with Natalizumab and quantify the results relative to the time from initial dosage and total doses taken.

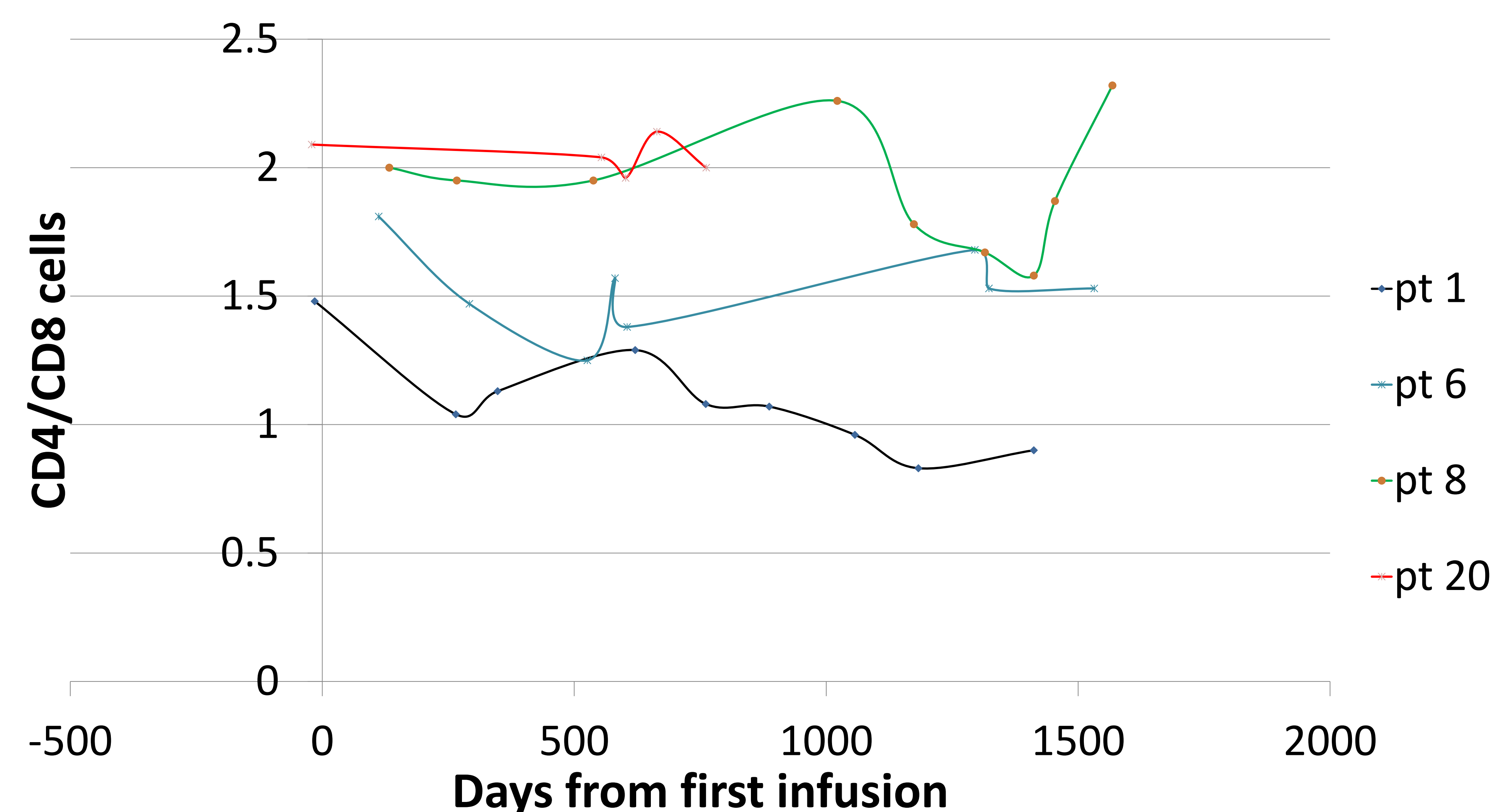
Methods

- Retrospective analysis on patient blood work was completed to collect data
- All MS patients undergoing treatment with Tysabri within the FHMS clinic were used excluding those that had fewer than 2 doses. Of those that qualified 14 of the 20 study patients had blood work available for analysis

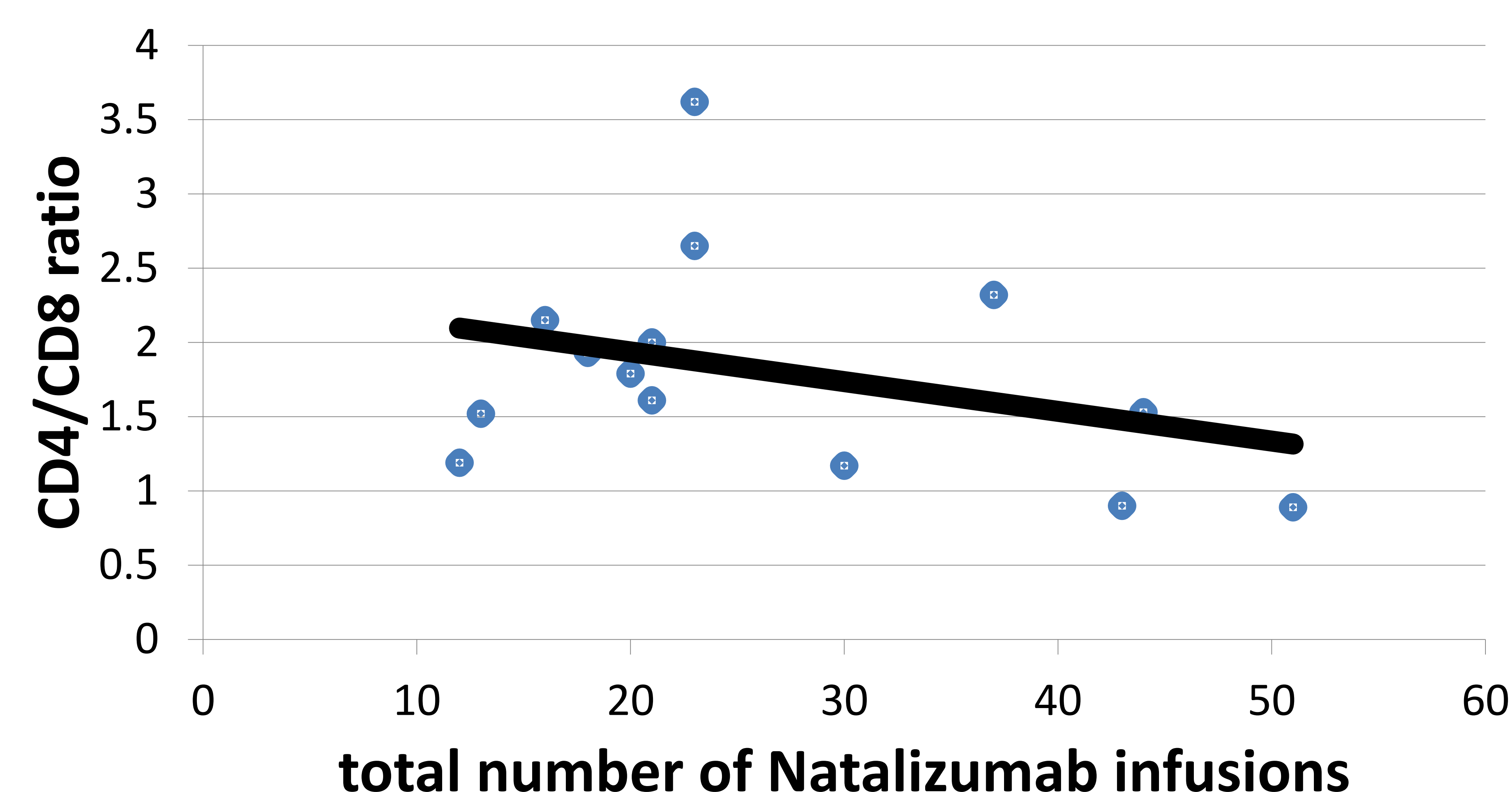
Results

- Of the 14 patients followed, 6 were seen to have a decrease in CD4/CD8 T-cell count of greater than 10% after 1-2 years relative to their initial value.
- These 6 patients were also seen to have a T-cell count decrease of up to 44% over the course of their treatment with Tysabri, with the largest decrease in T-cell count present at the 1-2 year treatment mark.
- Of the remaining 8 patients, 5 had no significant change, higher or lower, in their T-cell count over both the initial time period of concern and over the total period within which they underwent treatment. The remaining 3 patients had increases in their T-cell count, upwards of 60%, over the treatment period.
- The Spearman Rank Correlation Coefficient was also determined for the t-cell count vs. the number of infusions received as to determine their association. The found rho value of -0.174 indicates a weak association between the decrease in CD4/CD8 T-cells with the an increase in the total number of doses of Natalizumab.

CD4/CD8 ratio after first day of infusion



CD4/CD8 ratio as per number of Natalizumab infusions



Conclusions

- It was found that the T-cell count in the peripheral blood of over half of the patients did not remain constant within the first 1-2 years of treatment with Tysabri. Decreases in the T-cell counts of these patients were large enough for opportunistic infections to be of concern
- The number of doses only marginally decreases the CD4/CD8 ratio over a long period of treatment time (greater than 2 years). This can be attested to the CD4/CD8 ratios re-stabilizing to their initial levels
- Physicians should place greater concern for non-CNS opportunistic infections for patients undergoing treatment with Tysabri, particularly within the first 1-2 years of treatment.
- CD4/CD8 T-cell levels are a convenient and easy method to observe patient immune levels to infections.

¹Steve O, Marra CM, Bar-Or A, *et al.* Altered CD4+/CD8+ T-Cell Ratios in Cerebrospinal Fluid of Natalizumab-treated Patients with Multiple Sclerosis. *Arch. Neurol.* 2006;63(10):1383-1387