Simultaneous Use of Immunoglobulin with Natalizumab Attenuates the JCV Stratify Index Elevation- a 2 Year Analysis

Ronald Bailey 1, Marco Pasco 1, Taif Kaisi 1, Shard Yakoot 2, Bhavesh Desai 2, Maria Aziz 1
1 The Neurology Group, Pomona, CA 2 California Specialty Pharmacy, Whittier, CA

OBJECTIVES
- To assess whether combined use of immunoglobulin with NTZ alters Stratify index.

BACKGROUND
- The incidence of progressive multifocal encephalopathy (PML) in Multiple Sclerosis (MS) increases exponentially with prolonged Natalizumab (NTZ) use.
- JCV Stratify (Stratify) is a sensitive test, but lacks specificity to determine NTZ course of action.1
- Use of immunoglobulin (IgG) in the treatment of MS is controversial.
- Off label immunoglobulin use has been limited to patients who are steroid non-responders, patients who have proven refractory to steroids because of prolonged use, or in whom steroids are contraindicated.

METHODS
- Subjects included MS patients (n = 36) enrolled in the Touch Program and treated with NTZ for 2 years.
- Baseline Expanded Disability Status Scale (EDSS) scores ranged from 2.0-8.0.
- Subjects were divided into 2 groups:
  1. Receiving immunoglobulin/NTZ (n = 20)
  2. Receiving NTZ alone (n = 16).
- Patients were evaluated with monthly blood testing, monthly neurological examination, and annual magnetic resonance imaging (MRI) scans.
- JCV DNA PCR probes in whole blood were used to determine JCV infection.
- NABs to NTZ were obtained at times of exacerbation.
- MS exacerbations were treated with 3 day courses of solumedrol or ACTHar gel.
- NTZ was administered at a dose of 300 mg IV q 28 days and those receiving IgG received 40 gm q month.

RESULTS
- All patients remained neurologically stable with respect to EDSS scoring throughout the study.
- 2 MS patients had exacerbations, one of which was treated with solumedrol and the other with ACTHar gel.
- No patient developed PML.
- There was no correlation between Stratify and DNA PCR probe determination in whole blood and urine over the two year interval.

DISCUSSION
- Although there is a trend showing difference between IgG/NTZ and NTZ treatments, the difference does not appear to be significant.
- Possible causes for lack of significance does not indicate a lack of relationship, instead this could be caused by the relatively small sample size of participants.
- One important aspect in the study is the consistency in the trends between the two therapies throughout the 2 year period.

CONCLUSION
- The immunomodulating effect of IgG is reflected in the disparities of Stratify index in those on combination therapy versus NTZ alone.
- The study continues to emphasize that Stratify is sensitive but not specific in determining NTZ use.
- The study suggests that the concomitant use of IgG with NTZ lowers elevations in Stratify index and may attenuate development of PML.
- The study may also point to a potential for decrease in risk for secondary autoimmune conditions that are associated with the use of other disease specific agents and various comorbidities linked with treatment.

REFERENCES
- Statistical Analysis: Simple descriptive statistics were done using SAS 9.4 and Excel. Cox Proportional Hazards survival model was performed using SAS 9.4 and Software R.
- Cox Proportional Hazards:
  The Cox model estimates the survival probability S(t) of a patient surviving at least until time t, S(t) = Pr(T > t)
  via the hazard function defined by:
  \( \lambda(t) = \frac{Pr(0 < T < t | T \geq t)}{S(t)} \)
  The hazard function is modeled as a function of input variables (e.g., EDSS score) via the equation:
  \( \lambda(t) = \lambda_0(t) \exp(\beta_1 X_1 + \ldots + \beta_n X_n) = \lambda_0(t) \exp(f(X)) \)

Disclosure: The authors have nothing to declare.