Transition From Natalizumab To Dimethyl Fumarate In Multiple Sclerosis Patients: Clinical and MRI Outcomes

M. Omar Waheed DO[1] and Ka-Ho Wong BS[1], Stacey L. Clardy MD PhD[1,2], Melissa M. Cortez DO[1], L. Dana DeWitt MD[1], Julia M. Klein APRN[1], M. Mateo Paz Soldan MD PhD[1,2], John D. Steffens MD[1], and John W. Rose MD[1,2]

1. Department of Neurology, University of Utah Health, Salt Lake City, UT 2. Department of Veterans Affairs Medical Center, Salt Lake City, UT

Objective

We assessed the outcomes of transitioning multiple sclerosis patients from natalizumab to dimethyl fumarate (DMF). Demographic data collected included age, gender, and ethnic background. Clinical assessments included number of clinical relapses within 12 months of transition and rate of continuation of therapy. In addition, we evaluated MRI activity within 12 months of initiation of therapy.

Background

- There are now a wide variety of available treatments for relapsing multiple sclerosis (RMS), some of which carry substantial risk of adverse effects.
- The best approach for transitioning patients between immunotherapies, including change from natalizumab to DMF, has not been established.

Design and Methods

- Retrospective chart review of all patients diagnosed with RMS who were prescribed natalizumab and oral DMF at the University of Utah Multiple Sclerosis Clinic (March 2012 to December 2017). Patients identified by pharmacy records in the electronic medical record.
- 512 RMS patients on treatment with natalizumab and/or oral DMF were screened. Patients who had received at least one dose of natalizumab and were subsequently transitioned to oral DMF were analyzed (n=27). 46 brain MRI's and 12 spinal cord MRI's were reviewed.

Table 1 – Patient Characteristics

	Natalizumab transition to oral DMF patients (n=27)
Gender (% n, female)	66.7 (18)
Age (mean, SD)	46.1 (10.9)
Time since MS diagnosis in years (mean, SD)	17.1 (6.6)
Race (%, n) Caucasian Hispanic	 92.6(25) 7.4(2)
Reason to switch from Natalizumab to DMF (%, n) JC Virus Positive Clinical or Radiological Relapse Other	 74.1(20) 18.5(5) 7.4(2)

Results

- Of 512 patients identified through chart review a total of 27 patients had transition from natalizumab to oral DMF.
- Prior to oral DMF initiation, average EDSS scores were 5.2 and after 12 months of DMF initiation EDSS scores increased to 5.3.
- Of the 27 patients transitioned from natalizumab to oral DMF, 5 patients demonstrated new T2 or enhancing lesions within 12 months of initiation (**see Figure 1**); only one of these patients experienced a clinical relapse within 12 months of initiating oral DMF (**see Figure 2**).
- 25 of the 27 patients remained on DMF after 12 months; 2 patients discontinued DMF within 12 months of immunotherapy transition, due to clinical relapse or new or active lesions.

Discussion

- In our retrospective review, 81.5% of patients had no clinical relapse, and no new or active lesions (n=22); 18.5% of patients had clinical relapse and/or new or active lesions (n=5), and 7.4 % discontinued DMF within 12 months of initiation (n=2).
- Transition from natalizumab to oral DMF was associated with a low risk of clinical activity during a 12 month observational period.
- However, our review of MRI scans indicates a modest increase in disease activity following transition. This suggests that careful selection and monitoring is required in patients transitioning from natalizumab to oral DMF.

Images

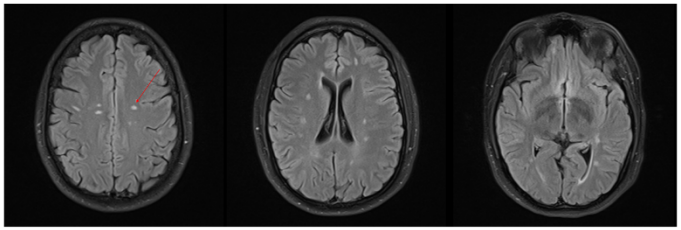

Figure 1: This patient tolerated DMF for the duration of the study without experiencing clinical relapse. She exhibited MRI activity (one new T2 lesion) within 1 year of initiating DMF

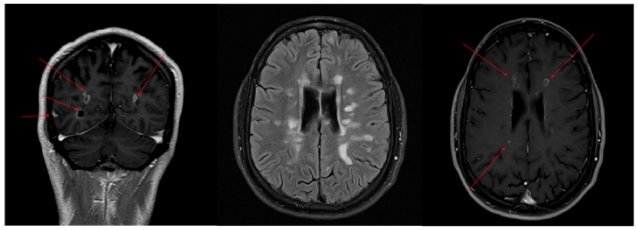

Figure 2: This patient experienced 1 clinical relapse within 6 months of initiation of DMF, characterized by left optic neuritis. MRI demonstrated numerous new enhancing lesions. This patient was the only one among this cohort to experience a relapse.

References

- Bridel C, et al. Update on multiple sclerosis treatments. Swiss Med Wkly. 201 Sept 23.
- Gajofatto A et al. Treatment strategies for multiple sclerosis: When to start, when to change, when to stop? 'world J Clin Cases 2015 Jul 16;3(7)545-55
- van Rossum, JA et al. Safety, anxiety and natalizumab continuation in JC virus-seropositive MS patients. March 2014. .