Evaluating Effect of Dimethyl Fumarate on Leukocytes Among Caucasian-, African- and Hispanic-American Patients with Multiple Sclerosis (MS)

Lana Zhovtis Ryerson[1] , Carrie L Sammarco[1], Tamar Bacon[1], Ashley Akhter[2], Lisa Laing[1], Ilya Kister[1]
[1]NYU MS Comprehensive Care Center, NYU Langone Medical Center, New York, NY, [2]NYU School of Nursing

BACKGROUND:

- Dimethyl fumarate (DMF) demonstrated significant efficacy in two randomized clinical trials for relapsing remitting multiple sclerosis (RRMS).[1,2] However, trials included few patients of African-American (AA) and Hispanic American (HA) backgrounds.
- Recent reports of Progressive Multifocal Leukoencephalopathy (PML) in patients treated with DMF, possibly related to leukopenia developing after the start of the drug, is of concern. [3,4]
- Identifying risk factors of leukopenia related to DMF may help reduce risk of PML.

OBJECTIVES:

- To evaluate DMF's effect on leukocyte count in Caucasian–American (CA), African-American (AA), and Hispanic-American (HA) patients with MS treated at the NYU MS Care Center in New York.

METHODS:

- Retrospective chart review was performed on all clinic patients who were started on DMF in the first year of drug availability.
- Ethnicity was derived from patient self-description.
- For each patient, we extracted from the Electronic Medical Record their complete absolute leukocyte counts (ALC) before DMF was started and during DMF therapy .
- Groups were compared using unpaired t – test for continuous and Fisher exact test for categorical variables.

RESULTS:

Table 1: Demographic characteristics

	Caucasian Americans (CA)	African Americans (AA)	Hispanic Americans (HA)
Number of patients	154	50	45
Age ± SD; (range); *p – value	47.3 ± 10.4; (26 – 73)	45.7 ± 10.2; (25 – 65); *p = 0.35	43.6 ± 9.8; (23-65); *p= 0.04
% Female; *p – value	68%	80% *p = 0.11	80% *p = 0.14
Duration of MS ± SD; (range); *p – value	14 ± 9.61; (2-47)	14±9.02; (2-47); *p = 0.88	15 ± 8.46; (2-46); *p= 0.68
Months on DMF ± SD; (range); *p – value	23 ± 6.66; (1-37)	22 ± 4.04; (1-33); *p = 0.71	21 ± 9.07; (2-33); *p = 0.97
% D/C *p – value	25%	24%; *p = 1.00	33%; *p = 0.26

* p – value as compared to CA

Figure 1: Absolute lymphocyte count (ALC) (uL) change from baseline (prior to DMF start) to last available ALC while on DMF

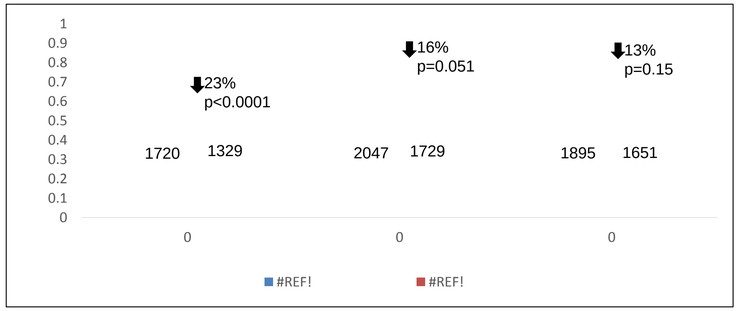


Figure 2: DMT prior to start of DMF in patients with Grade II/III lymphopenia (n = 44)

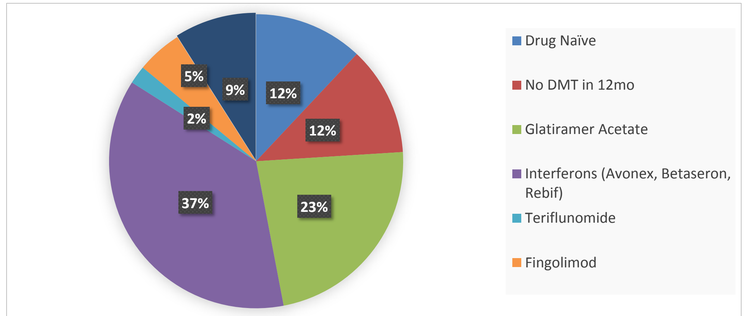
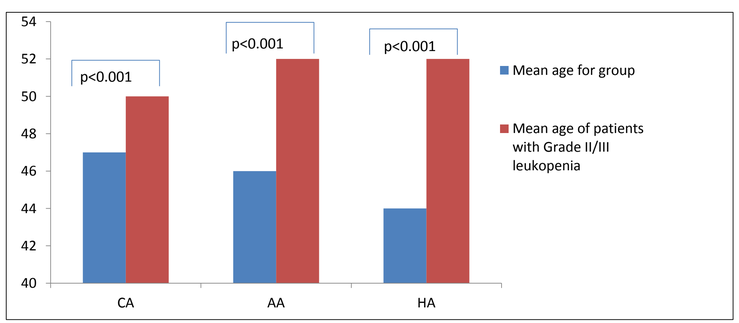


Figure 3: Age of patients with Grade II/III lymphopenia



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Contact Information:lana.zhovtisryerson@nyumc.org

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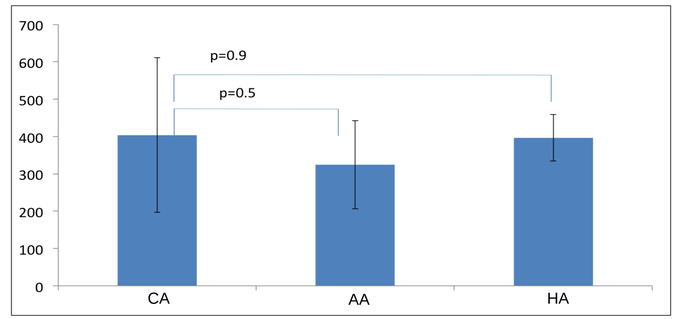
Table 3: Patient characteristics with Grade II/III Leukopenia

	Caucasian Americans (CA)	African Americans (AA)	Hispanic Americans (HA)
Grade II ALC <800cells/uL	16% (n=25)	6% (n=3, p= 0.09)	7% (n=3, p = 0.1)
Grade III ALC <500cells/uL	8% (n=13)	0 (n=0, p=0.04*)	0 (n=0, p=0.04*)

* p – value as compared to CA

Figure 4: Days to first lymphopenic result



CONCLUSIONS:

- Statistically significant drop in ALC (p<0.0001) was seen in CA group after start of DMF; trend to significance in AA (p=0.51); and non-significant decrease in HA (p=0.15).
- No specific DMT use prior to DMF start was identified as a risk for developing leukopenia.
- Significantly more CA patients developed grade II or higher leukopenia compared to AA (p= 0.004, Fisher exact test), and HA (p= 0.007, Fisher exact test)
- Time to first lymphopenic result varied from 324 days in AA to 404 days in CA with no significant differences noted between the 3 groups.
- Patients who developed Grade II/III lymphopenia were significantly older in all 3 ethnic groups, consistent with previously reported data.[5]

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