United States
Network of
PEDIATRIC MULTIPLE SCLEROSIS
Centers
www.usnpmsc.org

Oral Disease Modifying Therapies in Pediatric Multiple Sclerosis: A US Network Experience

University at Buffalo
The State University of New York

Osman Farooq[1], T. Charles Casper[2], Emmanuelle Waubant[3], Lauren Krupp[4], Tanuja Chitnis[5], Mark Gorman[6], Jayne Ness[7], Moses Rodriguez[8], Marc Patterson[8], Leslie Benson[6], Anita L. Belman[5], Cody S. Olsen[2], John Rose[2], Greg Aaen[9], Jennifer Graves[3], Yolanda Harris[7], Tim Lotze[10], Jan-Mendelt Tillema[8], Bianca Weinstock-Guttman[1] for the US Network of Pediatric Multiple Sclerosis Centers

[1]Pediatric MS Center of the Jacobs Neurological Institute at the University of Buffalo, [2]Data Coordinating and Analysis Center for the US Network of Pediatric Multiple Sclerosis Centers, University of Utah School of Medicine, [3]Regional Pediatric MS Center at the University of California at San Francisco,[4]Lourie Center for Pediatric MS, [5]Partners Pediatric MS Center at the Massachusetts General Hospital for Children, [6]Children's Hospital Boston, [7]UAB Center for Pediatric-Onset Demyelinating Disease at Children's of Alabama, [8]Regional Pediatric MS Center at Mayo Clinic Rochester, [9]Loma Linda University, [10]Texas Children's Hospital, Baylor College of Medicine

Background

- Disease modifying therapies (DMTs) are known to reduce relapses and delay disability in multiple sclerosis.
- DMTs have traditionally been administered parenterally
- New oral DMTs have been recently FDA approved for the treatment of adults with MS.
- Little is known about the safety, tolerability and efficacy of this new therapy in the pediatric population.

Objectives

- To evaluate safety, tolerability and preliminary efficacy of the new FDA approved oral DMTs in pediatric MS patients.

Methods

- Retrospective longitudinal study design within the US Network of Pediatric MS Centers (USNPMSC).
- Pediatric MS patients who initiated one of the 3 new FDA approved oral DMTs: fingolimod, dimethyl fumarate and teriflunomide for at least one dose before 18 years of age were included in this study.
- Data compiled from a database at the Data Coordinating & Analysis Center for USNPMSC.

RESULTS

Oral DMT patients were identified in the USNPMSC Pediatric MS and Other Demyelinating Diseases database in April 2014. The data compiled below is abstracted as of August 18, 2014 (median of 9 months follow-up).

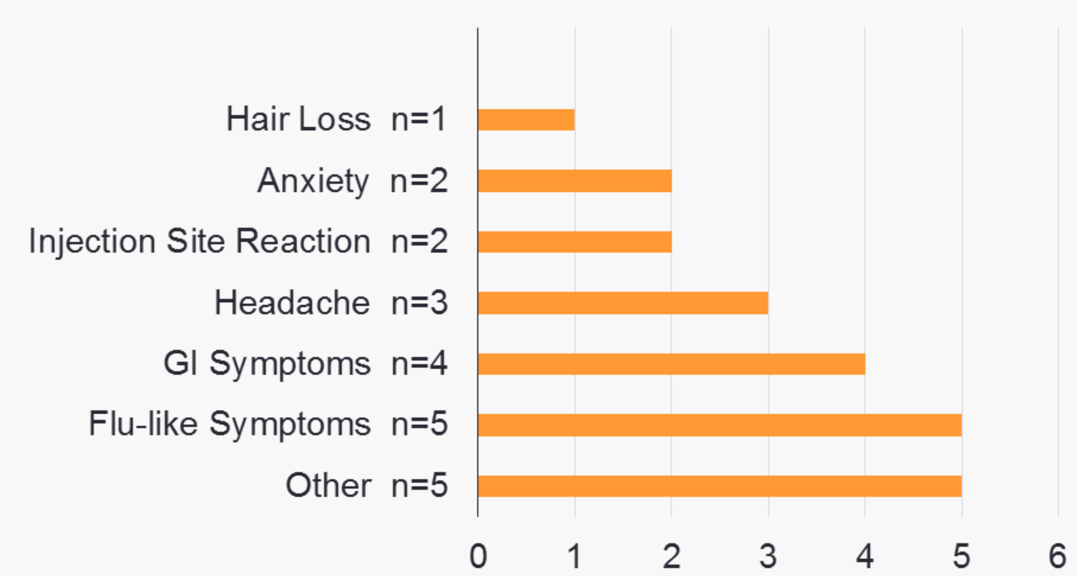
28 patients were identified across 7 participating sites. Eight patients received fingolimod, 17 received dimethyl fumarate, and 3 received both oral DMTs. Twenty-three patients were previously treated with other DMTs and 5 were treatment naïve.

Prior to oral DMTs, there were a total of 49 relapses. After starting oral DMTs, there were a total of 14 relapses.

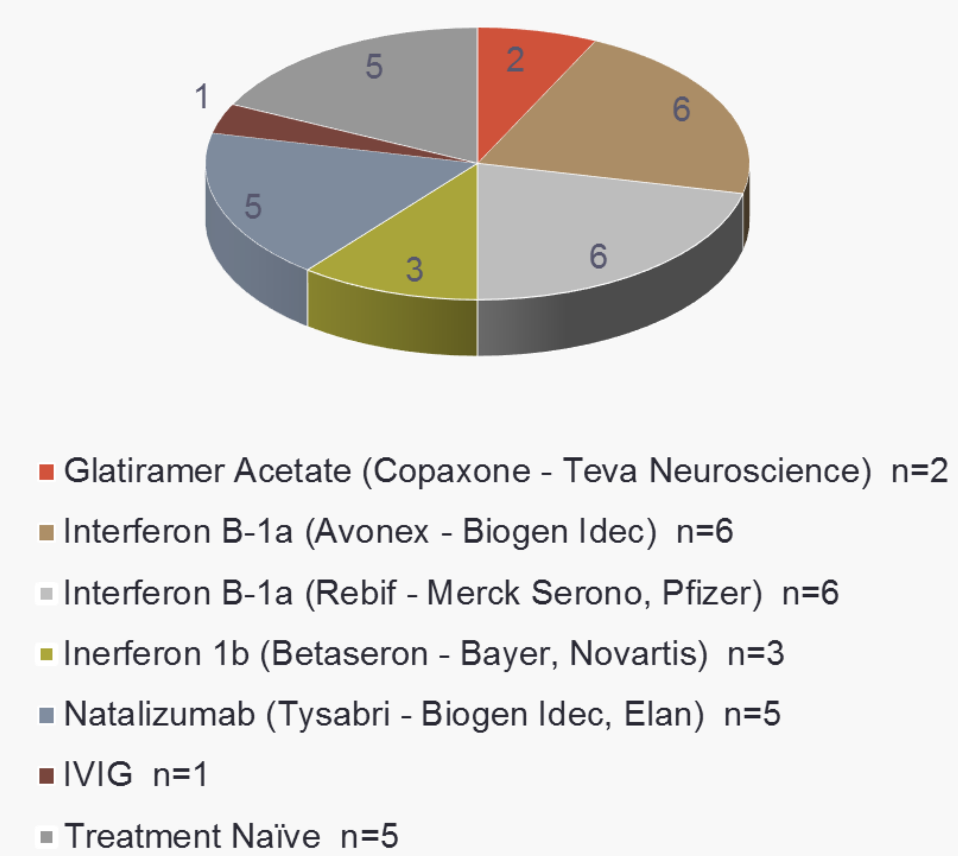
•Follow-up time prior to oral DMT - 55.7 patient-years
•Follow-up time after oral DMT - 21.6 patient-years
•Overall relapse rate prior to oral DMTs was 0.879 relapses per patient-year
•Overall relapse rate after start of oral DMT was 0.6531 relapses per patient-year.

Demographics	
Total number of patients in cohort	28
Male:Female ratio	1:1.5
Race	
Black	N=7
White	N=17
Mixed/Other	N=4
Ethnicity	
Hispanic	N=6
Not Hispanic	N=21
Unknown	N=1
Age	
Median	14.3 years
Mean (SD)	13.8 years (3.4)
Min, Max	3.32, 17.3

Side Effects of Previous DMTs

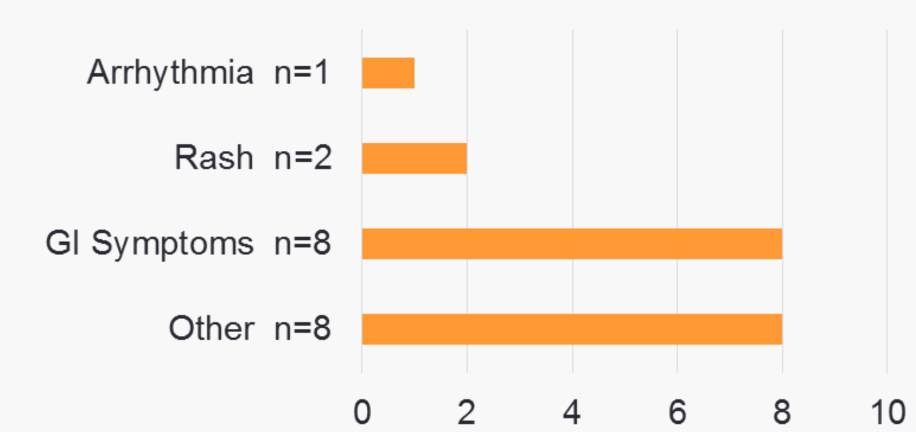


Previous DMTs prior to switch



Reason For Discontinuing Previous DMTs	N
Ineffective	8
Side Effects	5
Other	6
Not Reported	4

Side Effects on New DMTs



Patients Receiving New Oral DMTs	N=28
Patients on Dimethyl Fumarate	N=17 (61%)
Patients on Fingolimod	N=8 (28%)
Patients on Both	N=3 (11%)
Patients on Teriflunomide	N=0 (0%)
Outcomes	
Switched from Fingolimod to Dimethyl Fumarate (efficacy concerns)	N=2 (7%)
Switched from Dimethyl Fumarate to Fingolimod (reason unknown)	N=1 (3.5%)

Conclusions

- Within the first 9 months of oral DMTs medication onset, no safety concerns emerged in our cohort of pediatric MS patients.
- The number of relapses decreased from 49 relapses on previous DMTs to 14 on the new oral DMTs, thereby implying improved efficacy.
- The new oral DMTs are a good option for the management of pediatric-onset multiple sclerosis.

Limitations

- Limited data as related to a small cohort group.
- These are preliminary results and longer follow-up time would be needed to make accurate assessments of the true safety, tolerability and efficacy of the new oral DMTs in the pediatric population.

References

- Chitnis T, Tenembaum S, Banwell B, Krupp L, et al. Consensus statement: Evaluation of new and existing therapeutics for pediatric multiple sclerosis. *Mult Scler.* 2012; 18(1):116-27
- Chitnis T. Pediatric demyelinating disease. *Continuum.* 2013; 19(4):1023-45
- Nicholas JA, Boster AL, Imitola J, O'Connell C, Racke MK. Design of oral agents for the management of multiple sclerosis: benefit and risk assessment for dimethyl fumarate. *Drug Des Devel Ther.* 2014;8:897-908
- Sanford M. Fingolimod: a review of its use in relapsing-remitting multiple sclerosis. *Drugs:* 2014; 74)12)1411-33
- Weinstock-Guttman B. An update on new and emerging therapies for relapsing-remitting multiple sclerosis. *Am J Manag Care.* 2013;19(17) 343-54
- Yeh EA, Weinstock-Guttman B. The management of pediatric multiple sclerosis. *J Child Neurol.* 2012; 27(11): 1384-93

This study is supported by the National Multiple Sclerosis Society (NMSS) and the National Institute of Neurological Disorders and Stroke (NINDS) through the following grants: HC0165 and 1R01NS071463