Clincal Experience with Tecfidera®

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OBJECTIVE

To describe management of persons with Multiple Sclerosis on Tecfidera® in a post-marketing outpatient clinic setting.

BACKGROUND

Background: Tecfidera® (Dimethyl fumarate) was FDA approved for use in persons with MS on March 27, 2013, making it the newest oral disease modifying agent (DMA) for MS. There are over 100,000 patient years of experience with a compound of dimethyl fumarate and its esters (Fumaderm®) used in Europe to treat psoriasis.

METHODS

Patients were placed on Tecfidera® if they were failing therapy with conventional DMA. Failure was defined as increase in clinical relapses, increase in radiologic disease activity, or intolerability to DMA side effects. Two people with new diagnoses of MS were started on Tecfidera® because of their refusal to take injectable agents. Patients had a comprehensive metabolic panel, complete blood count with differential, platelets and urine analysis at baseline, and then every two months for the first six months, and then every three thereafter.

CONCLUSIONS

Our results in a real world setting are similar to the clinical trials in terms of adverse events, tolerability and drop out rate. In our small sample size, eosinophilia appeared only in the patients with gastrointestinal side effects severe enough to necessitate discontinuation of Tecfidera.

REFERENCES

Biogen Idec's TECFIDERA (Dimethyl Fumarate) Approved in US as a First-Line Oral Treatment for Multiple Sclerosis. Biogen Idec Press Release. Mar 27, 2013

Results

Thirty patients began therapy with Tecfidera® between April 2013 and January 2014. Five patients discontinued therapy (16.67% drop out rate). Of the remaining twenty-five patients, twelve patients had minimal or no side effects. Thirteen patients had more pronouced side effects, primarily gastrointestinal, but were able to continue with Tecfidera®. The primary reason for drop out for all five patients was intolerable gastrointestinal side effects; additionally one of these patients developed splenomegaly which occurred just over a week after starting Tecfidera® and resolved after the drug was stopped. We instituted a slower titration than recommended by the manufacturer, which appeared to lessen symptoms for some patients. Other strategies which seemed to ameliorate side effects included taking the medication with fat-containing food, use of yogurt and probiotics, anticholinergic medications for GI symptoms, simethicone for gas pain, antiemetics for nausea and baby aspirin for flushing. Of interest, lab data is available for three out of the five patients who discontinued the medication due to gastrointestinal side effects and revealed eosinophilia in all three patients. None of the other twenty-five patients showed eosinophilia.

Demographics

Age	44.2 years (mean), range = 24 – 66 years
Gender	Female= 24 Male= 6
EDSS	1.89 (mean), range = 1 - 6.5
Disease Duration	12.8 years (mean), range = 0.5 – 38 years
Prior Disease-Modifying Therapy	*Interferon beta 1a IM = 7 Interferon beta 1a SC = 11 Interferon beta 1b = 8 Glatiramer acetate = 15 Natalizumab = 1 Mitoxantrone = 1 No DMT= 2 *Some patients were on more than one DMA prior to Tecfidera®

Titration Schedule

The following titration schedule was utilized for the majority of patients starting Tecfidera®

120 mg once per day for 7 days (Days 1-7)
120 mg twice per day for 7 days (Days 8-14)
240 mg once per day for 7 days (Days 15-21)
120 mg q am and 240 mg in q pm for 7 days (Days 22-28)
240 mg twice per day (Days 29 and on

Patient	Baseline Eosinophils % (absolute number)	Two months post-Tecfidera initiation Eosinophils % (absolute number)
1	1.7 % (0.2)	9.5 % (0.7)
2	0.9 % (NA)	4.6% (NA)
3	3 % (0.2)	11 % (1)