Fingolimod versus dimethyl fumarate in first-ever treatment of multiple sclerosis: the Lausanne real-life experience

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Objective: To study the long-term efficacy and tolerance of fingolimod (FTY) and dimethyl fumarate (DMF), in early treated treatment-naïve MS patients.

Methods: Retrospective analysis (82 patients from the Lausanne prospective MS registry).

Inclusion criteria:

- RRMS (McDonald 2010 criteria),
- FTY or DMF as first-line treatment,
- treatment initiation within 36 months of disease onset
- and treatment duration > 12 months.

Data collected: (i) total n. of relapses, time from onset to treatment initiation, EDSS, n. of T2 lesions (0-2, 3-8, >9), n. of infra-tentorial and spinal cord lesions and total n. of T1 Gd+ lesions at treatment onset. (ii) n. of relapses, EDSS, total n. of new or enlarged T2 lesions and of Gd+ lesions on brain and spinal cord MRI at last follow-up. We defined a subgroup of highly active treatment-naïve patients as follows: ≥2 relapses in the year before treatment initiation and ≥1 Gd+ T1 lesion at treatment onset.

Definitions : EDSS progression: 1.0-point increase if baseline EDSS score ≤2.0, 0.5 increase if baseline EDSS >2.0.

NEDA-3 : no relapses, no EDSS progression and no new or enlarged T2 lesions or Gd+ lesions on follow-up MRIs.

Results :

Median disease duration prior to treatment : 10 months (1-35). Median follow-up : 43 months (16-133, FTY>DMF). More **relapses prior to treatment** in the FTY group (RR 3.21, 95 % CI 1.08-9.48, p=0.03). At last follow-up 83.3% of the FTY and 90.5 % of the DMF-treated patients were relapse free (p<0.05).

	Total (N=82)	Fingolimod (N=61)	Dimethyl fumarate (N=21)	*P* value
Age, years at disease onset, (median, range)	31, 16-60	30.9, 16-60	32.1, 19-60	0.575
Sex, F/M (n)	57/25	40/21	17/4	0.173
Disease duration prior to treatment initiation, months (median, range)	10, 1-35	12.7, 1-35	6.6, 1-35	0.265
Treatment duration, months (median, range)	40, 13-133	43, 13-133	32, 13-44	**0.011**
Follow-up duration, months (median, range)	43, 16-133	48, 16-133	32, 20-44	**0.000**
Relapses prior to treatment				
- **Median, range**	1, 1-6	2, 1-4	1, 1-6	**0.042**
- **>2 relapses in the first year (%)**	37.8	45.9	14.3	**0.004**
Initial EDSS (mean, ±SD)	1.84, ±0.56	1.85, ±0.57	1.76, ±0.49	0.505
Highly active patients (%)	18.3	19.7	14.3	0.582
Baseline MRI				
- **>9 T2 lesions (%)**	81.5	81.7	81	0.651
- **Gd+ lesions**				
○ **%**	59.5	52.5	80	0.037
○ **Median, range**	1, 0-26	1, 0-26	1, 0-8	0.953
- **Infratentorial lesions (%)**	70	66.1	81	0.756
- **Spinal cord lesions* (%)**	70	73.9	57.1	0.314

Table 1: Demographic, clinical and MRI characteristics of the whole population (total) and FTY and DMF-treated subgroups.

Risk of relapse : Higher highly active patients independently of treatment choice (RR 4.4, 95% CI 1.64-11.76, p=0.003).

EDSS progression : 11.5 % of FTY and 14.3% of DMF patients (p = 0.734). 71.4% of patients with spinal cord lesions at onset (vs 30.5 % in all patients).

Occurrence of new T1 Gd+ : see below. reduced in both groups (FTY RR 0.31, 95 % CI 0.168 – 0.577, p<0.001, DMF RR 0.18, 95 % CI 0.061 – 0.52, p<0.001).

	Fingolimod			Dimethyl Fumarate		
	Prior to treatment	At last FU	*P* value	Prior to treatment	At last FU	*P* value
Relapses						
- **Median no / patient, range**	2, 1-4	0, 0-2	**0.002**	1, 1-6	0, 0-3	**0.000**
EDSS (mean, ±SD)	1.85, ±0.57	1.77, ±0.92	0.135	1.76, ±0.49	1.74, ±1.22	0.566
MRI						
- **New or enlarged T2 lesions**	n.a	0, 0-12	n.a	n.a	0, 0-20	n.a
- **GD+ lesions (%)**	51.8	16.4	**0.000**	80	14.3	**0.009**
- **Spinal cord lesions (%)**	73.9	12.1	**0.000**	57.1	16.7	0.102

NEDA 3: see below. Patients with persistent disease activity had higher median infra-tentorial T2 lesion load (2.09 vs 1.2 p=0.036).

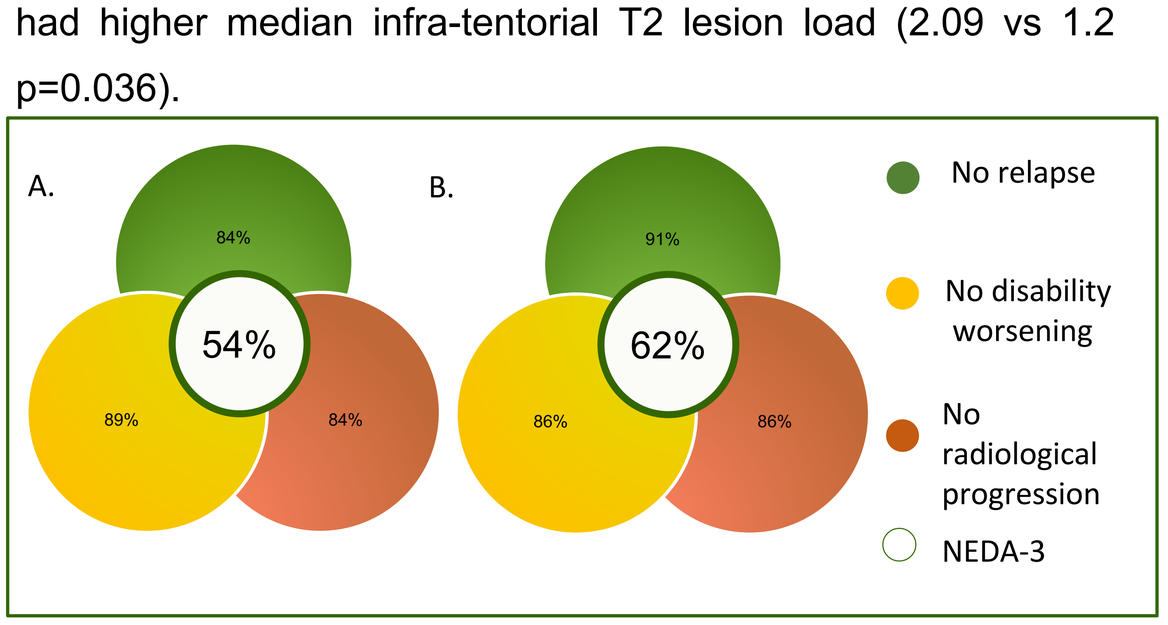

Figure 1. Proportions of NEDA-3 patients at last follow-up in A) fingolimod and B) dimethyl fumarate-treated groups, with analysis of their subcomponents. Similar efficacy in both groups (p=0.258).

Adherence to treatment : at last follow-up, 62.3 % (n=38) of FTY and 81 % (n=17) of DMF patients still on treatment (p = 0.2).

Reasons for discontinuation : disease progression, pregnancy planning, personal convenience, JC virus positivity in patients older than 50 (estimated high risk of PML).

Serious side effects : none.

Discussion : FTY's group higher clinical activity prior to treatment initiation suggests a neurologist's tendency to prescribe FTY for more clinically active patients.

The majority of patients in both groups were relapse free at last follow-up and had significant reduction in new supratentorial and spinal cord T2 lesions or T1 Gd+ lesions. When applying the NEDA 3 criteria, similar efficacy with both drugs, arguing in favour of efficient early immunomodulation in MS patients.