Switching therapy: how and why in a real word setting cohort of persons with Multiple Sclerosis in Catania

C. Leone, A. Zanghì, E. D'Amico, S. Messina, C. G. Chisari, A. M. Caramma, S. Lo Fermo, F. Patti and M. Zappia.

Department G. F. Ingrassia, section of Neurosciences, Multiple Sclerosis Centre, University of Catania, Italy

Introduction: Thirteen disease-modifying drugs are currently available as first-line or second-line treatments of Multiple Sclerosis (MS); however, no universal guidelines exist to decide when and how exactly patients with relapsing-remitting MS (pwRRMS) need to switch therapy. We described modalities and reasons of switching therapies in a large cohort of pwRRMS.

Methods: A retrospective analysis of data from pwRRMS who underwent a therapeutic switch between January 2005 and December 2014 was performed. PwRRMS having other immune-related disease and without a recent follow-up were excluded. We divided them in four groups based on the switch type: A=lateral (among same therapy lines); B=escalation (from a first to a second-line therapy); C=de-escalation (from a second to a first-line therapy); D=multiple switches We identified all interferons and, . glatimarer acetate as first-line therapy and natalizumab, fingolimod, cyclophosphamide, mithoxantrone as second-line therapy. Cyclophosphamide and mithoxantrone were used with the induction scheme, based on a more aggressive approach as starting therapy followed by a less aggressive, first-line therapy. The different switch reasons were clustered in four domains: sub-optimal response, tolerability/safety issues, *"per protocol"* (end-of-treatment) and miscellaneous. Frequency distributions were computed and compared between lateral and escalation groups.

Table 1 Demographic and clinical characteristics

	TOTAL	A	B	C	D	p-VALUE
N.	387	104	187	59	37	0,001
AGE	41,6±10,6	44,3±11,4	40,97±10,2	38,9±9,6*	41,9±10,2	
AGE AT ONSET	32,6±10	34,5±10,8	32,3±9,8	31,6±9,1	30,3±9,2	
LAG_TIME	3,5±5,3	3,7±5,5	3,5±5,1	3,6±4,7	3,7±4,3	
MONTHS AT SWITCH	43,1±41,4	48,8±40,4	49,2±46,4	20,34±15,5	32,3±30,7	0,00
EDSS AT DIAGNOSIS	2±1,3	1,9±1,1	2±1,3	2,3±1,4	2,2±1	
EDSS AT SWITCH	2,4±1,6	2±1,3§	2,7±1,7	1,5±1,4§	2,8±1,6	0,00
MONTHS OF FIRST TREATMENT	43,1±41,4	48,8±40,4	49,2±46,4	20,3±15,5	32,3±30,7	0,00
T1 MRI BRAIN at SWITCH	10,2±13,7	7,36±9,9	12,7±14,7*	7,15±11,8	9,9±17,3	
n.T2 MRI BRAIN at switch	39,9±35,5	49,8±38,2 §	49,8±38,2	28,4±30,9§	35±30,6	0,00
n.T2 MRI spine at switch	2,4±2,3	1,9±1,2§	3,07±2,5	1,58±1,6§	1,3±1,5	0,00
n.T1 Gad+ MRI BRAIN/SPINE at switch	0,6±2	0,4±1,2	0,8±2,7	0,3±1,1	0,7±1,5	
RELAPSE 1Y b switch	0,7±0,8	0,5±0,6§	0,7±0,8	0,6±0,8	1±1*	
REASONS for SWITCHING:						
SUBOPTIMAL RESPONSE	55,8%	57,3%	64%	8,6%	85,7%ª	0,001

n= number, EDSS=expanded disability status scale. Post hoc test : * significatively different from group 0,§ significatively different from group 1,ª significatively different from other groups ; 1yb=one year before;
p-value obtained with Anova test.

Results: The mean time of follow-up from the switch was 52.1±30.8 months. Out of 513 pwRRMS who switched therapy, 387 were included in the analysis(Table 1). One-hundred and four (26.9%) pwRRMS were in the lateral group, 187 (48.3%) in the escalation, 59 (15.2%) in the de-escalation and 37 (9.6%) in the multiple switches group. Overall, the most frequent reason of switching therapy was the sub-optimal response (55.8%), with the highest value in the multiple switches group (85.7%). The second most frequent reason of switching therapy was tolerability/safety issues reason (21.5%)(Table 2, Figure 1). The frequency of sub-optimal response and tolerability/safety issues reason was not significantly different between the escalation (64% and 21.5%, respectively) and lateral (57.3% and 29.1%, respectively) group. (Figure 2,3).

Table 2 Reason for switching between groups

	TOTAL	A	B	C	D
SUBOPTIMAL RESPONSE	55,8%	57,3%	64,0%	8,6%	85,7%
SIDE EFFECTS	21,5%	29,1%	21,5%	17,2%	5,7%
CLINICAL DECISION	18,9%	9,6%	9,7%	72,4%	6%
MISCELLANEUS	31,8%	4,2%	4,8%	1,8%	2,6%

Fig 1. Reasons for switching in all patients

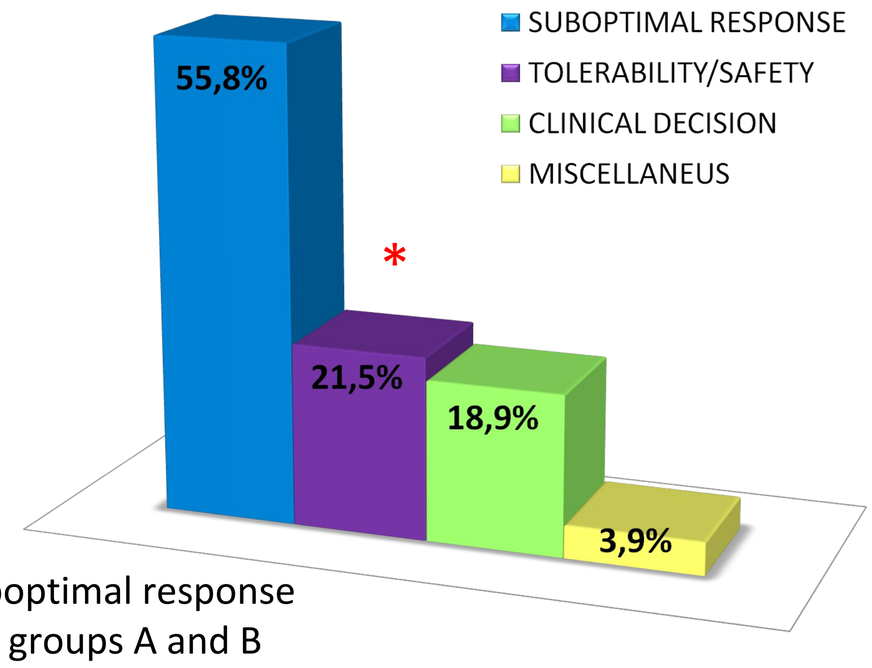

Fig 2. Suboptimal response between groups A and B

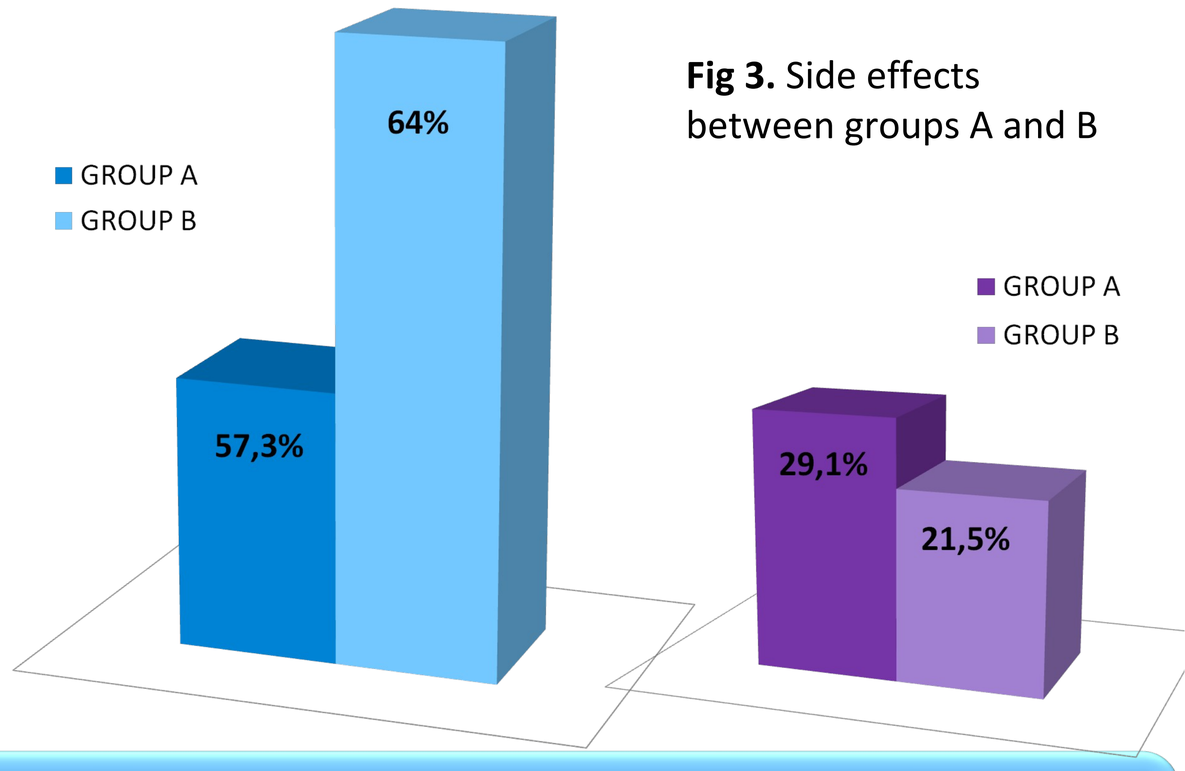

Fig 3. Side effects between groups A and B

Conclusions

A retrospective analysis of our clinical experience revealed that the most frequent reason of switch was the sub-optimal response to previous drugs, with similar frequency in the lateral and escalation groups.

References:
1.Rush et al.,Aggressive Multiple Sclerosis:proposed defintion and treatment algorithm, Nat.Rev.Natur.2015 Jul;11(7):379-89.
2.Comi G, Induction vs. escalating therapy in Multiple Sclerosis:practical implications, Neurol Sci (2008) 29:S253–S2.
3.Trojano M et al., New Natural History of Interferon-β-Treated Relapsing Multiple Sclerosis,Ann Neurol 2007;61:300–30655
4.Patti F et al., Effects of interferon beta-1a and -1b overtime: 6-year results of an observational head-to-head study Deceased Acta Neurol Scand 2006: 113: 241–247
Pozzilli C et al., Post-marketing survey on clinical response to interferon beta in relapsing multiple sclerosis: the Roman experience Neurol Sci (2005) 26:S174–S178

Sin
XLVI CONGRESSO NAZIONALE
10-13 OTTOBRE 2015 – GENOVA
WebPoster