Switching from Natalizumab to Fingolimod with no washout. Results of a pilot explorative study.

Poretto V, MD; Miante S, MD; Seppi D, MD; Rinaldi F, MD; Margoni M, MD; Perini P, MD; Favaretto A, MD; Federle L, MD; Puthenparampil M, MD; Gallo P, MD, PhD.

Multiple Sclerosis Centre of Padova, Department of Neuroscience, University Hospital of Padova, Italy

BACKGROUND

An increased risk of clinical and/or radiological MS reactivation has been observed switching from natalizumab to fingolimod with a washout interval of three months, and mainly occurs in up to 50% of the patients between the second and sixth month after natalizumab break. Indeed, the three-month washout period, initially recommended for safety, exposes the patients not only to disease relapses, but, in some cases, to a severe rebound.

OBJECTIVE

To investigate, in a preliminary pilot study in a small number of patients, the effects of a 'no-washout switching' on clinical and MRI parameters and on the short-term risk of adverse events in MS patients.

MATERIALS AND METHODS

In the period October 2013 – April 2015 we prospectively enrolled in the study 10 patients who stopped natalizumab for the high risk of developing progressive multifocal leukoencephalopathy. Patients were asked to start fingolimod 4 weeks after the last natalizumab infusion (i.e., when the next natalizumab administration was programmed). The study was approved by the local Ethics Committee. Six patients were females, 4 males, and the mean age at study entry was 41.9±10.0 (range 29-59). Mean number of natalizumab infusions was 34.5±8.6 (range 24-47). After fingolimod initiation, patients were assessed clinically at 1, 3 and 6 months, while brain MRI was performed at 3 and 6 months.

Pts	sex	age	N. of infusions	washout period (months)	1st MRI (+ 4 m)	2nd MRI (+ 7 m)	Relapse	EDSS T0	EDSS (last)
1	F	33	24	1	-	-	0	1,5	1,5
2	M	50	36	1	-	-	0	4	5,5
3	F	40	35	1	-	-	0	3,5	3,5
4	F	49	29	1	-	-	mild left ON (+6 m)	1,5	1,5
5	M	59	24	1	-	-	0	3,5	3,5
6	F	29	47	1	1 New WML	-	0	1,5	1,5
7	M	38	36	1	-	-	0	3,5	3,5
8	F	37	45	1	-	-	0	2	2
9	F	20	31	1	-	-	0	1,5	1,5
10	F	40	27	1	-	-	0	6,5	6,5
Mean value		39,5	33,4					2,9	3,05
SD		11,17	8,01					1,63	1,80

Table 1. Demographic data and clinical and radiological FU of ten patients that discontinued natalizumab therapy and start fingolimod one month after the last infusion. SD= standard deviation, +4m and +7m= 4 and 7 months from the last infusion of natalizumab, T0= time at the last dose of natalizumab, ON = optic neuritis. No statistically difference was observed between EDSS at T0 and the last EDSS.

RESULTS

Only one out of 10 patients had a mild relapse during the study period. This was a 49 years old woman who experienced a mild optic neuritis in the left eye after 6 months of fingolimod therapy, with no evidence of MRI activity. The relapse was treated with high doses of steroids and was followed by a complete recovery. At the first MRI time-point, only one patient (a 29 year old woman) had one new T2 white matter lesion. No new Gadolinium enhancing lesions was observed at month 3 and 6. The mean EDSS score was stable throughout the study. No side effects or adverse events (especially infections) were registered during the study.

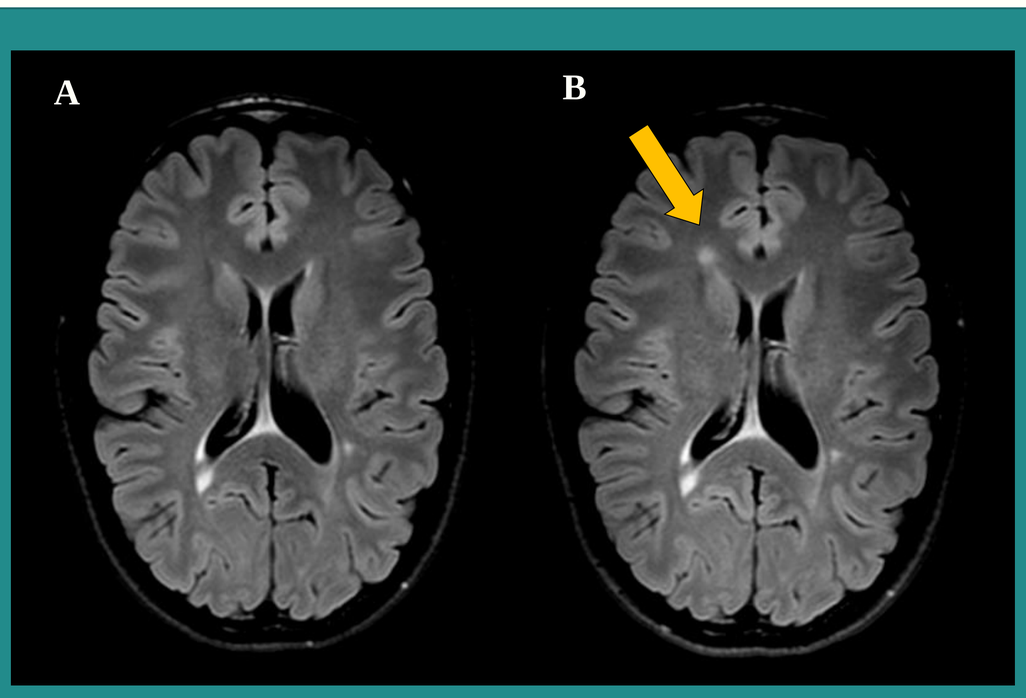

Figure 1. Axial FLAIR image of the patient who experienced neuroradiological relapse. Image A shows MRI performed one month after Natalizumab discontinuation (at the begining of Fingolimod therapy). The following MRI timepoint performed three months later showed the appearance of a new frontal periventricular white matter lesion (image B).

DISCUSSION

In this pilot explorative study, we observed that the lack of a washout period, when switching from natalizumab to fingolimod, is safe and reduces the risk of MS reactivation. Thus, fingolimod is a safe and effective therapeutic option after natalizumab.