Natalizumab withdrawal in Multiple Sclerosis-RR patients: what to expect?

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Background - Natalizumab (NAT) is the first monoclonal antibody approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). While pivotal and postmarketing studies demonstrated the impressive efficacy and the good tolerability profile of natalizumab, progressive multifocal leukoencephalopathy (PML), is a risk associated with long-term therapy. In order to minimize the risk of PML, treatment with NAT is often stopped after 2 years. However, it's quite controversial the features of clinical and radiological disease's activity after NAT-withdrawal. Moreover which treatment strategy should be followed after NAT treatment is still unknown.

Objective – To evaluate effects of natalizumab discontinuation on clinical and radiological disease activity within twelve months after cessation.

Methods – We retrospectively collected data from 30 patients with MS who discontinued natalizumab, since an high anti-JCV antibody index. Mean change scores of annualized relapse rate (ARR) and expanded disability status scale (EDSS) were calculated for detection of disease activity before, during and after the treatment with NAT. We collected MRI scans performed at baseline, during NAT treatment start, and at 3rd, 7th and 12th months after NAT discontinuation.

		Totale			Recidiva alla sospensione			Non recidiva alla sospensione		
	Tot f/m	30 20/10			15 10/5			15 10/5		
		media	DS	intervallo	media	DS	intervallo	media	DS	intervallo
Età all'esordio		28,0	± 8,6	[16-45]	27,6	± 7,8	[17-39]	28,4	±9,5	[16-45]
EDSS esordio		1,5	± 0,6	[0-3]	1,4	± 0,6	[0-2,5]	1,6	± 0,6	[1-3]
Ricadute 1°anno (esclusa diagnosi)		0,9	± 0,9	[0-3]	0,9	± 0,9	[0-3]	1,0	± 0,9	[0-3]
Ricadute nel corso della 1°tp		3,0	± 1,5	[1-10]	2,8	± 2	[1-5]	3,9	± 1,7	[2-10]
Trattamenti pre-natalizumab		1,2	± 0,7	[0-4]	1,4	± 0,8	[1-4]	1,1	± 1,1	[0-3]
N°lesioni all'ultima MRI pre-natalizumab	Gd +	1,8	± 0,6	[0-6]	2,1	± 1,5	[0-6]	1,7	± 1,1	[0-5]
	T2	1,3	± 1,2	[0-4]	0,8	± 1,3	[0-4]	0,5	± 1	[0-4]
Durata malattia prima di natalizumab (mesi)		85,7	± 85,0	[4-307]	109	± 102	[12-307]	62,2	± 58,3	[4-190]
EDSS pre-natalizumab		3,0	± 1,8	[1-6,5]	3,1	± 1,9	[1-6,5]	3,4	± 1,7	[1-6,5]
ARR pre-natalizumab		**2,06**	**± 0,9**	**[1-4]**	**2,44**	**± 0,9**	**[1-4]**	**1,66**	**± 0,7**	**[1-3]**
Ricadute in natalizumab		0,5	± 0,7	[0-2]	0,4	± 0,6	[0-2]	0,8	± 0,9	[0-2]
Età sospensione		39	± 9	[21-56]	40,2	± 7,8	[25-56]	37,9	± 10	[21-54]
Durata malattia alla sospensione (mesi)		127	± 93	[20-362]	154,4	± 110	[43-362]	115,8	± 70	[20-257]
Totale infusioni di natalizumab		39,5	± 17	[13-74]	38,3	± 15	[13-74]	45,1	± 18	[13-70]
EDSS alla sospensione		3,15	± 2	[1-6,5]	3,2	± 2,1	[1-6,5]	3,5	± 2,1	[1- 6,5]
EDSS ad 1 anno dalla sospensione		3,4	± 2,1	[1-6,5]	3,5	± 2,1	[1-6,5]	3,3	± 2,2	[1- 6,5]

Results – Overall, patients relapse-free were 48% at one year after discontinuation. 48% of the patients had relapses after discontinuation of NAT and 4% of the patients experienced a rebound phenomenon within twelve months. Patients in the relapse group had higher 1-year pre-NAT treatment ARR (2.44) than the relapse-free group (1.66) **(p value = 0.0129*).** EDSS and MRI did not show any significant difference between the groups (p values = 0.738 and 0.633 respectively).

Conclusion – Our data suggest that ARR during the year previous NAT treatment start could be a predictor of relapses after NAT withdrawal. No differences have been found in clinical or magnetic resonance imaging recurrence of disease activity amongst the groups.

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