

EFFECT OF EARLY TREATMENT INITIATION IN REAL-WORLD SETTINGS ON DISABILITY PROGRESSION: A SERIES OF 281 RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS, RENNES, FRANCE

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Introduction

- Disease-Modifying Treatment (DMT) options for Relapsing-Remitting Multiple Sclerosis (RRMS) largely evolved for the last twenty years
- Natural history studies demonstrated Multiple Sclerosis (MS) as a two-stage disease: the first phase from MS clinical onset to irreversible Expanded Disability Status Scale (EDSS) score of 3 is highly variable in duration and corresponds to focal inflammation [1]
- Extensions of randomized clinical trials pointed out that early treatment was beneficial to reduce the time of conversion from the first attack to clinically definite MS, compared with delayed treatment [2,3,4]
- Some observational studies tend to show a greater benefit of early treatment initiation but results need to be confirmed [5,6,7]

Objective: To measure early treatment initiation effect in real-world settings on disability in a series of relapsing-remitting MS patients from the Rennes MS expert centre in France

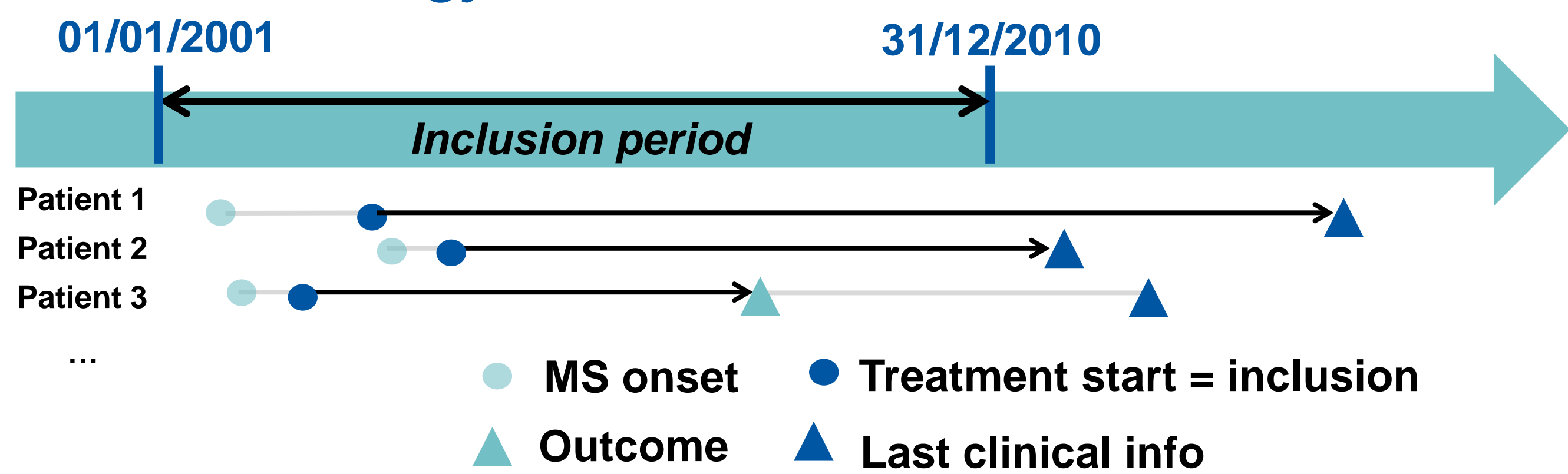
Methods

Study population

- RRMS clinical onset between 01/01/2001 and 31/12/2010
- Initiating an approved DMT over this period
- At least 5 years of follow-up and 3 visits in the MS expert centre

➔ N= 281 patients

Scheme of methodology:



Outcome

- Primary outcome: time to reach an irreversible EDSS score of 3
- Secondary outcomes: time to reach an irreversible EDSS score of 4 and to convert into secondary progressive MS (SPMS)

Exposure

Treatment initiated within 12 months following MS onset was considered as early treatment

Statistical analysis

Cox model adjusted on sex, age at treatment initiation, number of relapses in the year before treatment initiation, EDSS score at treatment initiation

Results

Exposure

- Median MS duration before treatment initiation: 1.2 years (min: 0.04 – max: 9.46)
- 120 patients initiated a treatment within 12 months following MS onset (= "Early" group)

Comparison of the two groups

	"Early" group	"Delayed" group	p
Women	93 (77%)	123 (76%)	0.941
Age ^(a) (years)	29.4 ± 8.5	33.2 ± 10.0	10 ⁻⁴
EDSS ^(a)			0.049
0	31 (26%)	57 (35%)	
1	61 (51%)	64 (40%)	
2	20 (17%)	36 (22%)	
≥ 3	8 (7%)	4 (3%)	
Number of relapses in the year before treatment initiation			<10 ⁻⁴
< 2	46 (38%)	120 (74%)	
2	54 (45%)	31 (19%)	
≥ 3	20 (17%)	10 (6%)	

^(a)At treatment initiation

Outcomes ("Early" group vs "Delayed" group)

- Irreversible EDSS score of 3: 23 patients (19%) vs 35 patients (22%), p=0.705
- Irreversible EDSS score of 4: 13 patients (11%) vs 20 patients (12%), p= 0.824
- SPMS: 7 patients (6%) vs 16 patients (10%), p= 0.307

Effect of early treatment initiation on disability progression

	Hazard Ratio ^(b) [95% confidence interval] ^(c)
Main analysis - Irreversible EDSS 3	
• Delayed (vs Early)	1.63 [0.89 ; 3.20]
• Time to treatment initiation	1.18 [0.98 ; 1.41]
Secondary analysis	
• Irreversible EDSS 4	
• Delayed (vs Early)	1.56 [0.68 ; 3.81]
• Time to treatment initiation	1.18 [0.92 ; 1.48]
• Conversion into SPMS	
• Delayed (vs Early)	2.03 [0.81 ; 7.77]
• Time to treatment initiation	1.13 [0.81 ; 1.46]

^(b)Adjusted on sex, age at treatment initiation, number of relapses in the year before treatment initiation, EDSS score at treatment initiation; ^(c)Bootstrap 95% Confidence interval

The risk of reaching an irreversible EDSS score of 3 increased by:
63% for patients in "delayed" group in comparison to patients in "early" group (with a confidence interval of [0.89 ; 3.20])
18% for every year of delay in treatment start after MS onset (with a confidence interval of [0.98 ; 1.41])

Discussion

- Our study suggests the benefit of early treatment initiation on disability progression, lack of significance was probably linked to a lack of statistical power
- Our results are in accordance with results of previous studies [5,6,7]. In particular, a Swedish recent study [7] showing that the risk of reaching an EDSS score of 4 increased by more than 7% for every year of delay in treatment start after MS onset
- Further analysis will be performed taking into account MRI data, and data from others MS centres in France

Literature

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