Risk of Cancer With Disease-Modifying Therapies in Multiple Sclerosis: A New-User Cohort Design in the French Nationwide Claims Database

P. Bosco-Lévy[1], M. Sabidó[2], E. Guiard[1], P. Diez[1], C. Foch[2], C. Favary[1], J. Jové[1], E. Boutmy[2], P. Blin[1]

[1]Univ. Bordeaux, INSERM CIC-P 1401, Bordeaux PharmacoEpi, Bordeaux, France; [2]Global Epidemiology, Merck Healthcare KGaA, Darmstadt, Germany

CONCLUSIONS

Results suggest a trend of increased risk of cancer in patients with MS who initiated immunosuppressants compared with immunomodulatory treatments.

Longer follow-up of this patient population is warranted.

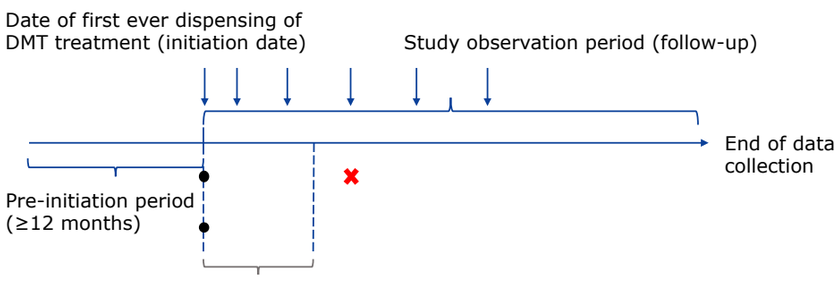
INTRODUCTION

- Debate continues on the risk of cancer in multiple sclerosis (MS), including the potential role of disease-modifying therapies (DMTs) in modifying this risk.
- There are limited data on the risk of cancer with DMT use and those available suggest that MS patients treated with immunosuppressant (IS) may be more likely to be at risk of cancer than those receiving immunomodulatory (IM) treatments.[1-4] Data has found a potential signal between interferon beta-1a and natalizumab, and increased risk of cancer. However, further evaluation with more robust evidence is required.[5]
- Population-based real-life studies can detect rare safety outcomes due to their large cohort sizes and long study durations without attrition of clinically relevant patient populations and can complement data from randomized controlled trials.

OBJECTIVES

To compare the incidence of any cancer (including and excluding non-melanoma skin cancer) in patients with MS initiating IM treatments vs IS treatments.

METHODS

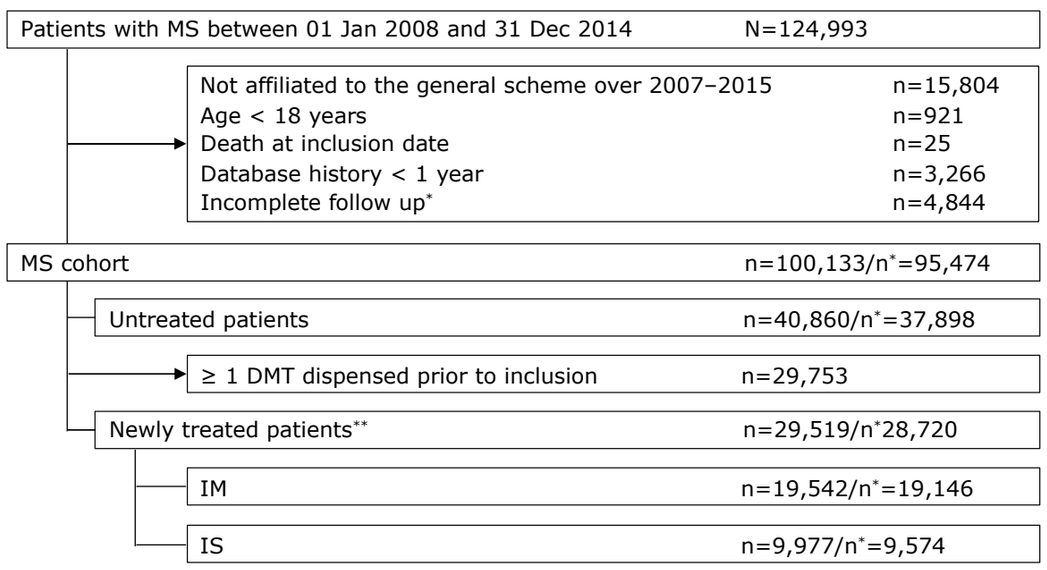


- A new-user cohort was conducted in SNDS, the French nationwide claims database, including all adult MS patients initiating a DMT between 2008–2014 and without a history of cancer in the previous 12 months.
- Patients were grouped into IM only or IS* only, according to the first DMT dispensed and regardless of subsequent DMTs.
- Outcome was any cancer diagnosis (ICD-10 hospitalization codes or specific anti-cancer treatment) after a 6-month induction period following DMT initiation.
  - An additional analysis with a 12-month induction period was also performed.
- Patients were followed from DMT initiation to the earliest date of cancer diagnosis, death, or end of follow-up (31 Dec 2015).
- Incidence rate (IR) of any cancer per 100,000 patient-years (PY) with 95% confidence interval (CI) were estimated for each DMT group.
- A Cox proportional hazards model was used with high dimensional propensity score adjustment or inverse probability of treatment weighting to control confounding and estimate hazard ratios (HR) with 95% CIs for IM vs IS.

*IM: interferons or glatiramer acetate. IS: teriflunomide, fingolimod, dimethyl fumarate, alemtuzumab, natalizumab, methotrexate, cyclophosphamide, mitoxantrone, mycophenolate mofetil, azathioprine, rituximab, or tacrolimus

RESULTS

Figure 1. Selection of Patients in the Newly Treated MS Sub-cohort



*Patients without history of malignancy. **One patient excluded due to receiving simultaneous IM/IS, then no further treatment.
IM, immunomodulatory; **IS**, immunosuppressant; **MS**, multiple sclerosis

Table 1. Baseline Characteristics of Newly Treated MS Patients*

	IM n=19,146	IS n=9,574
Demographic characteristics		
Mean (SD) age at initiation date, years	38.8 (11.0)	46.6 (13.2)
Sex female, n (%)	14,258 (74.5)	6,569 (68.6)
Main comorbidities, n (%)		
Autoimmune disease	845 (4.4)	616 (6.4)
COPD	616 (3.2)	462 (4.8)
Diabetes	448 (2.3)	396 (4.1)
Conditions associated with chronic alcohol consumption	149 (0.8)	106 (1.1)
HIV	1 (0.0)	3 (0.0)
Over the 1-year pre-initiation period		
≥1 Hospitalization, n (%)	15,282 (79.8)	7,411 (77.4)
≥1 Medical visit, n (%)	19,063 (99.6)	9,529 (99.5)
≥1 General practitioner visit, n (%)	18,479 (96.5)	9,246 (96.6)
≥1 Neurologist visit, n (%)	15,084 (78.8)	7,026 (73.4)
History of medication before initiation date		
≥1 corticosteroid dispensed, n (%)	8,729 (45.6)	4,130 (43.1)
≥1 dispensing of sexual hormones (among women), n (%)	4,993 (35.0)	1,922 (29.3)

*Patients without history of malignancy

COPD, chronic obstructive pulmonary disease; **HIV**, human immunodeficiency virus; **IM**, immunomodulatory; **IS**, immunosuppressant; **MS**, multiple sclerosis; **SD**, standard deviation

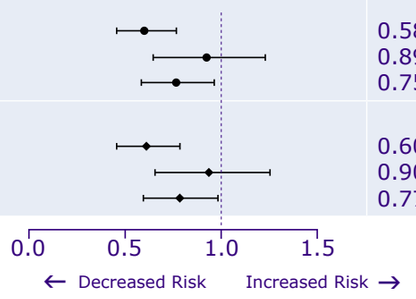
Table 2. IR of Malignancies in Newly Treated MS Patients and Without History of Malignancy (6-month Induction Period)

	Newly treated with IM n=19,146		Newly treated with IS n=9,574	
	Event (n)	IR per 100,000 PY	Event (n)	IR per 100,000 PY
Any malignancies, including NMSC	235	265	193	596
Any malignancies, excluding NMSC	231	261	188	580
All solid tumours, including NMSC	221	249	175	539
All solid tumours, excluding NMSC	217	245	170	524
All haematological malignancies / lymphoma	14	16	22	67

IM, immunomodulatory; **IR**, incidence rate; **IS**, immunosuppressant; **MS**, multiple sclerosis; **NMSC**, non-melanoma skin cancer; **PY**, patient year

Table 3. Risk of Malignancy According to DMT Exposure in the hdPS Trimmed Population of Newly Treated MS Patients Without History of Malignancies (6-month Induction Period)

	Events (n)	HR [95% CI] IM vs IS
Malignancies, including NMSC		
Unadjusted analysis	267	0.58 [0.45, 0.76]
Adjusted analysis	267	0.89 [0.65, 1.22]
IPTW analysis	267	0.75 [0.59, 0.96]
Malignancies, excluding NMSC		
Unadjusted analysis	261	0.60 [0.46, 0.78]
Adjusted analysis	261	0.90 [0.66, 1.25]
IPTW analysis	261	0.77 [0.60, 0.98]



CI, confidence interval; **DMT**, disease-modifying therapy; **hdPS**, high-dimensional propensity score; **IM**, immunomodulatory; **IPTW**, inverse probability of treatment weighting; **IS**, immunosuppressant; **HR**, hazard ratio; **MS**, multiple sclerosis; **NMSC**, non-melanoma skin cancer

Limitations

- Definitions of IM and IS used in this analysis were general and included treatments with diverse mechanisms of action. Further analysis is required to analyze their effect.
- Difference in follow-up between IM and IS cohorts. The median follow-up of patients initiating IM was 4.7 years, while that of patient initiating IS was 2.8 years.
- Subsequent DMTs were not considered. During the follow-up period, half of patients initiating IM (51%) remained exclusively treated with IM, and 92% initiating an IS remained exclusively treated with such therapy.

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