

From NATALIZUMAB and EDMUS

European Database for Multiple Sclerosis

to TYSEDMUS

Tysabri® in French EDMUS Databases

and OFSEP

Observatoire Français de la Sclérose En Plaques

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Natalizumab (Tysabri®)

2006

Polman et al. NEJM 2006; 354: 899-910

EFFICACY as compared to placebo, at 2 years

Accumulation of Disability	42 %	↘
Relapse Rate	68 %	↘
MRI Activity	92 %	↘

TOLERANCE

SAFETY

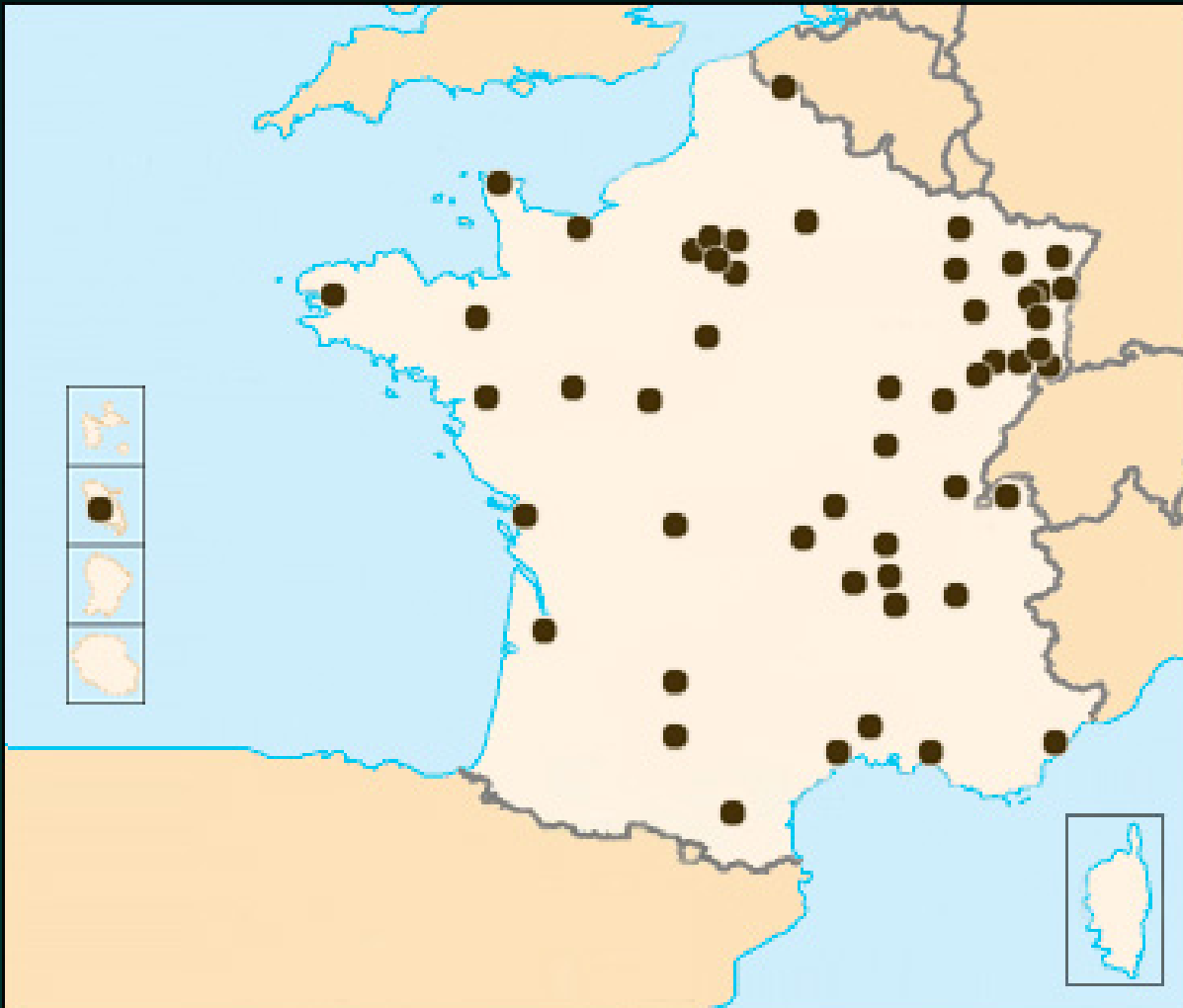
2007

Marketing Approval in France

Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) & Risk Management Plan

The Care of MS in France (1)

The EDMUS Network



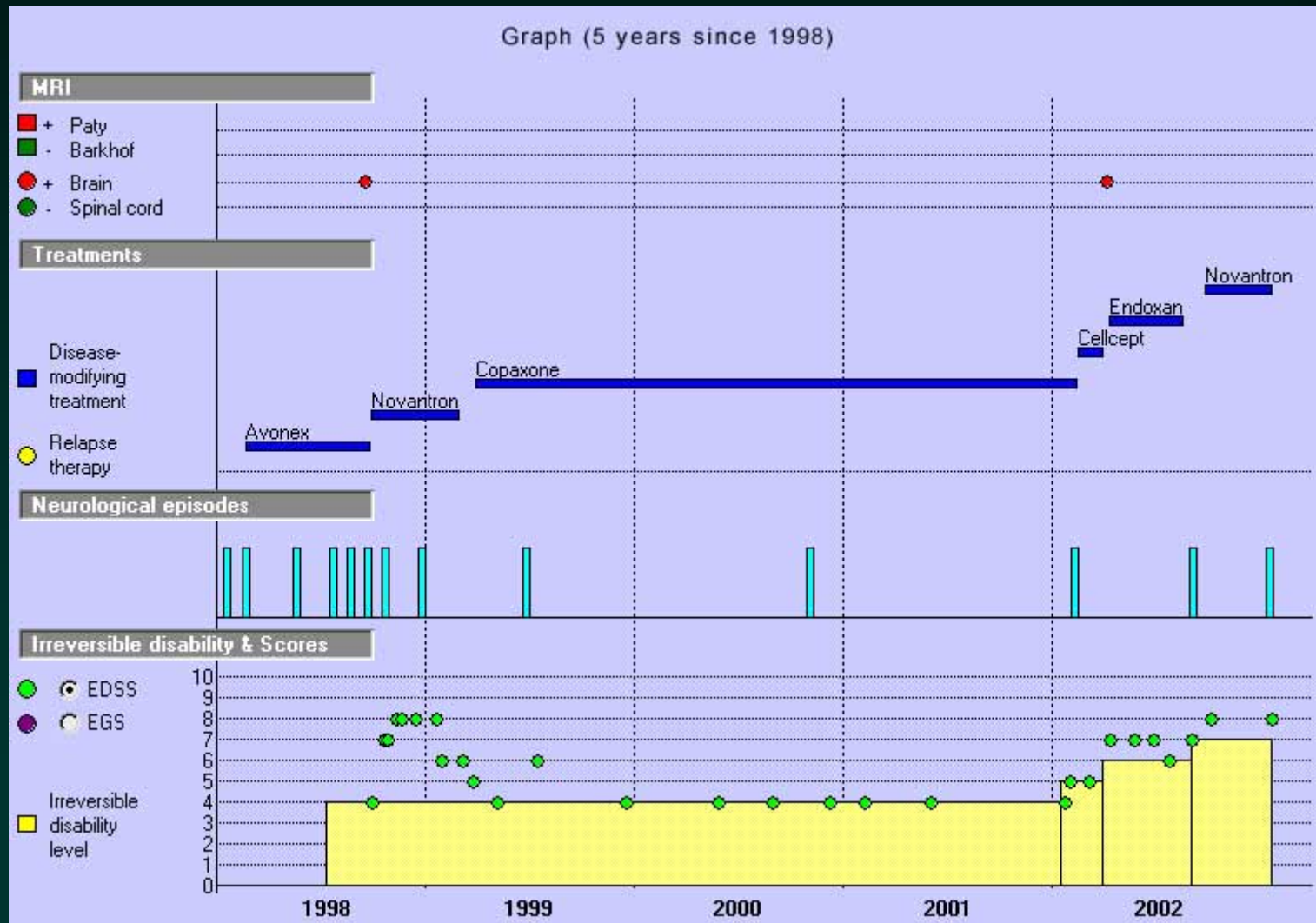
63 Centres

28 University Hospital
Referral MS Centres

18 City and Hospital
Health Regional Networks

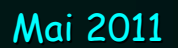
The Care of MS in France (2)

The EDMUS Software





285 Centres
40 Countries



Use of EDMUS in France

Electronic Medical Record

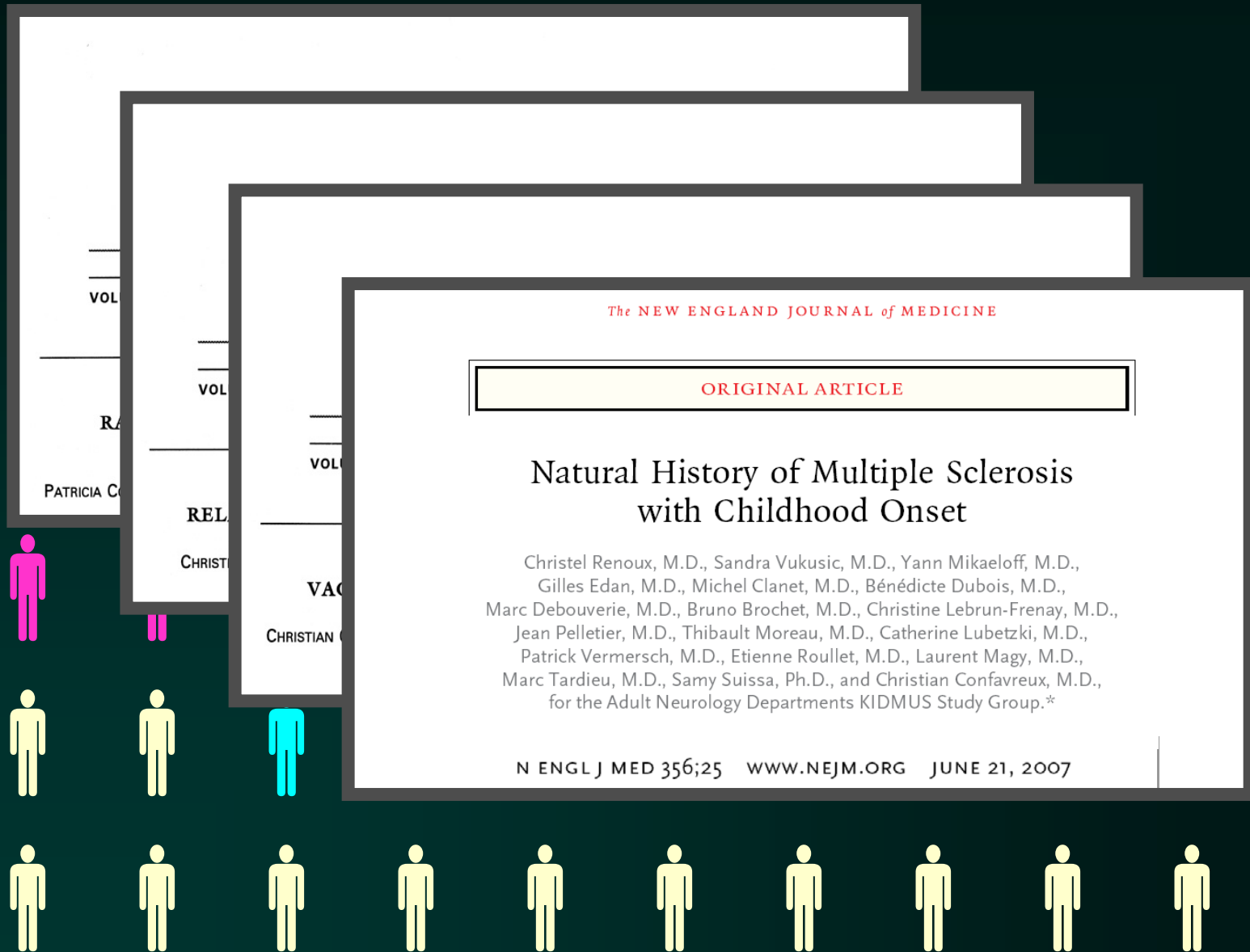
Fully Integrated in Daily Medical Practice

Directly

Indirectly

"Subcontracted"

The Care of MS in France (3)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Natural History of Multiple Sclerosis
with Childhood Onset

Christel Renoux, M.D., Sandra Vukusic, M.D., Yann Mikaeloff, M.D.,
Gilles Edan, M.D., Michel Clanet, M.D., Bénédicte Dubois, M.D.,
Marc Debouverie, M.D., Bruno Brochet, M.D., Christine Lebrun-Frenay, M.D.,
Jean Pelletier, M.D., Thibault Moreau, M.D., Catherine Lubetzki, M.D.,
Patrick Vermersch, M.D., Etienne Roulet, M.D., Laurent Magy, M.D.,
Marc Tardieu, M.D., Samy Suissa, Ph.D., and Christian Confavreux, M.D.,
for the Adult Neurology Departments KIDMUS Study Group.*

N ENGL J MED 356;25 WWW.NEJM.ORG JUNE 21, 2007

History

TYSEDMUS

Observational prospective phase IV pharmaco-epidemiological follow-up study of patients with MS and treated with natalizumab in France based on the French network of neurologists using EDMUS

Sponsor

AFSSAPS

Supports

Fondation Eugène Devic EDMUS

Hospices Civils de Lyon

Société Française de Neurologie (SFN)

Fédération Française de Neurologie (FFN)

Biogen Idec France (Unconditional Grant)

Coordination

LYON EDMUS Coordinating Centre

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Dr STANKOFF Bruno, Dr Frédéric TAITHE, Dr Eric THOUVENOT,
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Patrick, Dr VIALLET François, Pr VIGHETTO Alain, Pr VUKUSIC
Sandra, Dr WIERTLEWSKI Sandrine, Dr ZIEGLER François,
and all the neurologists involved in the regional city-hospital MS
networks.

Objectives

Primary

Establish the **Safety Profile** of NTZ (short to long term) in real life settings

Determine the **Incidence of Adverse Events**, notably

- infusion-related events, hypersensitivity reactions,
- development of anti-NTZ antibodies,
- infections: serious, opportunistic,
- pregnancies and pregnancy outcomes,
- malignancies

Secondary

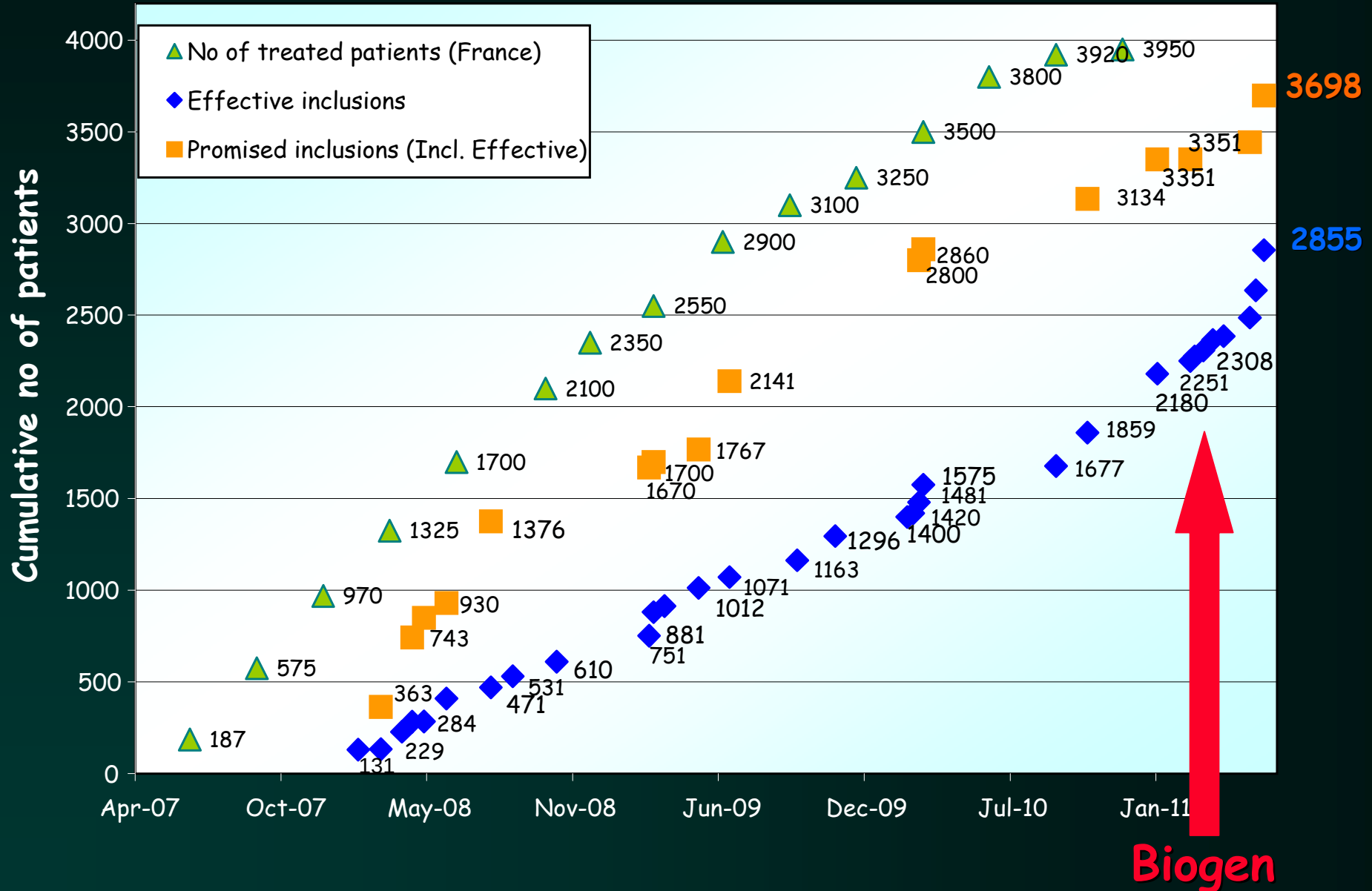
Describe the **Evolution** of patients treated with NTZ (relapses, EDSS, MRI)

Determine the **Conditions of Use** of NTZ in real life settings

Compare the incidence of serious and/or opportunistic infections and malignancies, between a **Non-Exposed Population** and the NTZ-exposed one

Inclusions

± 4000



Characteristics at Inclusion

Age (mean $\pm$ SD)	37.7 $\pm$ 9.8 yr
Female : Male Ratio	3 : 1
Disease Duration (mean $\pm$ SD)	9.1 $\pm$ 6.7 yr
Disease Course (% patients with RRMS)	96 %
Prior Disease-Modifying Treatments (% patients)	
Immunomodulators	88 %
Immunosuppressants	22 %
None	10 %
Nb Relapses in the Previous 12 Months (mean $\pm$ SD)	1.9 $\pm$ 1,2
EDSS score (mean $\pm$ SD)	3.6 $\pm$ 1,8
Brain MRI with Gad+ Lesions	55 %

Follow-up

Duration

Mean $\pm$ SD

20.1 $\pm$ 13.9 months

Median [Range]

19.5 [0 - 57] months

425 (16%) patients definitively stopped natalizumab

487 treatment discontinuations

- 32 % = Adverse Events, Allergy, Persisting Neutralizing Antibodies, ...
- 23 % = Lack of Efficacy (Relapses, Secondary progression)
- 45 % = Pregnancy, Convenience, ...

Safety

164 Serious Adverse Events among 128 patients (4.5%)

Severity	Description	Infusion No	NTZ Stopped
Death	PML	18	-
	Acute Leukoencephalopathy (mycoplasma)	19	-
	Cardiac arrest	14	-
	Cardiac arrest	2	-
	Completed suicide by defenestration	14	-
	Completed suicide by drug overdose	18	-
Persistent or significant disability	Carotid Artery Dissection, Sylvian Infarction	21	NO
Life-threatening	PML	32	YES
	Encephalitis due to herpes simplex	23	YES
	Urticaria, extended	2	YES
	Suicide attempt by drug overdose & cutting femoral vein	17	Unknown
	Suicide attempt by drug overdose	18	NO
	Suicide attempt	11	NO
	Cardio-respiratory arrest due to drowning	10	NO

Severity	Description	Infusion No	NTZ Stopped
Hospitalisation	PML	19	YES
	PML	39	YES
	PML	34	YES
	PML	Unknown	YES
	PML	Unknown	YES
	PML	Unknown	YES
	B-cell lymphoma,	33	YES
	Small cell lung cancer	27	YES
	Rectum cancer	7	YES
	Breast Cancer	Unknown	YES
	Breast cancer	43	NO
	Uterus cancer	26	NO
	Skin cancer	30	NO
	Anaphylactic shock	2	YES
	14 Allergic reactions	2x9, 3x2, 5x2, 6x1	YES
	Acute retinal necrosis due to VZV	21	YES
	Meningitis due to Enterovirus	1	YES
	Herpes Zoster shingles	3	NO
	Tuberculosis (Mycobacterium avium)	29	Unknown
	Cytolytic hepatitis	34	YES

Efficacy

At Starting
NTZ

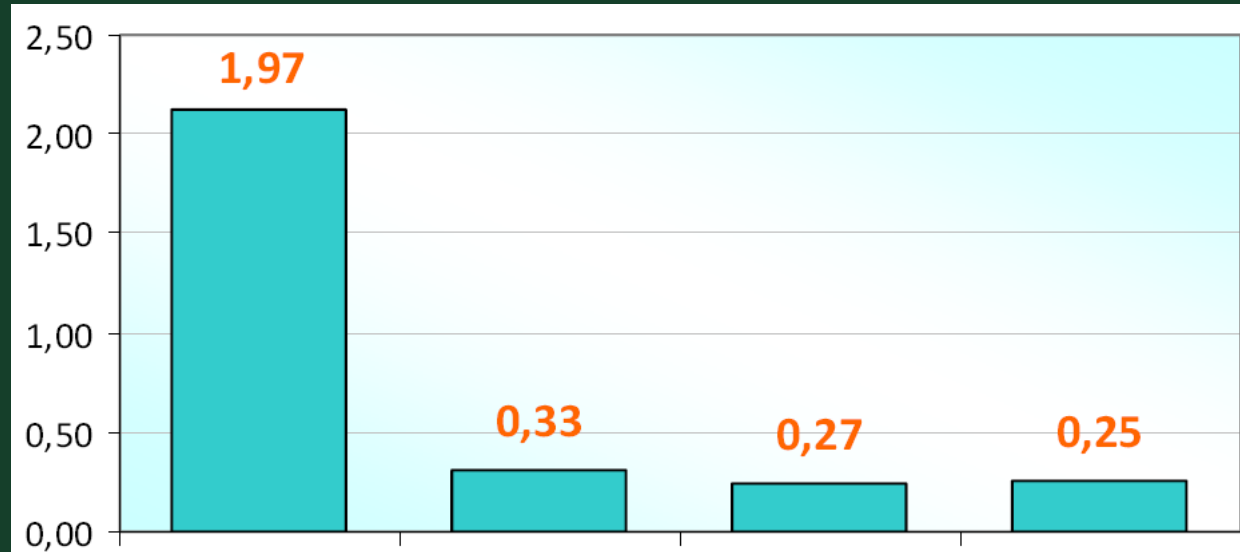
Year 1
NTZ

Year 2
NTZ

Year 3
NTZ

Relapses

(Mean Annualized Relapse Rate)



EDSS Score (Mean $\pm$ SD)

3.7 $\pm$ 1.8

3.3 $\pm$ 1.9

3.4 $\pm$ 1.9

3.5 $\pm$ 2.0

The Observatoire Français de la SEP (OFSEP)



▲ Investissements d'avenir : 200 millions d'euros pour les 10 lauréats de l'appel à projets "Cohortes"

Les 10 projets lauréats de l'appel à projets "Cohortes" du programme "Investissements d'avenir" ont été présentés par Valérie Pécresse et René Ricol, commissaire général à l'investissement. Inscrit dans l'action "Santé et Biotechnologies", l'appel à projets "Cohortes" est doté de 200 millions d'euros et assure un financement sur la durée.

Communiqué - Valérie Pécresse
25 janvier 2011

Valérie Pécresse, ministre de l'Enseignement supérieur et de la recherche, et René Ricol, commissaire général à l'investissement, ont dévoilé **les 10 projets lauréats de l'appel à projets "Cohortes"**. Inscrit dans l'action "Santé et Biotechnologies", l'appel à projets "Cohortes" est doté de 200 millions d'euros et assure un financement sur la durée.



PROJET OFSEP

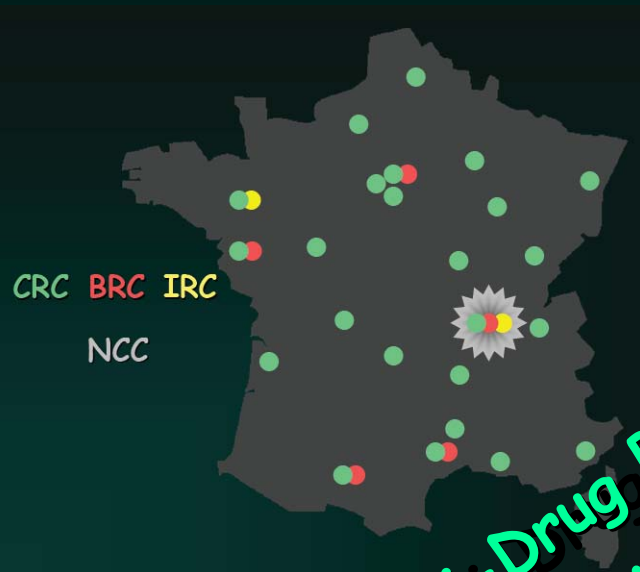
10.341.968 € over 10 years



MINISTÈRE
DE L'ENSEIGNEMENT SUPÉRIEUR
ET DE LA RECHERCHE
COMMISSARIAT GÉNÉRAL
À L'INVESTISSEMENT

The National MS Cohort

A "Large Epidemiologic Tool"



Increase
Enrich
Diversify

Supplementary Nests

Inaugural Cohorts
Centers
Clinical Epidemiology

Pharmaco-Epidemiology

Safety, Tolerance,
Conditions of Prescription

AFSSAPS

Pharmaco-Economy

Cost / Efficacy

CNAMTS, RSI, MSA

Pharmacology

Efficacy

HAS, CT

FOR WHOM ?

Physicians, Researchers,
Health Authorities,
Industry

WHERE ?

France and ROW

FOR WHAT ?

Promote Research ...
... Clinical,
Translational,
Basic

Permanent Multi-Drug Pharmacological Surveillance System
for Multiple Sclerosis in France