

Myopathies inflammatoires: quels traitements fondés sur des preuves

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Polymyositis and Dermatomyositis

Anthony Bohan, M.D., and James B. Peter, M.D., Ph.D.

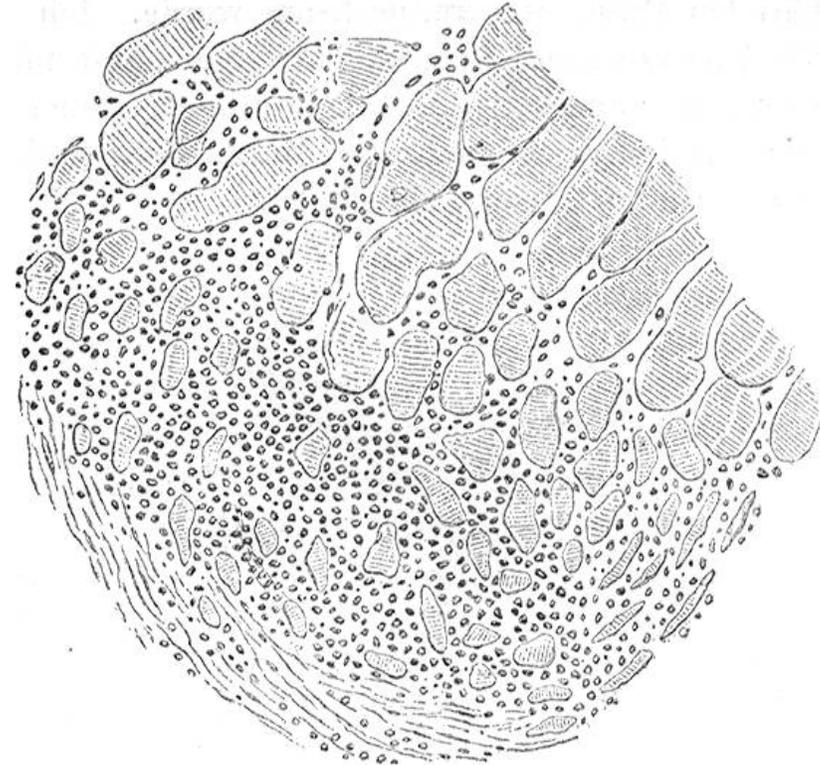
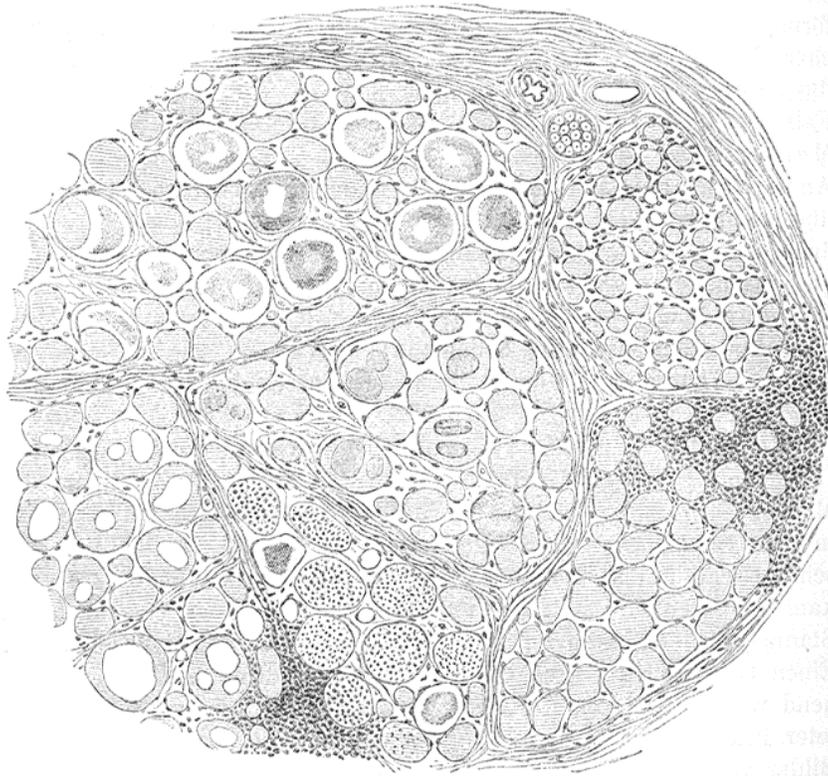
1. Symetric and proximal acute muscle weakness
2. Increase level of muscle enzyme (CK, Transaminases, LDH)
3. Myopathic changes (EMG)
4. Pathological pattern (Necrosis/regénération, inflammation)
5. **Skin rash**

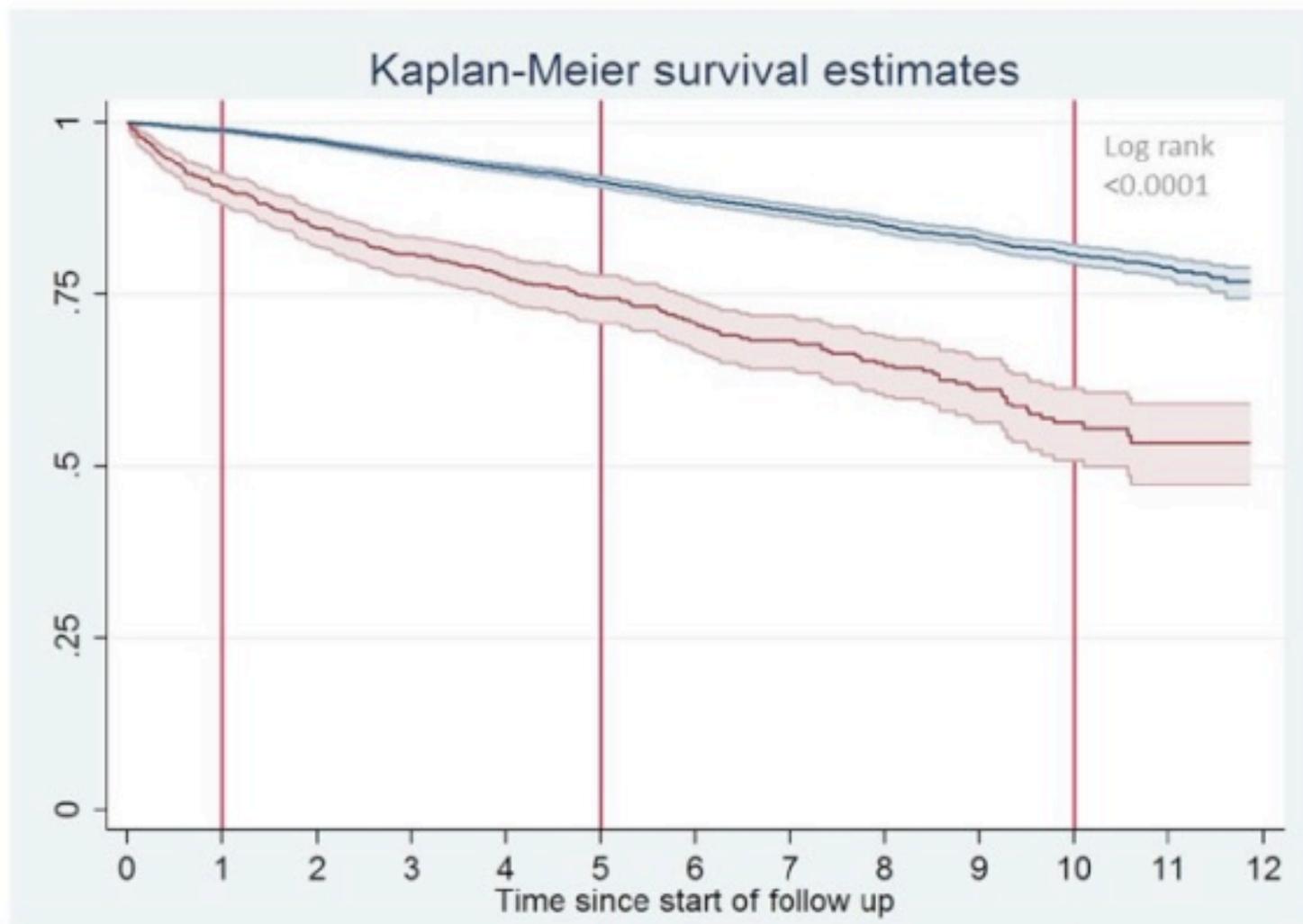
MORVE CHRONIQUE DE FORME ANOMALE;

Par le docteur POTAIN, médecin de l'hôpital Necker.

Sur le visage, on remarquait une sorte d'érythème à teinte

livide et un peu violacée occupant les paupières

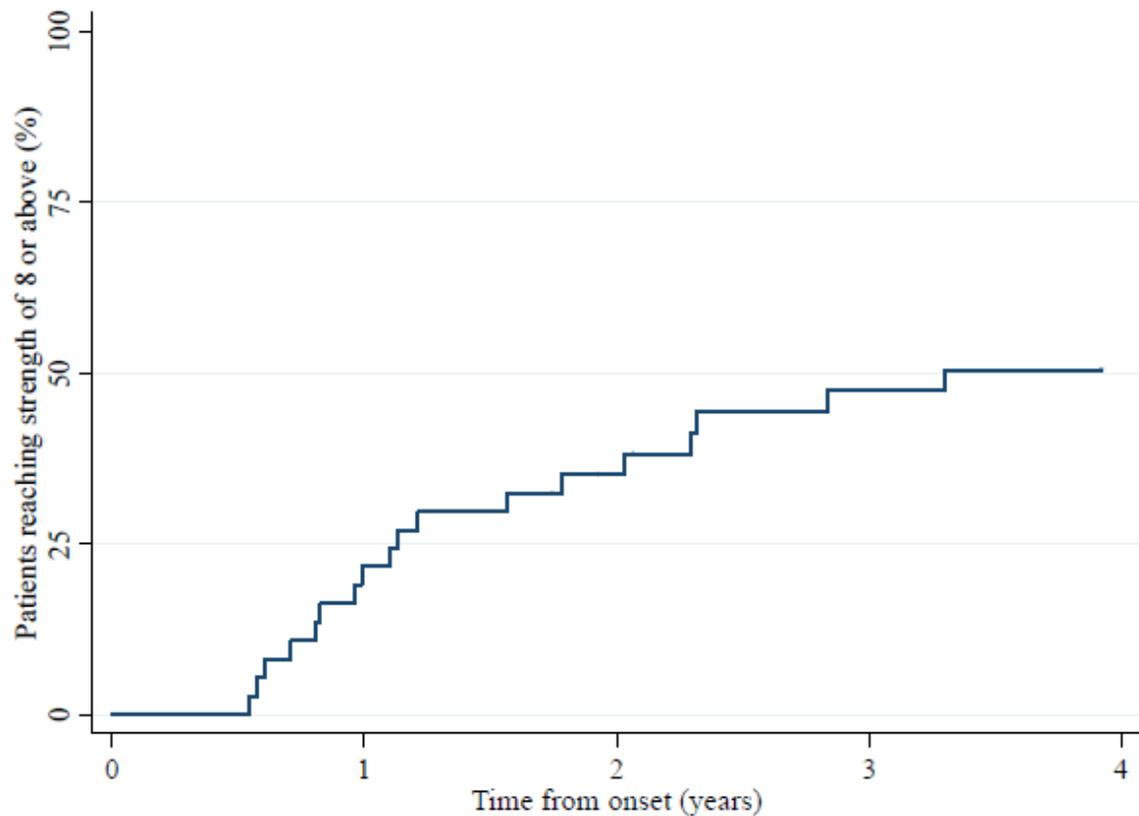




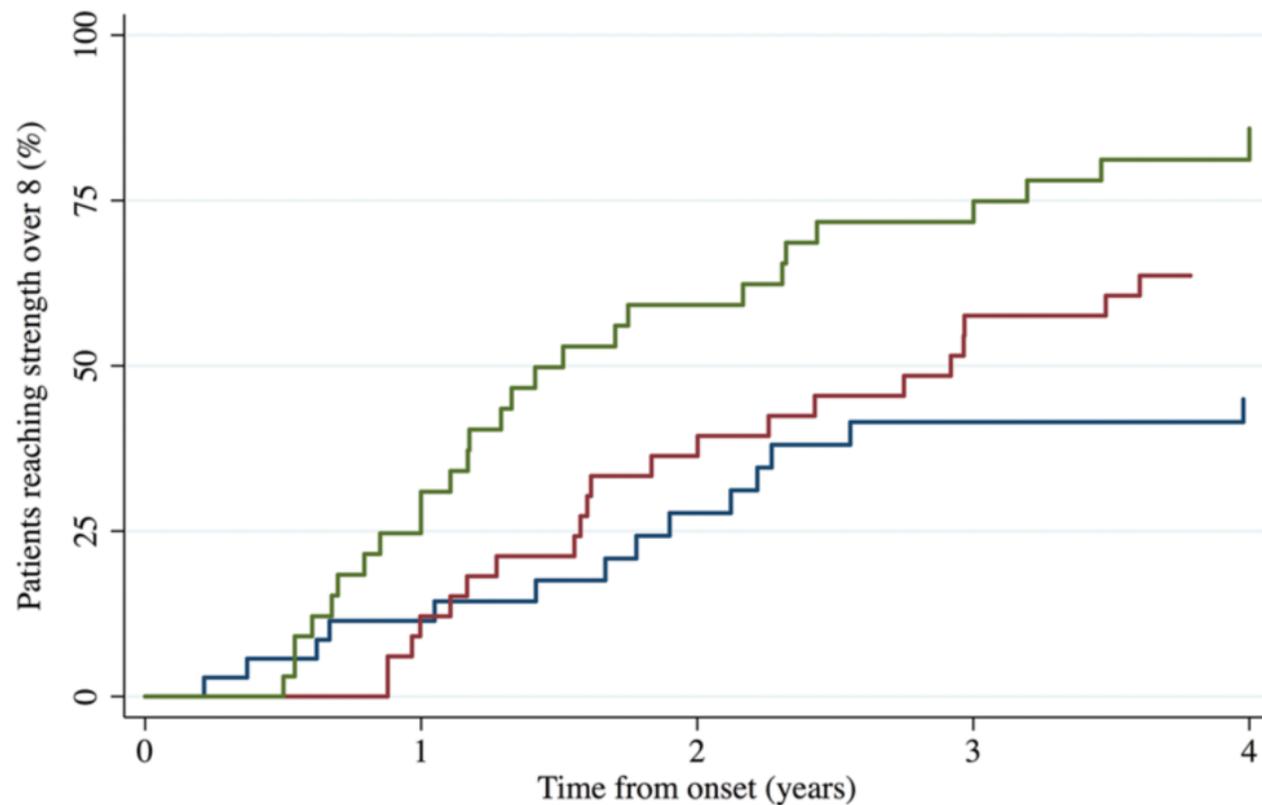
At risk, n	716/7100	648/7013	327/4037
Dead at end of interval, n	66/77	100/448	53/318
Cumulative mortality, %	9/1	23/7	31/12

Figure 2 Kaplan-Meier curves of death in idiopathic inflammatory myopathy (red line) and general population (blue line).

strength recovery over time in SRP+ patients



HMGCR+ patients



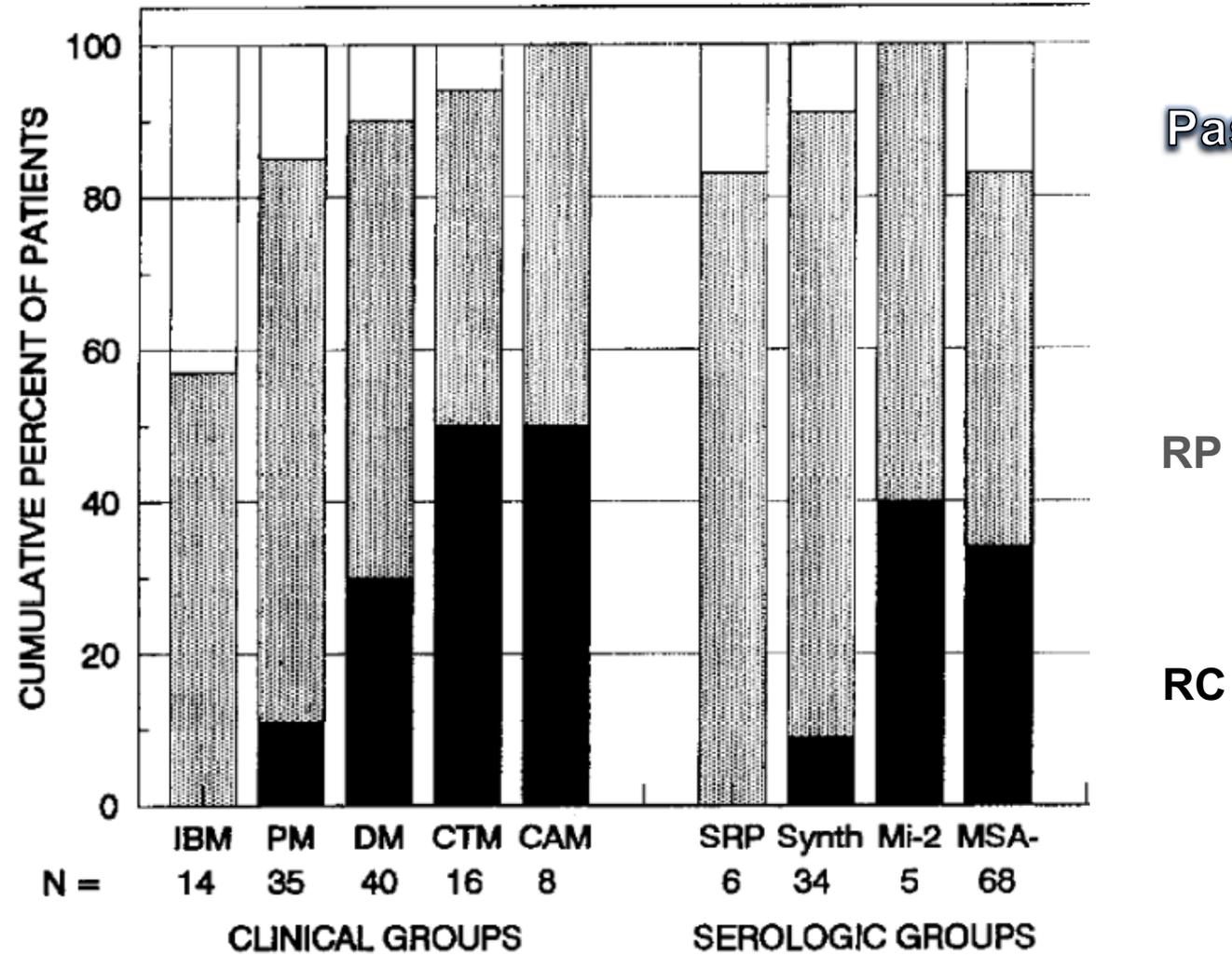
1- Induire la rémission

Corticoïdes

- Aucun RCT

Myositis + CT seuls

Open
Label



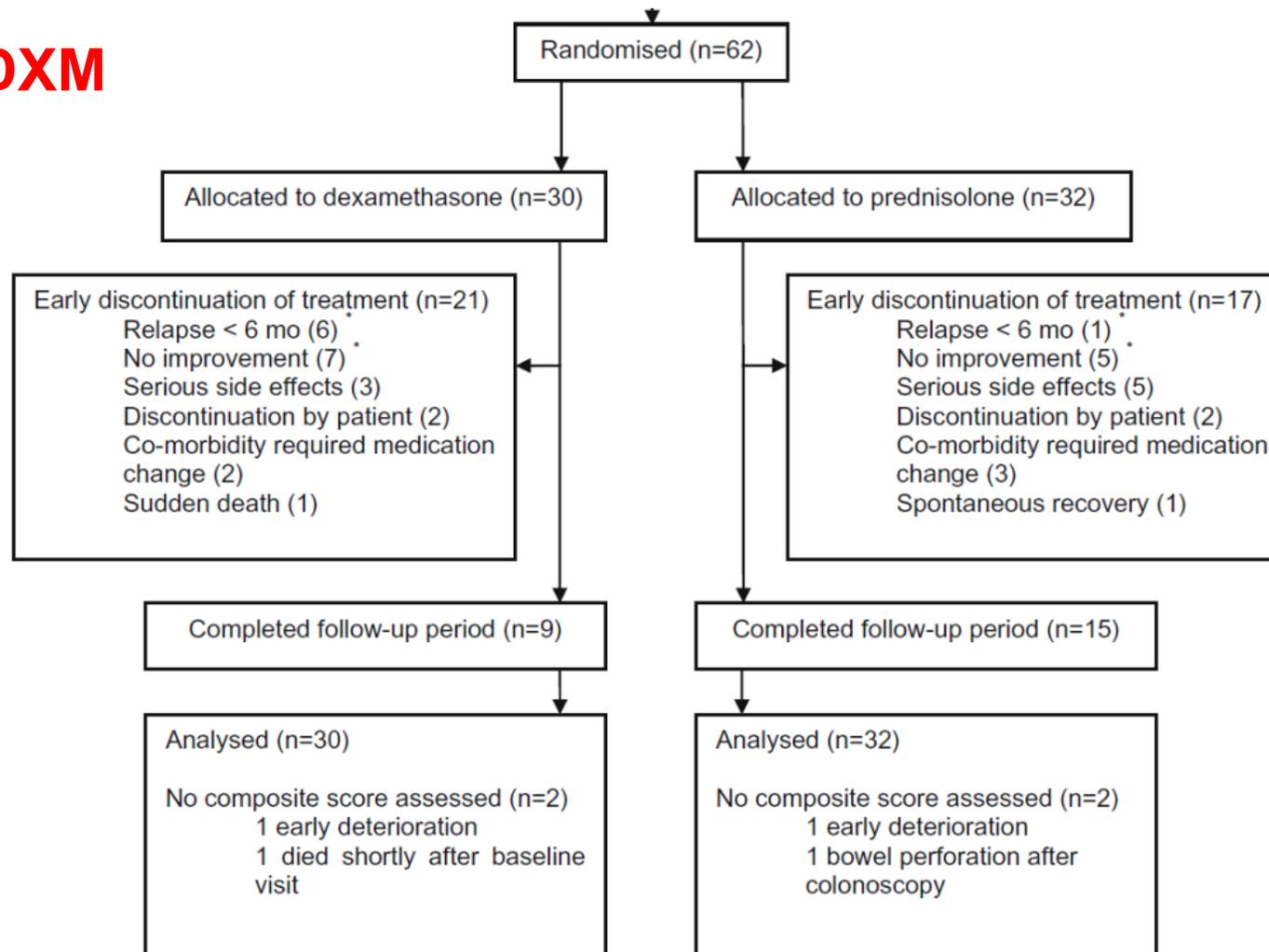
Pas R

RP

RC

Naïfs PDN vs DXM

18 Mois
RCT



Pas de différence (Composites MMT – Rechutes – tolérance – Dlr)

97% EI NS

Rechutes > 50%

Réfractaires + ACTH

6 Mois
OL
↓
CSM >20%

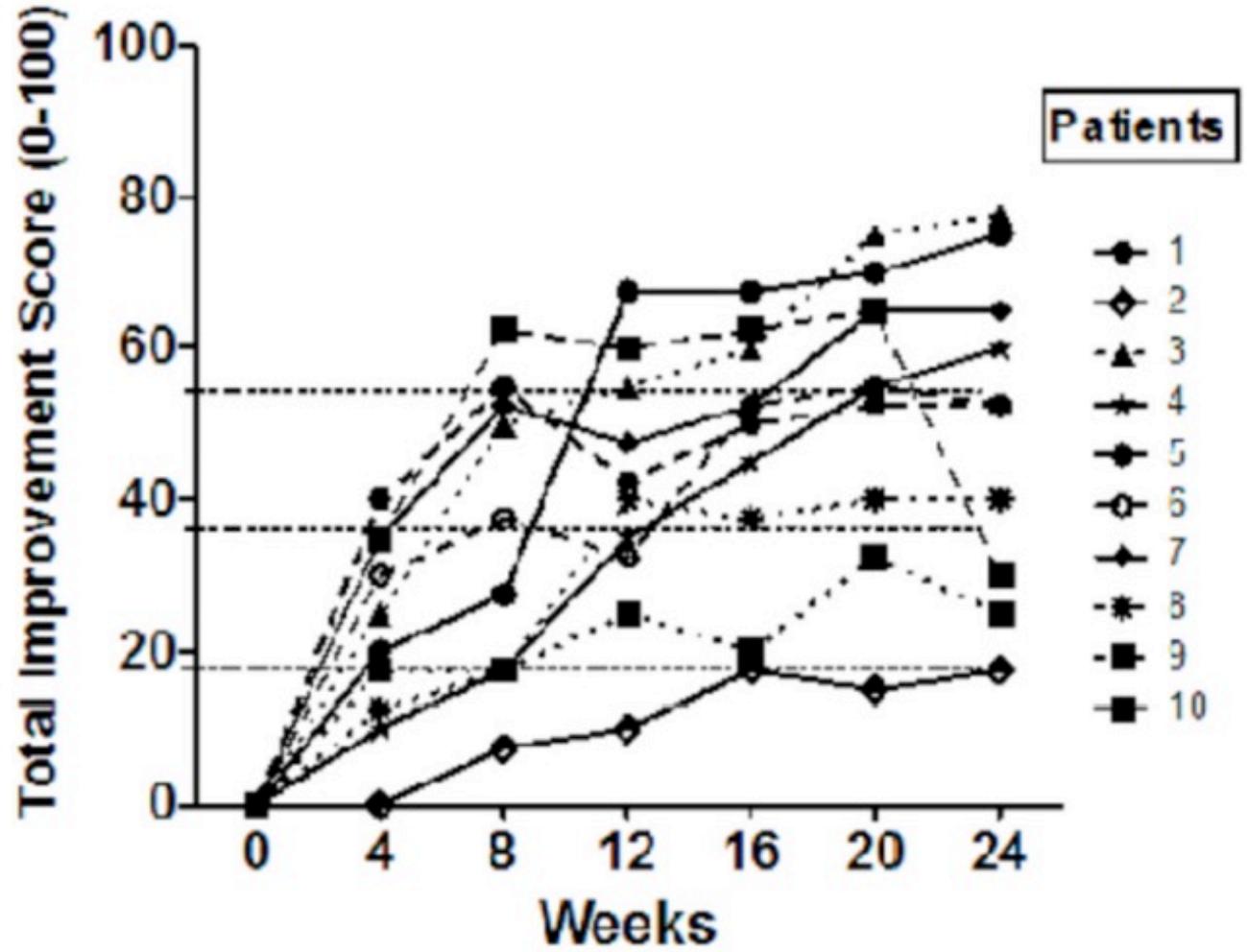
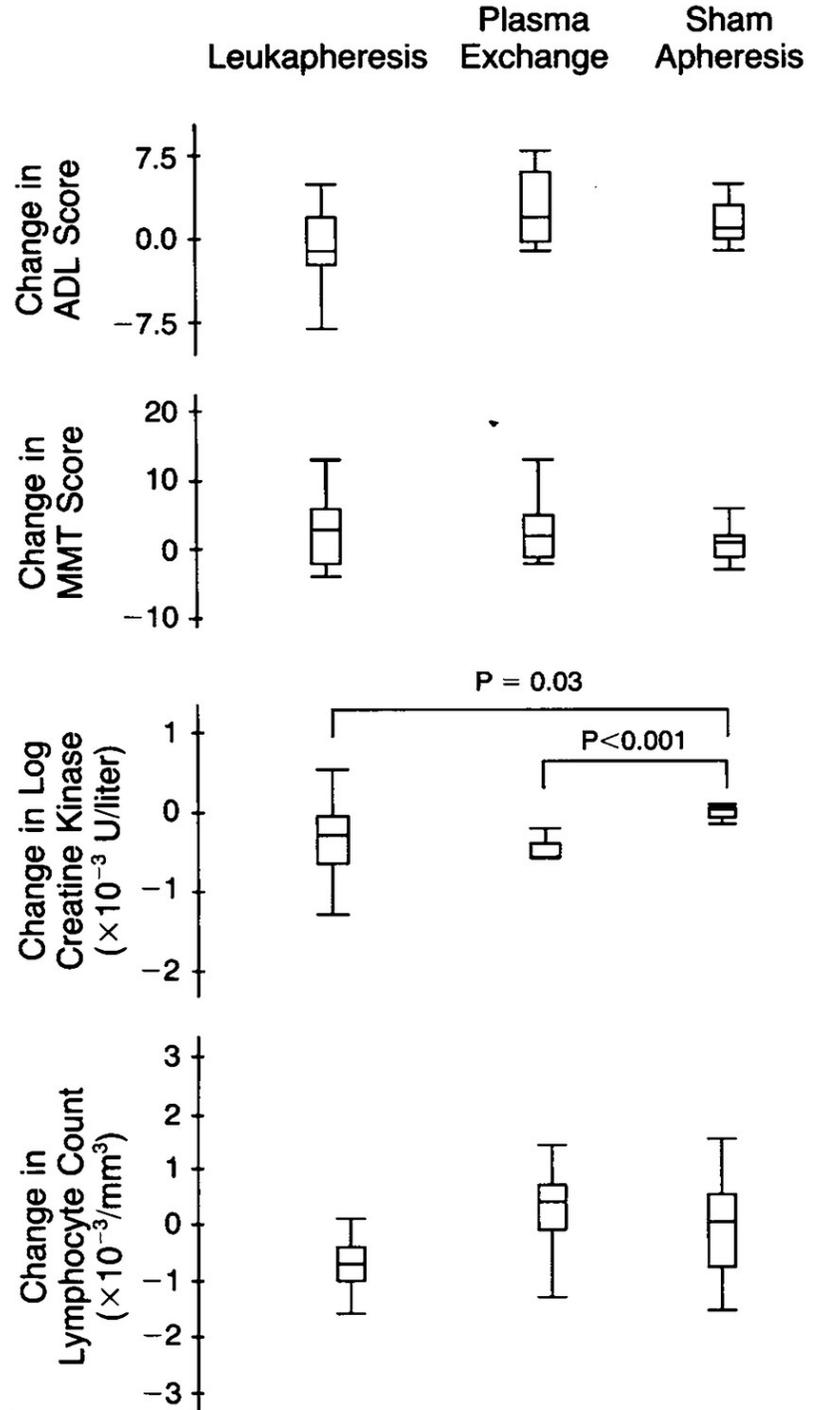


Figure 1 Primary outcome criteria as DOI (A) and secondary outcome criteria as 2016 American College of Rheumatology-European League Against Rheumatism myositis response criteria (B). DOI, definition of improvement .

PM/DM réfractaires + Aphérèse

1 Mois
RCT

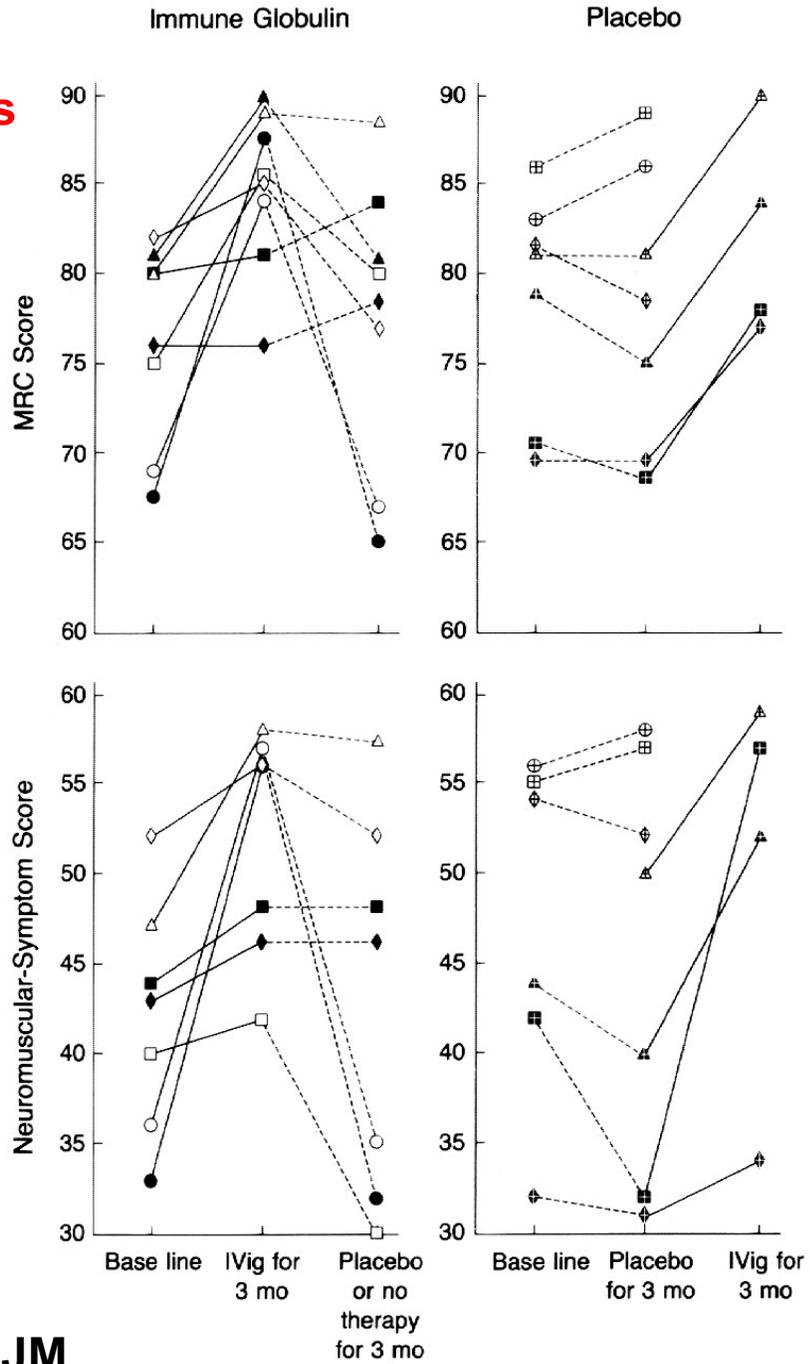
Pas de bénéfice



**DM réfractaires
N=16**

**6 Mois
RCT
Cross over**

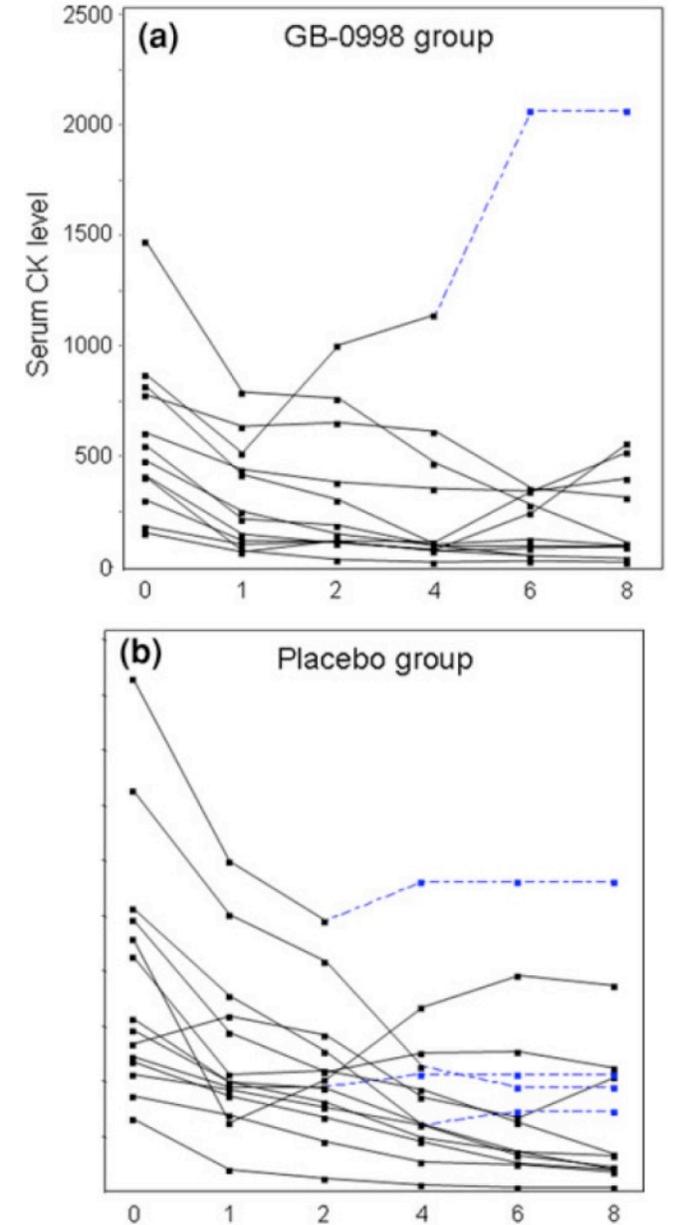
**MMT
A M3 Mieux**



**PM réfractaires
N=35**

**6 Mois
RCT
Cross Over**

**MMT
Pas Mieux à M2
BIAIS ?**



PM/DM réfractaires
N=35

4-6 Mois
OPL

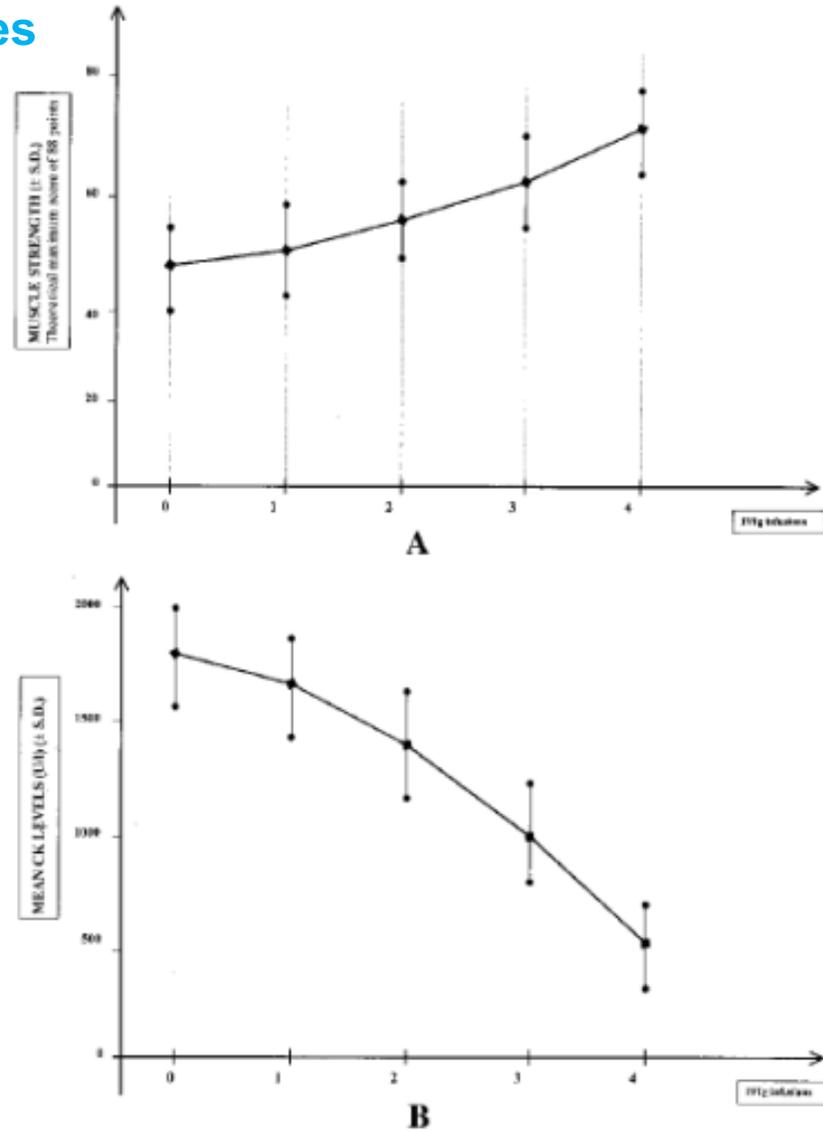


Figure 1. Clinical (A) and biologic (B) evolution of 35 patients with polymyositis receiving intravenous immunoglobulin (IVIg) therapy. Bars show the mean \pm SD. CK = creatine kinase.

DM réfractaires
N=120
IgPRO RCT vs PBO
COMMENCE
OP: 6 mois TIS >20%

1- Induire la rémission

CT 1 mg/kg - Bolus dans les formes sévères ?

IgIV dans les formes sévères dans les pratiques

EP dans les formes sévères discuté

Décroissance lente

Table 1 Diagnosis, disease course, and outcome

	Diagnosis at baseline <i>N</i> (%)	Diagnosis at follow-up <i>N</i> (%)	Deceased <i>N</i> (%)	Surviving patients		
				Rankin 0–2 (independent) <i>N</i> (%)	Monophasic course <i>N</i> (%)	Polyphasic or chronic continuous course <i>N</i> (%)
Polymyositis	0	0	–	–	–	–
Dermatomyositis (DM)	24 (39)	23 (38)	6 (26)	14 (61)	6 (26)	10 (43)
DM + CTD	0	1	0	1 (100)	0	1 (100)
DM + malignancy	1	6	5 (83)	1 (17)	0	0

- **75 % SAS DMARD + à 3.5 ans**
- **> 90% des MNAI à 3 ans**

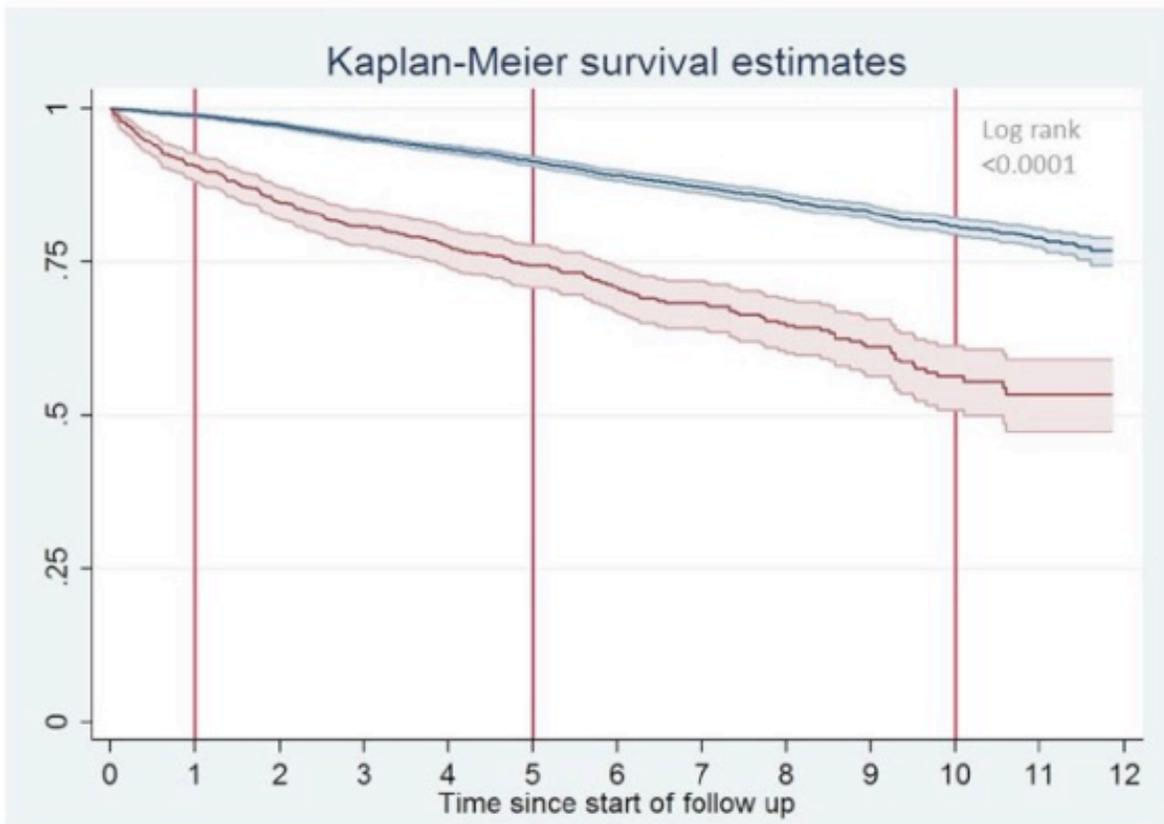
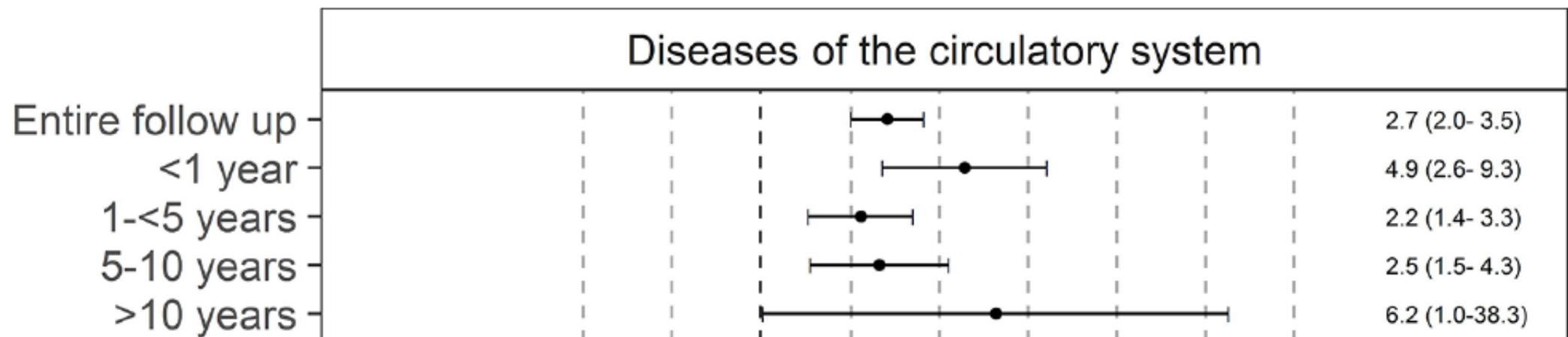


Table 2 Causes of death of all who died during follow-up and the main diagnosis for hospitalisation up to 1 month prior to death in patients with idiopathic inflammatory myopathy (IIM) identified from the National Patient Register 2002–2011 as well as the general population cohort

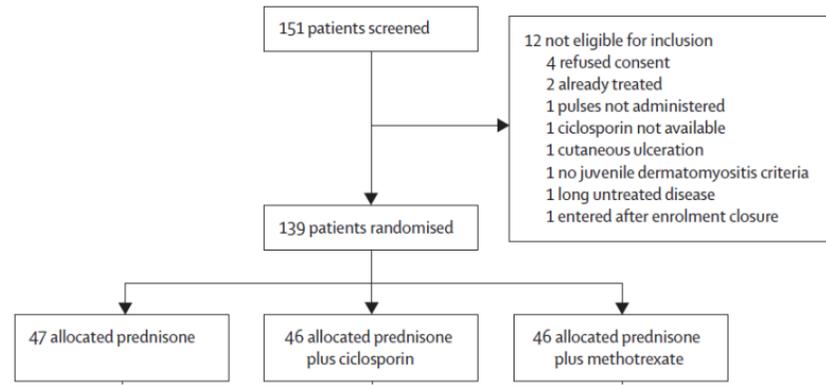
	IIM patients	General population comparators	p Value*
Death from all causes	224	870	
Diseases of the circulatory system	21 (20.8)	91 (28.7)	0.08

Number of individuals (percent of total number) in each subgroup if not stated otherwise.



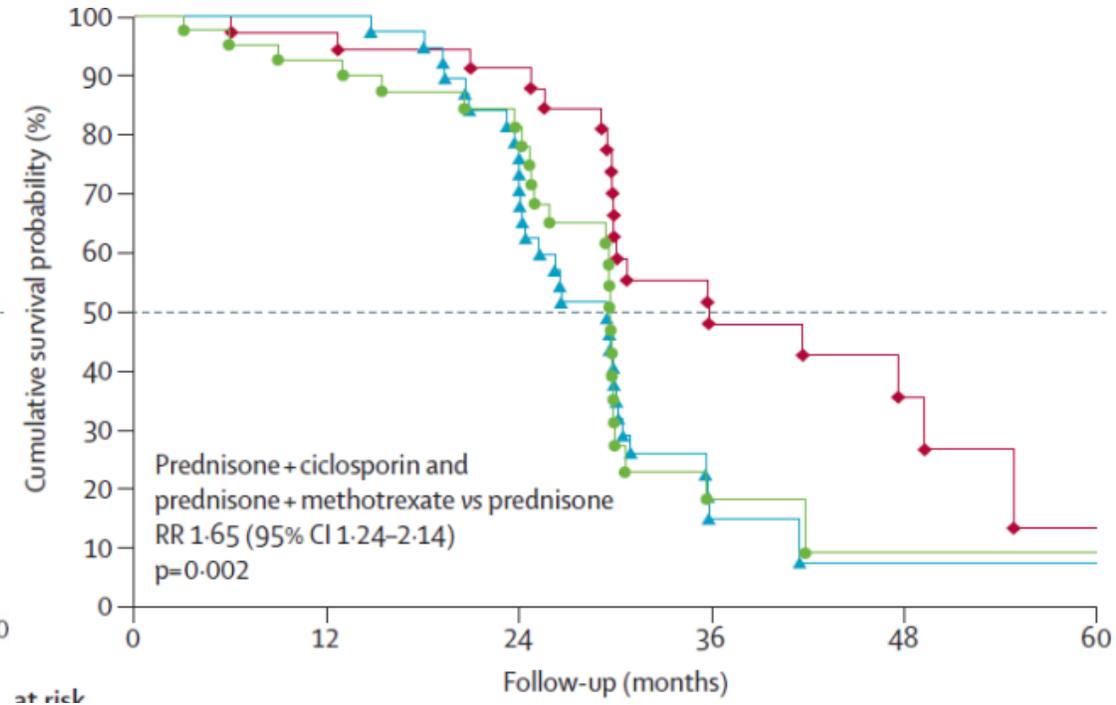
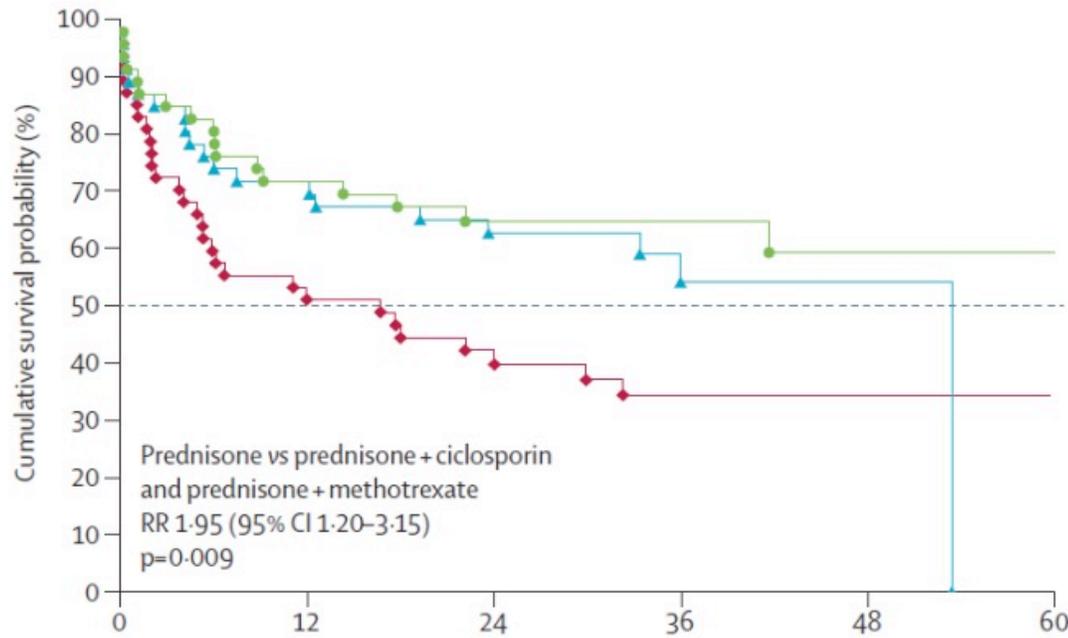
2- Maintenir la rémission

jDM réfractaires N=151
CT vs CT + Ciclà vs CT + MTX



PRINTO LANCET 2016

- ◆ Prednisone
- ▲ Prednisone + ciclosporin
- Prednisone + methotrexate



6 Mois
 RCT
 Open

IMACS
 A M6-12 Mieux

Prometheus

**PM/DM N=50
CT vs CT + MTX**



**12 Mois
RCT**

**EPARGNE CT (doses cumulées)
NS à 62% des inclusions**

**PM N=16
CT vs CT + AZA**



**3 Mois
RCT
Blind**

**MMT/CK
ECHEC**

**PM N=16
CT vs CT + AZA**



**3 ans
Extension
ouvert**

**MMT/CK
EFFICACE**

1- MMF - Calcineurines

2- Combo ?

PM/DM N=25
AZA + MTX os vs MTX IV / 2s



12 = 6 + 6 Mois
RCT
Cross over

Efficace + mais de différence

Villalba, et al arthritis 1998
Majithia, et al Rheumatology 2005

PM/DM/jDM réfractaires

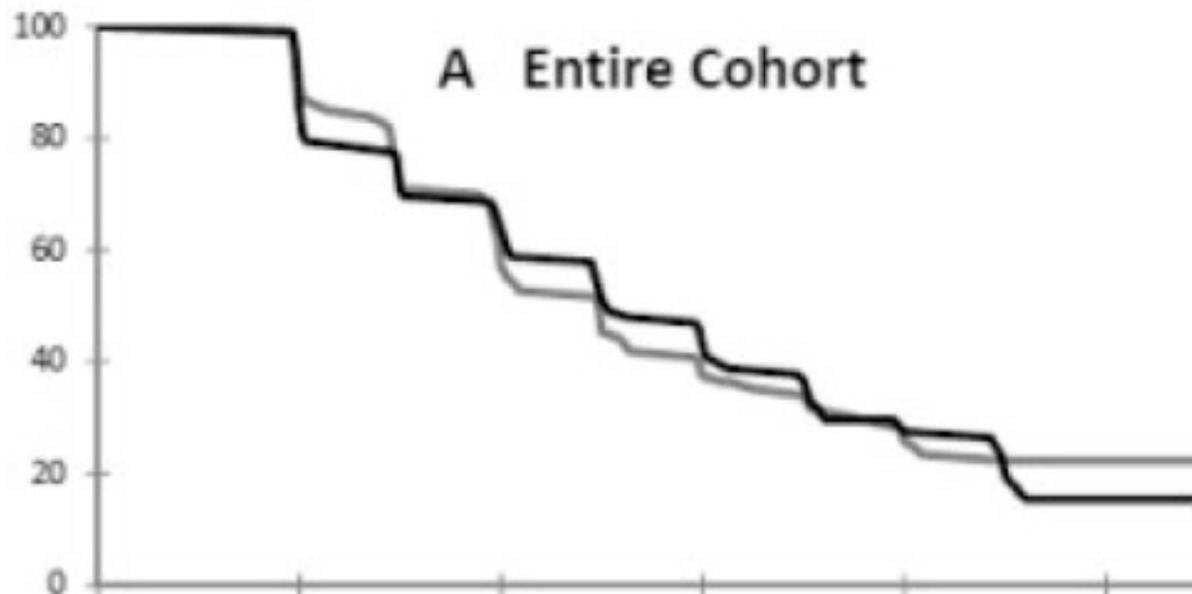
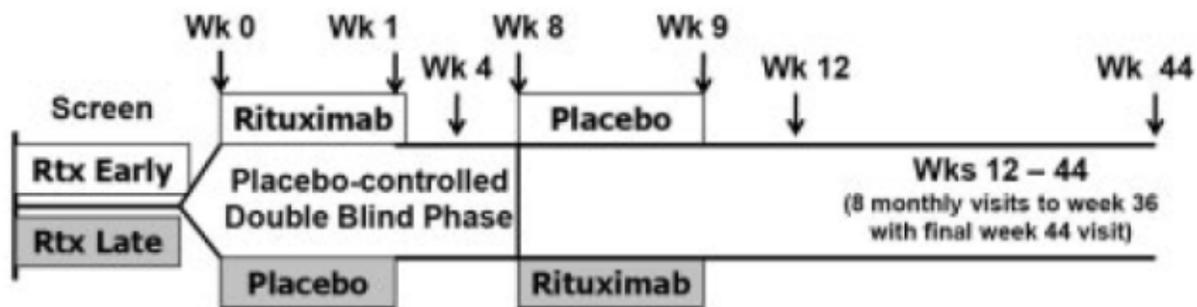
N=200

RTX



**2 mois
RCT
Delay started**

**IMACS à w8
ECHEC
mais 86% Critères + à M6**



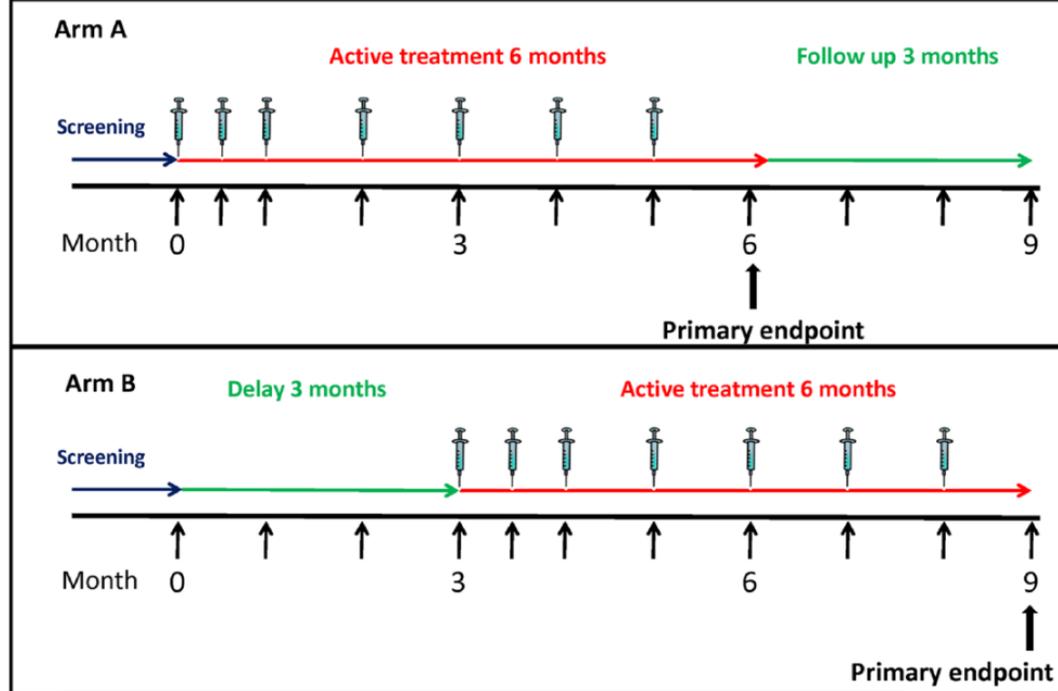
**Jo1 +
Mi2 +**

**PM/DM réfractaires
N=20
Abatacept add on**



**6 Mois
RCT blind
Delayed-start**

**IMACS 50% Réponse à M6
À M3 Aba > Contrôle**

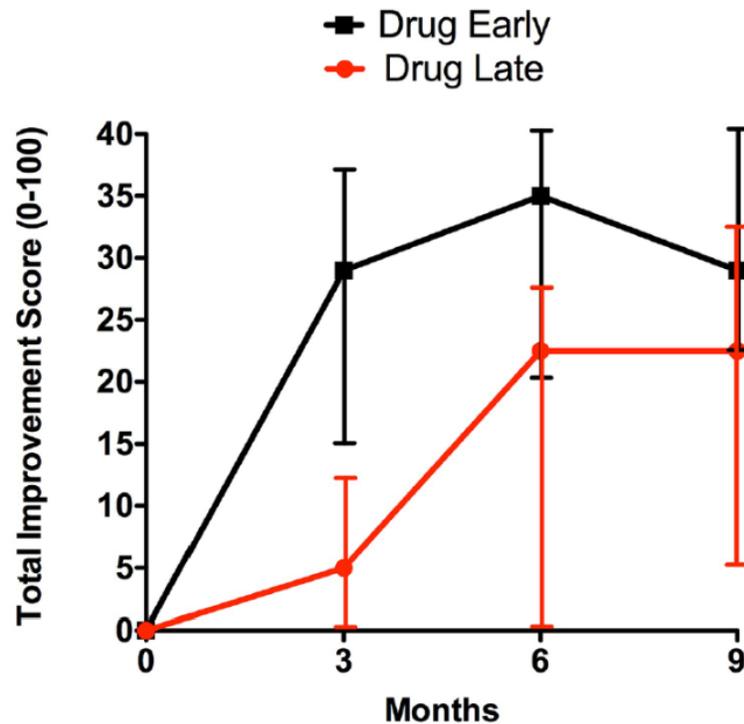


**PM/DM réfractaires
N=150
Abatacept vs PBO
EN COURS**

**ICI-Myositis
PHRC-K ?**

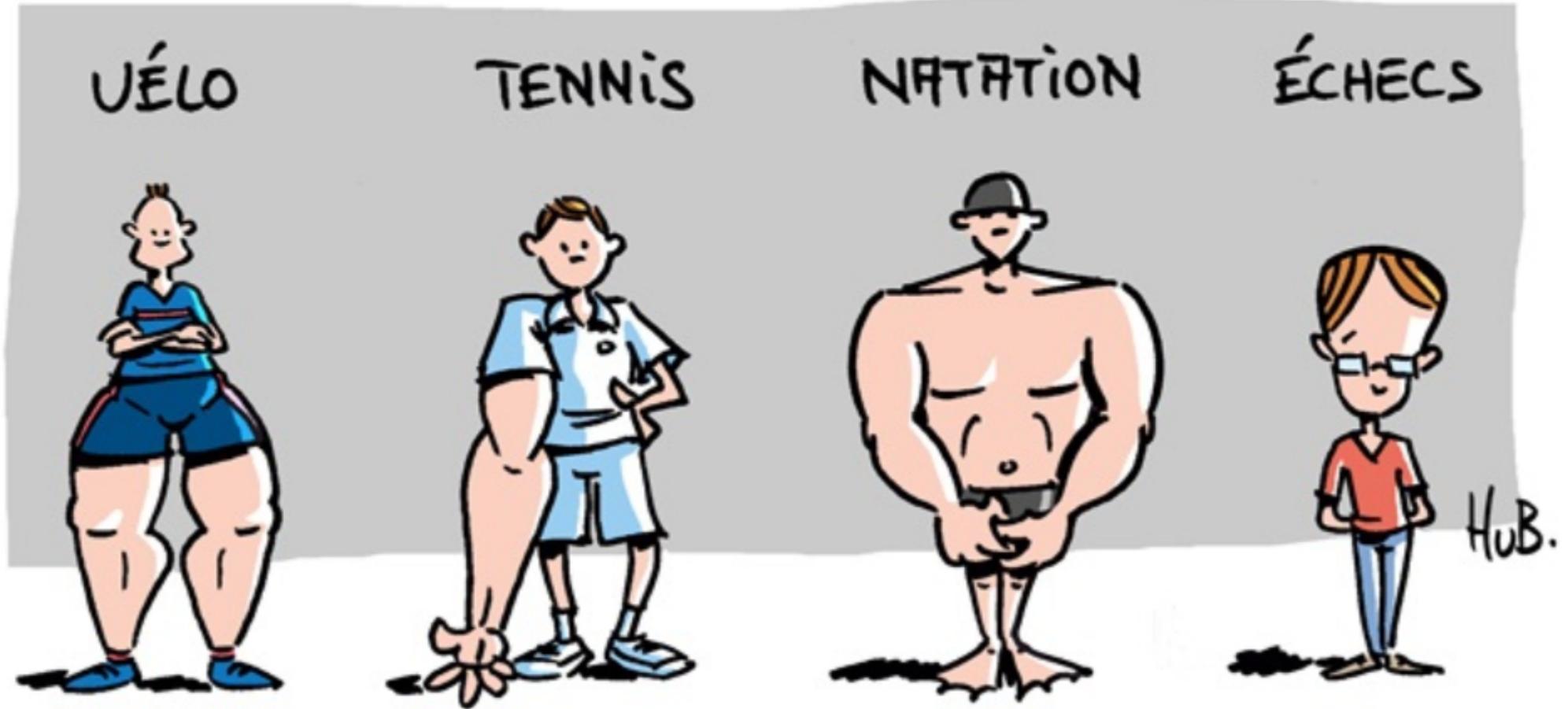
**Anti-IL-6
RCT = en cours**

**Anti-TNF
RCT = ECHEC**



**JE Selam et al NEJM 2019
Tjarnuld et al ARD 2017**

POUR VOTRE SANTÉ, FAITES DU SPORT!



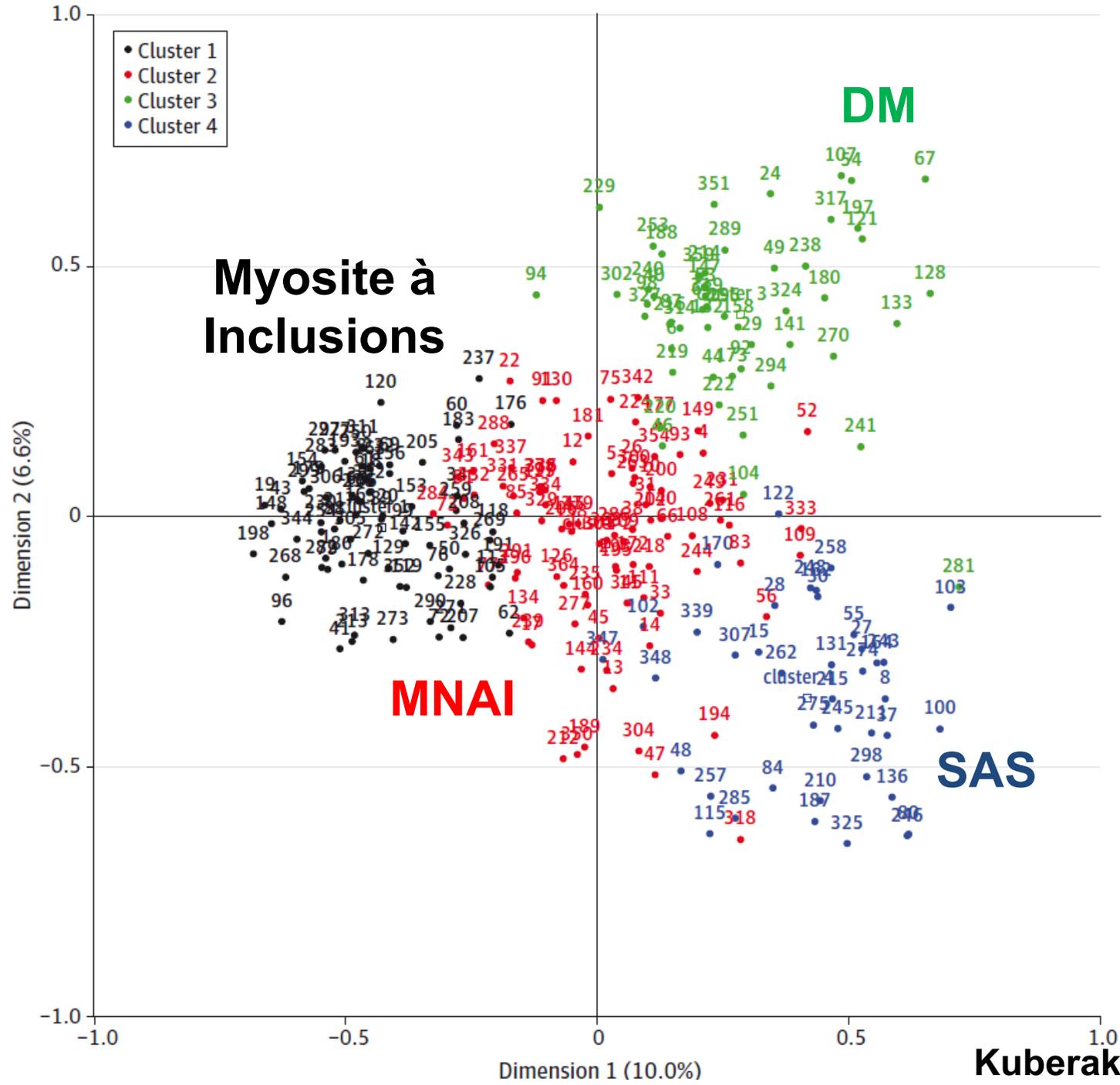
2- Maintenir la rémission

1- IS systématique MTX/AZA

2- Switch

3- RTX

4- Un traitement sur mesure



Treatment to last follow-up duration (yrs)	4.9 [3.1; 8.9]
Normal strength	40%
Deltoid (MRC)	5 [4; 5]
Psoas (MRC)	4 [2; 5]
Chronic ventilation	3%
CS use	57% (n=20/35)
CS dose (mg/day)	8 [5; 10]
IS monotherapy	20%
IVIg monotherapy	31%
IS+IVIg	31%
IVIg use	69%
- IVIg duration (yrs)	1.7 [1.3; 3.4]
- IVIg discontinuation ≥ 6 months	31%
Immunosuppressant (IS)	54%
- MTX	26%
- AZA	17%
- MMF	3%
- RTX	3%
- RTX/MTX	6%
CK level (IU/L)	299 [200; 559]
Remission	62% (n=21/34)
- Remission without IVIg	21% (n=7/34)
- Treatment-free remission	0%
mRS	1 [0; 2]
Course	
- Monophasic	0%
- Polyphasic (recurrence after treatment-free remission)	0%
- Chronic	100%

Evaluation immediately before IVIG			
Creatine kinase (IU/liter)	8916	2323	3517
Strength			
Arm abductors			
Contraction against resistance			
Right	4	4+	4
Left	4	4+	4
Weight resisted (kg)			
Right	2.7	5.0	2.7
Left	2.7	5.0	3.2
Most recent evaluation			
Time since first IVIG (mo)	9	19	15
Creatine kinase (IU/liter)	1755	64	877
Strength			
Arm abductors			
Contraction against resistance			
Right	5	5	5
Left	5	5	5



PERGAMON

Neuromuscular Disorders 16 (2006) 334–336



www.elsevier.com/locate/nmd

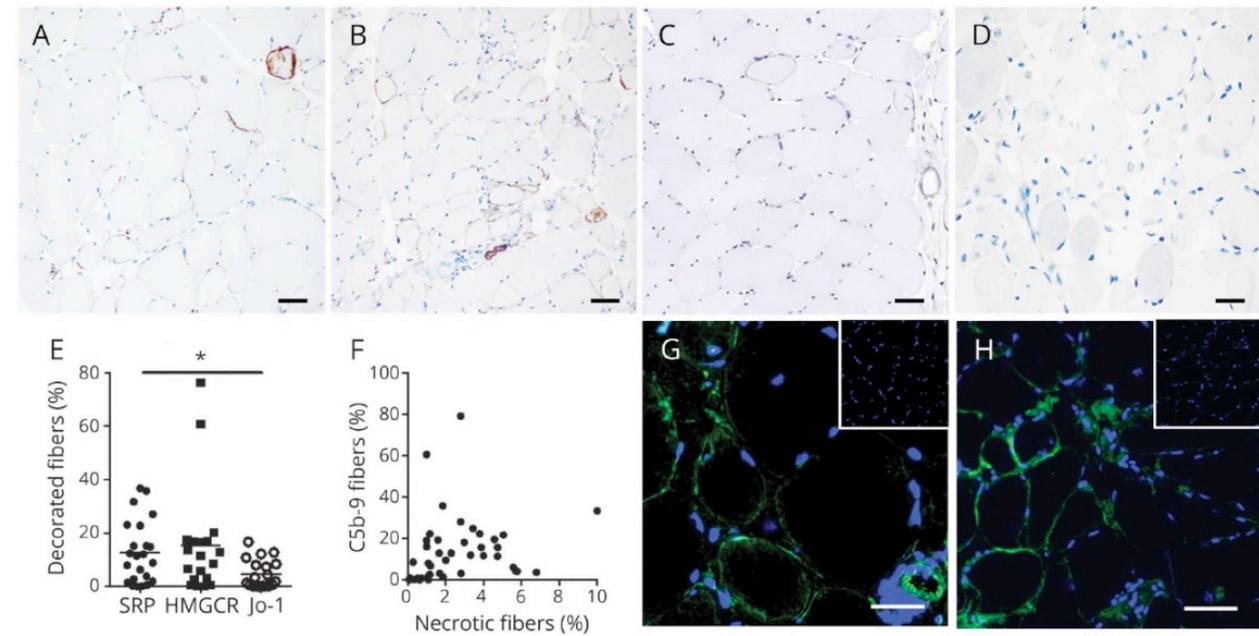
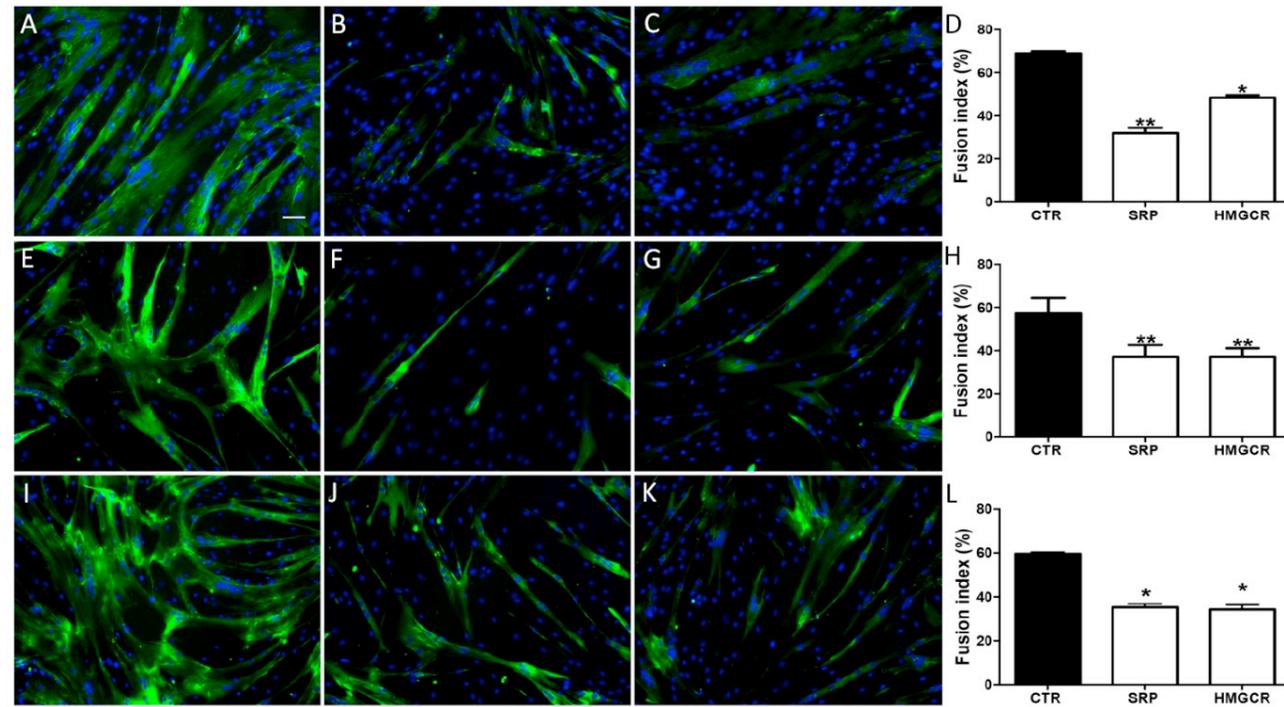
Case report

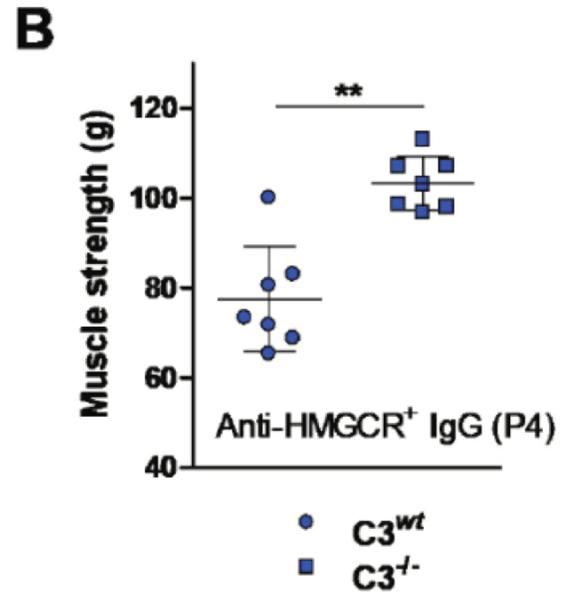
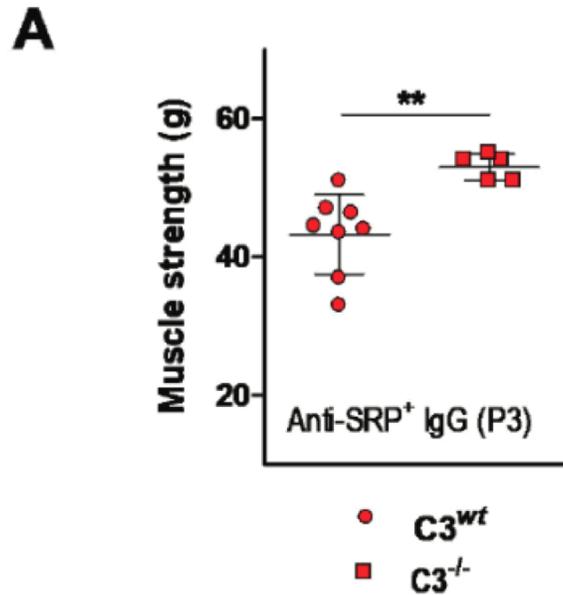
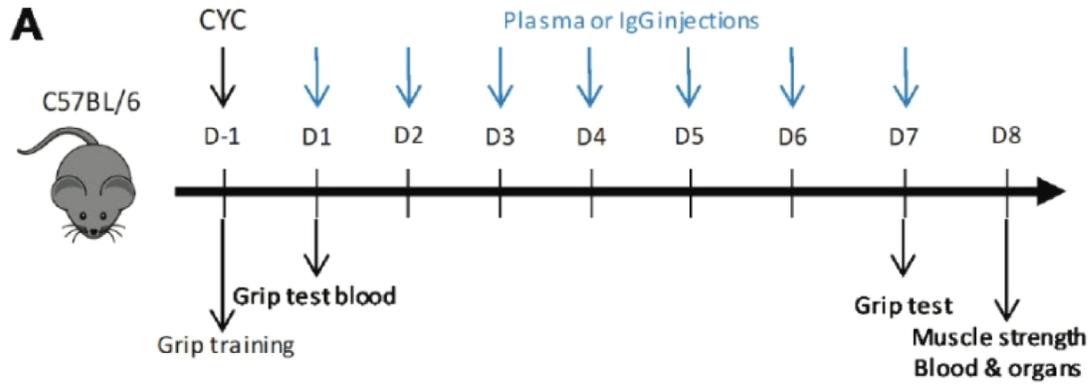
Marked efficacy of a therapeutic strategy associating prednisone and plasma exchange followed by rituximab in two patients with refractory myopathy associated with antibodies to the signal recognition particle (SRP)

Jean-Benoit Arlet ^a, Dalia Dimitri ^b, Christian Pagnoux ^b, Olivier Boyer ^c, Thierry Maisonobe ^d, François-Jérôme Authier ^e, Coralie Bloch-Queyrat ^a, Claire Goulvestre ^f, Farhad Heshmati ^a, Marielle Atassi ^b, Loïc Guillevin ^a, Serge Herson ^b, Olivier Benveniste ^b, Luc Mouthon ^{a,*}

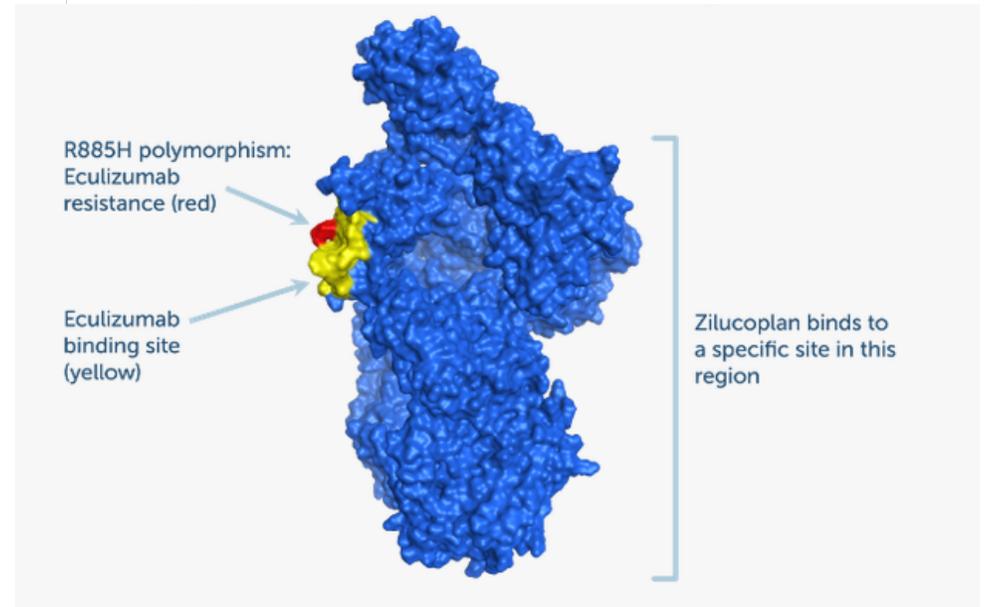
- **SRP + RTX efficace 13/17**
- **HMGR + RTX inefficace**

Pinal-Fernandes et al. 2016
O. Landon et al. JNMP 2019
Allenbach et al. NMD 2017

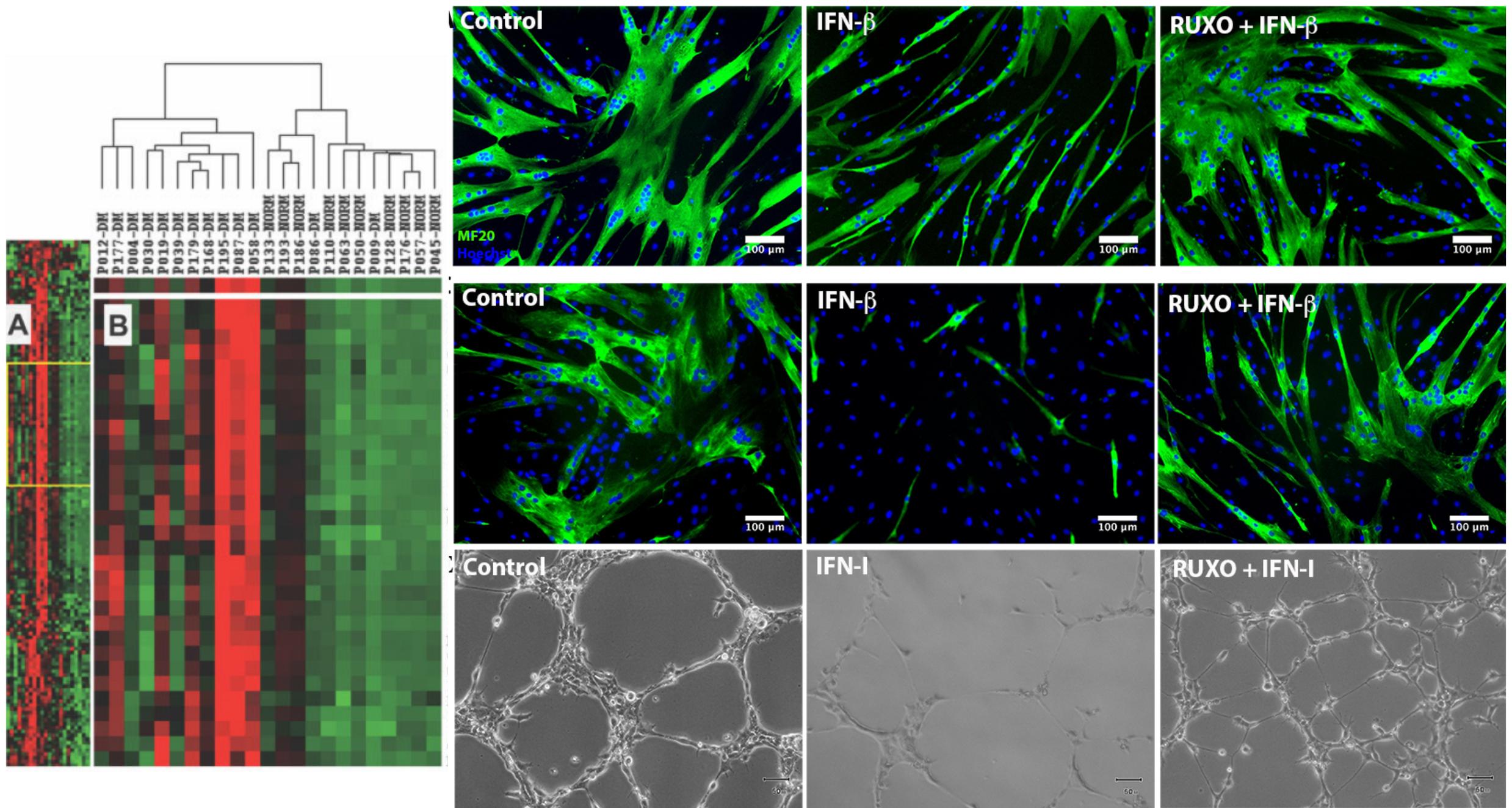




RCT ZILUCOPLAN

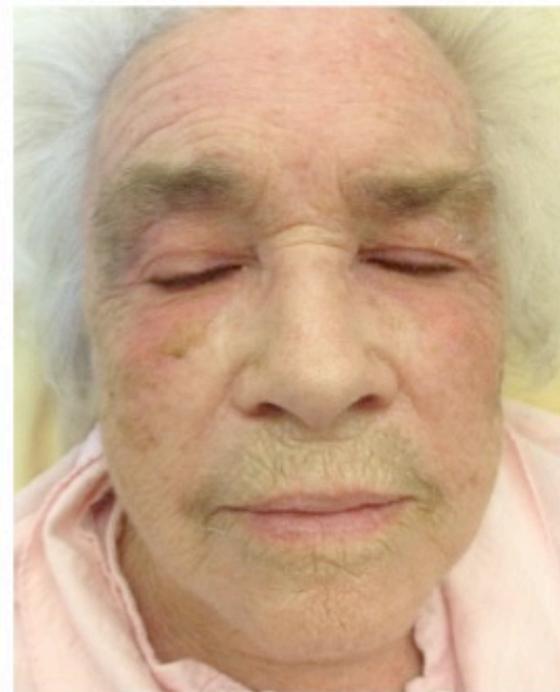
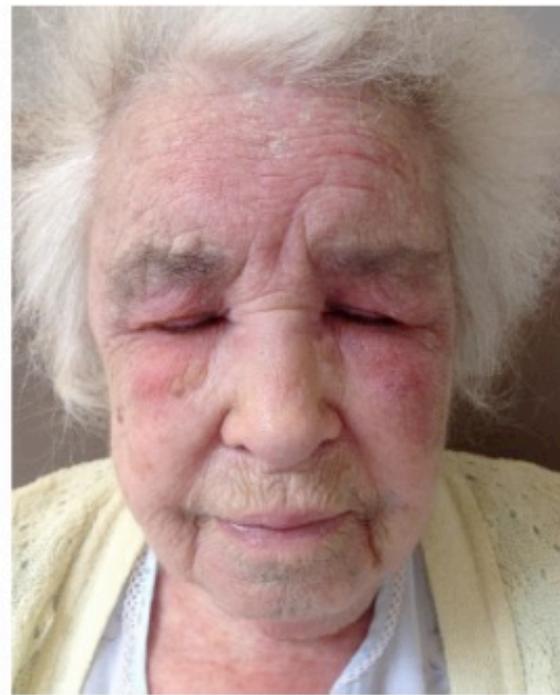


C5a – C5b

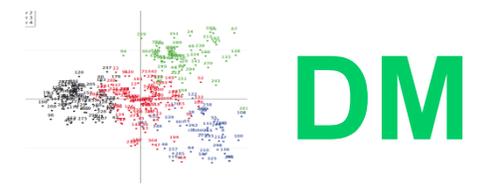


Greenberg et al. Annals of Neurol 2005

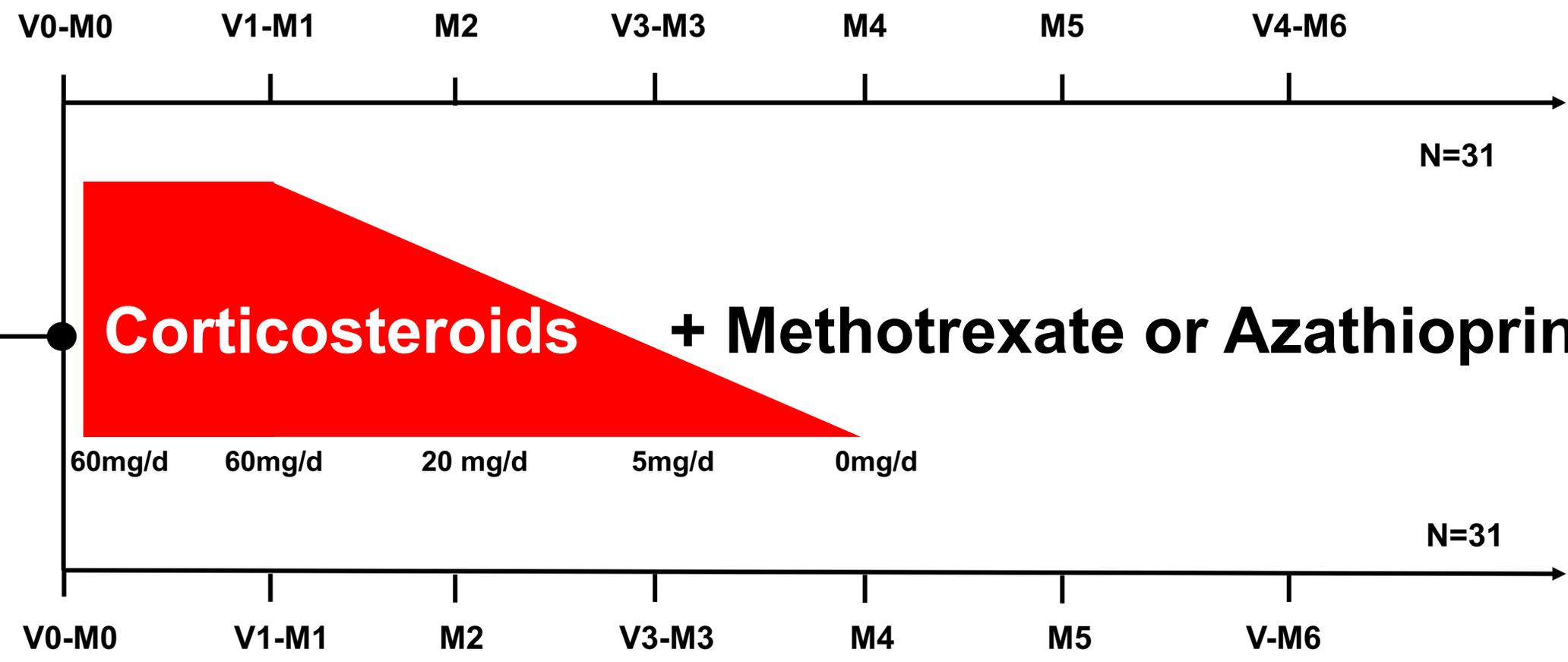
Ladislau et al. Brain 2018



PHRC - N 2018 : BIRD



Baricitinib



Placebo

Screening visit

60mg/d 60mg/d 20 mg/d 5mg/d 0mg/d

N=31

N=31

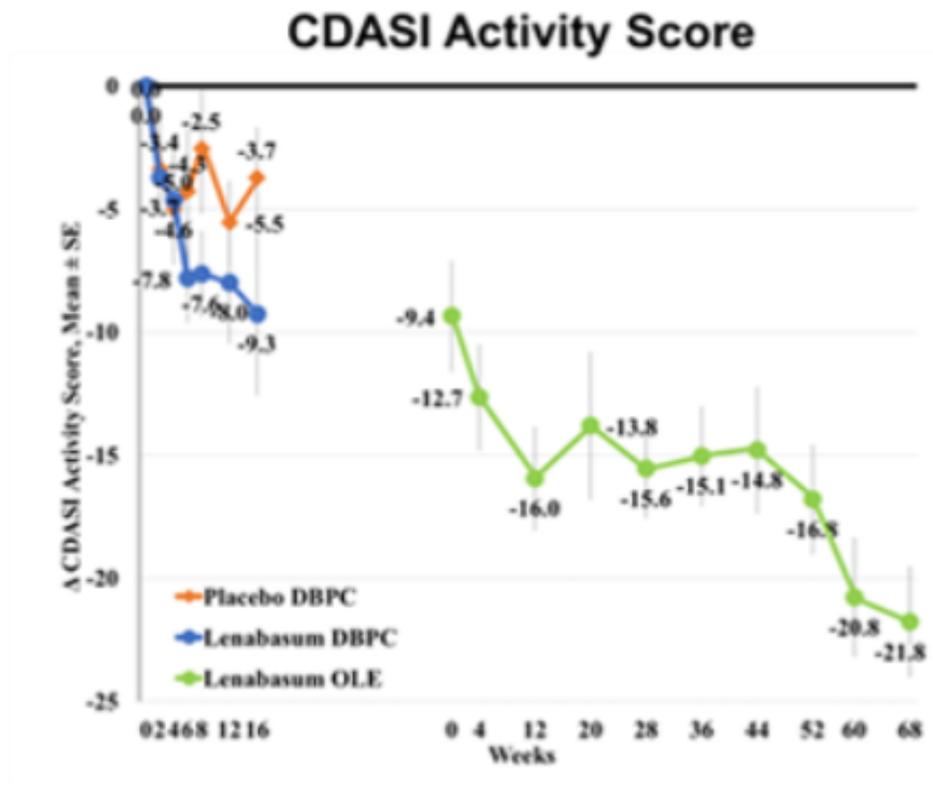
**DM réfractaires
N=20
LENABASUM**



**4 mois
RCT
RCT**

**CDASI
Efficace**

**DM réfractaires
N=150
LENABASUM**



4- Un traitement sur mesure et futur

- **MNAI EP – IgIV sévère ? SRP + RTX – HMGCR IgIV dépendance**
Avenir MNAI anti-complément
- **Avenir anti-IFN**