Rola przeciwciał neutralizujących w terapiach SM (ciągle dyskutowana)

Konrad Rejdak

Katedra i Klinika Neurologii

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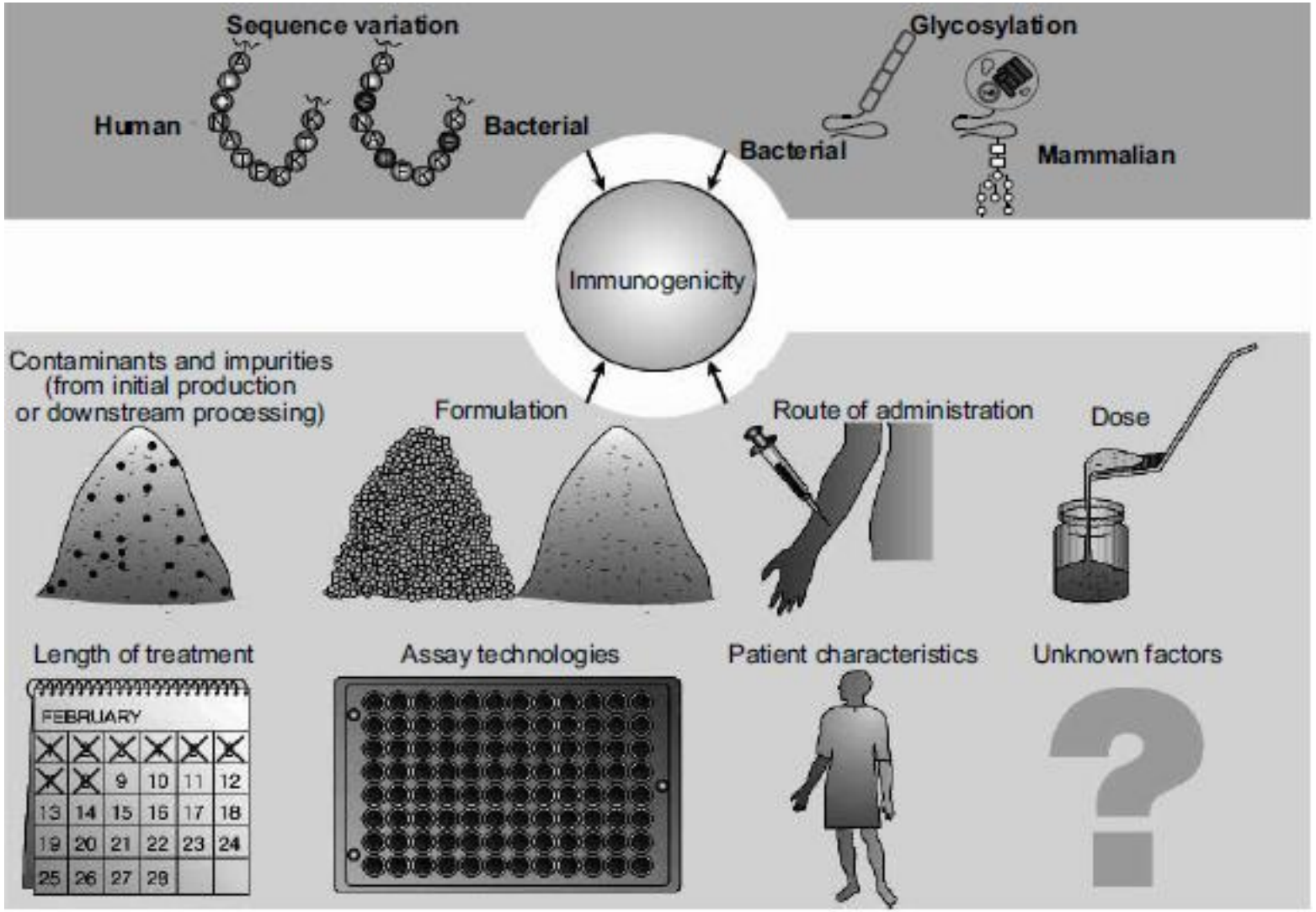
Immunogeniczność preparatów biologicznych



Rossman, 2004

Następstwa kliniczne obecności przeciwciał neutralizujących

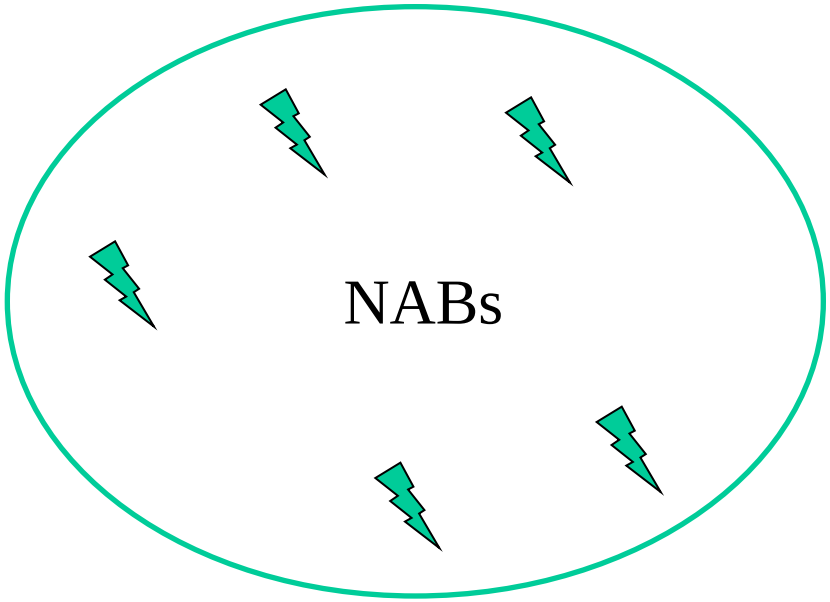
Disease/Condition	Consequence of Antibody	Biotherapeutic Agent	Reference
Diabetes	Loss of efficacy	Insulin	Meager[3]; Fineberg et al.[2]
Acute myocardial infarction		Streptokinase Staphylokinase	Rosenschein et al.[41] Vanderschueren et al.[42]
Adenosine deaminase deficiency		Adenosine deamidase	Chaffee et al.[43]
Cervical dystonia		Botulinum toxin	Rollnik et al.[11]
Hemophilia A		Factor VIII	Lusher; 2000.[5]
Malignant carcinoid tumors		Interferon alpha-2	Freund et al.[7]; Quesada et al.[10]
Multiple sclerosis		Interferon beta	IFNB MS Study Group.[34]; PRISMS Study Group.[20]; Sorensen et al.[35]
Cancer		Interleukin-2 (IL-2)	Prümmer.[44]
Hypogonadotropic azoospermic men		Gonadotropin-releasing hormone	Blumenfeld et al.[45]
Cutaneous T-cell lymphoma		Denileukin diftitox	Olsen et al.[46]
Hypogonadotropic hypogonadism		Human chorionic gonadotropin	Claustrat et al.[47]
Carcinoma		GM-CSF*/IL-3	Ragnhammar and Wadhua.[48]
Anemia	Neutralization of native protein	Erythropoietin	Casadevall et al.[4]; Prabhakar and Muhlfelder.[49]

Rossman, 2004

Immunogeniczność preparatów immunomodulujących w SM

INF β

GA



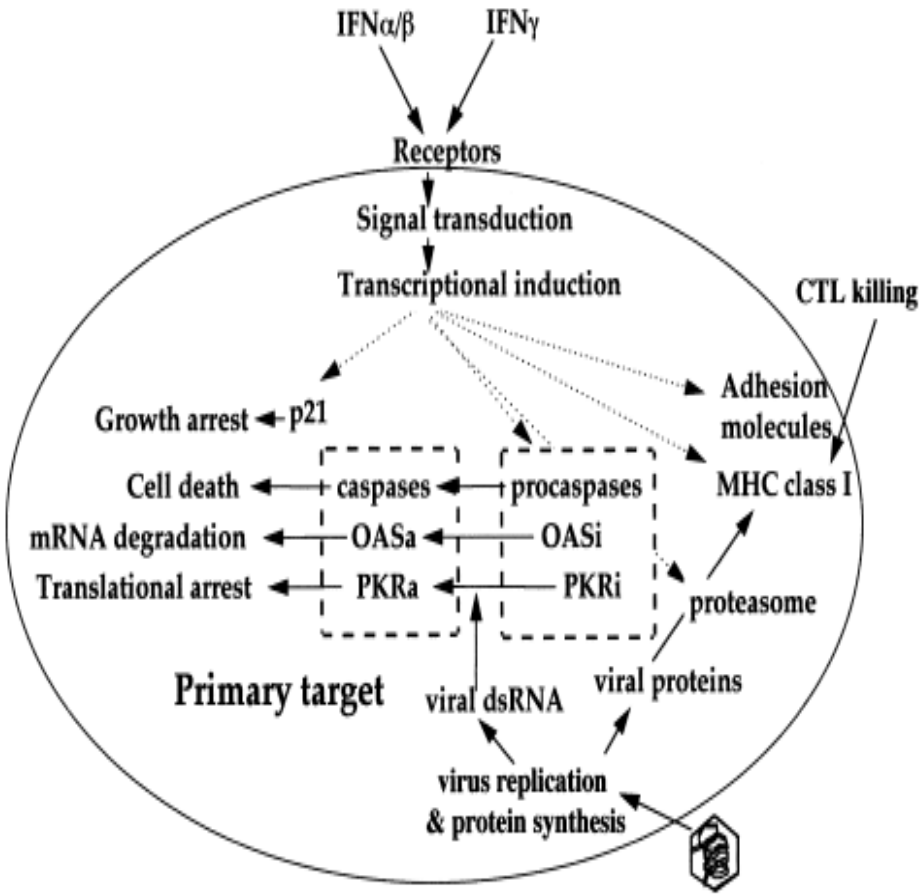
Przeciwciała monoklonalne:
natalizumab

Biologia interferonów

INF są ewolucyjnie starą rodziną białek o małej masie

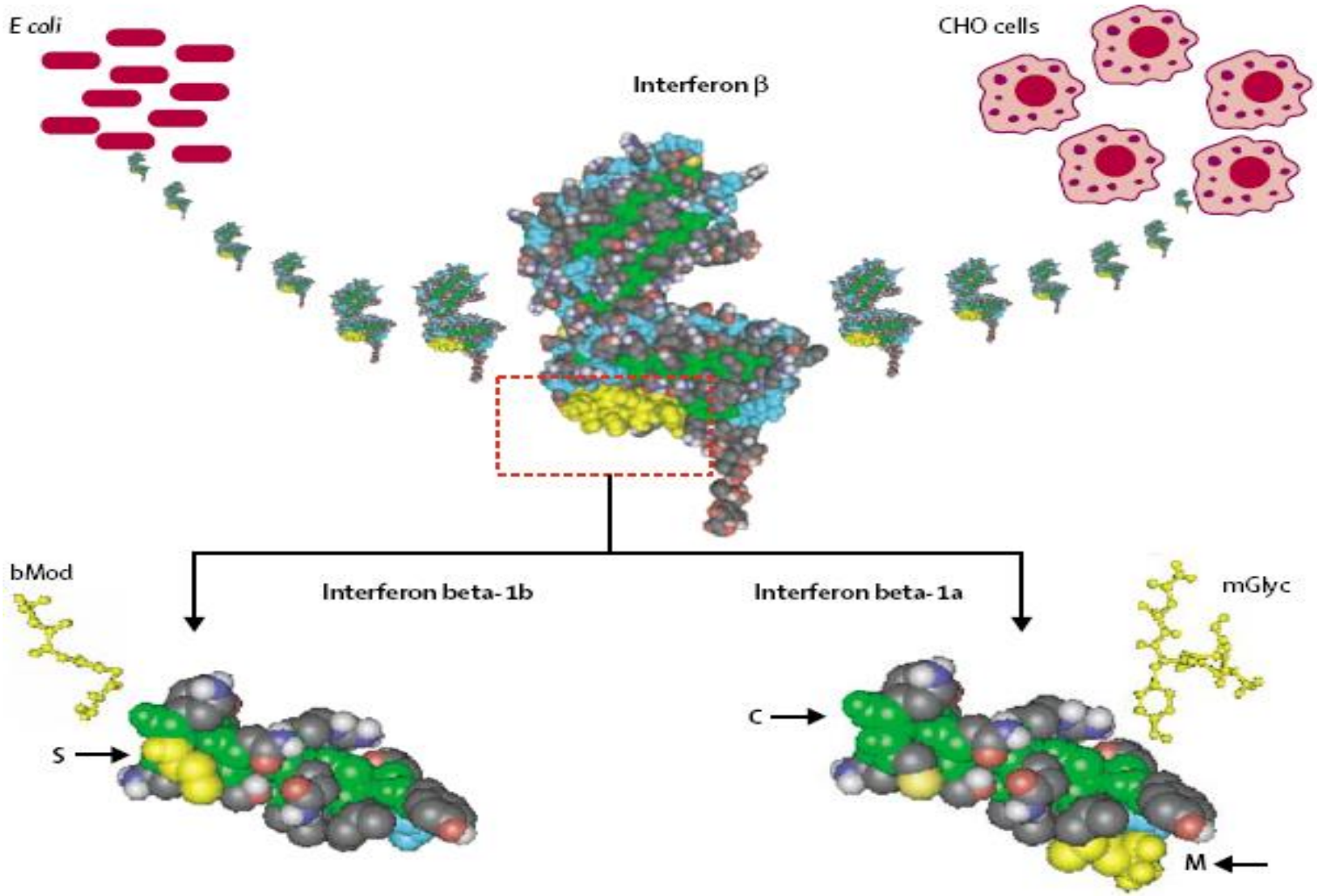
Klasyfikowane są jako cytokiny o strukturze helisy:
Typ I: α, β, τ, ω
Typ II: γ

Funkcje:
- obrona przeciwwirusowa,
- regulacja wzrostu komórek,
- aktywacja immunologiczna



Goodbourn et al., 2000

Interferon beta jako środek terapeutyczny

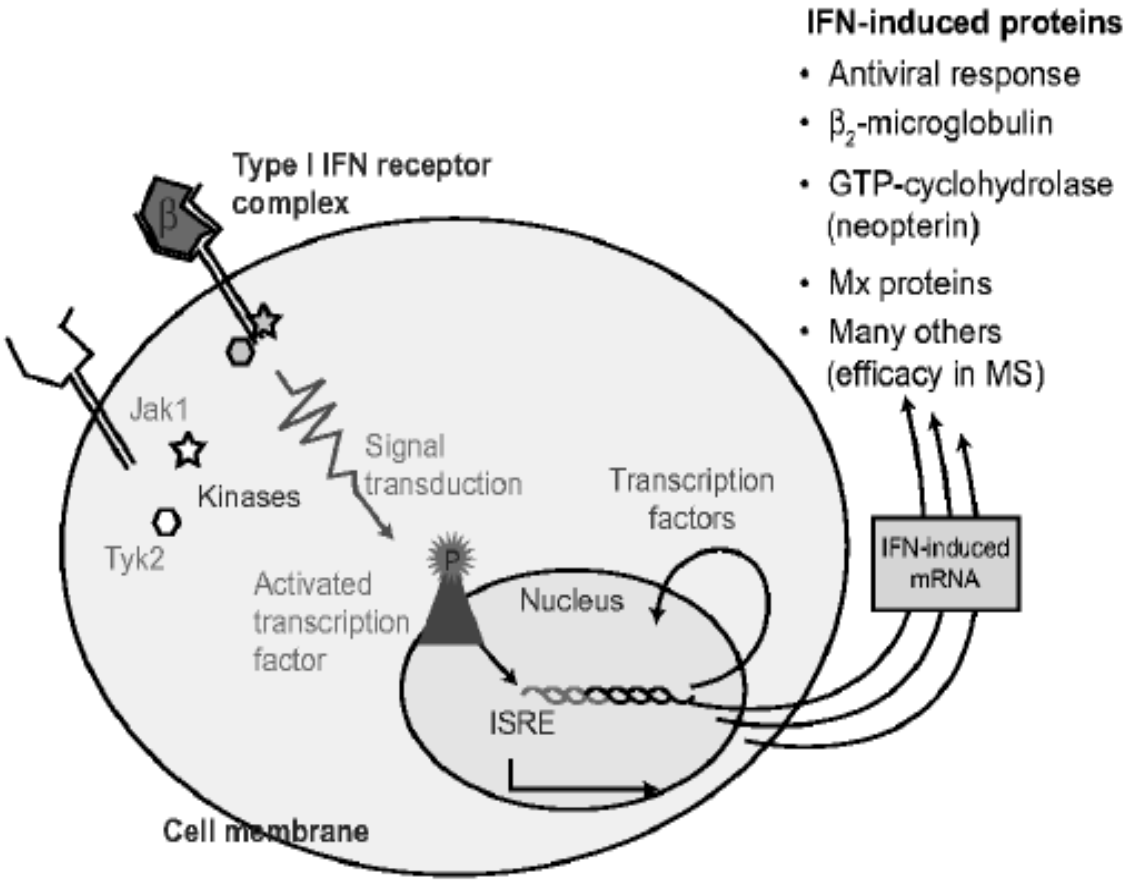


Hemmer et al., 2005

Aktywność biologiczna IFN:

INF beta jest produkowany w bezpośredniej odpowiedzi na infekcję wirusową przez większość rodzajów komórek, w szczególności fibroblasty.

Ulega procesowi glikozylacji



IFN = Interferon; ISRE = Interferon-stimulated response element; Jak1 = Janus kinase 1; Tyk2 = Tyrosine kinase 2.

Noronha, 2007

Wskaźniki bioaktywności INF-beta

Wskaźniki specyficzne:

Myxovirus resistance 1 protein (MxA)

Wskaźniki niespecyficzne:

2’5’ oligoadenylate-synthetase (OAS)

β_2 microglobulin

Neopterin

Tumor necrosis factor apoptosis inducing ligand (TRAIL)

A comparative study of the relative bioavailability of different interferon beta preparations

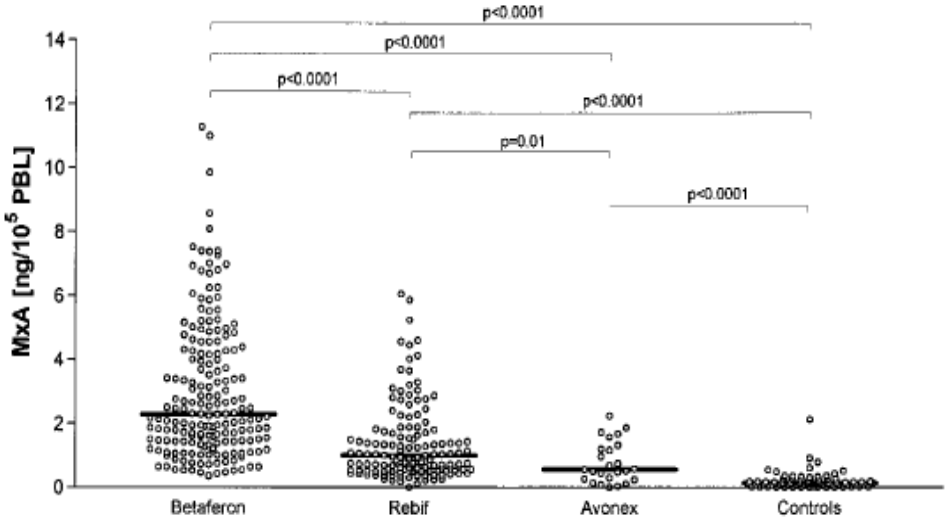
F. Deisenhammer, MD; I. Mayringer, MD; J. Harvey, PhD; E. Dilitz, MD; T. Gasse, MD; D. Stadlbauer, MD; M. Reindl, PhD; and T. Berger, MD

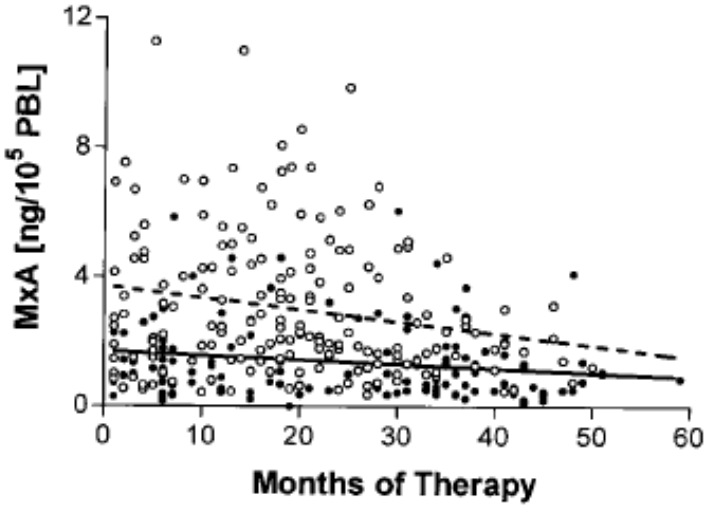
Porównanie względnej bioaktywności różnych preparatów interferonu beta

Table 2 In vitro stimulation of MxA in untreated blood from 10 healthy volunteers

	Interferon protein weight, pg			MxA, ng/mL			*p* Values as compared with baseline		
IU	Betaferon	Rebif	Avonex	Betaferon	Rebif	Avonex	Betaferon	Rebif	Avonex
0	0	0	0	10.5	10.5	11.4	—	—	—
1	31	4	5	19.2	12.2	13.2	0.388	0.784	0.865
5	156	18	25	21.6	13.6	16.2	0.106	0.635	0.662
10	313	37	50	29.8	15.9	18.1	0.039	0.421	0.583
100	3125	367	500	47.7	36.7	40.7	0.002	0.006	0.026
500	15,625	1833	2500	53.1	52.2	50.0	0.004	0.003	0.006
1000	31,250	3667	5000	47.8	55.6	57.1	0.001	0.001	0.004

The left-hand section gives the interferon protein weight of the different preparations by international units. The middle section shows the MxA response according to IUs. The right-hand section shows the statistical results of comparison (Student's *t*-test) between MxA levels at the corresponding IUs and the baseline MxA level.





Urinary neopterin and nitric oxide metabolites as markers of interferon β-1a activity in primary progressive multiple sclerosis

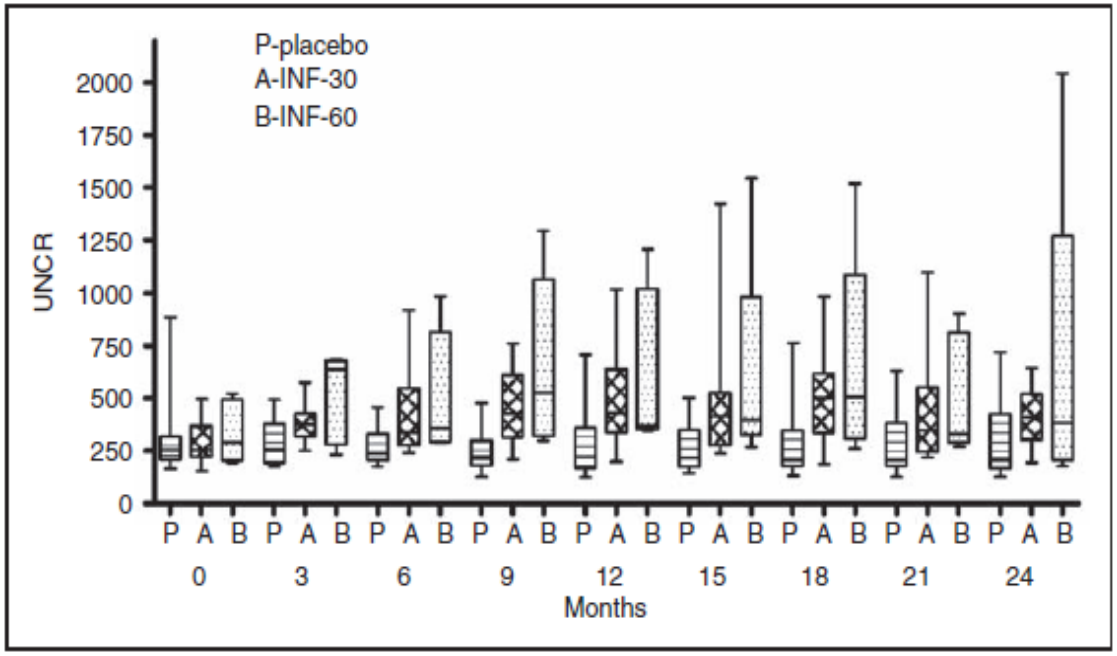
K Rejdak[1], SM Leary[2], A Petzold[2,4], AJ Thompson[2], DH Miller[2] and G Giovannoni[3]

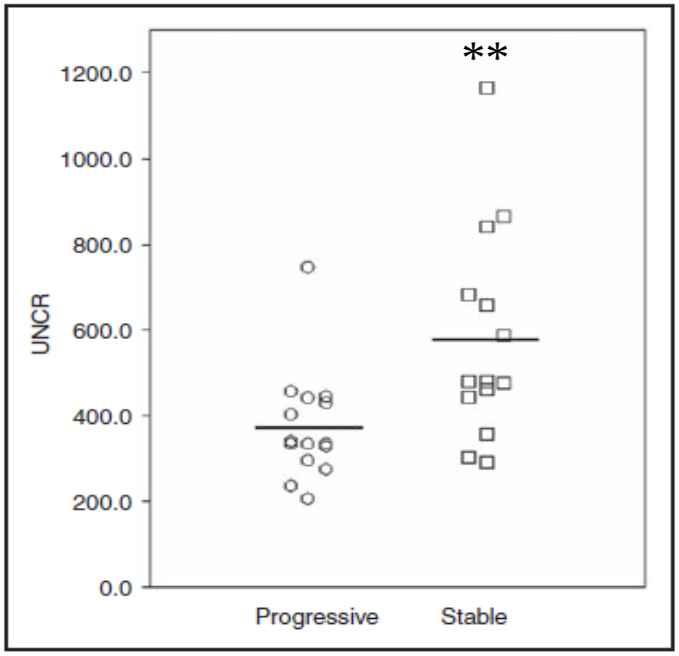
Multiple Sclerosis
0(00) 1–7

Table 1. Baseline characteristics of patients available for intention-to-treat analysis. Data presented as medians (range)

	Placebo-treated ($n=20$)	IFNβ-1a 30 μg/week ($n=15$)	IFNβ-1a 60 μg/week ($n=14$)
Sex (F/M)	15/5	10/5	6/8
Age (years)	43 (30–59)	51 (29–58)	53 (25–59)
Disease duration (years)	8 (3–19)	6 (2–17)	6 (3–21)
EDSS	5 (2–7)	5.5 (3.5–7)	5 (2–6.5)
UNCR (μmol/mol)	254.8 (165.5–884.8)	259.2 (154.5–810.6)	384.9 (164.5–967.3)
NOxCR (mmol/mol)	62.3 (18.1–156.9)	63.0 (28.7–247.9)	93.0 (19.8–284.6)

EDSS, Expanded Disability Status Scale; UNCR, neopterin/creatinine; NOxCR, nitrate and nitrite/creatinine.



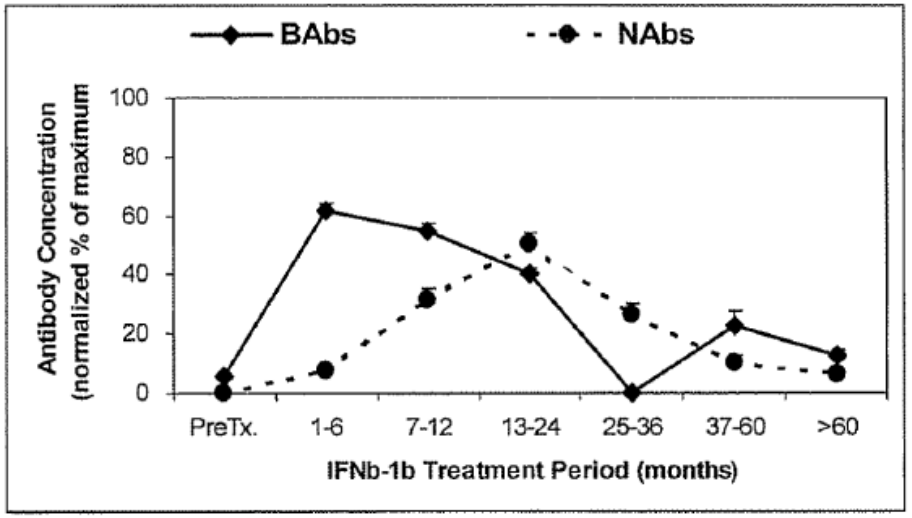


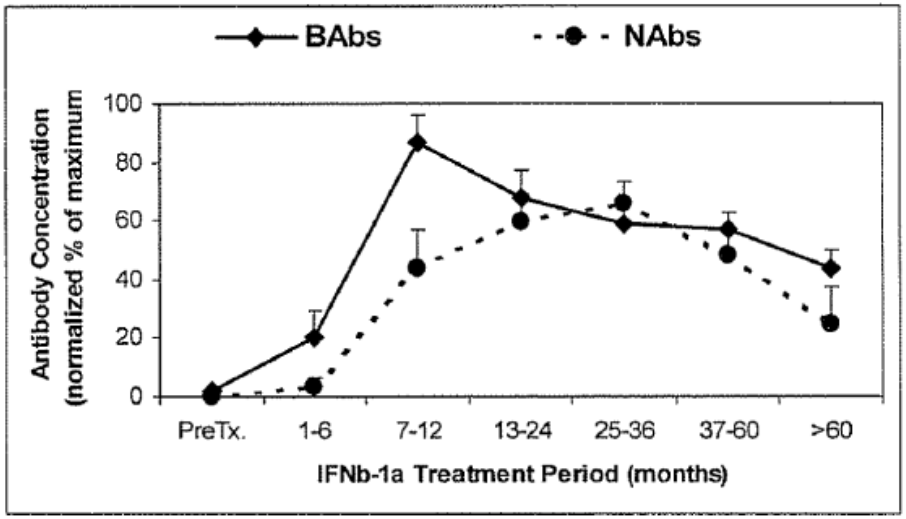
Oznaczanie obecności P-ciał u pacjentów leczonych INF-beta

Przeciwciała wiążące

vs.

Przeciwciała neutralizujące

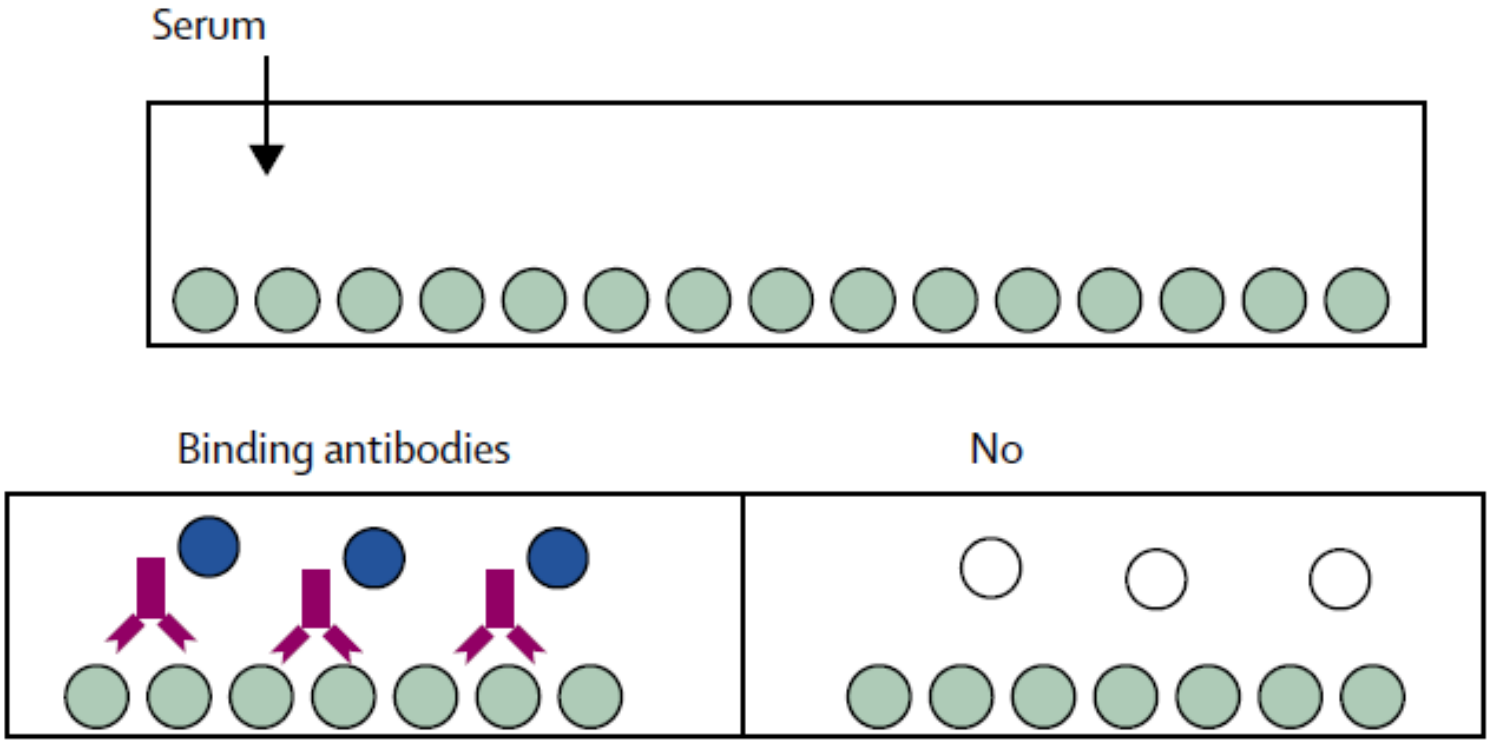




Oger, Gibbs., 2007

Oznaczanie obecności P-ciał u pacjentów leczonych INF-b

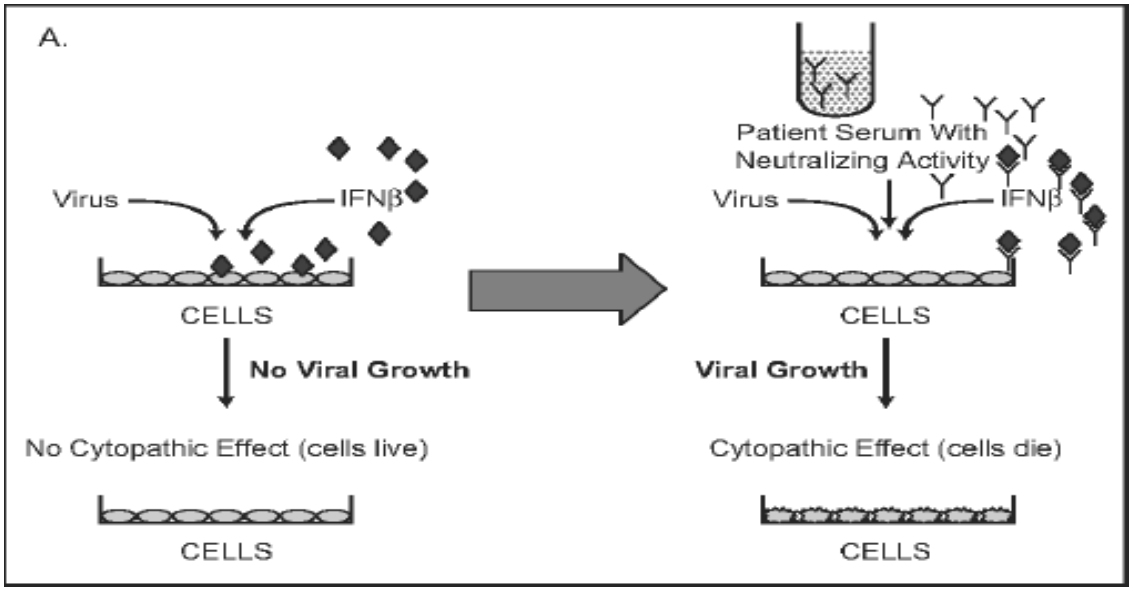
Przeciwciała wiążące



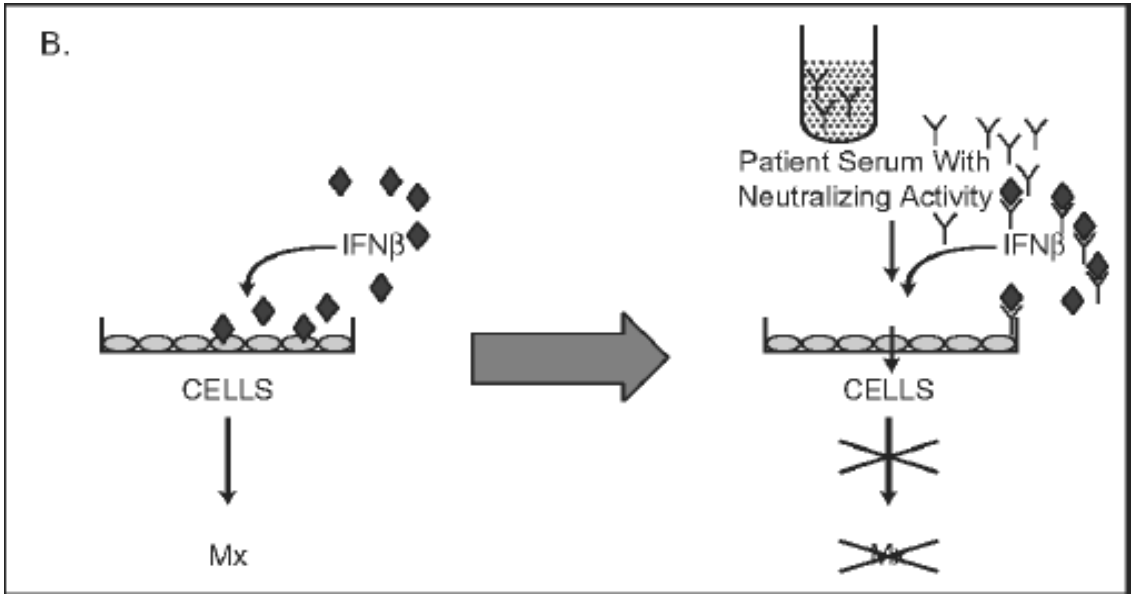
Hemmer et al., 2005

Oznaczanie obecności P-ciał u pacjentów leczonych INF-b

Efekt cytopatyczny



Oznaczenie białka MxA
i indukcji ekspresji
genu MxA



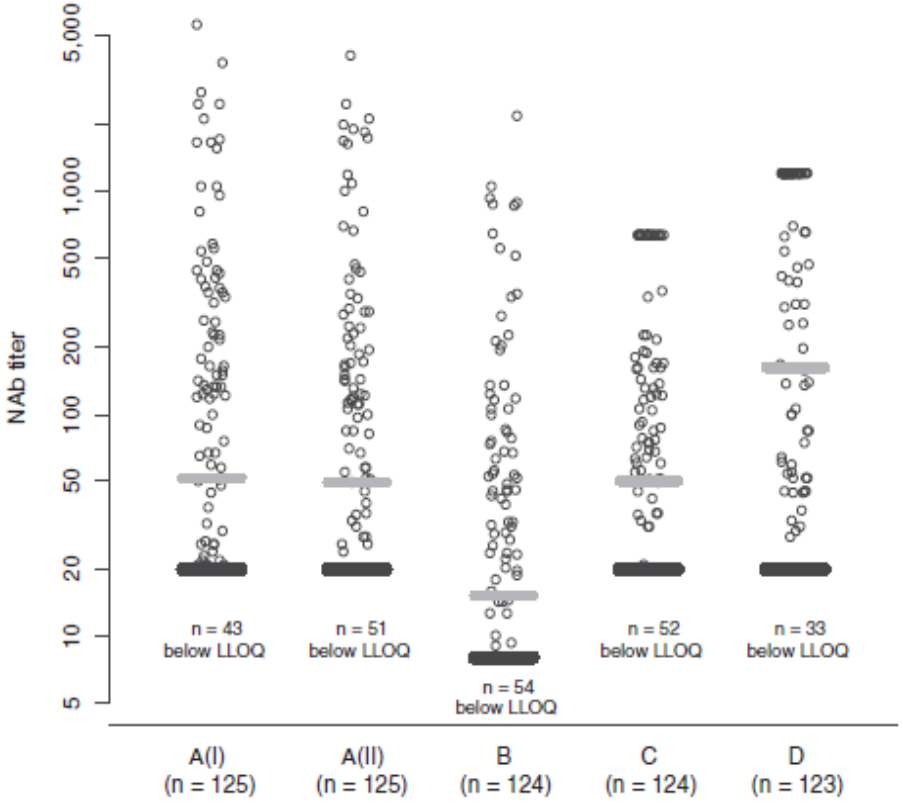
Deisenhammer et al., 2007

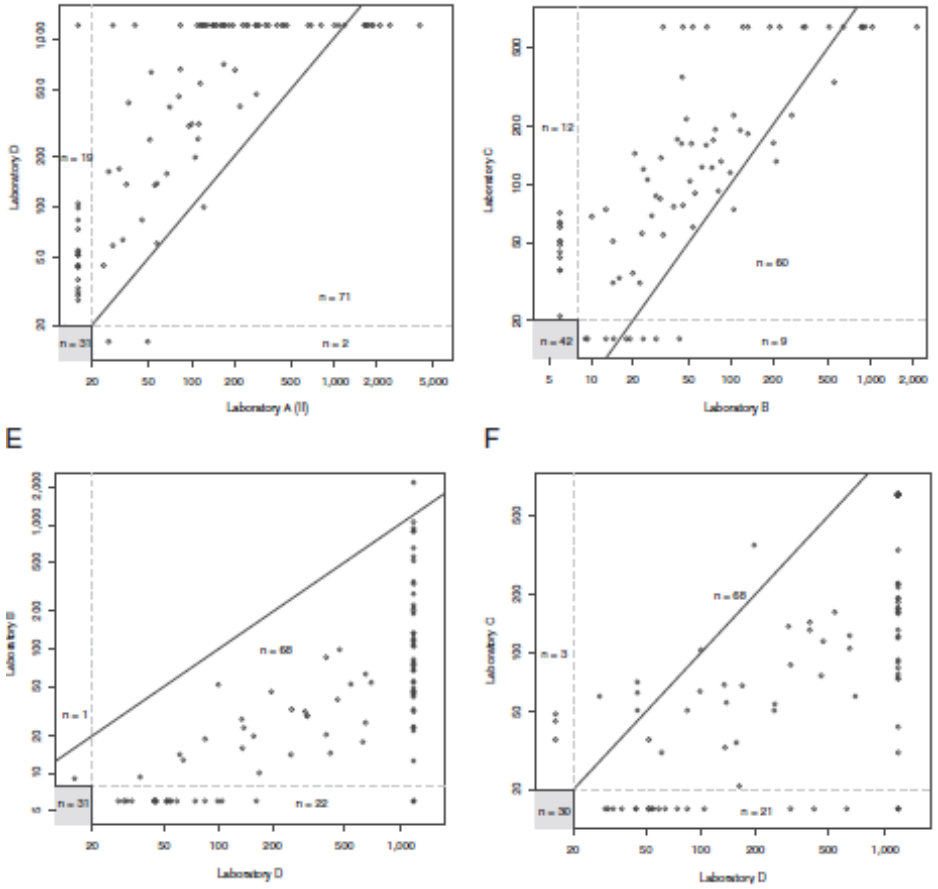
Oznaczanie obecności P-ciał u pacjentów leczonych INF-b

Variability in detection and quantification of interferon β-1b–induced neutralizing antibodies

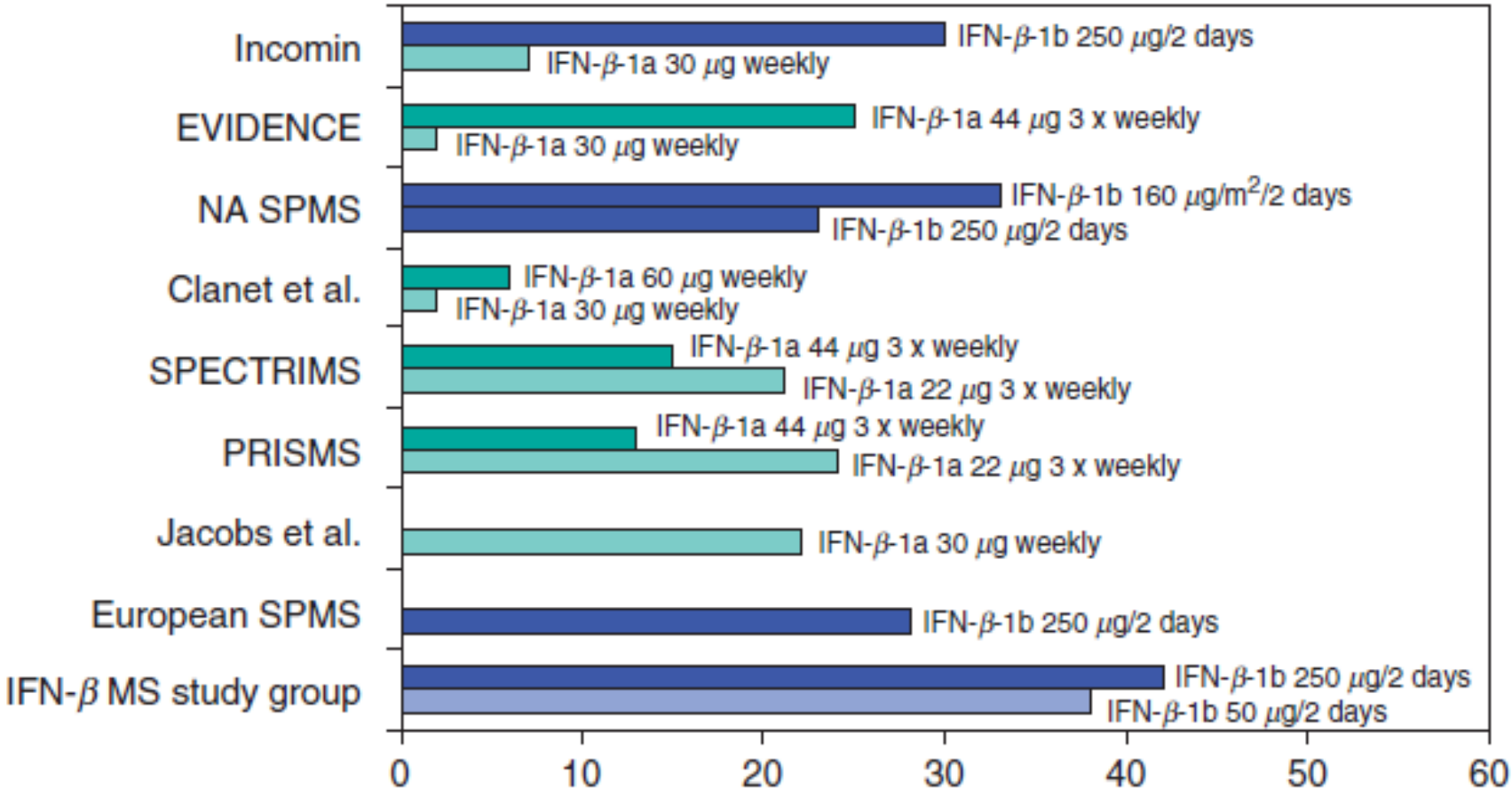
Hans-Peter Hartung[1,12*], Bernd Kieseier[1], Douglas S Goodin[2], Barry GW Arnason[3], Giancarlo Comi[4], Stuart Cook[5], Massimo Filippi[4], Douglas R Jeffery[6], Ludwig Kappos[7], Timon Bogumil[8], Brigitte Stemper[9], Rupert Sandbrink[1,9], Yukiko Nakada[10], Haruhiko Nakajima[10], Susanne Schwenke[9], Stephan Lehr[9], Jürgen Heubach[9], Christoph Pohl[9,11] and Joachim Reischl[9]

Journal of Neuroinflammation 2012, **9**:129





Immunogeniczność intereferonu beta



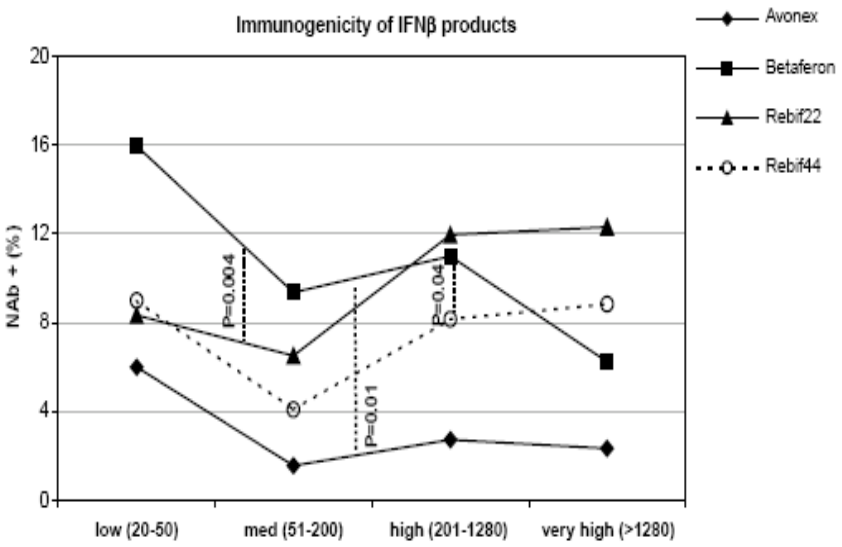
Noronha, 2007

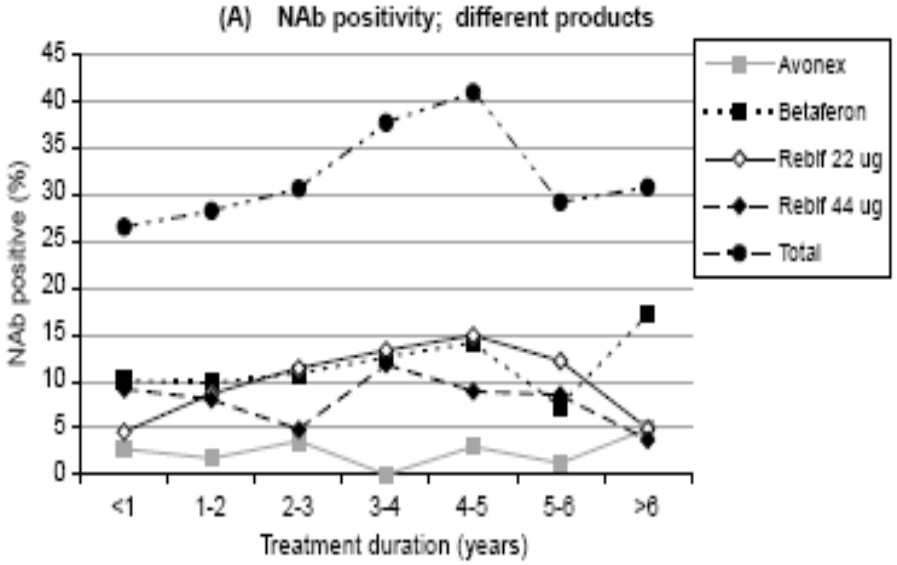
Interferon beta preparations for the treatment of multiple sclerosis patients differ in neutralizing antibody seroprevalence and immunogenicity

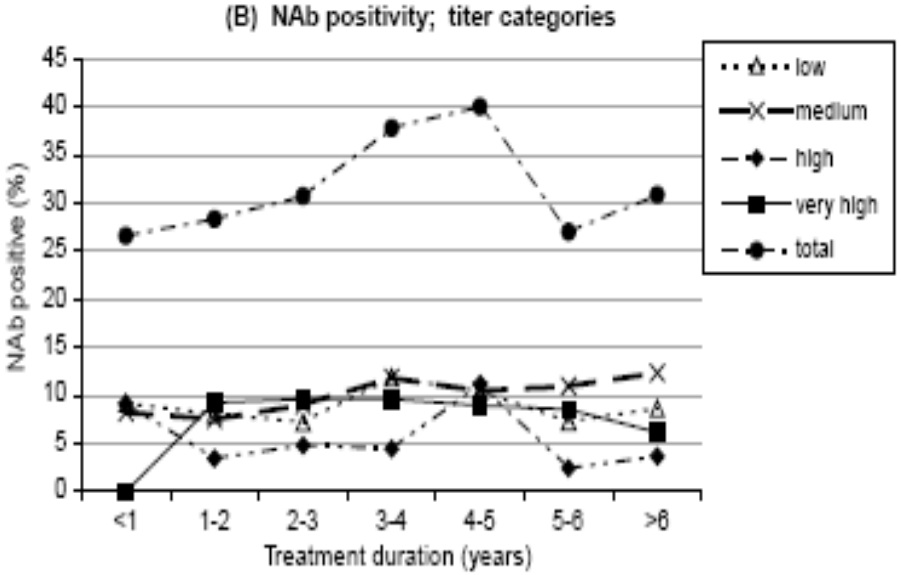
A Sominanda[1], U Rot[2], M Suoniemi[1], F Deisenhammer[3], J Hillert[1] and A Fogdell-Hahn[1]
Multiple Sclerosis 2007; 13: 208–214

Table 1 The frequency of neutralizing antibodies against IFNβ in 1115 IFNβ-treated MS patients

NAb positive	n (%)
No. of patients ($n=1115$)	356 (32%)
Male ($n=282$)	89 (32%)
Female ($n=833$)	267 (32%)
Avonex ($n=257$)	34 (13%)
Betaferon ($n=288$)	125 (43%)
Rebif22 ($n=276$)	108 (39%)
Rebif44 ($n=294$)	89 (30%)
Rebif22 and Rebif44 ($n=570$)	197 (35%)







Appearance and disappearance of neutralizing antibodies during interferon-beta therapy

P. Soelberg Sorensen, MD, DMSc; N. Koch-Henriksen, MD, DMSc; C. Ross, MD; K.M. Clemmesen, MD; K. Bendtzen, MD, DMSc; and the Danish Multiple Sclerosis Study Group*

NEUROLOGY 2005;65:33–39

Pojawianie się i znikanie Nabs

Table 2 Follow-up time of patients for each IFN-beta preparation and for all patients

	24 mo	30 mo	36 mo	42 mo	48 mo	54 mo	60+ mo
Betaferon 250 μg /2 day*	191	163	158	133	130	84	67
Avonex 30 μg 1 × weekly*	70	50	46	27	24	9	4
Rebif 22/44 μg 3 × weekly*	170	127	120	86	73	19	8
All patients†	455	375	361	279	256	138	103

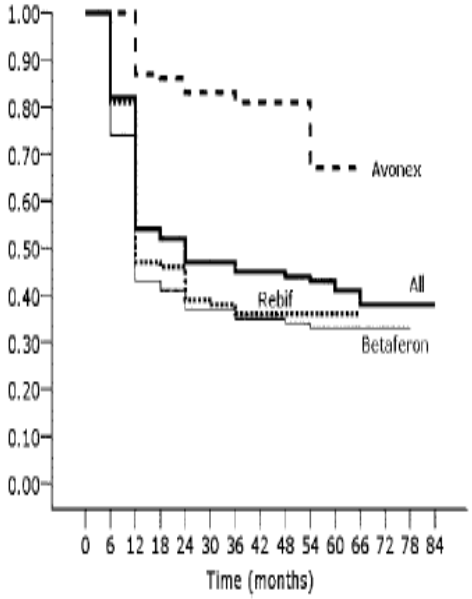


Figure 1. Probability of remaining neutralizing antibody (NAB)-negative (free of NAB-positive tests). Life-table

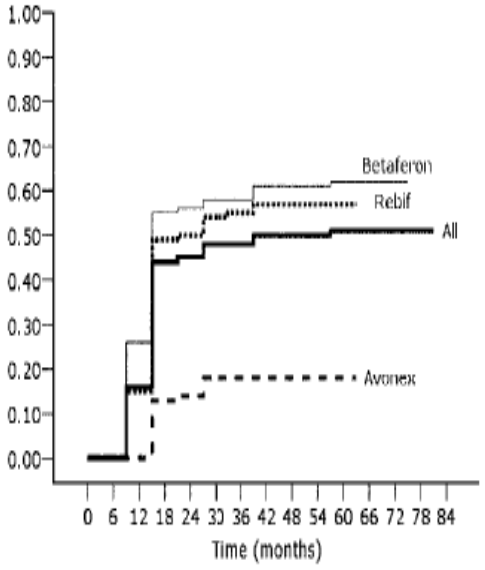


Figure 2. Cumulative probability of becoming definitely neutralizing antibody (NAB)-positive (at least two consecutive NAB-positive tests with neutralizing capacity ≥20%).

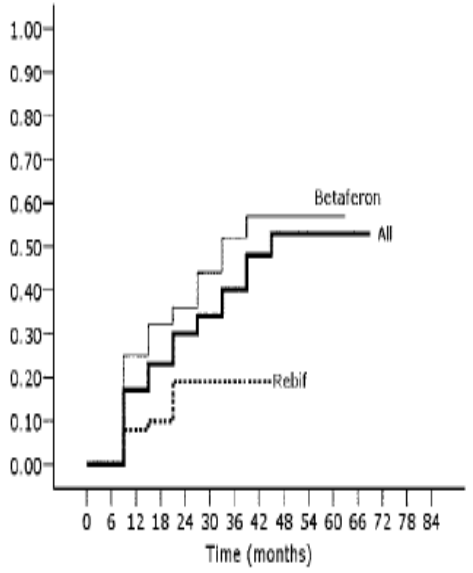


Figure 4. Cumulative probability of reverting to definite NAB-negative status (at least two consecutive neutralizing antibody [NAB]-tests with neutralizing capacity <20%) in

Interferon-beta: the neutralizing antibody (NAb) titre predicts reversion to NAb negativity

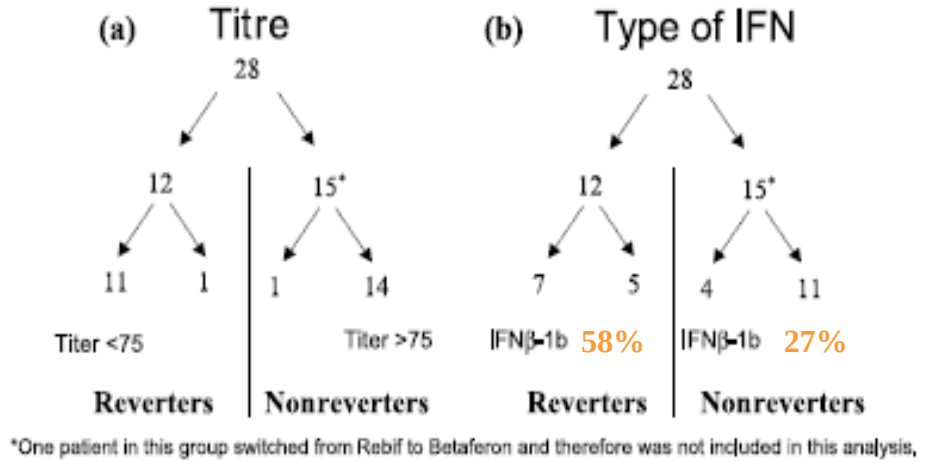
*C Gneiss, M Reindl, A Lutterotti, R Ehling, R Egg, M Khalil, T Berger and F Deisenhammer**
Department of Neurology, University of Innsbruck, Anichstrasse 35, 6020 Innsbruck, Austria
Multiple Sclerosis *(2004)* **10,** 507–510

Prawdopodobieństwo powrotu do stanu sero-negatywnego zależy od:

-Wysokości mian wyjściowych

-Typu interferonu

beta 1b > beta 1a



*One patient in this group switched from Rebif to Betaferon and therefore was not included in this analysis.

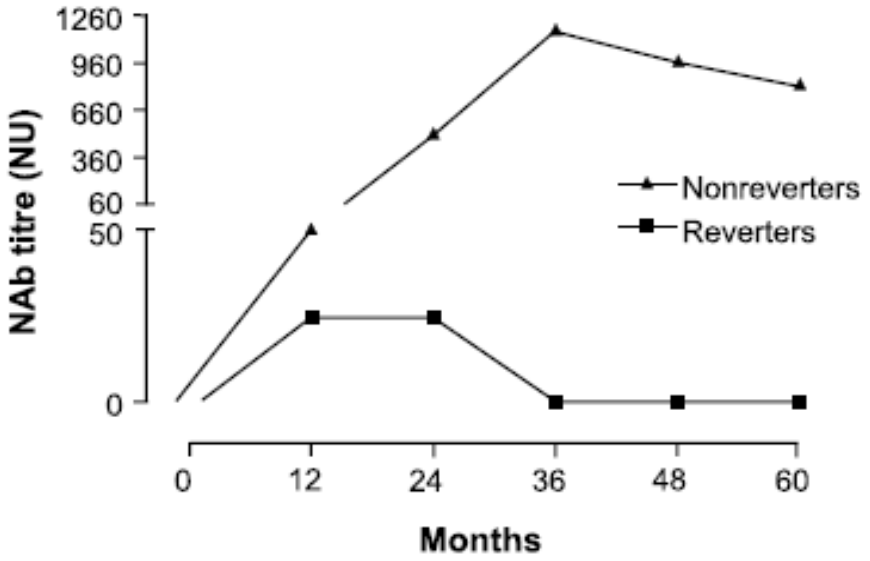


Figure 2 *Longitudinal development of NAbs against IFNβ in reverters and nonreverters.*

Czy Nabs zaburzają aktywność biologiczną interferonu beta?

Biological activity of interferon betas in patients with multiple sclerosis is affected by treatment regimen and neutralising antibodies

A Bertolotto, A Sala, S Malucchi, F Marnetto, M Caldano, A Di Sapio, M Capobianco, F Gilli

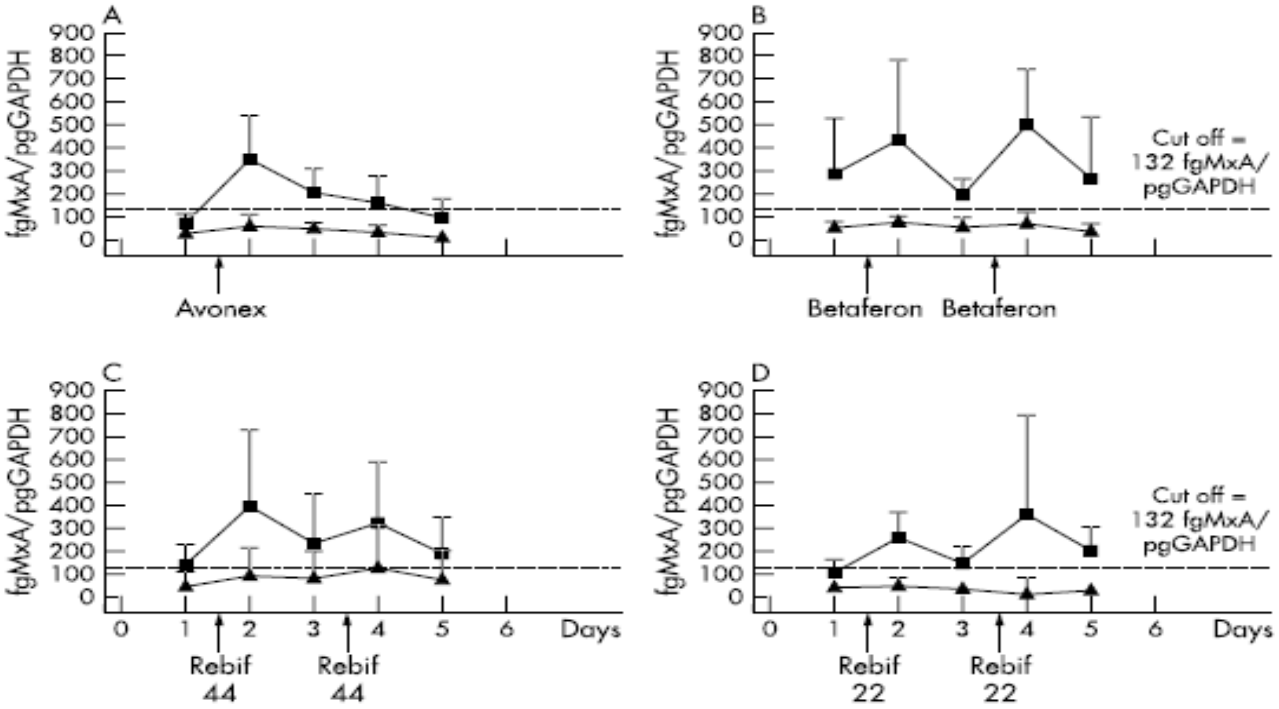
See Editorial Commentary, p 1234

J Neurol Neurosurg Psychiatry 2004;75:1294–1299. doi: 10.1136/jnnp.2004.037259

Table 1 Demographic and clinical characteristics of 62 patients with MS treated with four different interferon beta regimens

	Avonex (n = 16)	Betaferon (n = 10)	Rebif 22 (n = 24)	Rebif 44 (n = 12)	Total (n = 62)
Sex (M/F)	5/11	4/6	7/17	6/6	22/40
Body mass*	1.763 (0.14), 1.51–1.97	1.724 (0.14), 1.55–1.94	1.753 (0.17), 1.50–2.10	1.764 (0.11), 1.59–1.95	1.753 (0.14), 1.50–2.10
Duration of disease*	8.0 (4.6), 1–18	10.0 (6.1), 4–26	8.4 (5.1), 1–2	6.7 (4.8), 1–18	8.0 (5.2), 1–26
Months of therapy*	16 (7), 5–29	35 (20), 4–60	21 (18), 3–60	11 (10)‡, 3–36	20 (17), 3–60
EDSS*	2.0 (1.0), 0–4.0	2.0 (1.0), 1.0–6.5	2.0 (1.0), 0–5.0	2.0 (1.0), 0–5.0	2.0 (1.5), 0–6.5
Nab status†					
NAb–	14 (88)	6 (60)	17 (71)	10 (83)	47 (76)
Persistent NAb+	2 (12)	3 (30)	5 (21)	2 (17)	12 (19)
Isolated NAb+	–	1 (10)	2 (8)	–	3 (5)

*Mean (SD), range.
†Number (%).
‡Since Rebif 44 was more recently approved for the treatment of MS than Avonex, Betaferon, and Rebif 22, the duration of treatment with Rebif 44 compared with the other three treatment regimens was statistically different.
EDSS, Expanded Disability Status Scale; F, female; M, male; MS, multiple sclerosis.



Czy Nabs zaburzają aktywność biologiczną interferonu beta?

CME

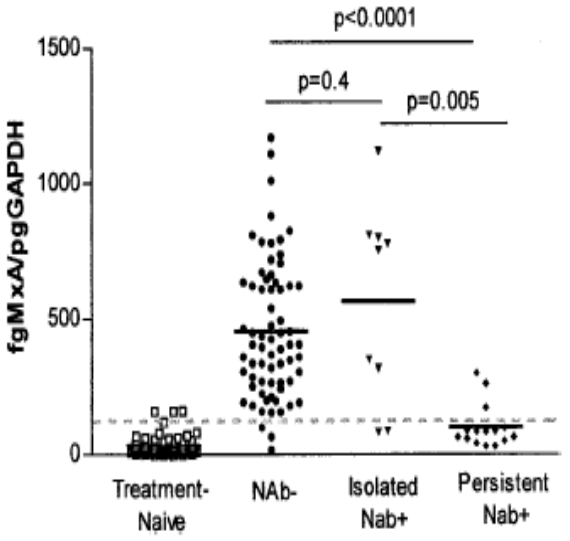
Persistent neutralizing antibodies abolish the interferon β bioavailability in MS patients

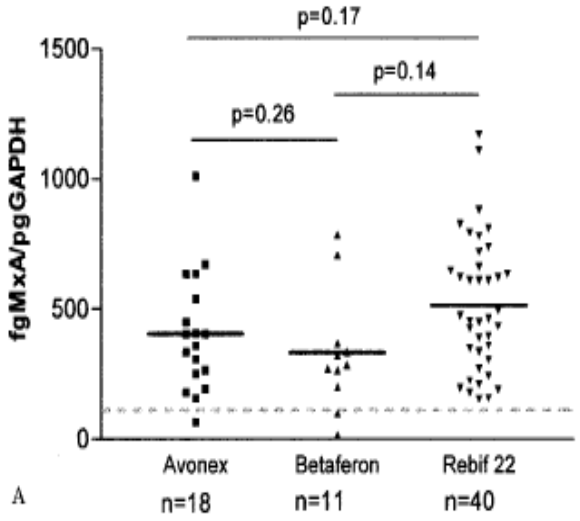
A. Bertolotto, MD; F. Gilli, PhD; A. Sala, PhD; M. Capobianco, MD; S. Malucchi, MD; E. Milano, MD; F. Melis, MD; F. Marnetto, PhD; R.L.P. Lindberg, PhD; R. Bottero, MD; A. Di Sapio, MD; and M.T. Giordana, MD

NEUROLOGY 2003;60:634–639

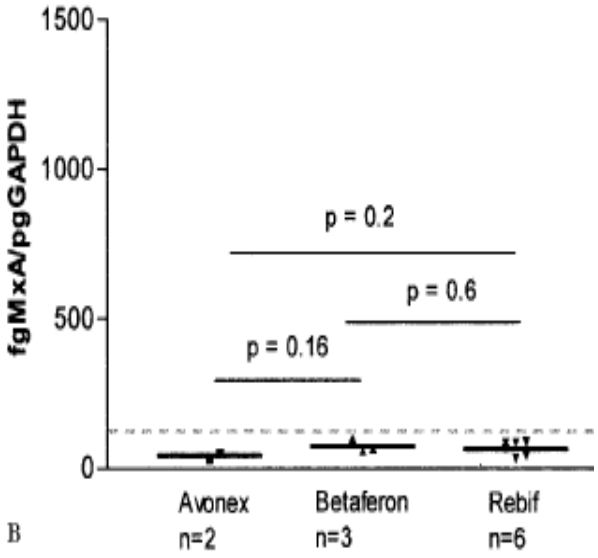
Table 1 Clinical characteristics of MxA tested patients

IFNβ therapy	No. patients	No. samples	Hours from last injection, mean ± SD (range)	Months of therapy, mean ± SD (range)
Treatment naïve	99	103	— —	— —
IFNβ treated	92	187	12.2 ± 1.7 (9–14)	21 ± 16 (7–69)
Avonex	22	29	12.1 ± 1.1 (11–14)	19 ± 10 (8–34)
Betaferon	17	39	12.3 ± 1.2 (10–14)	32 ± 21 (9–69)
Rebif 22	53	119	12.1 ± 1.4 (9–13)	19 ± 15 (7–62)





A



B

Czy Nabs zaburzają aktywność kliniczną interferonu beta?

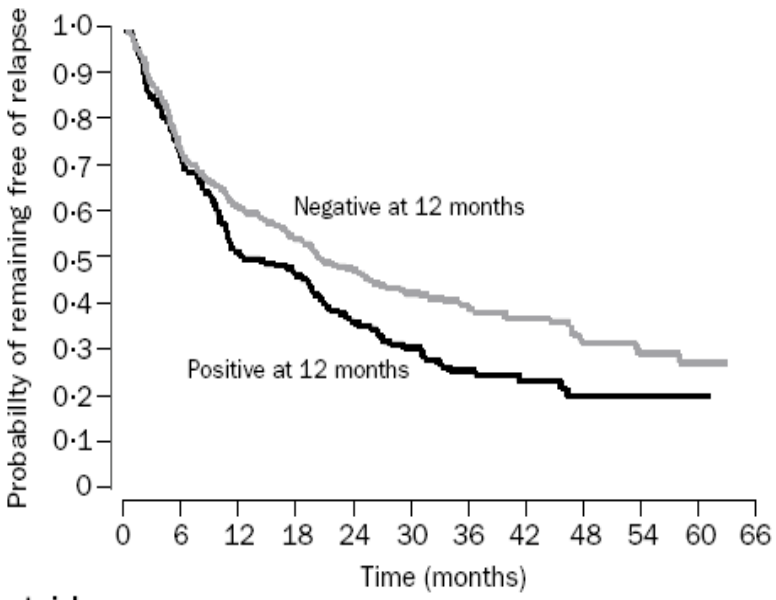
Clinical importance of neutralising antibodies against interferon beta in patients with relapsing-remitting multiple sclerosis

Lancet 2003; **362:** 1184–91

*Per Soelberg Sorensen, Christian Ross, Katja Maria Clemmesen, Klaus Bendtzen, Jette Lautrup Frederiksen, Kai Jensen, Ole Kristensen, Thor Petersen, Soren Rasmussen, Mads Ravnborg, Egon Stenager, Nils Koch-Henriksen, and the Danish Multiple Sclerosis Study Group**

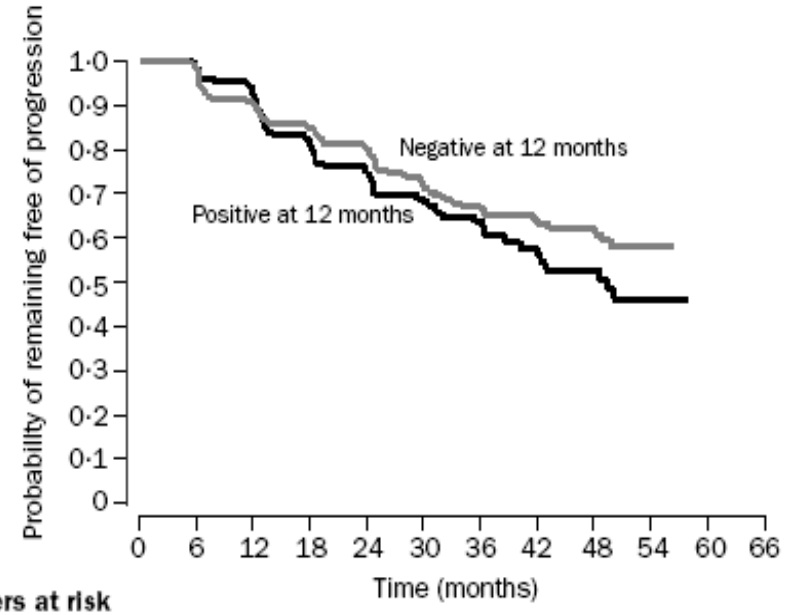
	Treatment				
	Rebif once a week (n=103)	Rebif three times a week (n=162)	Avonex (n=82)	Betaferon (n=194)	All (n=541)
Age (years)	37·5 (20–55)	39·2 (16–67)	40·3 (14–67)	39·3 (19–62)	38·1 (14–67)
Sex ratio (female:male)	2·22:1	2·24:1	2·15:1	1·77:1	2·04:1
EDSS	2·85 (0–5·5)	2·99 (0–6·5)	2·56 (0–5·5)	2·80 (0–5·5)	2·84 (0–6·5)
Relapses*	3·16 (2–10)	2·80 (2–8)	2·52 (1–6)	2·95 (0–8)	2·88 (0–10)
Disease duration (years)	7·34 (0–35)	5·88 (0–27)	7·41 (0–24)	7·66 (0–51)	7·04 (0–51)

Data are mean (range) except for sex ratio. *During past 2 years.



Numbers at risk

Positive	183	135	95	80	64	45	30	18	11	8	3
Negative	355	265	216	182	155	112	79	60	41	24	15



Numbers at risk

Positive	182	182	172	142	117	80	70	36	29	16	
Negative	355	353	318	282	250	139	114	65	55	28	

Kliniczno-radiologiczny paradoks w odniesieniu do obecności Nabs

Neutralizing antibodies to interferon beta-1b multiple sclerosis: a clinico-radiographic paradox in the BEYOND trial

Douglas S Goodin[1], Hans-Peter Hartung[2], Paul O'Connor[3], Massimo Filippi[4], Barry Arnason[5], Giancarlo Comi[6], Stuart Cook[7], Douglas Jeffery[7], Ludwig Kappos[8], Timon Bogumil[9], Volker Knappertz[2,9], Rupert Sandbrink[2,10], Karola Beckmann[10], Rick White[11], John Petkau[11] and Christoph Pohl[10,12] for the BEYOND Study Group

Group	Value	P-value* NAb-negative vs.	P-value* Glatiramer acetate vs.
IFNβ-1b 250 μg			
Cumulative number of new T2 lesions up to LAS (mean)			
Negative, $n=518$	1.9		<0.0001
All positive (≥20 NU/ml), $n=314$	5.2	<0.0001	0.066
Low, $n=157$	4.4	<0.0001	0.76
Medium, $n=79$	5.0	<0.0001	0.026
High, $n=78$	7.1	<0.0001	0.08
Glatiramer acetate, $n=415$	4.6	<0.0001	
Absolute change in T2-lesion volume up to LAS (median)			
Negative, $n=514$	0.18		<0.0001
All positive (≥20 NU/ml), $n=312$	0.75	<0.0001	0.45
Low, $n=156$	0.65	<0.0001	0.96
Medium, $n=79$	0.74	0.0056	0.85
High, $n=77$	1.4	<0.0001	0.058
Glatiramer acetate, $n=409$	0.68	<0.0001	
IFNβ-1b 500 μg			
Cumulative number of new T2-lesions up to LAS (mean)			
Negative, $n=475$	2.2		<0.0001
All positive (≥20 NU/ml), $n=334$	4.7	<0.0001	0.40
Low, $n=140$	2.8	0.0099	0.09
Medium, $n=77$	4.8	0.0005	0.73
High, $n=117$	7.0	<0.0001	0.0010
Glatiramer acetate, $n=415$	4.6	<0.0001	
Absolute change in T2-lesion volume up to LAS (median)			
Negative, $n=469$	0.25		<0.0001
All positive (≥20 NU/ml), $n=330$	0.74	<0.0001	0.83
Low, $n=139$	0.36	0.057	0.19
Medium, $n=75$	0.97	0.024	0.92
High, $n=116$	1.2	<0.0001	0.058
Glatiramer acetate, $n=409$	0.68	<0.0001	

Kliniczno-radiologiczny paradoks w odniesieniu do obecności Nabs

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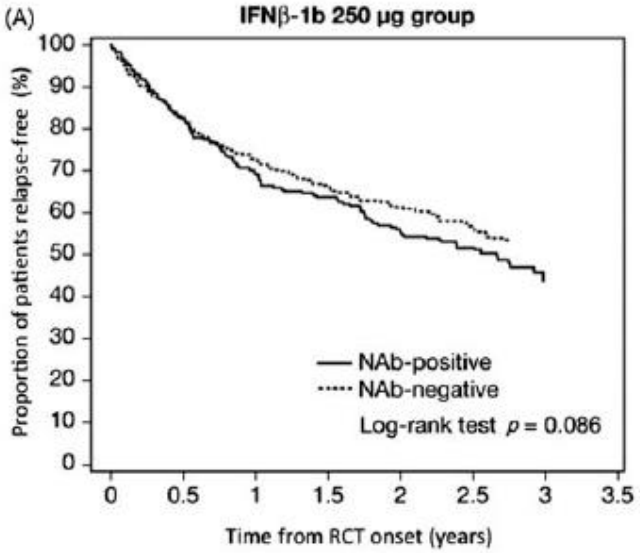
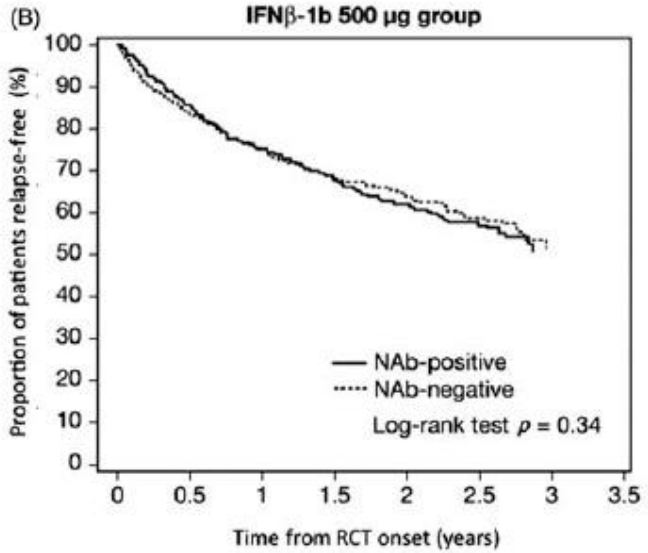
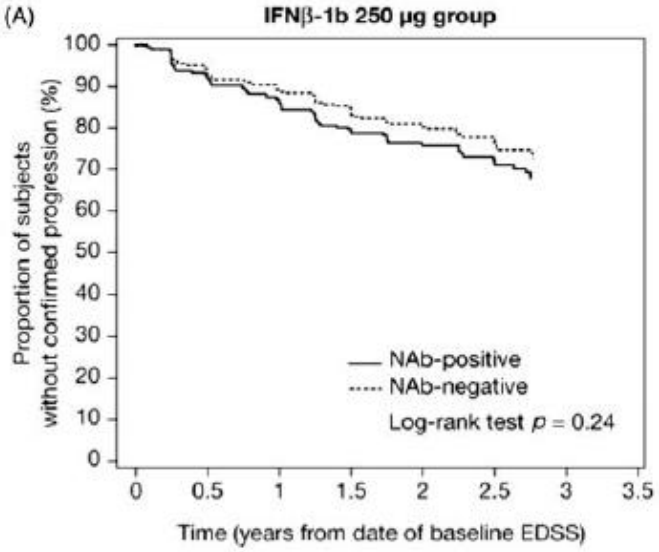
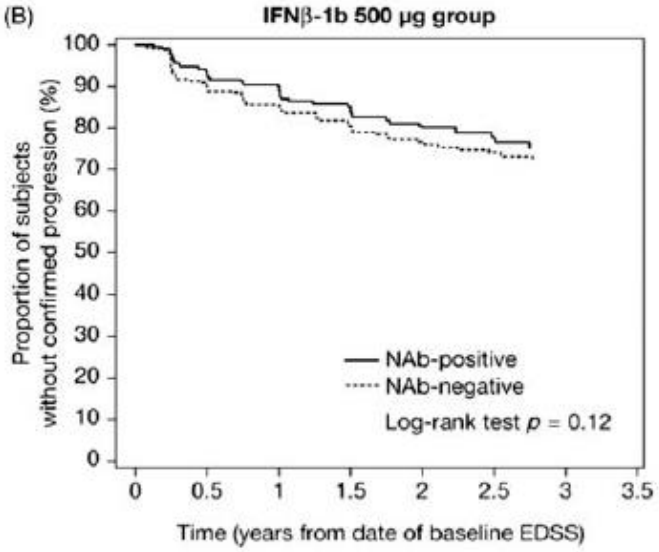
Douglas S Goodin[1], Hans-Peter Hartung[2], Paul O'Connor[3], Massimo Filippi[4], Barry Arnason[5], Giancarlo Comi[6], Stuart Cook[7], Douglas Jeffery[7], Ludwig Kappos[8], Timon Bogumil[9], Volker Knappertz[2,9], Rupert Sandbrink[2,10], Karola Beckmann[10], Rick White[11], John Petkau[11] and Christoph Pohl[10,12] for the BEYOND Study Group









Clinical and Experimental Immunology ORIGINAL ARTICLE doi:10.1111/j.1365-2249.2007.03467.x

A case study on the effect of neutralizing antibodies to interferon beta 1b in multiple sclerosis patients followed for 3 years with monthly imaging

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Table 1. Demographic, clinical and magnetic resonance imaging (MRI) characteristics of patients at enrolment time.

Patient no.	Age	Gender	Years of MS	EDSS score	No. of CELs
1	28·0	Female	4·0	1·5	0
2	45·0	Female	2·0	5·5	4
3	23·0	Female	4·0	5·0	13
4	30·9	Female	5·9	2·0	3
5	35·0	Male	7·0	2·0	4
Mean ± s.d.	32·4 ± 8·3	4 F/1 M	4·6 ± 1·9	3·2 ± 1·9	4·8 ± 4·9

CELs: contrast-enhancing lesions; EDSS: Expanded Disability Status Scale; MS: multiple sclerosis.

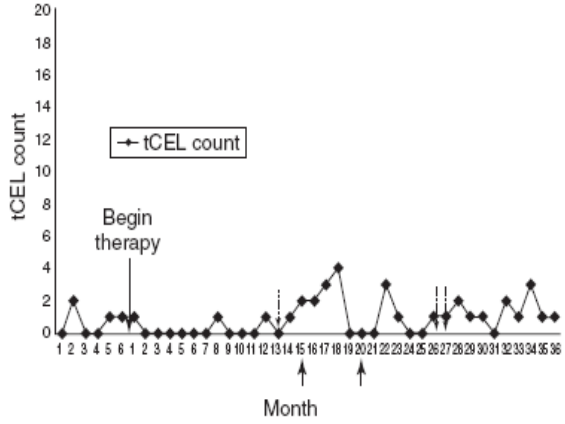

Fig. 1. The graph represents NAb development in relation to tCELs evolution in patient 1. Neutralizing antibodies (Nab) development

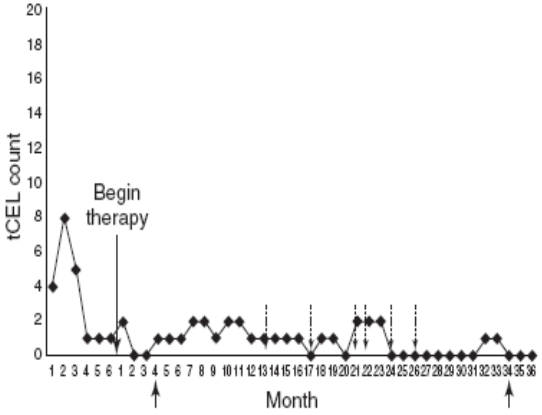

Fig. 2. The graph represents NAb development in relation to tCELs evolution in patient 2.

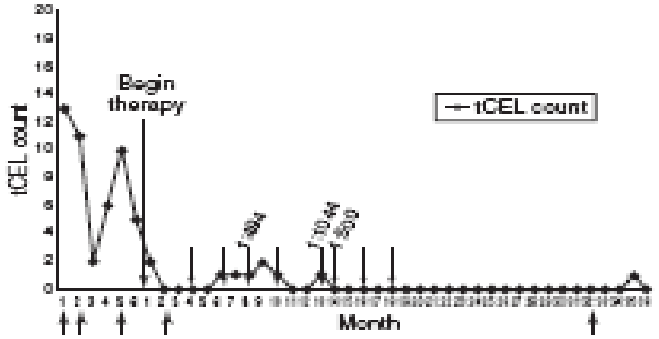

Fig. 3. The graph represents NAb development in relation to tCELs evolution in patient 3.

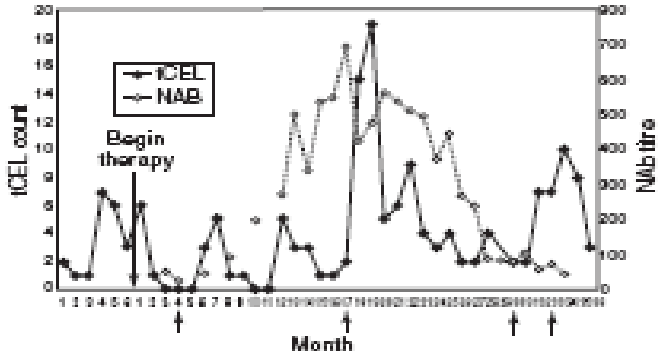

Fig. 4. The graph represents NAb development in relation to tCELs evolution in patient 4.

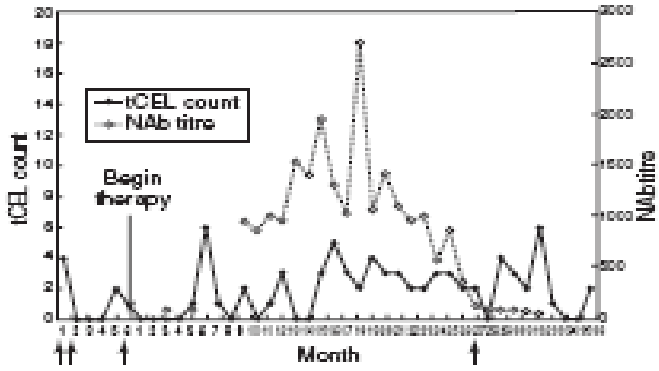

Fig. 5. The graph represents NAb development in relation to tCELs evolution in patient 5.

Aktualne rekomendacje

EFNS TASK FORCE/CME ARTICLE

Guidelines on use of anti-IFN-β antibody measurements in multiple sclerosis: report of an EFNS Task Force on IFN-β antibodies in multiple sclerosis

P. S. Sørensen[a], F. Deisenhammer[b], P. Duda[c], R. Hohlfeld[d], K.-M. Myhr[e], J. Palace[f], C. Polman[g], C. Pozzilli[h] and C. Ross[i] for the EFNS Task Force on Anti-IFN-β Antibodies in Multiple Sclerosis

Neutralising antibodies to interferon β in multiple sclerosis

Expert panel report

J Neurol (2007) 254:827–837
DOI 10.1007/s00415-006-0486-3

Hans-Peter Hartung
Chris Polman
Antonio Bertolotto
Florian Deisenhammer
Gavin Giovannoni
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Andrew Pachner
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Finn Sellebjerg
Krysztof Selmaj
Per Soelberg Sorensen

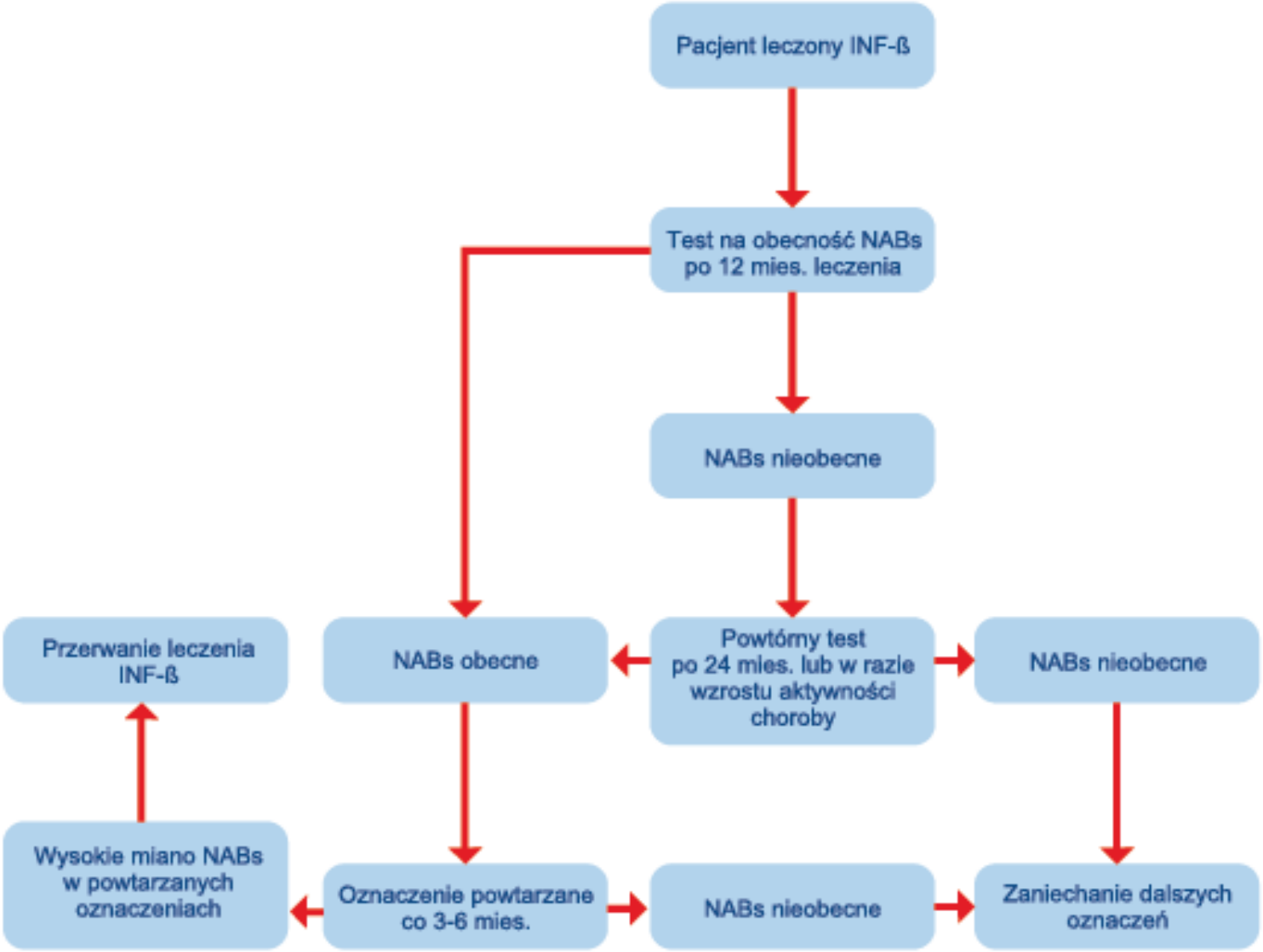
Neutralizing antibodies to interferon beta: Assessment of their clinical and radiographic impact: An evidence report

AMERICAN ACADEMY OF NEUROLOGY

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

D.S. Goodin, MD; E.M. Frohman, MD, FAAN; B. Hurwitz, MD; P.W. O'Connor, MD; J.J. Oger, MD, FRCPC, FAAN; A.T. Reder, MD; and J.C. Stevens, MD, FAAN

Algorytm postępowania w oparciu o rekomendacje



Algorytm postępowania w oparciu o rekomendacje

Konsorcjum Neutralizing Antibodies on Interferon Beta in Multiple Sclerosis (NABINMS) w ramach Programu Ramowego KOMISJI EUROPEJSKIEJ, składające się z europejskich naukowców i lekarzy klinicystów.

Panel 1: **Definitions applied by the expert panel as a starting point for their discussions**

NAb titres

- Cut-offs need to be determined and appropriately validated for individual laboratories and will be agent-specific; EMA recommends using interferon beta-1a in assays independent of the therapeutic interferon-beta product used
- Titres most often applied in routine clinical practice differ between the products used (table 1)

Clinical status of patient

Doing well

No relapses; no or limited MRI activity (CELs and/or new T2 lesions)

Intermediate disease activity

One relapse during therapy; no or limited MRI activity (CELs and/or new T2 lesions)

Doing poorly

Multiple relapses or one relapse and extensive MRI activity (multiple CELs and new T2 lesions)

CEL=contrast-enhancing lesion. EMA=European Medicines Agency. NAb=neutralising antibody.

Panel 2: **Recommended features of the common assay* for neutralising antibodies**

- Developed by the three marketing authorisation holders (Merck-Serono, Biogen, and Bayer) at the request of CHMP
- Based on the inhibition of MxA induction in A549 cells
- MxA is detected by a rat monoclonal antibody
- The Kawade equation[37] is used to define the titre as the dilution that reduces interferon beta by ten to one laboratory units
- CHO-derived interferon beta is used as standard antigen
- Assay validation shows good inter-laboratory (CV 1·9–5·3%) and intra-laboratory (CV 0·4–4·4%) reproducibility

CHMP=Commission for Human Medicinal Products of EMA. CHO=Chinese hamster ovary cell. CV=coefficient of variability. MxA=myxovirus resistance protein A. EMA=European Medicines Agency. *As reported by the EMA.[75]

Polman i wsp., 2010

Algorytm postępowania w oparciu o rekomendacje

	Stan dobry**	Średnia aktywność choroby**	Stan zły**
Negatywne miano NAb			
Zalecenie diagnostyczne	Powtórzyć po 12 mies.	Powtórzyć po 12 mies.	Nie powtarzać
Zalecenie dotyczące leczenia	Bez zmian	Rozważyć kontynuację bieżącego leczenia*	Zmienić leczenie
Małe miano NAb			
Zalecenie diagnostyczne	Powtórzyć po 3-6 mies. Jeżeli małe miano utrzymuje się, rozważyć test MxA	Powtórzyć po 3-6 mies. Jeżeli małe miano utrzymuje się, rozważyć test MxA	Nie powtarzać. Rozważyć MxA w celu uzyskania dodatkowych informacji
Zalecenie dotyczące leczenia	W przypadku braku aktywności biologicznej MxA rozważyć zmianę leku na preparat spoza grupy interferonów beta	W przypadku braku aktywności biologicznej MxA rozważyć zmianę leku na preparat spoza grupy interferonów beta	Zmienić leczenie
Duże miano NAb			
Zalecenie diagnostyczne	Powtórzyć po 3-6 mies.	Powtórzyć po 3-6 mies.	Nie powtarzać
Zalecenie dotyczące leczenia	Jeżeli duże miano utrzymuje się, rozważyć zmianę leku na preparat spoza grupy interferonów beta	Jeżeli duże miano utrzymuje się, rozważyć zmianę leku na preparat spoza grupy interferonów beta	Zmienić leczenie

Polman i wsp., 2010

Co robić gdy Nabs hamują aktywność kliniczną IFNbeta ?

Steroidy i immunosupresja jest nieskuteczna

Zamiana pomiędzy preparatami INF – nieefektywna

Octan glatirameru

Inne leki – np. doustne ?

Podsumowanie

- Konieczne jest wprowadzenie uniwersalnego i wiarygodnego testu do oznaczania obecności Nabs
- NAbs redukują biologiczną i kliniczną skuteczność IFN β
- IFNβ powinien być odstawiony u pacjentów z utrwalonymi mianami NAb +dodatnimi i przy braku aktywności biologicznej IFN β
- Alternatywne leczenie dla pacjentów Nab pozytywnych powinno opierać się na lekach o innej budowie o niskiej lub braku immunogeniczności, które wykażą odpowiednią skuteczność i bezpieczeństwo dla pacjentów