

# Helse Vest Forskningspris 2022

«Paradigmeskift i MS-behandling»

Solstrand Nov-2022

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**Kjell-Morten Myhr**

Professor | Overlege | Senterleder

Neuro-SysMed

Universitetet i Bergen & Haukeland universitetssjukehus



TUSEN TAKK!

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# Presentasjon

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- Paradigmeskift i MS-behandling
  - MS
  - Utvikling i MS-behandlingen
- Hvordan har vi fått dette til?



# Multipel Sklerose

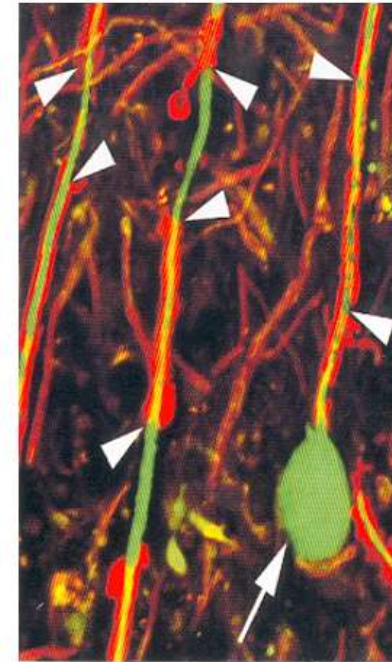
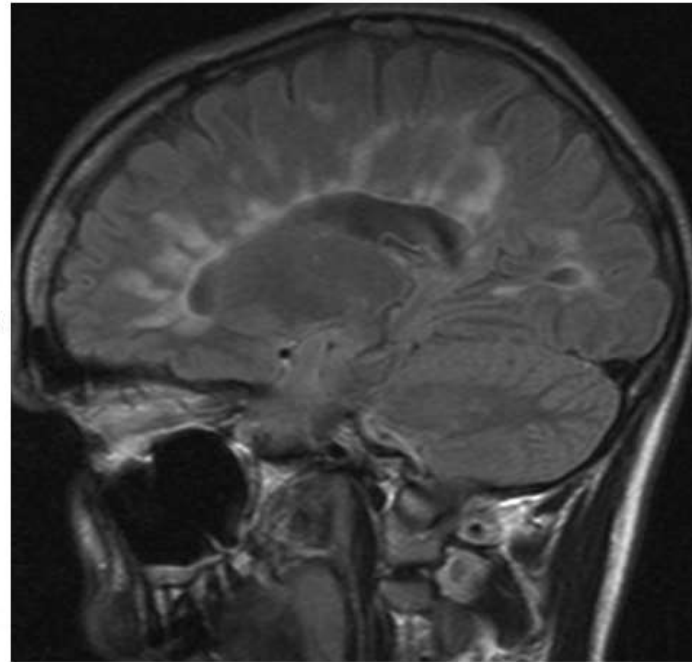
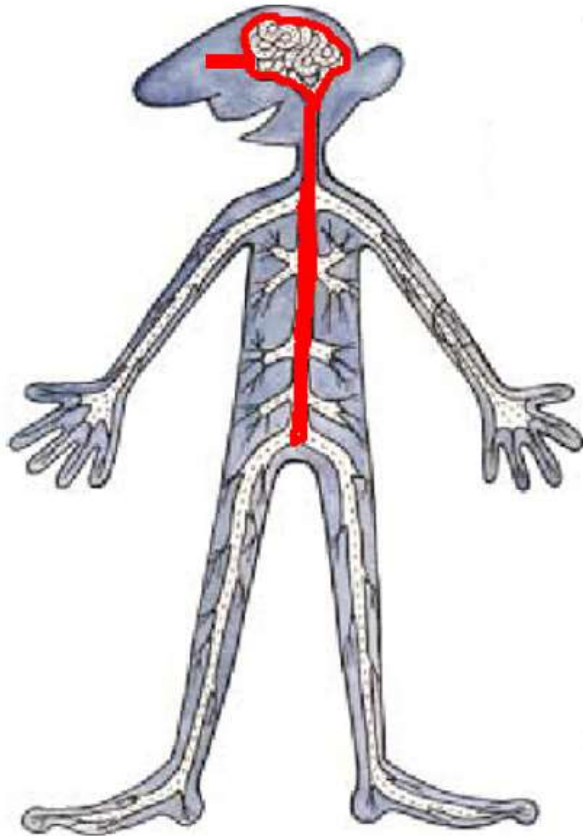
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# Multipel Sklerose



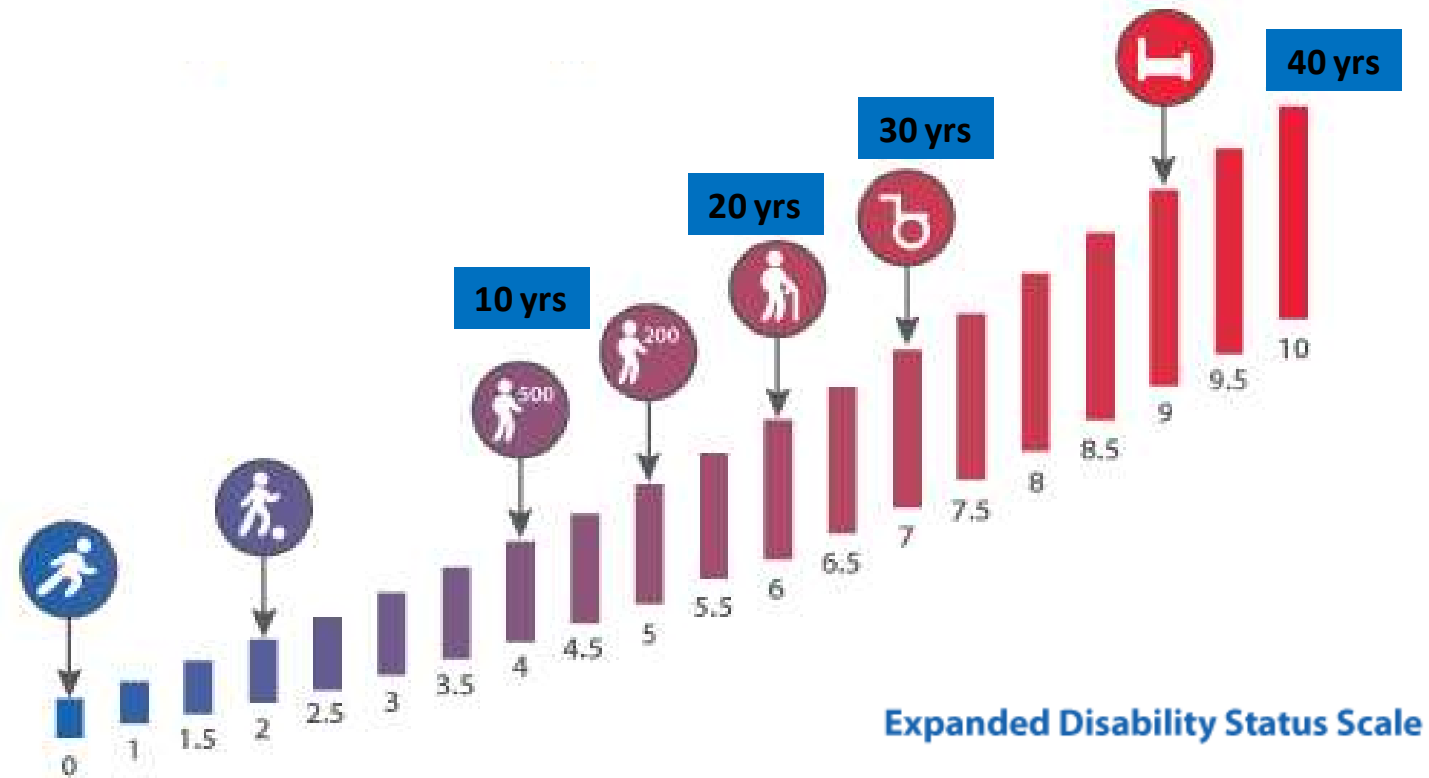
# Multipel Sklerose (MS) – er en alvorlig sykdom

- Debut i 20-40 års alder
- Kvinner/Men: 2:1
- 13000 Pasienter i Norge; 5-600 nye per år



Trapp B, Mørk SJ, Bø L. et al. NEJM 1998

# Prognose uten behandling



KM Myhr et al. Mult Scler 2001

# Tidlig irreversibel skade

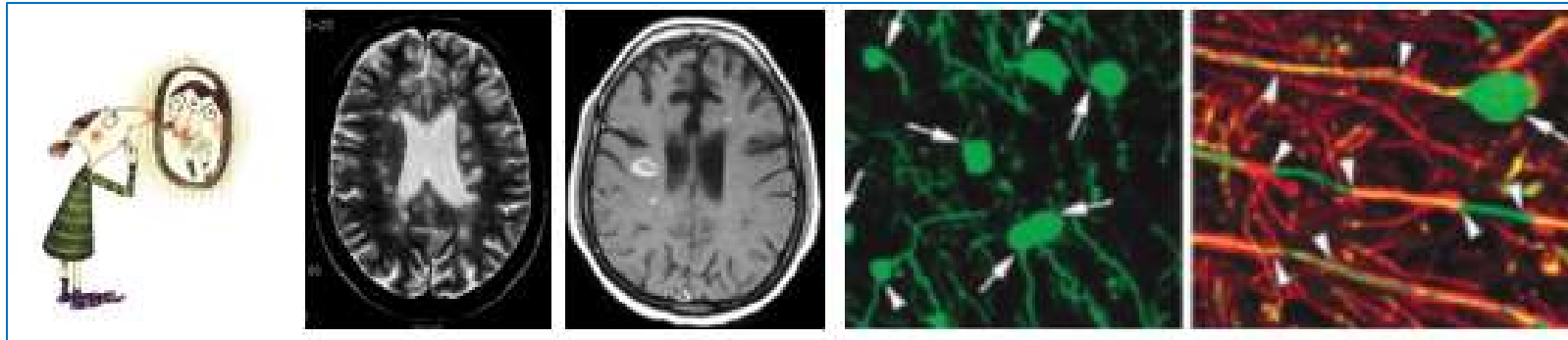


TABLE 2. DISTRIBUTION AND NUMBER OF TRANSECTED AXONS IN MULTIPLE-SCLEROSIS LESIONS.

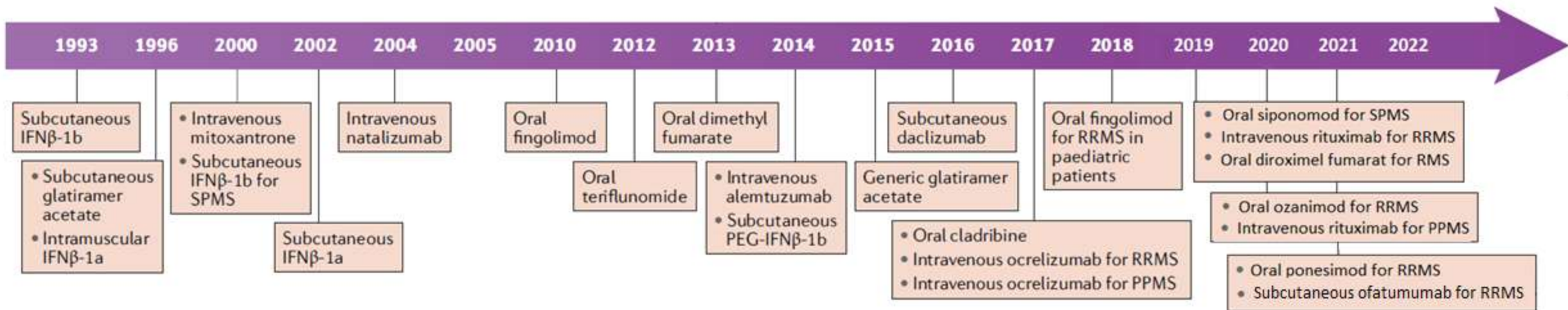
| TISSUE (NO. OF PATIENTS)   | NO. OF LESIONS ANALYZED | NO. OF TRANSECTED AXONS/mm <sup>3*</sup> |
|----------------------------|-------------------------|--|
| Active lesions (3)         | 5                       | 11,236±2775                              |
| Chronic active lesions (4) | 13                      |  |
| Edge                       |                         | 3138±688                                 |
| Core                       |                         | 875±246                                  |
| Nonlesion white matter (5) | 11                      | 17±2.8                                   |
| Control white matter (4)   | 5                       | 0.7±0.7                                  |

-> Utgjør ca. 25% av «Axoner/mm<sup>3</sup>»

Forebygge  
&  
Stoppe

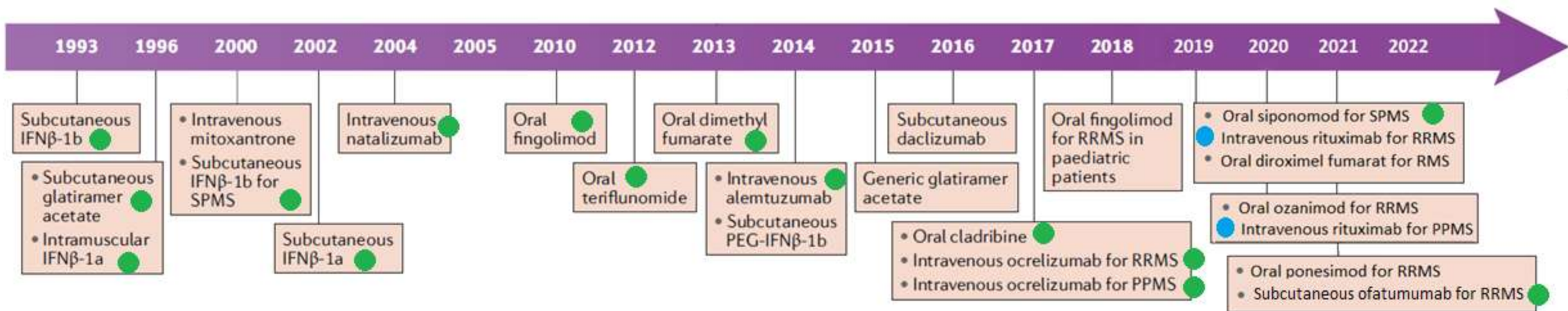


# MS-behandlingar godkjent i FDA/EMA \* (> 20 siste ~ 30 år)



\* FDA = Food and Drug Administration (USA) ; EMA = European Medicines Agency (Europa)

# HUS & Norge har bidratt aktivt i utviklingen

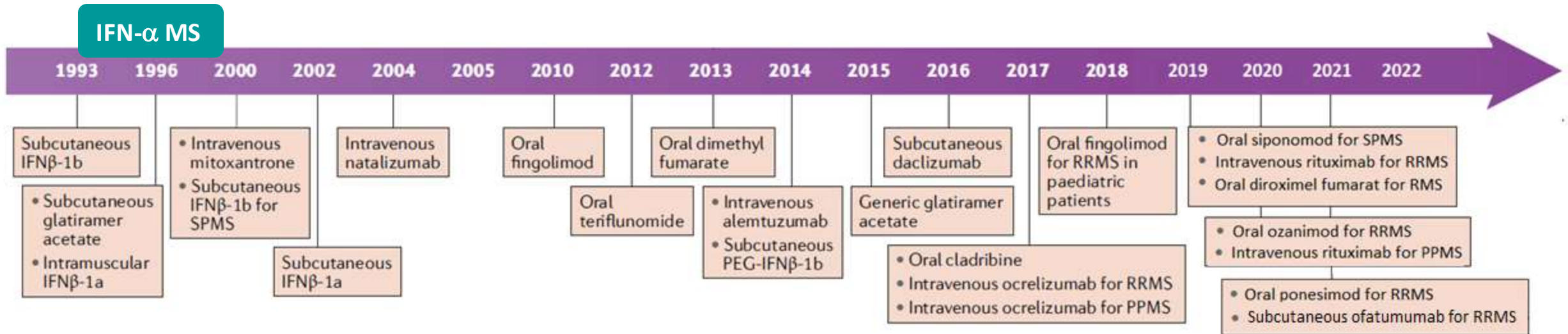


\* FDA = Food and Drug Administration (USA) ; EMA = European Medicines Agency (Europa)

• Godkjent for bruk av beslutningsforum (ikke av FDA/EMA) ([HUSsom pådriver](#))

• Studiedeltakelse fra Haukeland universitetssjukehus

# MS-behandlinger godkjent i FDA/EMA \*(siste ~ 30 år)



\* FDA = Food and Drug Administration (USA) ; EMA = European Medicines Agency (Europa)

# NOROC-MS: IFN- $\alpha$ vs Placebo ved MS (13 avdelinger)

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March 01, 1999; 52 (5) ARTICLES

## Interferon- $\alpha$ 2a reduces MRI disease activity in relapsing-remitting m

K.M. Myhr, T. Riise, F.E. Green Lilleås, T.G. Beiske, E.G. Celius, A. Edland, D. Jensen, J.P. Larsen, R. Nilsen, M.W. Nortvedt, A.I. Smievoll, C. Vedeler, H.I. Nyland  
First published March 1, 1999, DOI: <https://doi.org/10.1212/WNL.52.5.1049>

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November 28, 2000; 55 (10) BRIEF COMMUNICATIONS

## Neutralizing antibodies to interferon (IFN) $\alpha$ -2a and IFN $\beta$ -1a or IFN $\beta$ -1b in MS are not cross-reactive

K.M. Myhr, C. Ross, H.I. Nyland, K. Bendtzen, C.A. Vedeler  
First published November 28, 2000, DOI: <https://doi.org/10.1212/WNL.55.10.1569>

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July 12, 2000; 55 (1) ARTICLE

## Quality of life as a predictor for change in disability

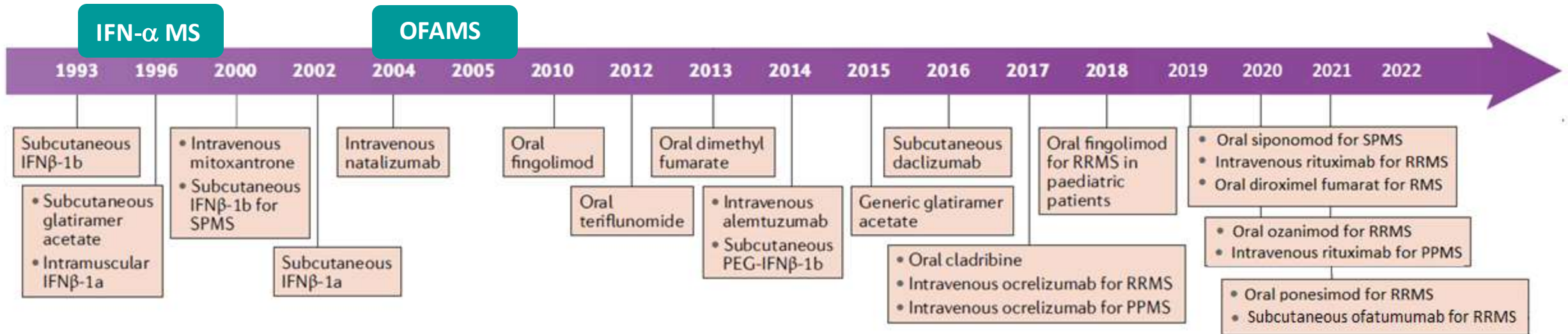
Monica W. Nortvedt, Trond Riise, Kjell-Morten Myhr, Harald I. Nyland  
First published July 12, 2000, DOI: <https://doi.org/10.1212/WNL.55.1.51>

*Multiple Sclerosis (1999) 5, 317–322*  
© 1999 Stockton Press All rights reserved 1352–4585/99 \$15.00  
<http://www.stockton-press.co.uk/ms>

## *Type I interferons and the quality of life of multiple sclerosis patients. Results from a clinical trial on interferon alfa-2a*

*MW Nortvedt\*<sup>1</sup>, T Riise<sup>1</sup>, KM Myhr<sup>2</sup>, HI Nyland<sup>2</sup> and BR Hanestad<sup>3</sup>*  
*<sup>1</sup>Department of Public Health and Primary Health Care, University of Bergen, Ulriksdal 8C, N-5009 Bergen, Norway;*  
*<sup>2</sup>Department of Neurology, Haukeland University Hospital, Bergen, Norway; <sup>3</sup>Bergen College, Bergen, Norway*

# MS-behandlinger godkjent i FDA/EMA \*(siste ~ 30 år)



\* FDA = Food and Drug Administration (USA) ; EMA = European Medicines Agency (Europa)

# OFAMS-MS: Omega-3 vs Placebo ved MS (14 avdelinger)

ORIGINAL CONTRIBUTION

## $\omega$ -3 Fatty Acid Treatment in Multiple Sclerosis (OFAMS Study)

*A Randomized, Double-Blind, Placebo-Controlled Trial*

Øivind Torkildsen, MD, PhD; Stig Wergeland, MD; Søren Bakke, MD; Antonie G. Beiske, MD, PhD; Kristian S. Bjerve, MD, PhD; Harald Hovdal, MD; Rune Midgard, MD, PhD; Finn Lilleås, MD; Tor Bård Bjørnarå, MD; Frøydis Dalene, MD; Grethe Kleveland, MD; Jan Schepel, MD; Inge Christoff Kjell-Morten Myhr, MD, PhD

*Arch Neurol.* 2012;69(8):1044-1051.

Negativ studie; men ~ 45 artikler / 7 PhD-arbeider

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& Neuroinflammation

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neurology open access journal



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January 2018; 5 (1) ARTICLE

OPEN ACCESS

## Neurofilament light chain predicts disease activity in relapsing-remitting MS

Kristin N. Varhaug, Christian Barro, Kjetil Bjørnevik, Kjell-Morten Myhr, Øivind Torkildsen, Stig Wergeland, Laurence A. Bindoff, Jens Kuhle, Christian Vedeler

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July 17, 2012; 79 (3) ARTICLES

## Vitamin D and disease activity in multiple sclerosis before and after treatment

Kristin I. Løken-Amsrud, Trygve Holmøy, Søren J. Bakke, Antonie G. Beiske, Kristian S. Bjerve, Bård T. Bjørnarå, Harald Hovdal, Finn Lilleås, Leiv Sandvik, Øivind Torkildsen, Stig Wergeland, Kjell-Morten Myhr

RESEARCH ARTICLE OPEN ACCESS

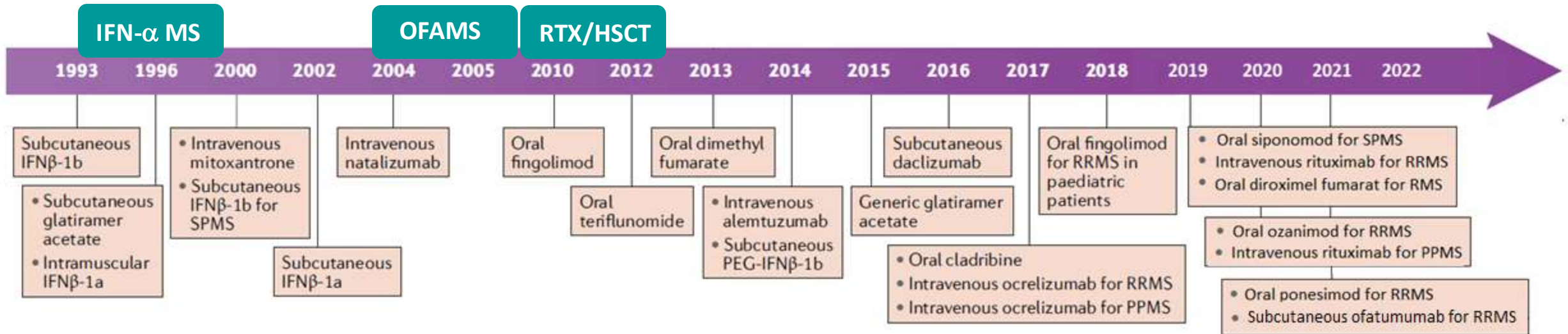
## The Effect of Smoking on Long-term Gray Matter Atrophy and Clinical Disability in Patients with Relapsing-Remitting Multiple Sclerosis

Ingrid Anne Lie, MD, Kristin Wesnes, MD, PhD, Silje S. Kvistad, MD, PhD, Iman Brouwer, MASc, Stig Wergeland, MD, PhD, Trygve Holmøy, MD, PhD, Rune Midgard, MD, PhD, Alla Bru, MD, Astrid Edland, MD, Randi Eikeland, MD, PhD, Sonia Gosal, MD, Hanne F. Harbo, MD, PhD, Grethe Kleveland, MD, Yvonne S. Sørenes, MD, Nina Øksendal, MD, Frederik Barkhof, MD, PhD, Hugo Vrenken, PhD, IR, Kjell-Morten Myhr, MD, PhD, Lars Bø, MD, PhD, and Øivind Torkildsen, MD, PhD

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*Neurol Neuroimmunol Neuroinflamm* 2022;9:e200008. doi:10.1212/NXI.0000000000200008

# MS-behandlinger godkjent i FDA/EMA \*(siste ~ 30 år)



\* FDA = Food and Drug Administration (USA) ; EMA = European Medicines Agency (Europa)

# Rituximab og stamcelle-behandling → RCT's 2008 → 2017

## ORIGINAL ARTICLE

The NEW ENGLAND JOURNAL of MEDICINE

### B-Cell Depletion with Rituximab in Relapsing–Remitting Multiple Sclerosis

Stephen L. Hauser, M.D., Emmanuelle Waubant, M.D., Ph.D., Douglas L. Arnold, M.D., Timothy Vollmer, M.D., Jack Antel, M.D., Robert J. Fox, M.D., Amit Bar-Or, M.D., Michael Panzara, M.D., Neena Sarkar, Ph.D., Sunil Agarwal, M.D., Annette Langer-Gould, M.D., Ph.D., and Craig H. Smith, M.D., for the HERMES Trial Group\*

N Engl J Med 2008;358:676-88.

## RESEARCH PAPER

Multiple Sclerosis 2009; 15: 229–237

### Early highly aggressive MS successfully treated by hematopoietic stem cell transplantation

J Fagius<sup>1</sup>, J Lundgren<sup>2</sup> and G Öberg<sup>3</sup>

## Nytt liv for MS-pasienten etter stamcelletransplantasjon

Per Martin Mo (35) er den første i Norge som har fått stamcelletransplantasjon mot alvorlig MS-sykdom. Han føler det som om han har vunnet i Lotto.



## Kristian er en av tre MS-rammede som har fått en helt spesiell behandling

MS rammer unge, friske mennesker av ukjent årsak. Behandlingen vi har i dag kan bare bremse utviklingen.



KVALITE STAMCELLEBEHANDLING. Kristian i Unndal er MS-ny. Han har bare hatt ett attack etter stamcellebehandlingen og kan fortsatt leve med dataveri Lina (3 1/2). FOTO: EIVIND SEMVÅSET



# Rituksimab og stamcelle-behandling → Behandlingsstudier

**MSJ** Experimental  
Translational  
Clinical

Original Research Article January–March 2021, 1–10

## Safety and efficacy of rituximab as first- and second line treatment in multiple sclerosis – A cohort study

Hilde Marie Torgauten, Kjell-Morten Myhr, Stig Wergeland, Lars Bø, Jan H Aarseth and Øivind Torkildsen

MULTIPLE  
SCLEROSIS  
JOURNAL | MSJ

Original Research Paper 2020, Vol. 26(14) 1889–1897

## Safety and efficacy of autologous hematopoietic stem cell transplantation for multiple sclerosis in Norway

Silje Agnethe Stokke Kvistad, Anne Kristine Lehmann, Linn Hereide Trovik, Einar Klæbo Kristoffersen, Lars Bø, Kjell-Morten Myhr and Øivind Torkildsen



FÅR FORSAKERDØD: Spesiallege Rudi Casle Haugen, professor Øivind Torkildsen ved Universitet i Bergen og leder Kjell-Morten Myhr ved forskningscenteret Neuro-SysMed arbeider alle med Hilde som stemmingsindikator med økt stress.  
Foto: Silje Stokke

## Får viktig forskning studie

Leder Kjell-Morten Myhr ved Neuro-SysMed okreltuzumab (Ocrevus) i en sammenlignende studie på et år.

Lene Moe  
lene.moe@helsevestre.no



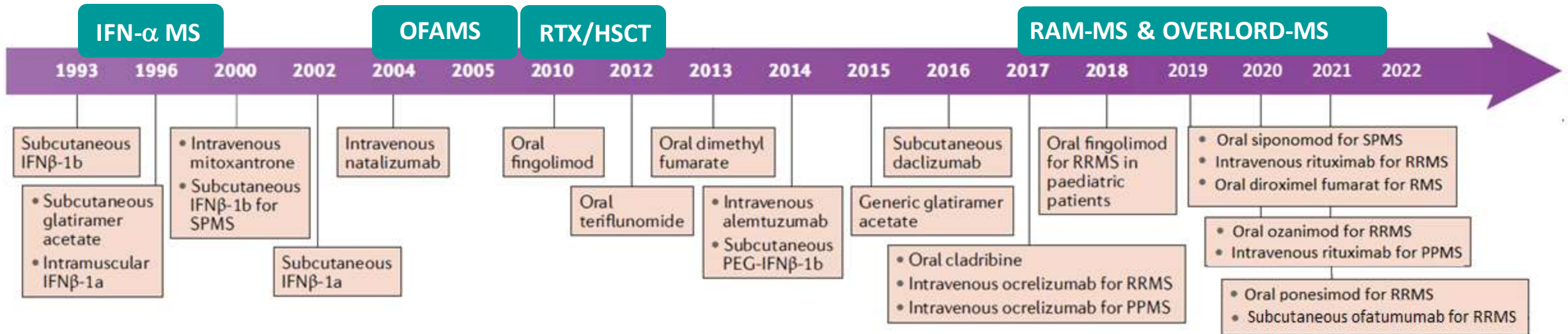
MOTTET: 11 fagfolk med bakgrunn fra blant annet sykepleie, nevrologi, besætnings- og transfusjonsmedisin møttes i København for å drøfte RAM-MS-studien (populært kalt stamcellestudien). Foto: Per-Øyvind Torkildsen

## Startet opp stamcellestudien i København

Den randomiserte studien på stamcelletransplantasjon, RAM-MS, starter nå å inkludere pasienter fra Sverige og Danmark.

Lene Moe  
lene.moe@helsevestre.no  
Publisert 2019-08-04 — 18:30

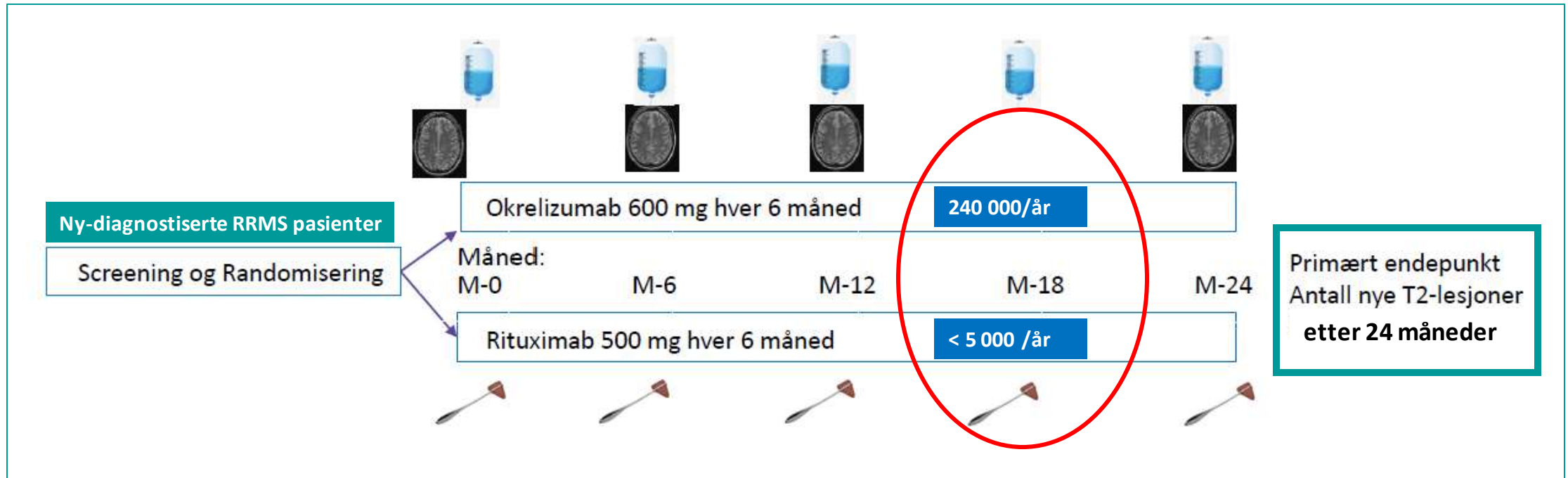
# MS-behandlingar godkjent i FDA/EMA \*(siste ~ 30 år)



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# Tidlig høyeffektiv behandling «OVERLORD-MS»

en «non-inferiority» studie



**Status: 213/211 = fullinkludert**



BE Rød



HM Torgauten



Ø. Torkildsen

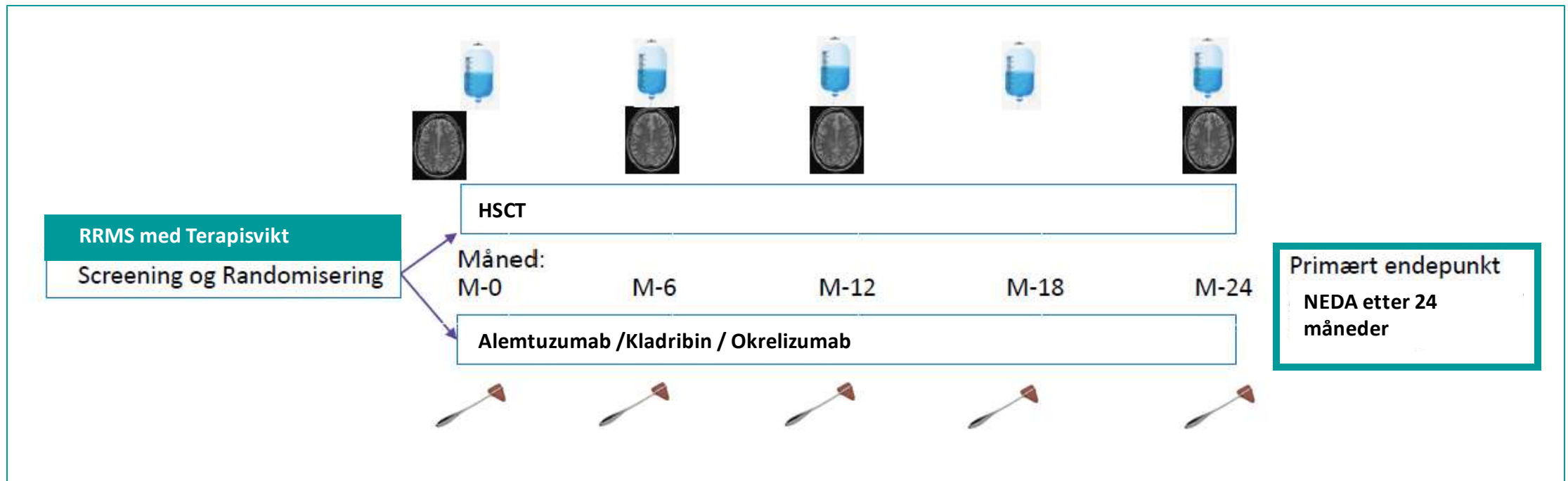


S. Wergeland



KM Myhr

# Stamcelle behandling ved terapisvikt; RAM-MS



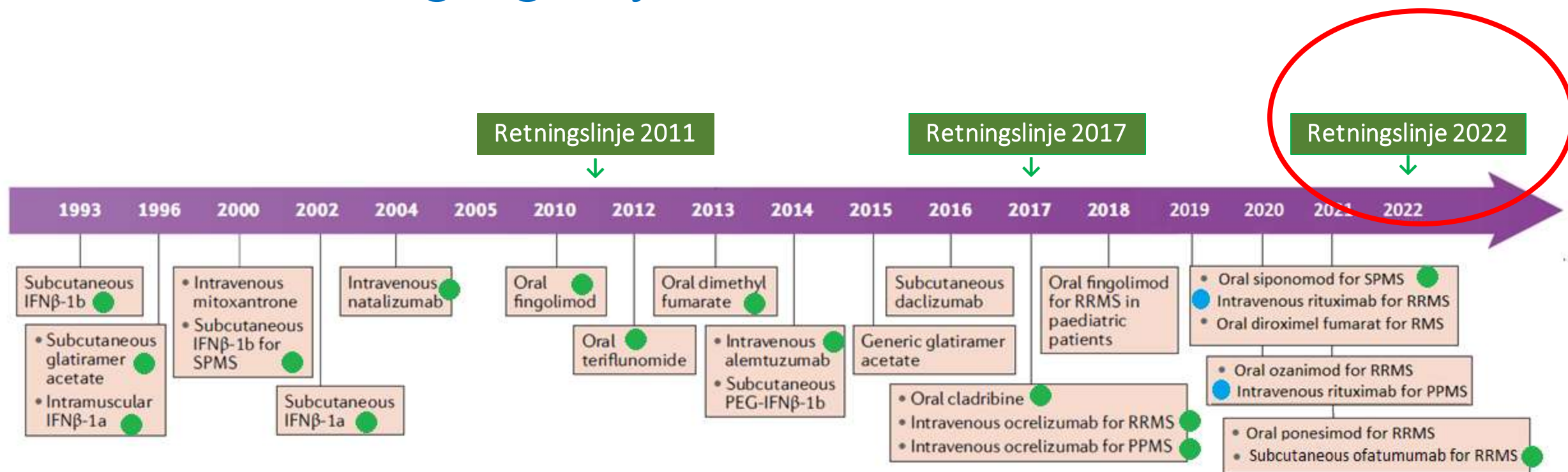
Status: 72 /100 inkludert pasienter



Ø. Torkildsen

L. Bø

# MS-behandlinger godkjent i FDA/EMA\*

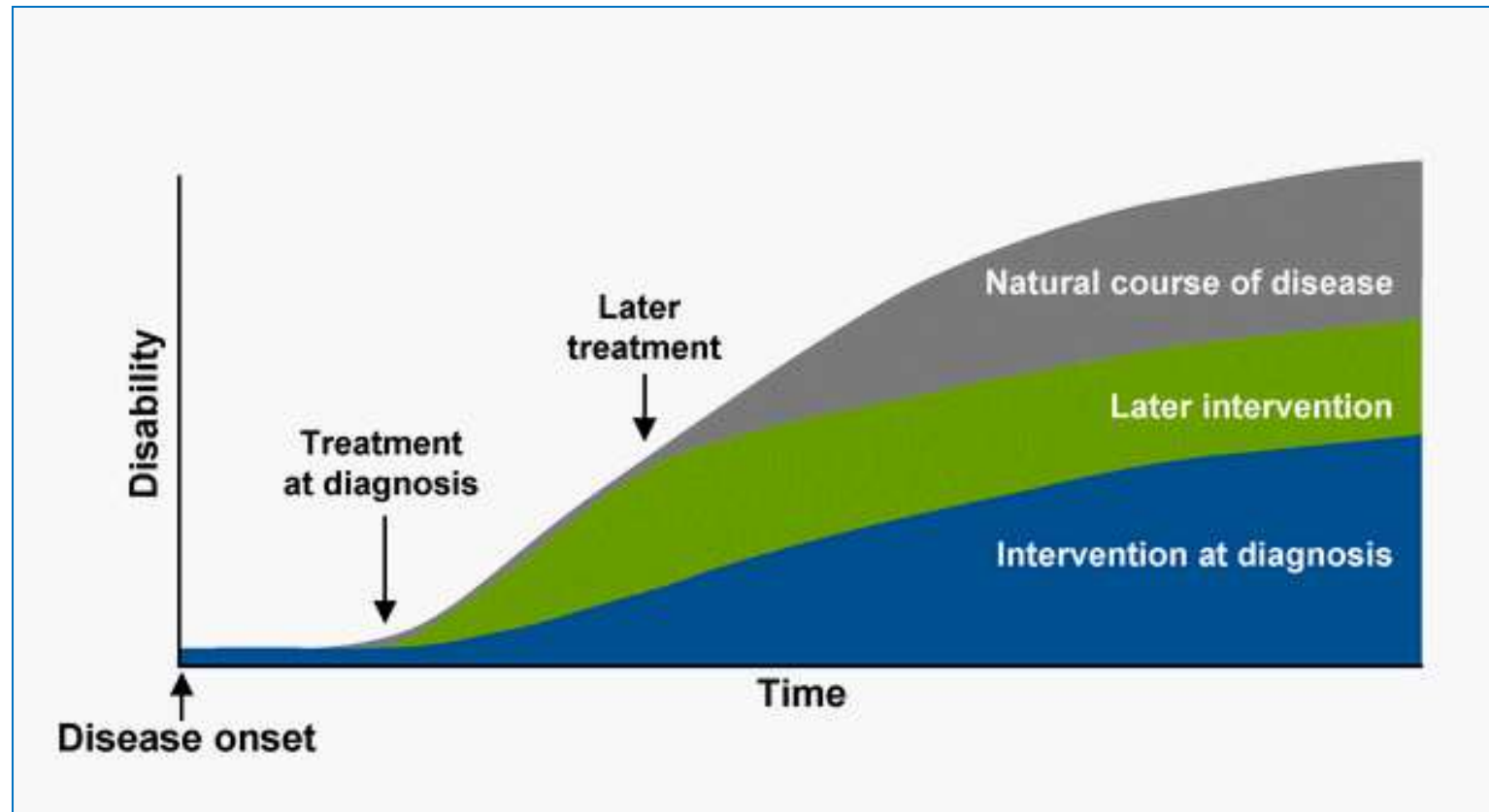


\* FDA = Food and Drug Administration (USA) ; EMA = European Medicines Agency (Europa)

• Godkjent for bruk av beslutningsforum (ikke av FDA/EMA) (HUS som pådriver)

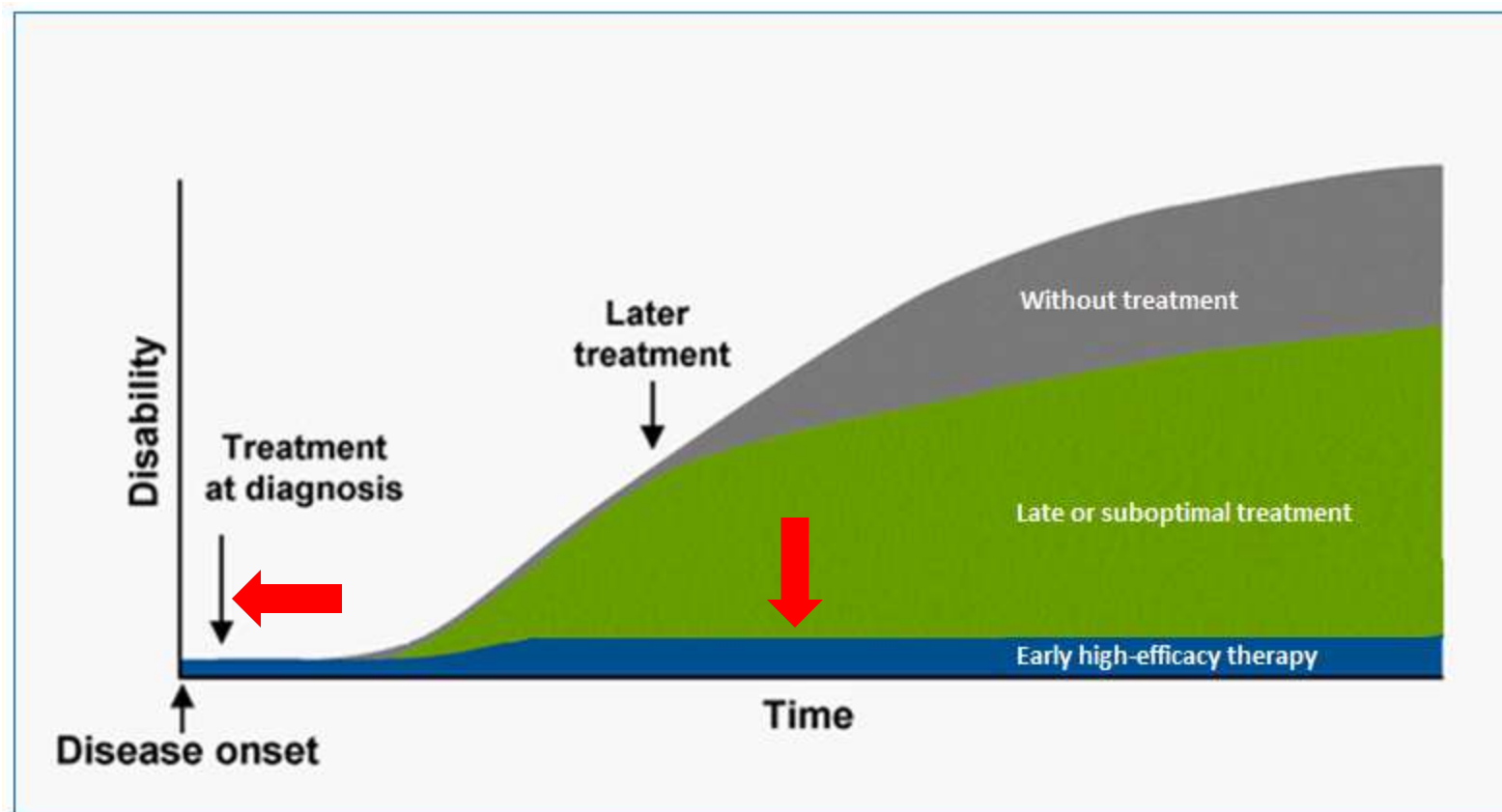
• Studiedeltakelse fra Haukeland universitetssjukehus

# Tidlig behandling → bedre effekt



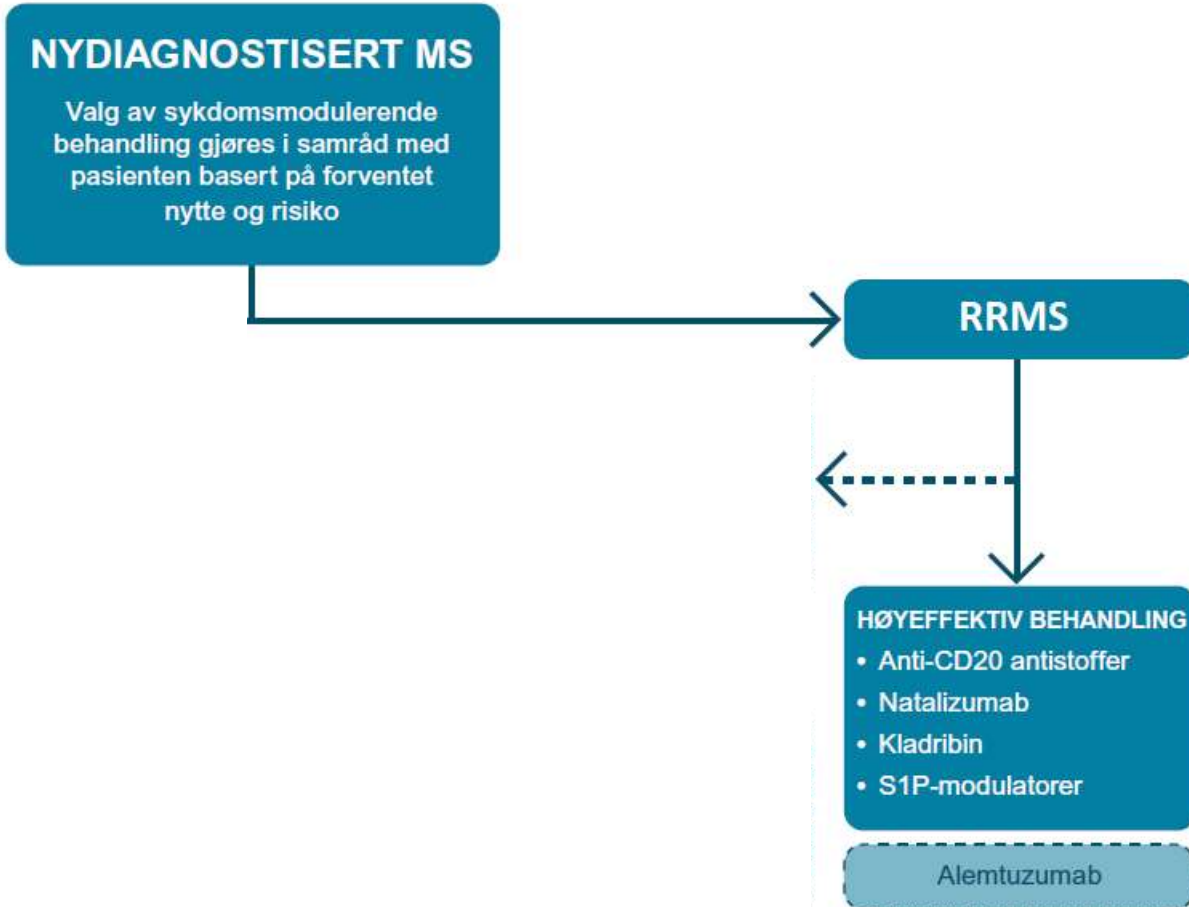
Giovannoni et al. 2016 – Modified by Myhr 2022

# Tidlig høyeffektiv behandling → bedre effekt



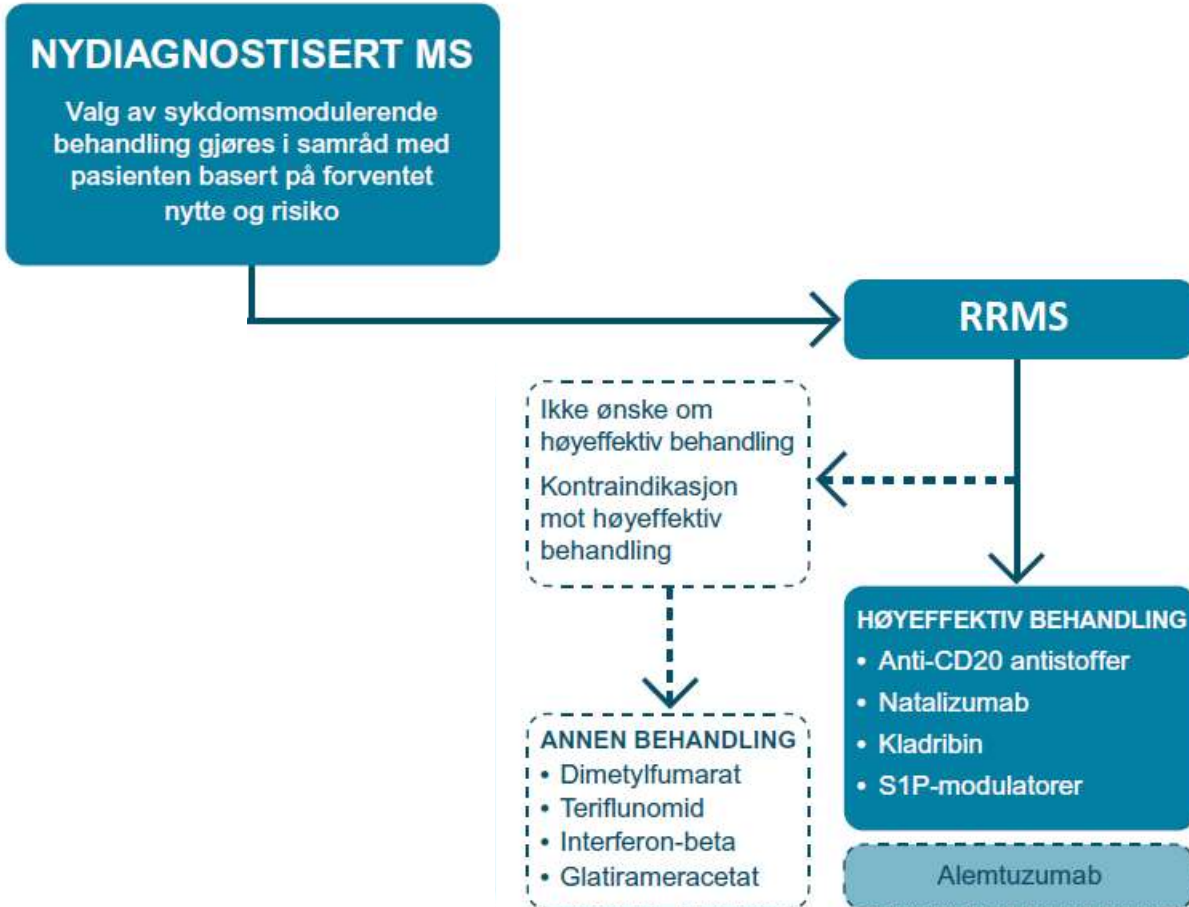
Giovannoni et al. 2016 – Modified by Myhr 2022

# MS-algoritme for oppstart av behandling

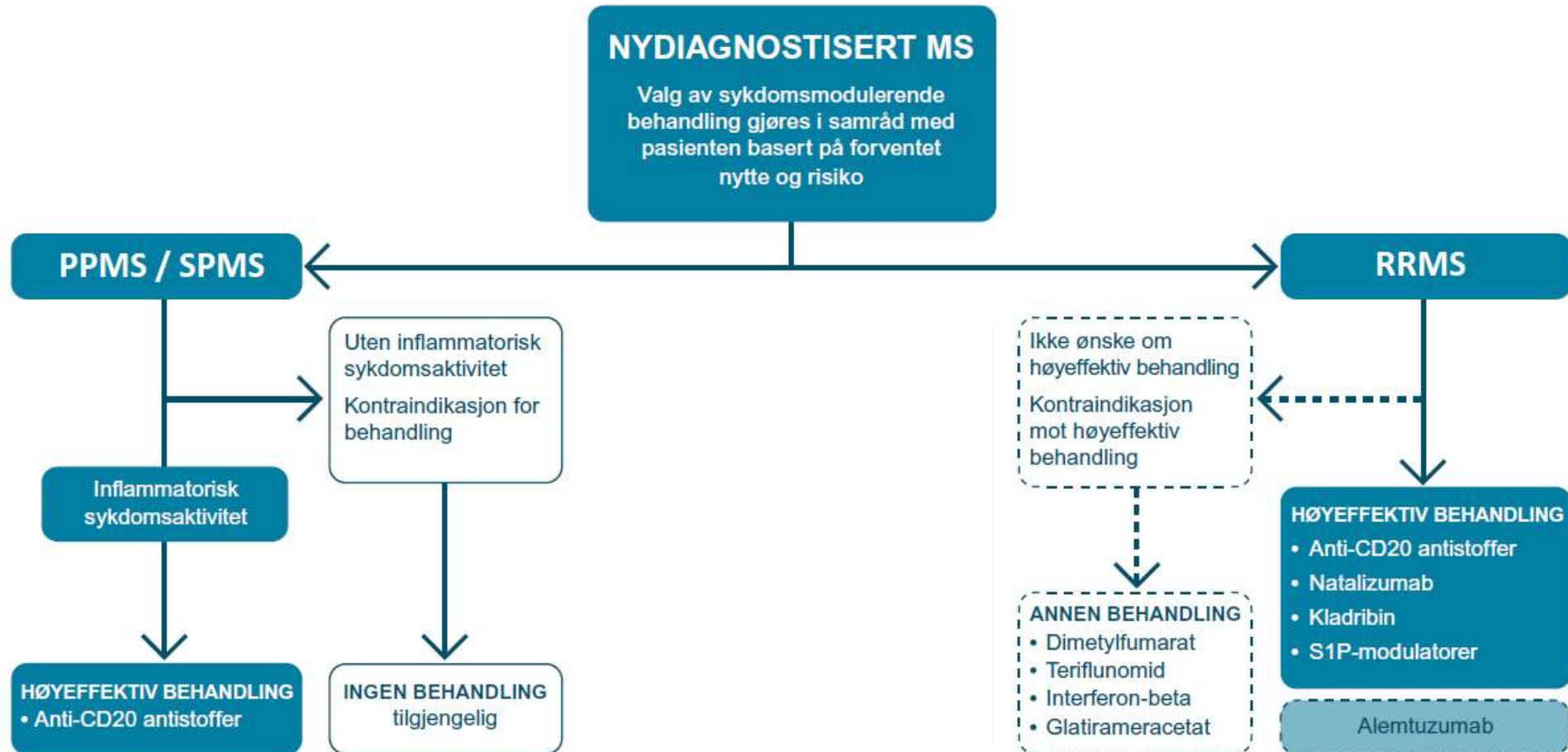




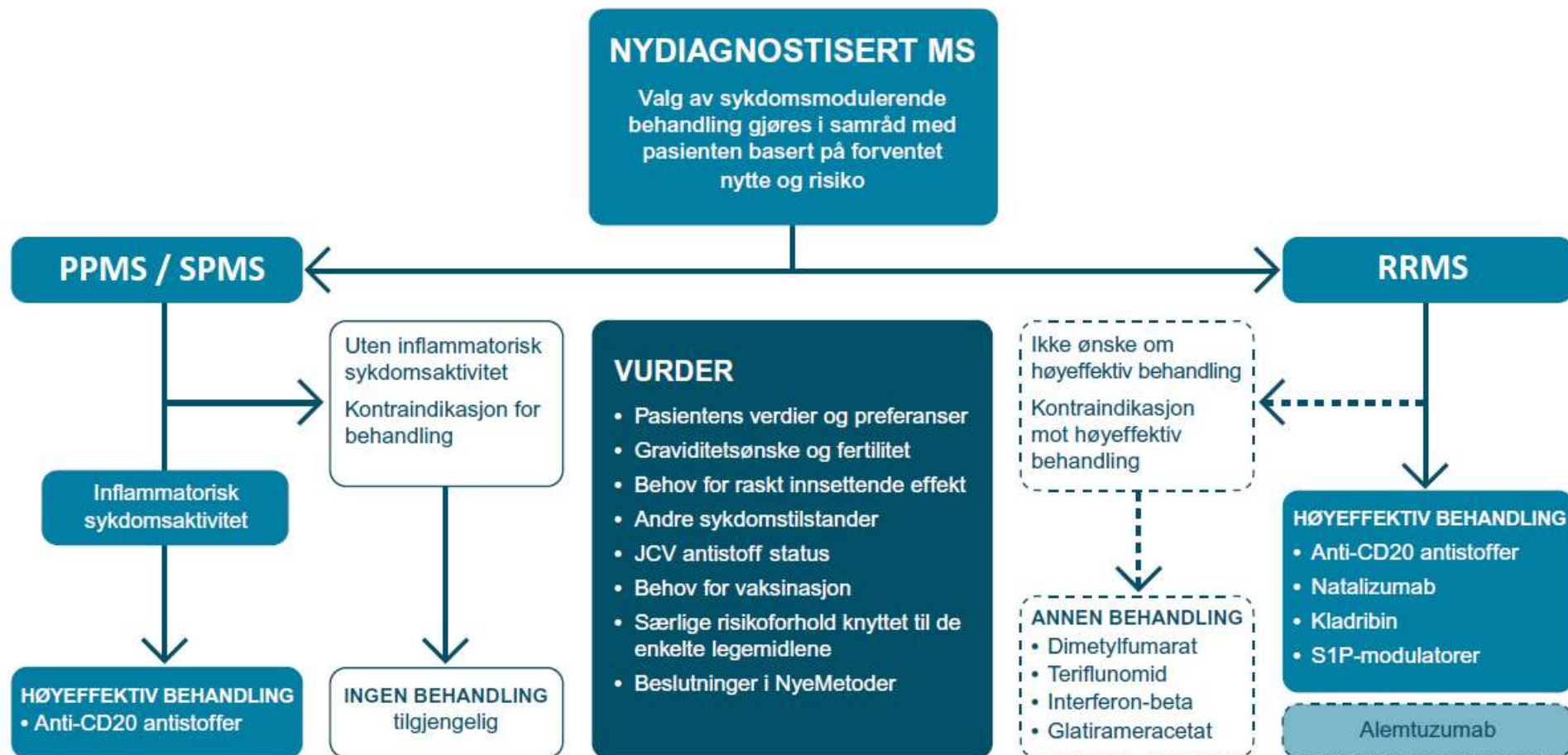
# MS-algoritme for oppstart av behandling



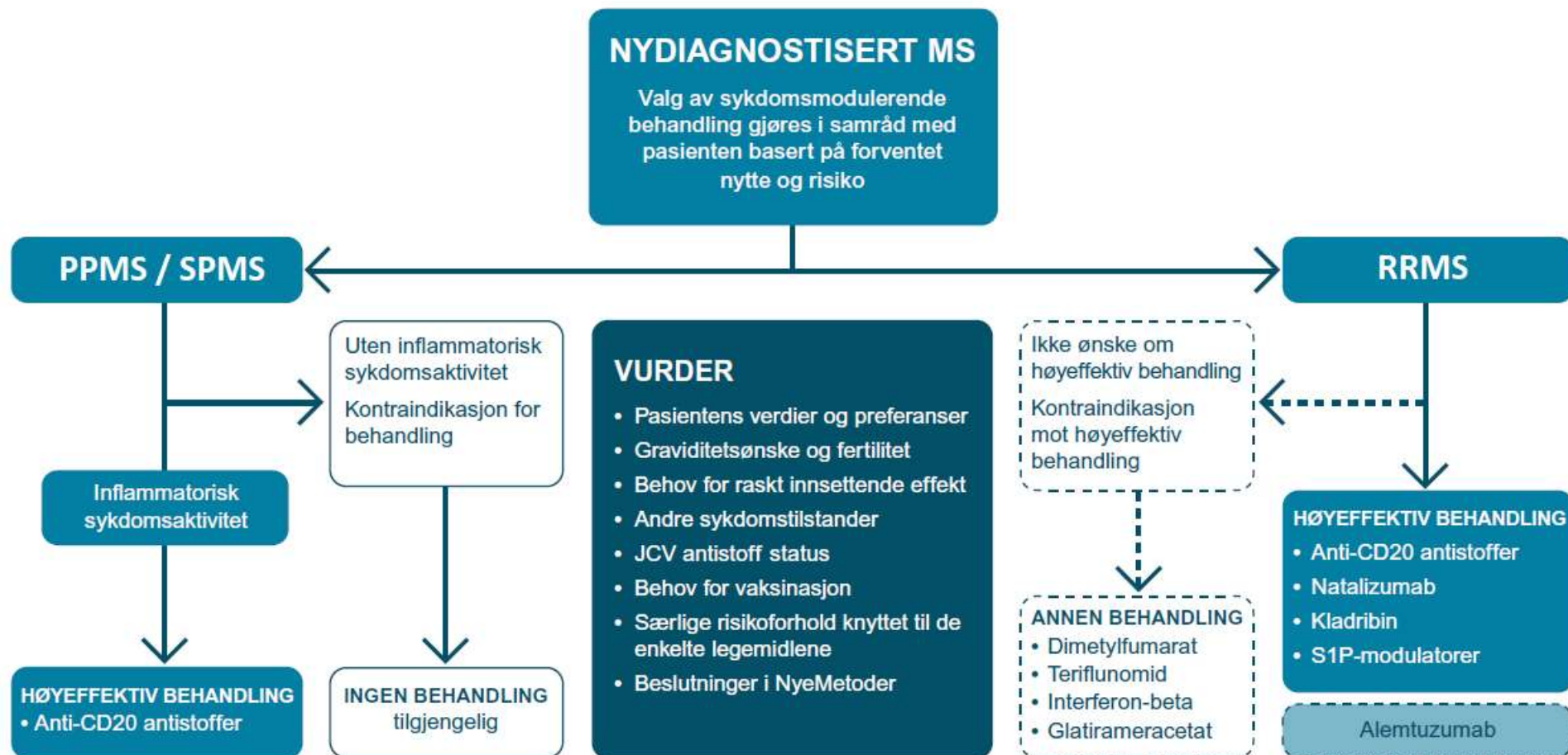
# MS-algoritme for oppstart av behandling



# MS-algoritme for oppstart av behandling



# MS-algoritme for oppstart av behandling



# Tidlig høyeffektiv behandling



# Hvordan

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# Hvordan

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- Lederskap; Sykehus & Avdeling/Klinikk – UiB & Institutt



- Mentorer, inspiratorer, veiledere



- Kolleger og samarbeidspartnere lokalt



- Samarbeidspartnere nasjonalt & internasjonalt (akademia/Industri)

- Pasienter & Pasientforening & Organisasjon

- Tverrfaglig personell

- Rekruttering; studenter, cand med – LIS / PhD

# Takk til alle PhD's



H Næss



J Dahl



NG Torkildsen



AG Beiske



ØG Torkildsen



T Smedal



T Rajalahti



SB Glad



S Wergeland



S Gavasso



K Løken-Amsrud



S Fjær



HMLBøe



K Bjørnevik



M Cortese



H Olberg



GH Bringeland



S Kvistad



K Wesnes



E Benjaminsen



A Bhan



IA Lie



E Skorve



J Willumsen



HM Torgauten



H Norborg



BE Rød



Akash Kapali



# Finansiering



The Research Council  
of Norway



efpia

HELSE VEST

HELSE NORD

HELSE MIDT-NORGE

HELSE SØR-ØST

NASJONALT PROGRAM

ms-forbundet  
MULTIPPEL SKLEROSE FORBUNDET

MS-Foreningen  
Bergen



Odd Fellow Ordenen

Kjell Almes Legat



NorCRIN

LMI | Legemiddelindustrien



Neuro-SysMed

fkb Forskningscenter  
for klinisk behandling  
Norges forskningsråd

Tusen takk for forskningsprisen!

