What's New in Research

GBS & CIDP

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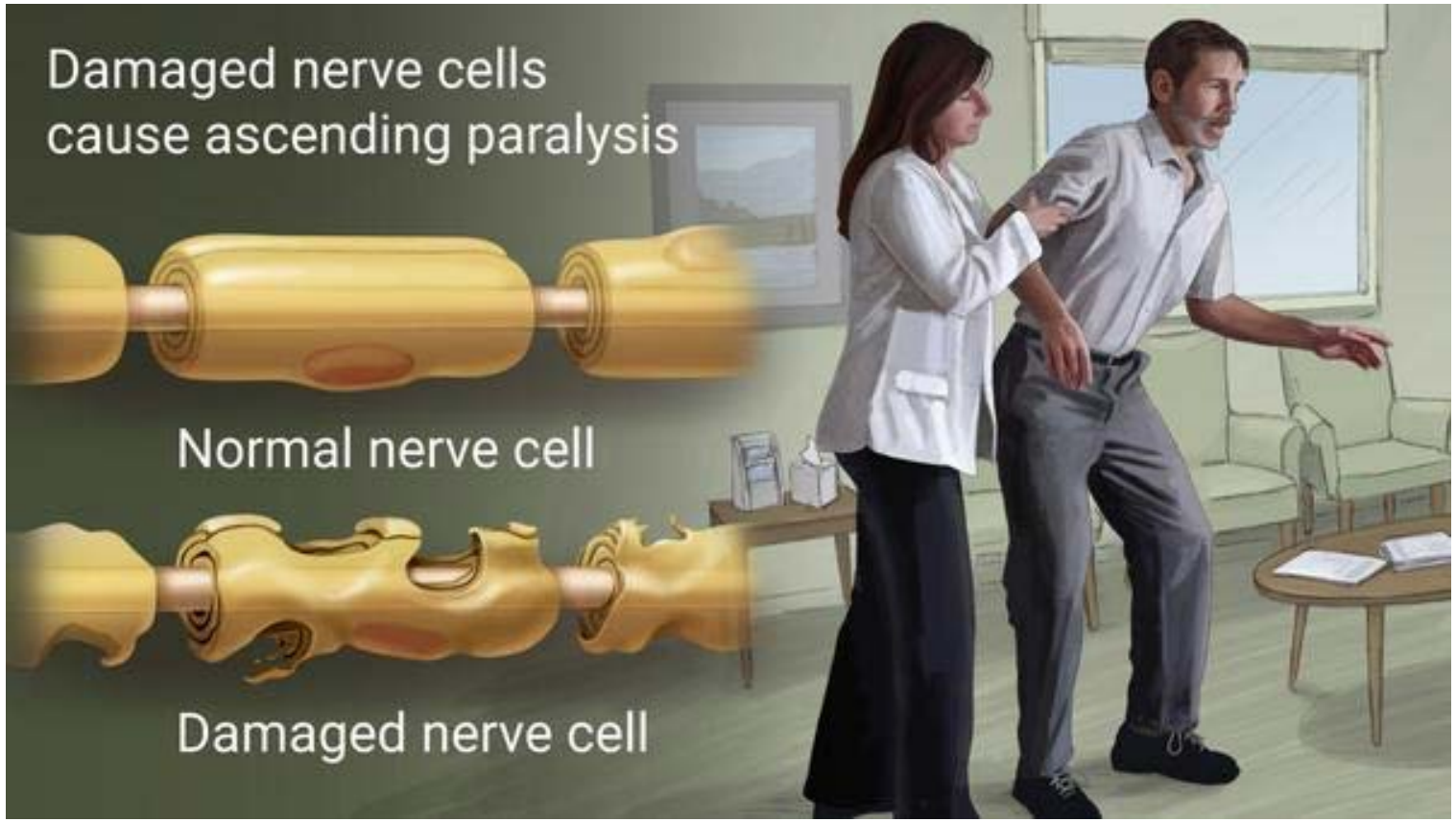
Where to Learn About Research?

- GBS-CIDP Foundation International
- clinicaltrials.gov

GBS


Damaged nerve cells
cause ascending paralysis
Normal nerve cell
Damaged nerve cell

Small Volume Plasma Exchange

- In Bangladesh < 10% of GBS receive IVIG or plasma exchange (PE).
- Researchers there developed a new technique that is based on the same principle as PE but is 25 times less expensive.
- Small Volume Plasma Exchange (SVPE):
  - blood is obtained from patients and cleared from the plasma just by gravity
  - can be done by the bedside of the patient
  - no need for electricity or complex machinery
- Pilot study in 20 patients with GBS showed that the procedure is feasible and safe during a follow-up of 6 months.

Safety and efficacy of eculizumab in Guillain-Barré syndrome: a multicentre, double-blind, randomised phase 2 trial

*Sonoko Misawa, Satoshi Kuwabara, Yasunori Sato, Nobuko Yamaguchi, Kengo Nagashima, Kanako Katayama, Yukari Sekiguchi, Yuta Iwai, Hiroshi Amino, Tomoki Suichi, Takanori Yokota, Yoichiro Nishida, Tadashi Kanouchi, Nobuo Kohara, Michi Kawamoto, Junko Ishii, Motoi Kuwahara, Hidekazu Suzuki, Koichi Hirata, Norito Kokubun, Ray Masuda, Juntaro Kaneko, Ichiro Yabe, Hidenao Sasaki, Ken-ichi Kaida, Hiroshi Takazaki, Norihiro Suzuki, Shigeaki Suzuki, Hiroyuki Nodera, Naoko Matsui, Shoji Tsuji, Haruki Koike, Ryo Yamasaki, Susumu Kusunoki, for the Japanese Eculizumab Trial for GBS (JET-GBS) Study Group**

Summary

Background Despite the introduction of plasmapheresis and immunoglobulin therapy, many patients with Guillain-Barré syndrome still have an incomplete recovery. Evidence from pathogenesis studies suggests the involvement of complement-mediated peripheral nerve damage. We aimed to investigate the safety and efficacy of eculizumab, a humanised monoclonal antibody against the complement protein C5, in patients with severe Guillain-Barré syndrome.

Methods This study was a 24 week, multicentre, double-blind, placebo-controlled, randomised phase 2 trial done at 13 hospitals in Japan. Eligible patients with Guillain-Barré syndrome were aged 18 years or older and could not walk independently (Guillain-Barré syndrome functional grade 3–5). Patients were randomly assigned (2:1) to receive 4 weeks of intravenous immunoglobulin plus either eculizumab (900 mg) or placebo; randomisation was done via a computer-generated process and web response system with minimisation for functional grade and age. The study had a parallel non-comparative single-arm outcome measure. The primary outcomes were efficacy (the proportion of patients with restored ability to walk independently [functional grade ≤2] at week 4) in the eculizumab group and safety in the full analysis set. For the efficacy endpoint, we predefined a response rate threshold of the lower 90% CI boundary exceeding 50%. This trial is registered with ClinicalTrials.gov, number, NCT02493725.

Findings Between Aug 10, 2015, and April 21, 2016, 34 patients were assigned to receive either eculizumab (n=23) or placebo (n=11). At week 4, the proportion of the patients able to walk independently (functional grade ≤2) was 61% (90% CI 42–78; n=14) in the eculizumab group, and 45% (20–73; n=5) in the placebo group. Adverse events occurred in all 34 patients. Three patients had serious adverse events: two in the eculizumab group (anaphylaxis in one patient and intracranial haemorrhage and abscess in another patient) and one in the placebo group (depression). The possibility that anaphylaxis and intracranial abscess were related to eculizumab could not be excluded. No deaths or meningococcal infections occurred.

Interpretation The primary outcome measure did not reach the predefined response rate. However, because this is a small study without statistical comparison with the placebo group, the efficacy and safety of eculizumab could be investigated in larger, randomised controlled trials.

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See **Comment** page 483

*Group members are listed at the end of this Article

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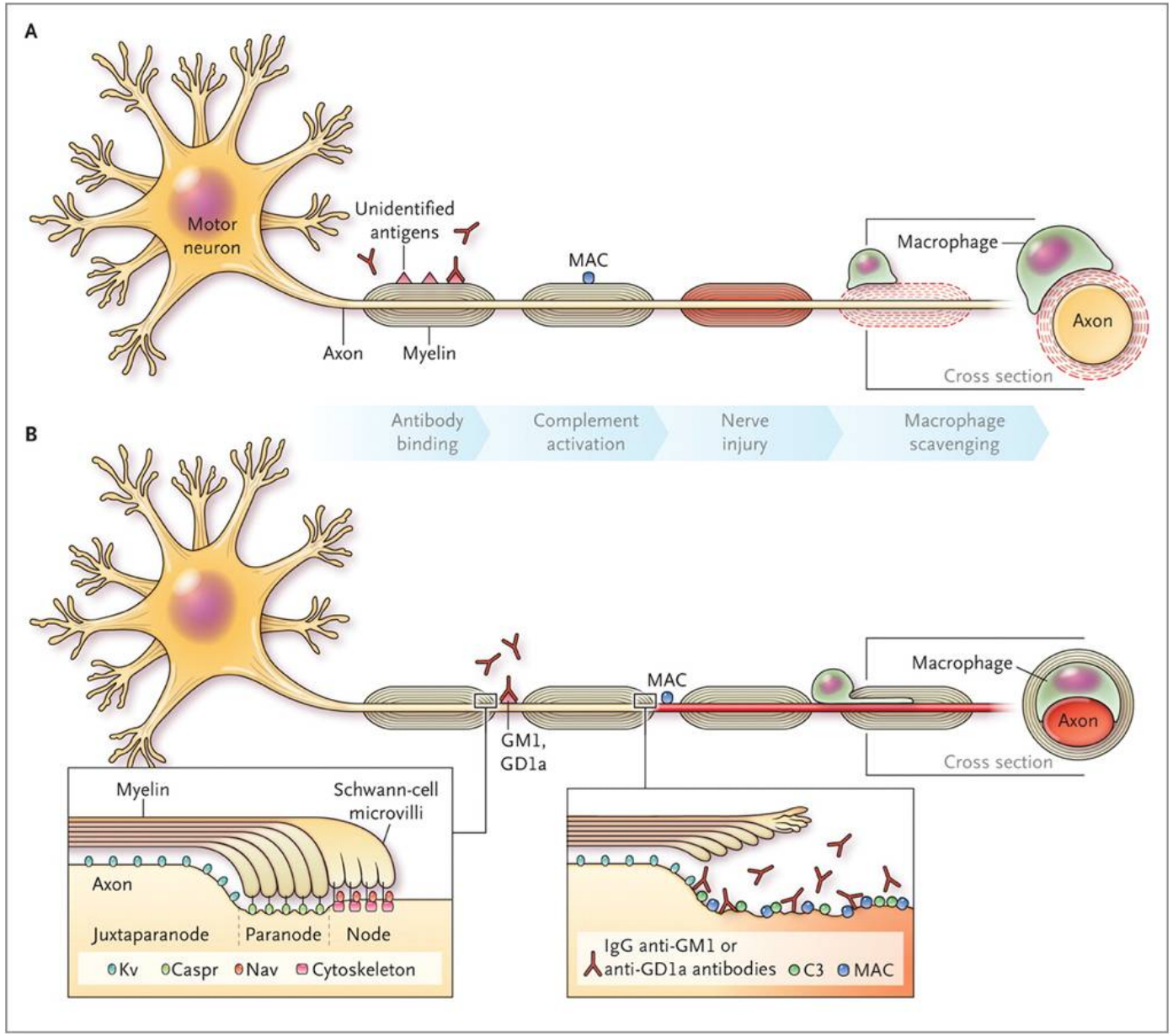
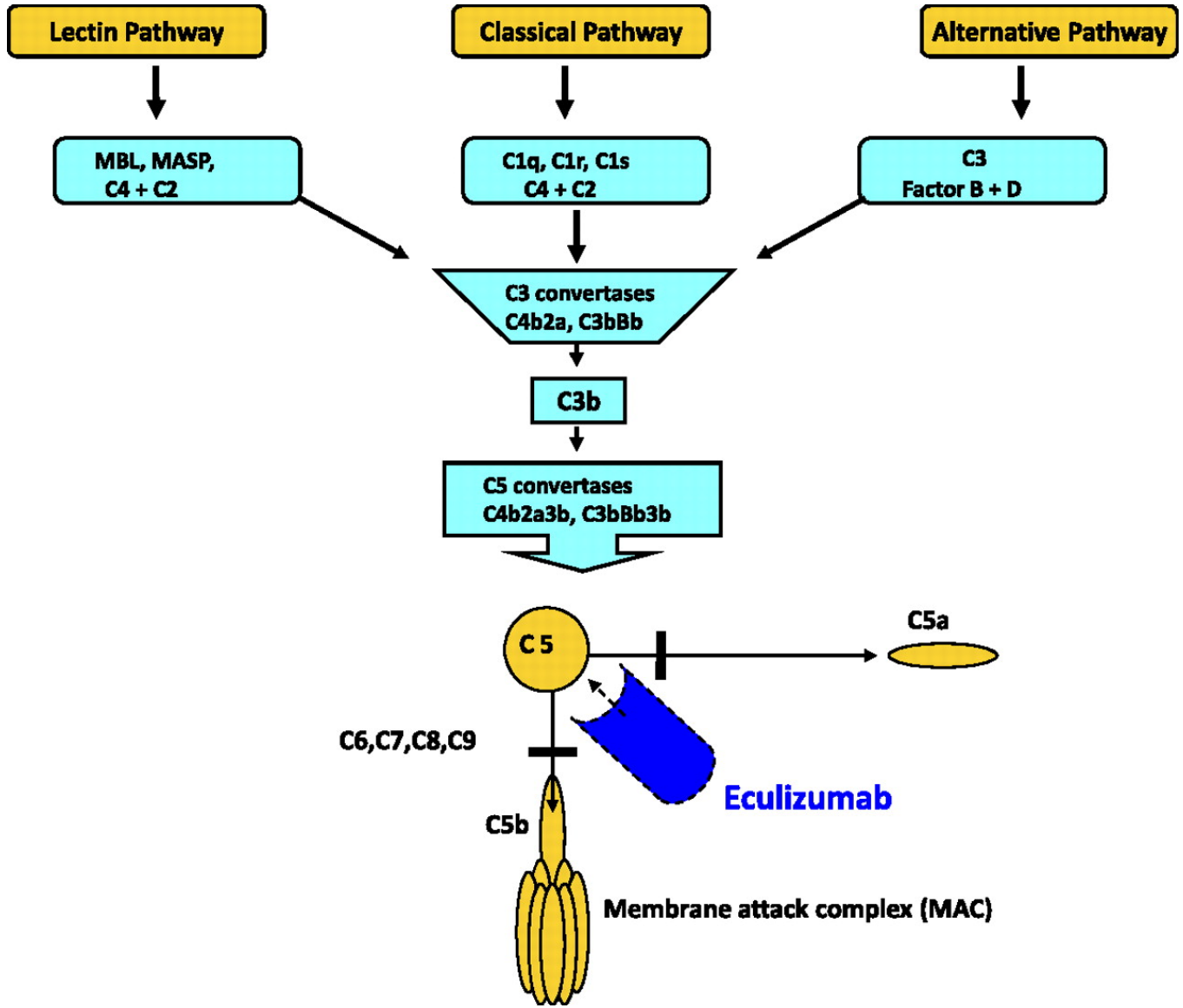
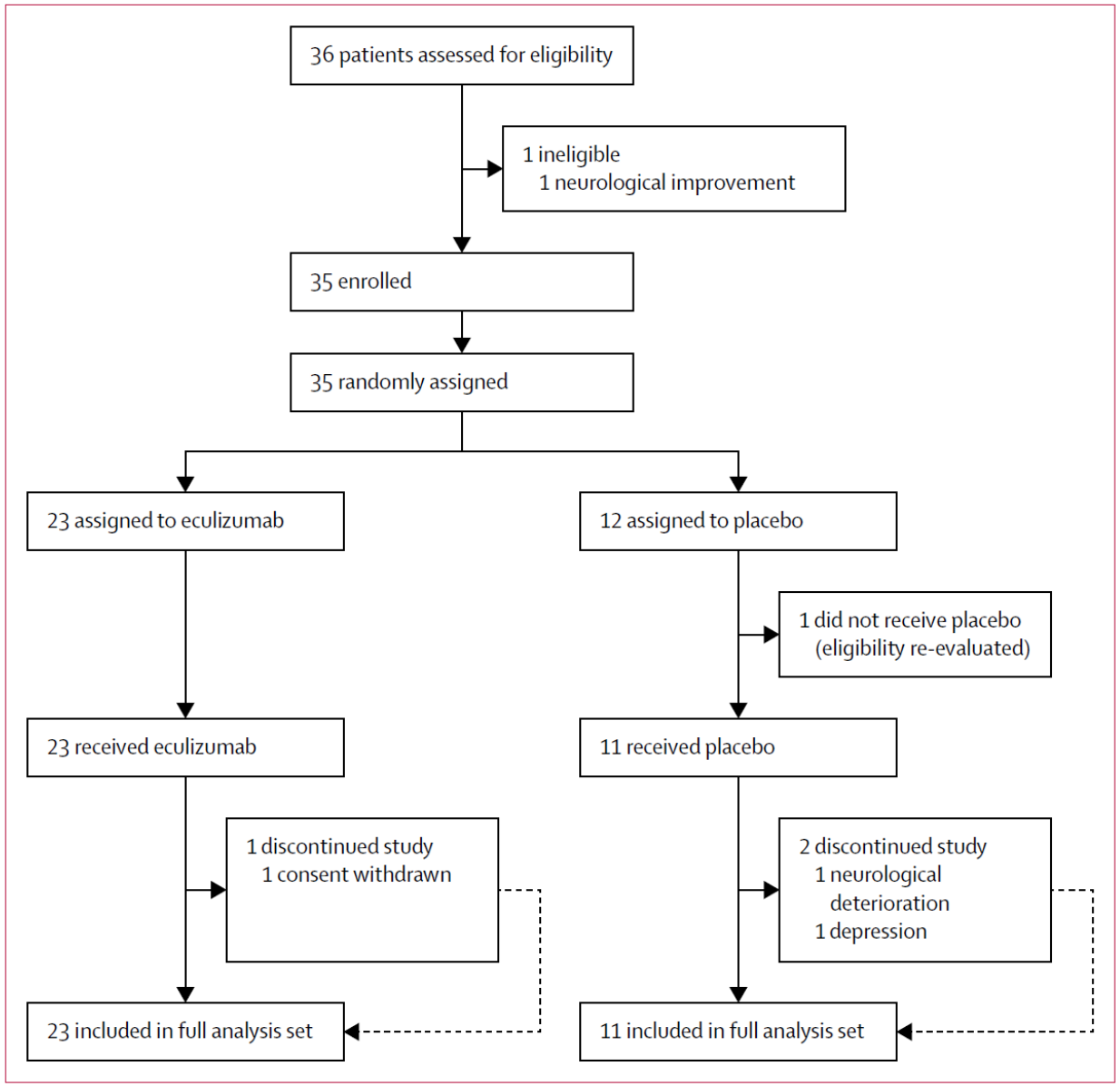

A
Motor neuron
Unidentified antigens
MAC
Macrophage
Axon
Axon
Myelin
Cross section
Antibody binding
Complement activation
Nerve injury
Macrophage scavenging
B
GM1, GD1a
MAC
Macrophage
Axon
Cross section
Myelin
Schwann-cell microvilli
Axon
Juxtaparanode
Paranode
Node
Kv
Caspr
Nav
Cytoskeleton
IgG anti-GM1 or anti-GD1a antibodies
C3
MAC


Lectin Pathway
Classical Pathway
Alternative Pathway
MBL, MASP,
C4 + C2
C1q, C1r, C1s
C4 + C2
C3
Factor B + D
C3 convertases
C4b2a, C3bBb
C3b
C5 convertases
C4b2a3b, C3bBb3b
C5
C5a
C6,C7,C8,C9
Eculizumab
C5b
Membrane attack complex (MAC)



Disease onset < 14 days
Patients unable to walk
Received IVIG

	Eculizumab (n=23)	Placebo (n=11)	Between-group difference (95% CI)	p value
Primary outcome				
Able to walk 5 m independently (functional grade ≤2)				
Week 4, % (90% CI)	61% (42 to 78)	45% (20 to 73)	15% (−20 to 51)	..
Number of patients	14/23	5/11	..	..
Secondary outcomes				
Improvement by one functional grade*†				
Week 4, % (95% CI)	66% (39 to 86)	61% (27 to 87)	5% (−31 to 40)	0·801
Patients with data	22	11	..	..
Week 24, % (95% CI)	95% (70 to 99)	91% (45 to 99)	4% (−17 to 24)	0·710
Patients with data	22	9	..	..
Able to walk 5 m independently (functional grade ≤2), sensitivity analysis*†				
Week 4, % (95% CI)	65% (37 to 85)	45% (16 to 79)	20% (−19 to 58)	0·325
Patients with data	22	11	..	..
Week 24, % (95% CI)	92% (67 to 98)	72% (32 to 93)	20% (−14 to 54)	0·187
Patients with data	22	9	..	..
Time to improvement by one functional grade (days)				
Median (95% CI)	19·0 (9·0 to 35·0)	22·0 (7·0 to 59·0)	−3·0‡	0·542
Patients with data	23	11	..	..
Able to run (functional grade ≤1)§				
Week 24, % (95% CI)	74% (52 to 90)	18% (2 to 52)	56% (27 to 85)	0·004
Number of patients	17/23	2/11	..	..

NEUROMUSCULAR ELECTRICAL STIMULATION IN EARLY REHABILITATION OF GUILLAIN-BARRÉ SYNDROME: A PILOT STUDY

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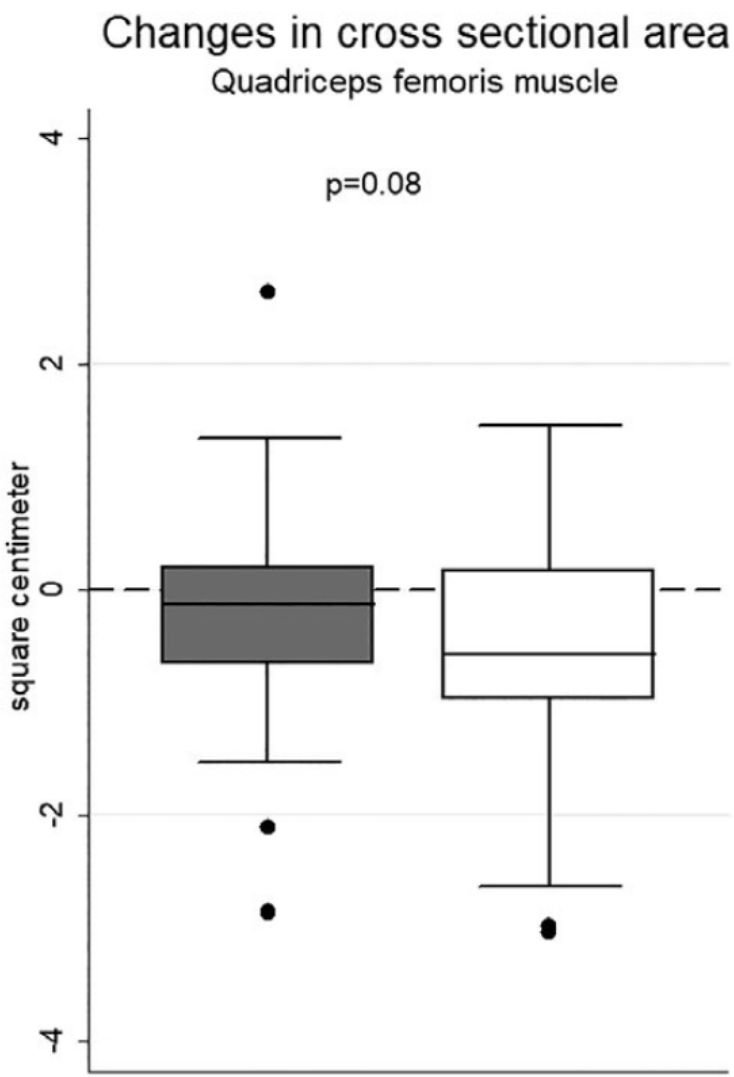
ABSTRACT: *Introduction*: In Guillain-Barré syndrome (GBS), patients often develop muscle atrophy from denervation and immobilization. We, therefore, conducted a pilot study of neuromuscular electrical stimulation (NMES) to evaluate feasibility, safety, and effect on muscle wasting in the early phase of GBS. *Methods*: Seventeen patients were randomized to receive 20 min of muscle fiber stimulation followed by 40 min of NMES of the right or left quadriceps muscle with the untreated side as control. Cross-sectional area (CSA) of the muscle measured by ultrasound and isometric knee extensor strength were the primary and secondary outcome measures. *Results*: No treatment related adverse effects were recorded. Change in CSA was -0.25 cm^2 (confidence interval [CI], -0.93–0.42) on the stimulated side versus -0.60 cm^2 (CI, -1.32–0.11) on the nonstimulated side (P = 0.08). No effect was observed on muscle strength. *Conclusions*: NMES seems safe and feasible in the early phase of GBS. Further studies are needed to explore effect on muscle function.

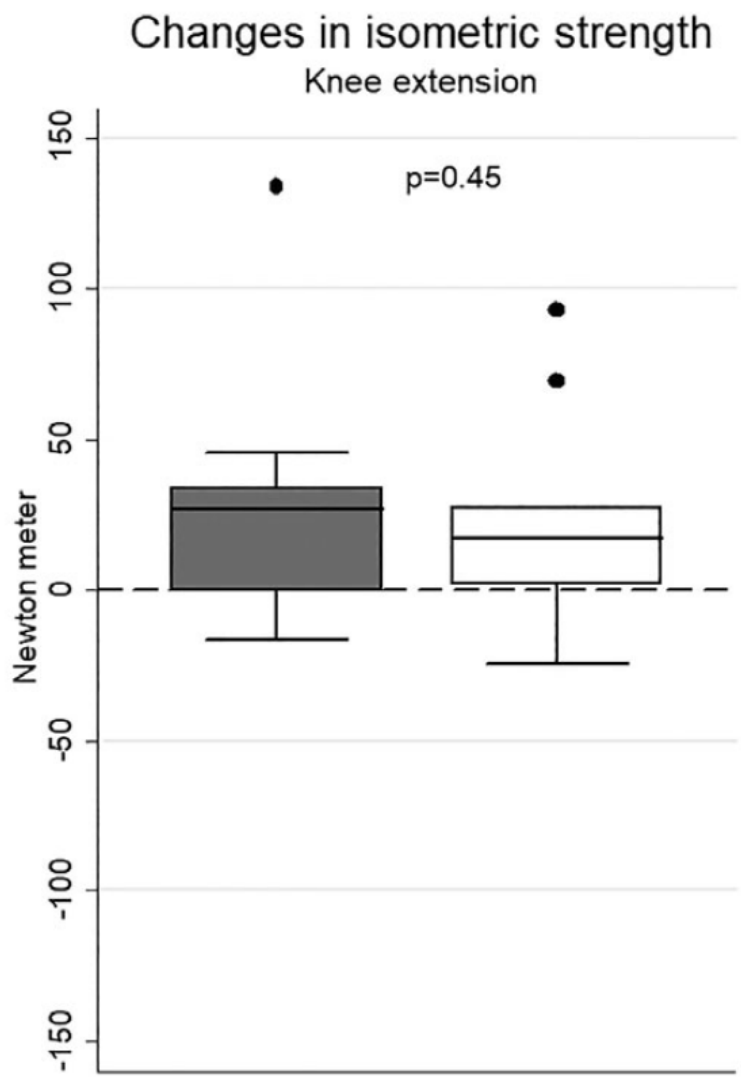
Muscle Nerve **59**:481–484, 2019

Guillain-Barré syndrome (GBS) is an acute polyradiculoneuropathy with subacute progressive muscle weakness, sensory symptoms, and pain.[1] GBS is a heterogeneous disorder ranging from mild impairment with fast recovery to complete paralysis including severe respiratory or autonomic failure. Recovery may take months to years and may be incomplete resulting in chronic disability.[2] Treatment with intravenous immunoglobulin (IVIg) or plasma exchange (PE) reduces the time to regain independent mobility.[3,4] Multidisciplinary rehabilitation is recommended as well[5] but in the acute phase may be challenging because of limited patient participation due to profound weakness.

Stiwell Med4

- 17 patients with GBS
- Direct muscle fiber stimulation and neuromuscular electrical stimulation initiated as soon as possible (maximal 2 weeks after onset of symptoms) and continued until discharge.
- 20 minutes of MFS and 40 min of NMES were applied every weekday.
- The stimulation intensity was titrated individually the point of maximal contraction or the highest tolerable intensity.
- Average duration ~1 month (range 10-95 days)


Changes in cross sectional area
Quadriceps femoris muscle
p=0.08
square centimeter
4
2
0
-2
-4


Changes in isometric strength
Knee extension
p=0.45
Newton meter
150
100
50
0
-50
-100
-150


SYSTEM

STUDY PROTOCOL Open Access

Observer blind randomised controlled trial of a tailored home exercise programme versus usual care in people with stable inflammatory immune mediated neuropathy

Claire M. White[1*], Robert D. Hadden[2], Sarah F. Robert-Lewis[1], Paul R. McCrone[3] and Jane L. Petty[1]

Abstract

Background: Inflammatory neuropathies such as Guillain-Barré syndrome, chronic inflammatory demyelinating polyradiculoneuropathy and paraproteinaemic demyelinating neuropathy are a heterogenous group of peripheral nerve disorders that affect around one to two people per 100,000. Whilst treatments such as intravenous immunoglobulin, plasma exchange and corticosteroids have generally positive results, long-term residual symptoms and associated activity limitations are common.

There is currently no standardised care for patients with ongoing activity limitation and participation restriction as a result of inflammatory neuropathy IN but data from observational studies and a randomised controlled trial suggest that exercise either alone or as part of a multidisciplinary rehabilitation programme may be beneficial in improving activity limitation. Tailoring the intervention for participants following physiotherapy assessment and incorporating patient preference for type and location of exercise may be important.

Methods/Design: The current study is a pragmatic, prospective, parallel observer-blind, randomised controlled trial to evaluate the efficacy and cost-effectiveness of a twelve week tailored home exercise programme versus advice and usual care. Seventy adults with stable immune mediated inflammatory neuropathy IN will be recruited to the study from two main sources: patients attending selected specialist peripheral nerve clinics in the South East and West Midlands of England and people with who access the GAIN charity website or newsletter. Participants will be randomised to receive either advice about exercise and usual care or a 12 week tailored home exercise programme. The primary outcome of activity limitation and secondary outcomes of fatigue, quality of life, self-efficacy, illness beliefs, mood and physical activity will be assessed via self-report questionnaire at baseline, 12 weeks and 12 months post intervention. Cost effectiveness and cost utility will be assessed via interview at baseline and 12 months post intervention.

Intention to treat analysis will be our primary model for efficacy analysis. Semi-structured interviews will be conducted with a selected sample of participants in order to explore the acceptability of the intervention and factors affecting adherence to the exercise programme.

Discussion: This is the first randomised controlled trial to compare the efficacy and cost-effectiveness of tailored home exercise with advice about exercise and usual care for adults with inflammatory neuropathy.

Trial registration: Current Controlled Trials ISRCTN13311697

Keywords: Inflammatory neuropathy, Activity limitation, Home exercise, Observer blind randomised controlled trial

Exercise Study Criteria

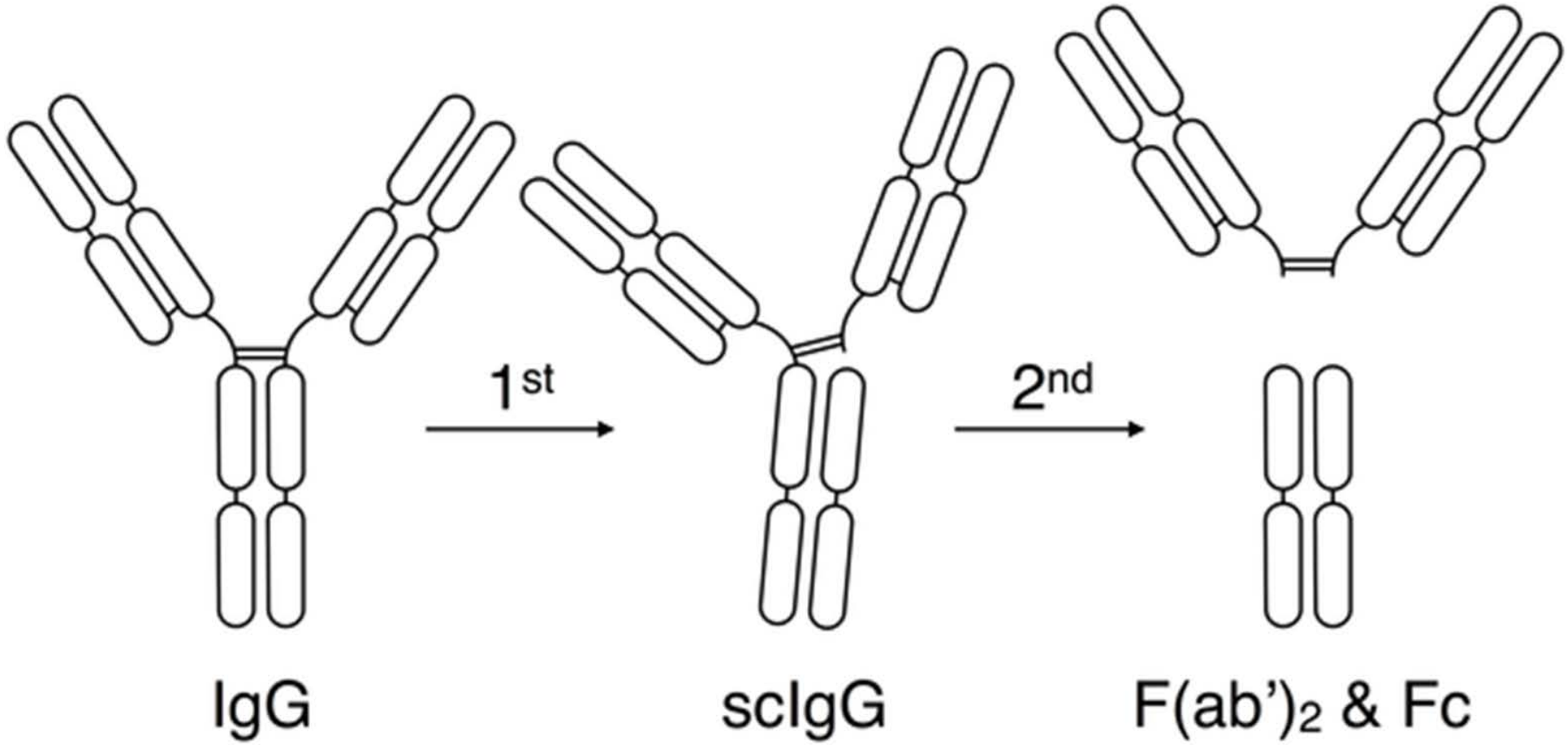
- Adults with stable weakness as a result of GBS or CIDP.
- They are able to walk 10 m, with or without walking aids.
- They are at least one year since onset if they have GBS.
- They are stable and on stable dosing of medications for CIDP.
- No PT in last 6 months.

Exercise Study Interventions

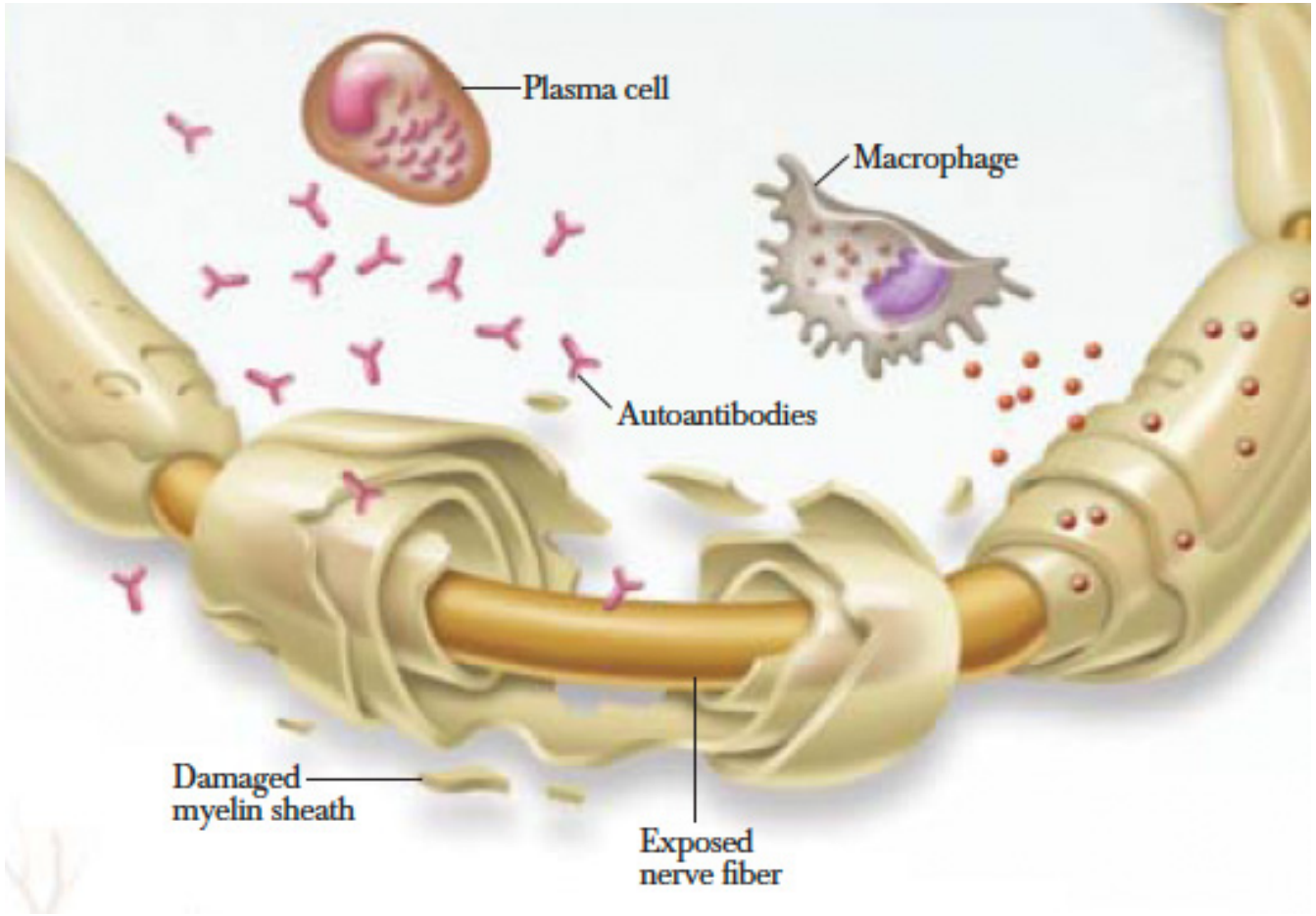
- PT program consisting of aerobic training and stamina building.

Imlifidase

- Enzyme from bacteria Streptococcus pyogenes that cleaves immunoglobulin G (IgG).
- Can inactivate human IgG antibodies.
- Clinically tested regarding efficacy and safety.
- Initial clinical studies focused on desensitization of HLA-immunized patients before kidney transplantation and treatment of antibody mediated graft rejection.


1st
2nd
IgG
scIgG
F(ab')2 & Fc

CIDP


Plasma cell
Macrophage
Autoantibodies
Damaged
myelin sheath
Exposed
nerve fiber

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journal homepage: www.elsevier.com/locate/jns

Current practice patterns in CIDP: A cross-sectional survey of neurologists in the United States

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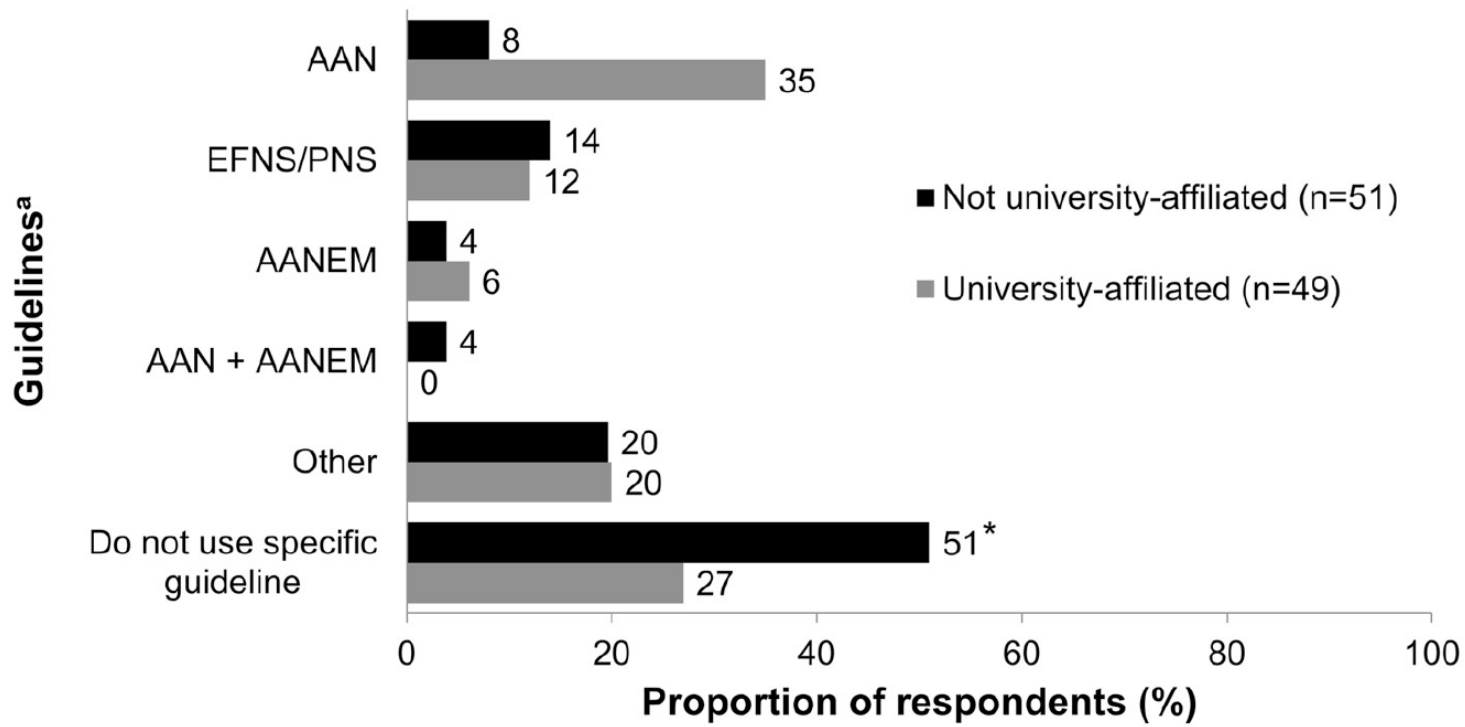
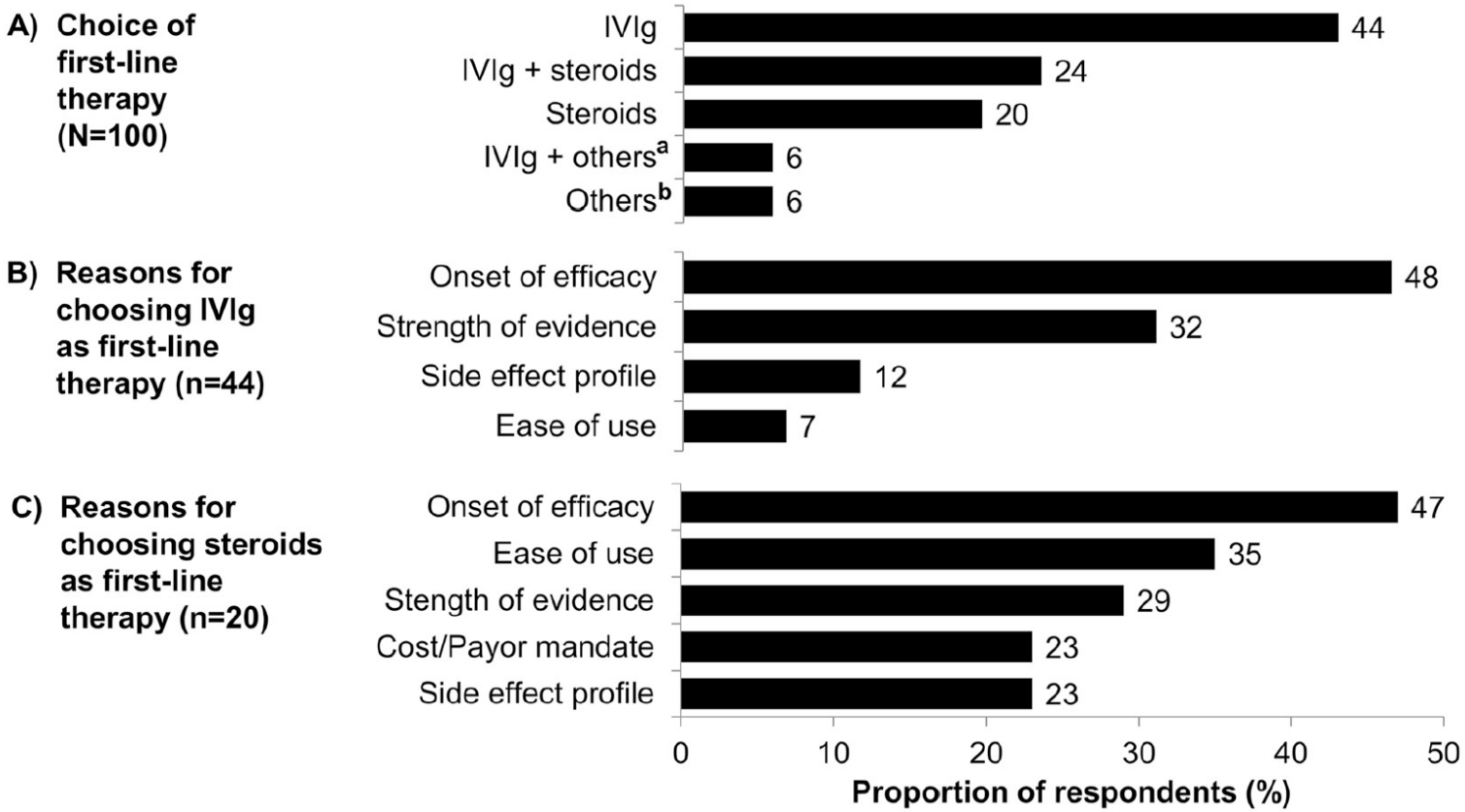
[b] California Pacific Medical Center, 2324 Sacramento Street, Suite 111, San Francisco, CA 94115, USA
[c] One Research, LLC, 1150 Hungry Neck Blvd. Suite C-303, Mt. Pleasant, SC 29464, USA
[d] Louisiana State University Health Sciences Center, School of Medicine, 1542 Tulane Avenue, Rm 721, New Orleans, LA 70112, USA


Washington
n=3
Oregon
n=2
California
n=14
Nevada
n=1
Arizona
n=2
Texas
n=4
Kansas
n=1
Nebraska
n=1
Minnesota
n=1
Missouri
n=5
Illinois
n=2
Wisconsin
n=4
Michigan
n=3
Ohio
n=4
Kentucky
n=1
Tennessee
n=5
Mississippi
n=1
Louisiana
n=2
Alabama
n=2
Georgia
n=1
Florida
n=10
North Carolina
n=5
WV
n=1
Virginia
n=1
Pennsylvania
n=5
New
York
n=10
Connecticut
n=1
New Jersey
n=4
Delaware
n=1
Maryland
n=2

Findings

- Cross-sectional survey of 100 community neurologists in the US.
- Only 13% cited using the European Federation of Neurological Societies/Peripheral Nerve Society guideline.
- Variability in treatment approaches existed regarding:
  - the dose of IVIg used
  - the length of IVIg therapy before determining response
  - the outcome measures used to determine IVIg response
  - the protocol for weaning off therapy


Guidelines[a]
AAN
EFNS/PNS
AANEM
AAN + AANEM
Other
Do not use specific guideline
8
35
14
12
4
6
4
0
20
20
51*
27
Not university-affiliated (n=51)
University-affiliated (n=49)
0
20
40
60
80
100
Proportion of respondents (%)


A) Choice of first-line therapy (N=100)
IVIg
IVIg + steroids
Steroids
IVIg + others[a]
Others[b]
44
24
20
6
6
B) Reasons for choosing IVIg as first-line therapy (n=44)
Onset of efficacy
Strength of evidence
Side effect profile
Ease of use
48
32
12
7
C) Reasons for choosing steroids as first-line therapy (n=20)
Onset of efficacy
Ease of use
Stength of evidence
Cost/Payor mandate
Side effect profile
47
35
29
23
23
0
10
20
30
40
50
Proportion of respondents (%)

IVIG Treatment

- For initial IVIg treatment, only 55% declared using the recommended loading dose of 2.0 g/kg.
- 39% reported using a loading dose of 0.3 - 0.6 g/kg every 2–4 weeks, which is more commonly used in immune globulin replacement.
- About 40% reported treating their patients for at least 3 months before determining treatment response.
- 25% reported giving IVIg for 6 months.
- A small minority (5%) said that they give IVIg for ≥12 months before assessing initial response.

CIDP Survey

- Implications for you?

Journal of Neurology (2019) 266:468–475
https://doi.org/10.1007/s00415-018-9158-3

ORIGINAL COMMUNICATION

Nerve echogenicity and intranerve CSA variability in high-resolution nerve ultrasound (HRUS) in chronic inflammatory demyelinating polyneuropathy (CIDP)

Anna Lena Fisse[1] · Kalliopi Pitarokoili[1] · Jeremias Motte[1] · Donata Gamber[1] · Antonios Kerasnoudis[1] · Ralf Gold[1] · Min-Suk Yoon[2]

Received: 5 November 2018 / Revised: 9 December 2018 / Accepted: 12 December 2018 / Published online: 15 December 2018

Abstract

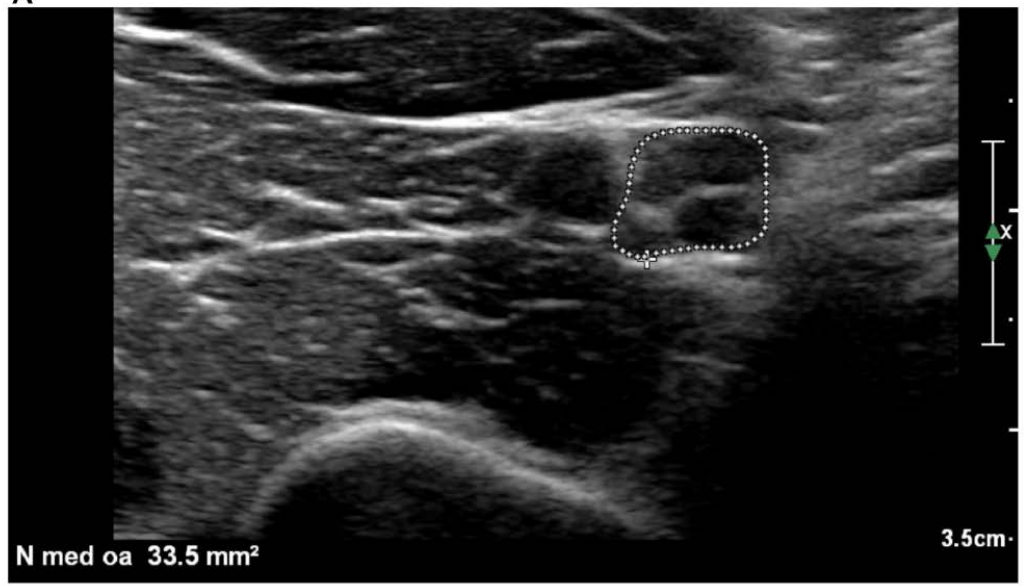
Objective HRUS is increasingly being used in the diagnosis and evaluation of autoimmune neuropathies such as CIDP. Recently, studies focused not only on changes of nerves size, but also the fascicular structure and the echogenicity changes in CIDP. However, little is known about the alterations of echogenicity in the long-term course in CIDP. The aim of this study was to evaluate echogenicity in CIDP patients in a long-term follow-up period and to analyze the benefit of the evaluation of echogenicity compared to nerve size.

Methods 20 patients fulfilling the definite diagnostic criteria of CIDP received clinical examination, nerve conduction studies and HRUS every 6 months over a median follow-up time of 34 months. Patients were divided into clinically stable/regressive disease course or progressive disease course according to the development of the inflammatory neuropathy cause and treatment overall disability sum score. Echogenicity of peripheral nerves was measured semi-automated and quantitative. Echogenicity was divided into three classes by fraction of black: hypoechogenic, mixed hypo-/hyperechogenic, hyperechogenic.

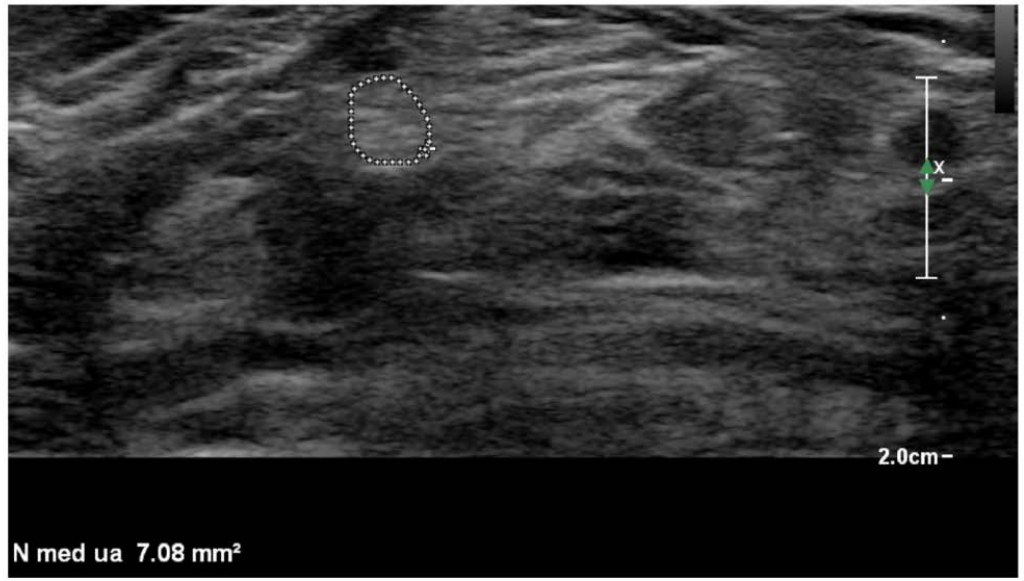
Results Patients with hyperechogenic arm nerves more frequently show clinical worsening, whereas patients with hypoechogenic arm nerves remain stable or even improved over time. In the long-term course of the disease, echogenicity mostly did not change, and if changes occured echogenicity did not correspond to ODSS changes.

Conclusion Echogenicity of the arm nerves in CIDP may be used as a prognostic marker, but not as a follow-up tool for evaluating clinical changes. Further studies in a larger cohort are needed to confirm these results.

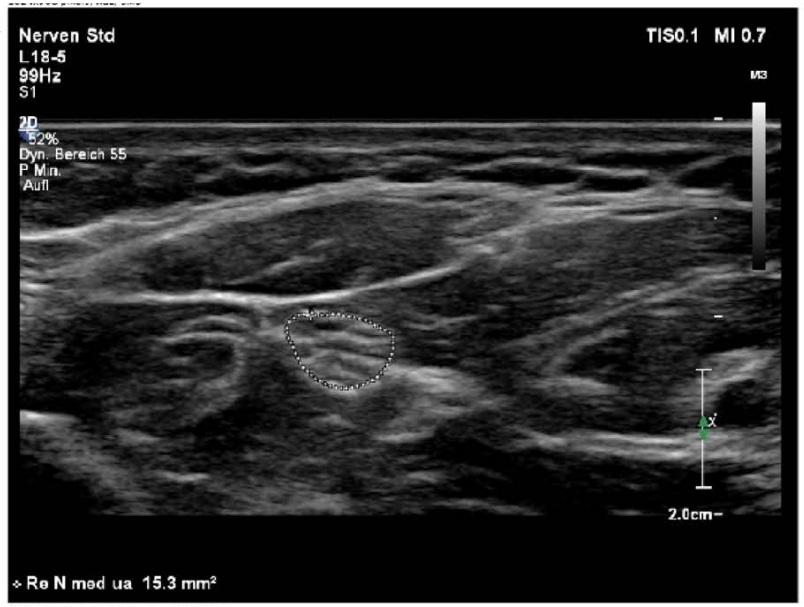
A



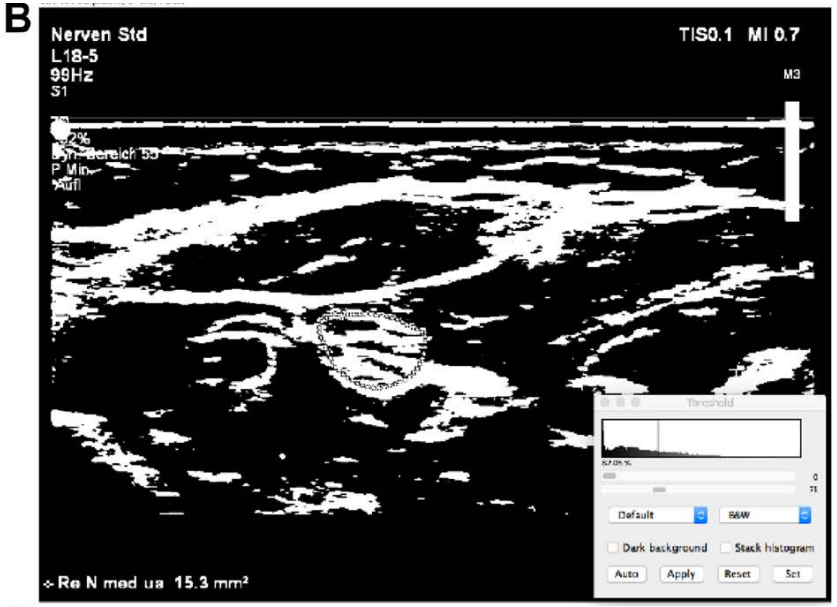
B



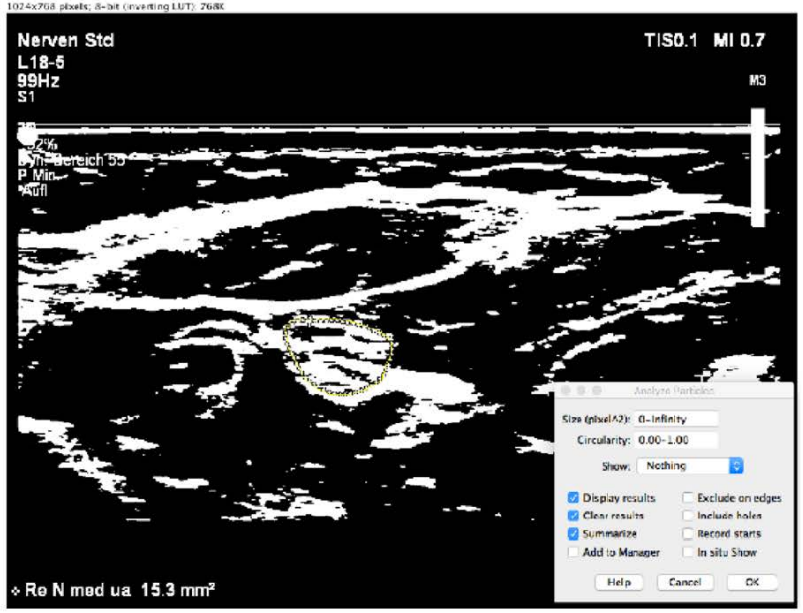
A



B



C



D

Summary

	Count	Total Area	Average Size	%Area	Mean
[redacted].jpg	70	3407	48.671	32.994	255

Echogenicity

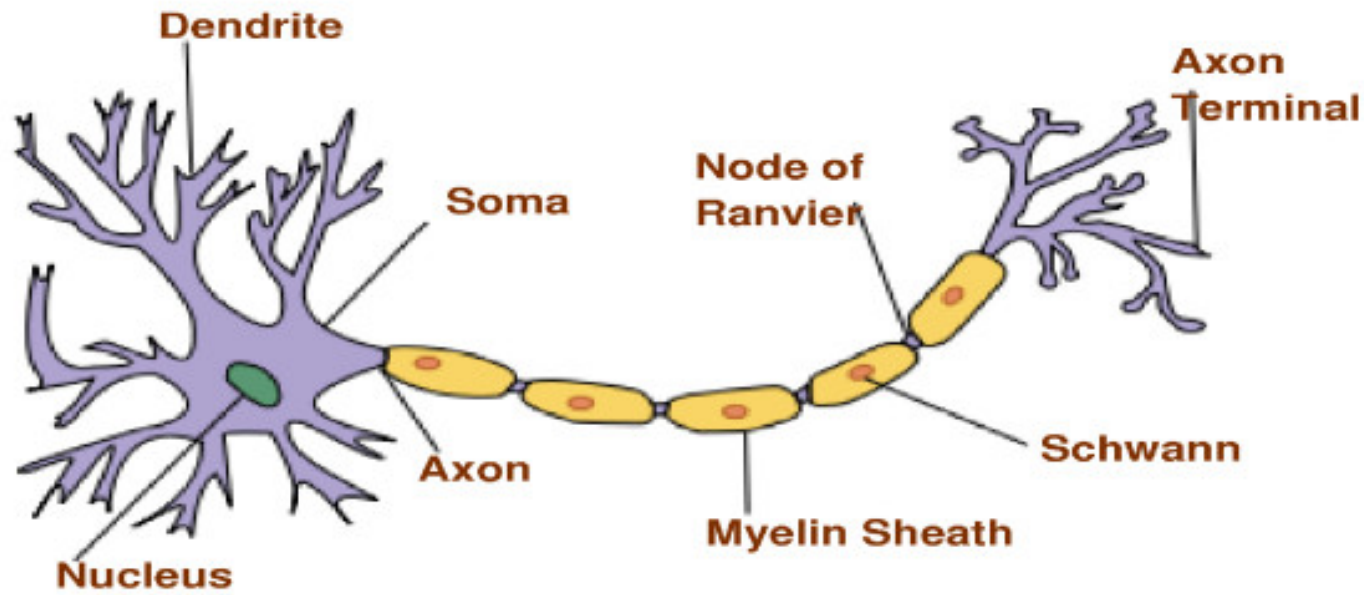
- hypoechogenic (fraction of black > 67%)
- hyperechogenic (fraction of black < 33%)

Findings

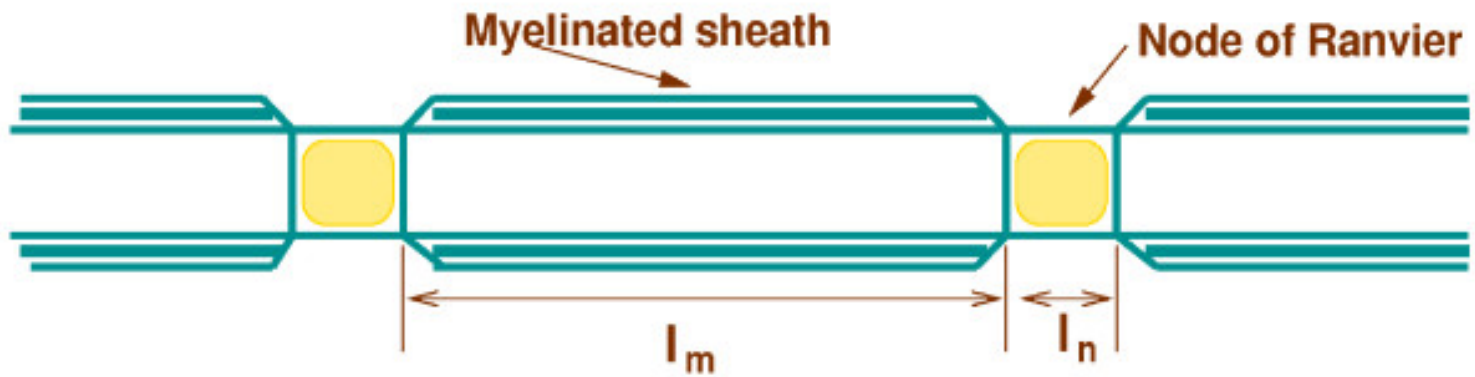
- 20 CIDP patients
- Patients with hyperechogenic arm nerves more frequently showed clinical worsening
- Patients with hypoechogenic arm nerves remained stable or even improved over time
- In the long-term course of the disease, echogenicity mostly did not change, and if changes occured echogenicity did not correspond to clinical measures
- Role for nerve ultrasound in prognosis

Nodopathies

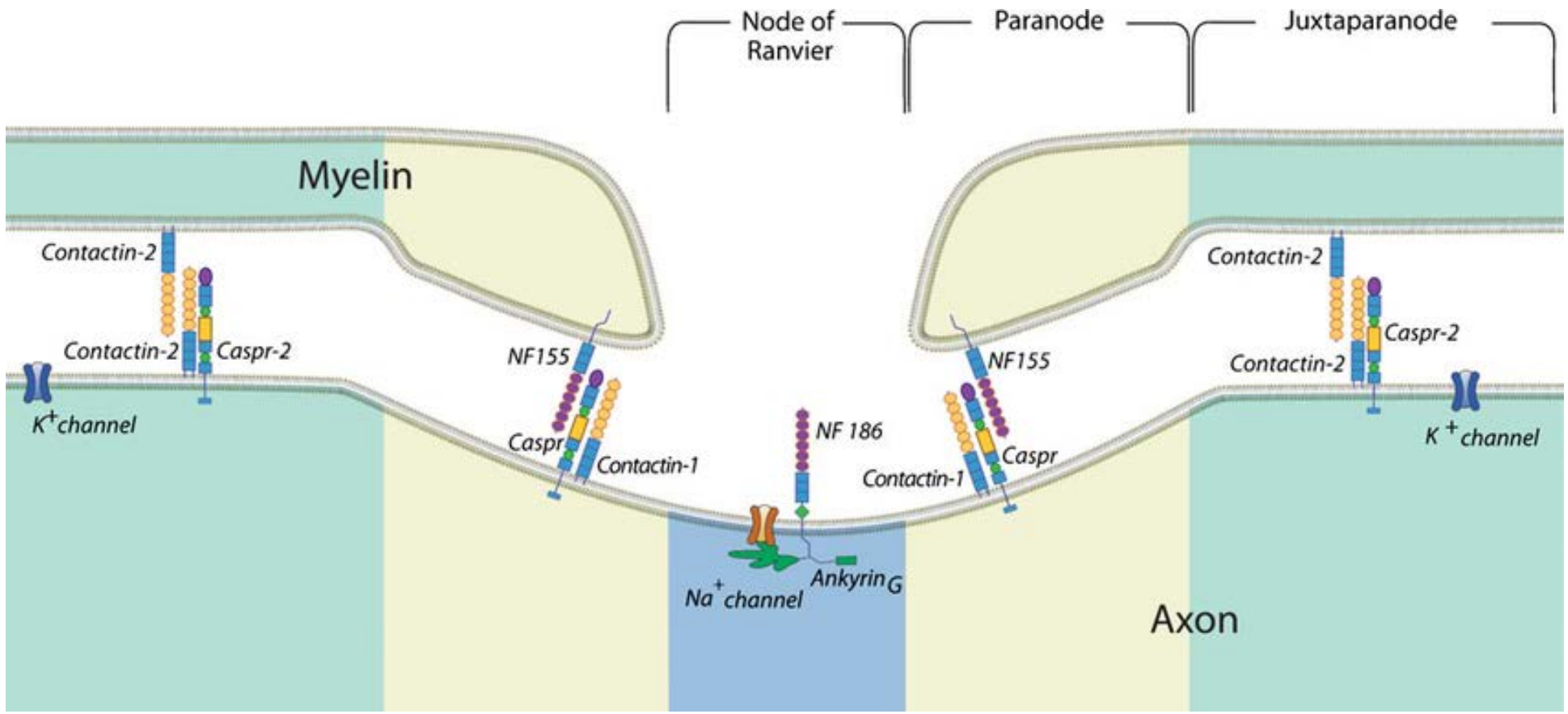
- In recent years, awareness that a small percentage of CIDP patients have distinct syndromes associated with specific antibodies, clinical features and poor response to standard treatments.
- Approximately 10% of CIDP patients.
- Antibodies are commercially available (but not easy to get)


Dendrite
Axon Terminal
Node of Ranvier
Soma
Axon
Schwann
Myelin Sheath
Nucleus

(a)


Myelinated sheath
Node of Ranvier
l_m
l_n

(b)

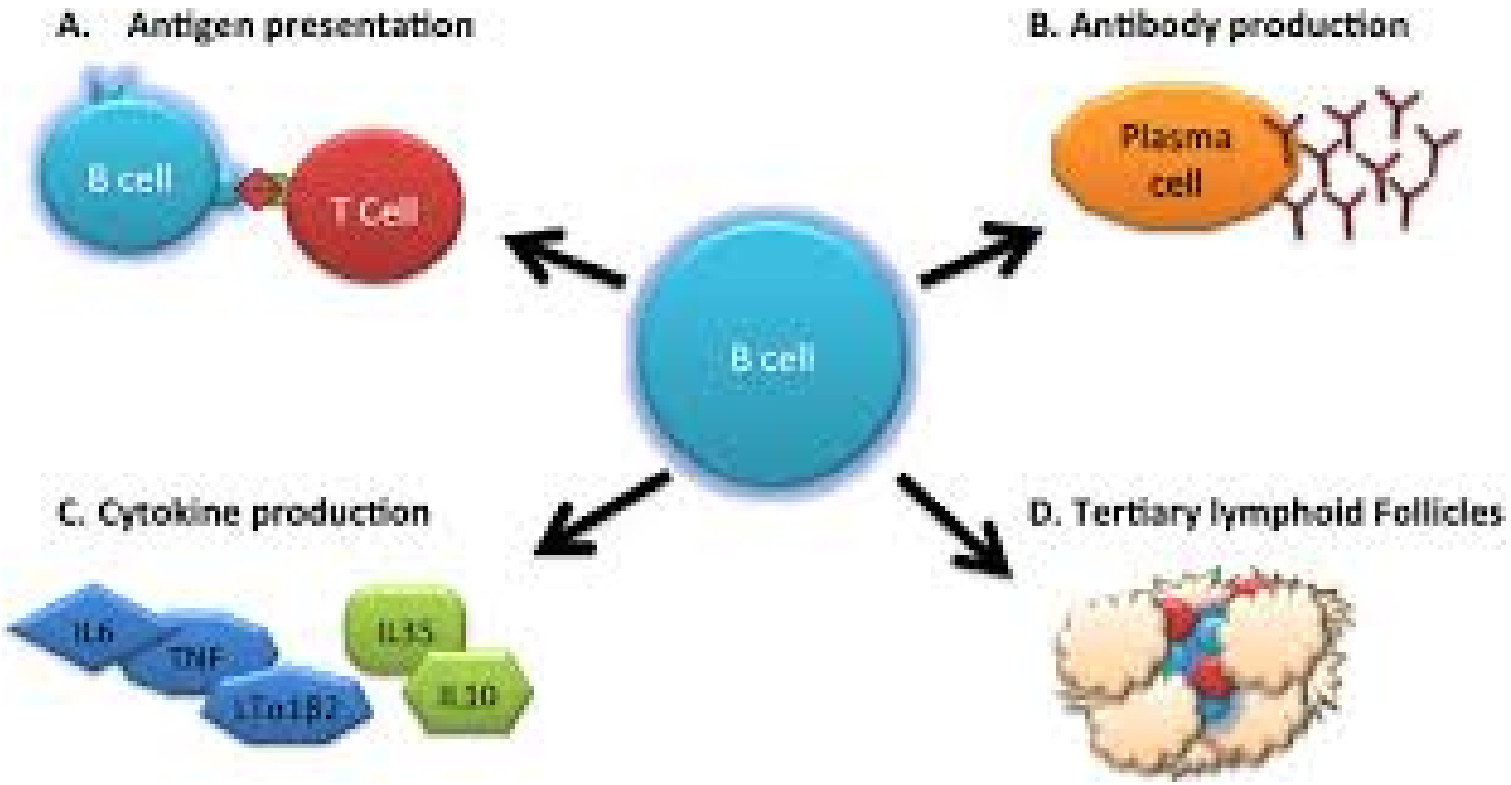

Node of Ranvier
Paranode
Juxtaparanode
Myelin
Contactin-2
Contactin-2
Caspr-2
K+channel
NF155
Caspr
Contactin-1
NF 186
Na+ channel
Ankyrin G
NF155
Contactin-1
Caspr
Contactin-2
Caspr-2
Contactin-2
K+channel
Axon

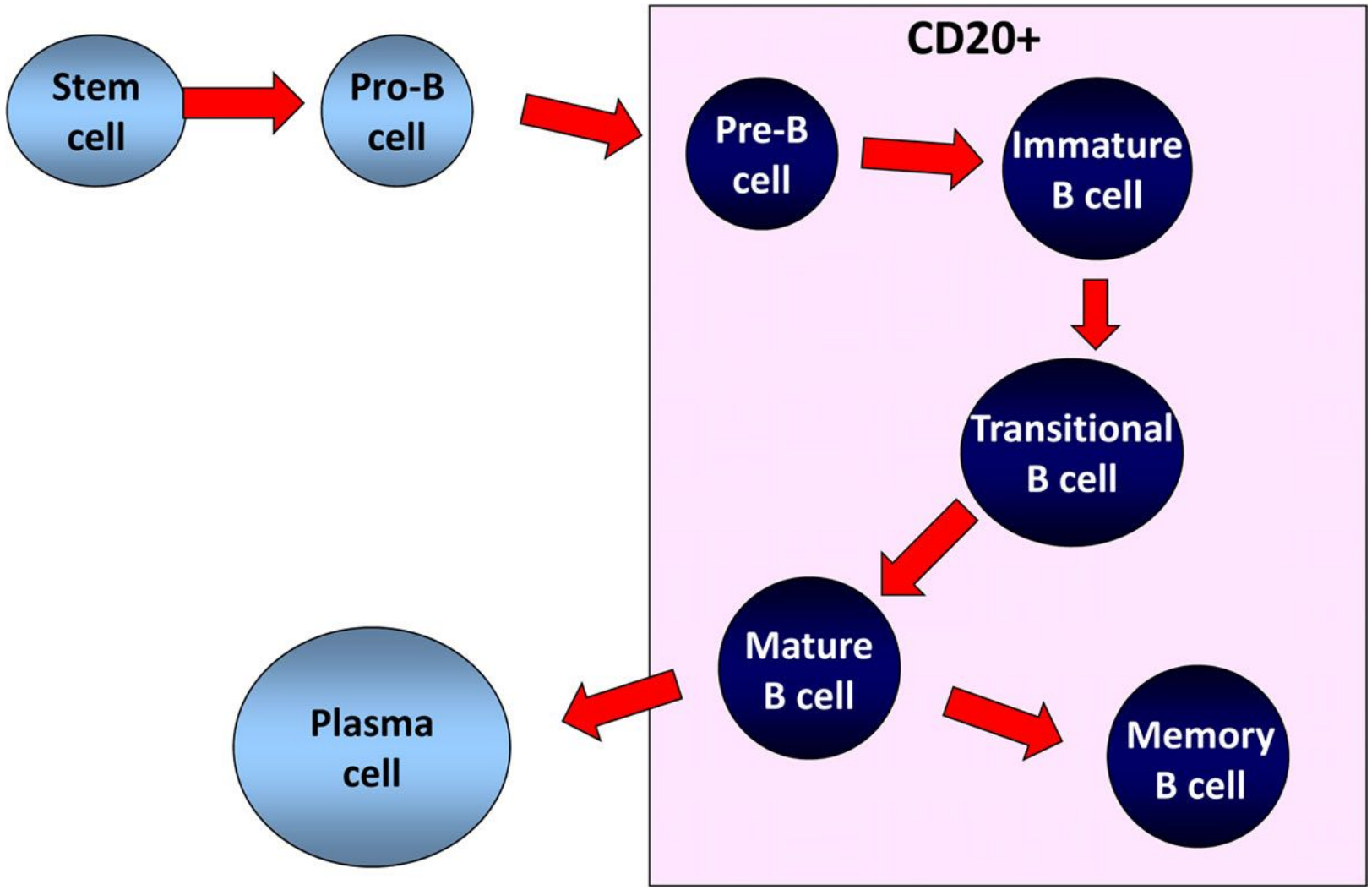
Neurofascin antibodies

- Younger age of onset
- Central nervous system involvement
- Enlarged nerves
- Distal weakness
- Tremor
- Poor response to IVIg and corticosteroids
- Responds to rituximab

Contactin antibodies

- Subacute: 8 to 12 weeks
- Weakness distal or diffuse
- Legs often > Arms
- May be mild or severe
- Sensory ataxia
- Progressive
- Treatment
  - Not often responsive to IVIg (<10%)
  - Prednisone (~75%)
  - Rituximab


A. Antigen presentation
B cell
T Cell
B. Antibody production
Plasma cell
B cell
C. Cytokine production
IL6
TNF
LTα1β2
IL35
IL10
D. Tertiary lymphoid Follicles


Stem cell
Pro-B cell
CD20+
Pre-B cell
Immature B cell
Transitional B cell
Mature B cell
Plasma cell
Memory B cell

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WILEY

RESEARCH REPORT

Rituximab in chronic inflammatory demyelinating polyradiculoneuropathy with associated diseases

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We aimed to analyse the response to rituximab in a cohort of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) patients with associated disorders. We conducted a clinical and electrophysiological retrospective monocentric study in 28 CIDP patients. Response to rituximab was defined as (a) a five-point increase in the Medical Research Council sum score or a one-point decrease in the Overall Neuropathy Limitations Scale score, compared to the score at the first rituximab infusion, or (b) the discontinuation of, or reduced need for, the last treatments before rituximab initiation. Twenty-one patients (75%) were responders to rituximab. The median time before response was 6 months (1-10 months). Only two patients needed to be treated again during a median follow-up of 2.0 years (0.75-9 years). Interestingly, the response rate was good in patients with associated autoimmune disease (5/8) and similar to the response rate observed in patients with a haematological disease (16/20) ($P = 0.63$). A shorter disease duration was associated with a better clinical response to rituximab (odds ratio 0.81, $P = 0.025$) and the response rate was better ($P = 0.05$) in common forms (83.3%) than in sensory forms (42.9%). No major adverse events were recorded. Rituximab is efficacious in CIDP patients with haematological or autoimmune disease. It improves clinical response and decreases dependence on first-line treatments.

KEYWORDS

CIDP, efficacy, rituximab, safety, treatment

Rituximab in CIDP with Associated Disorders

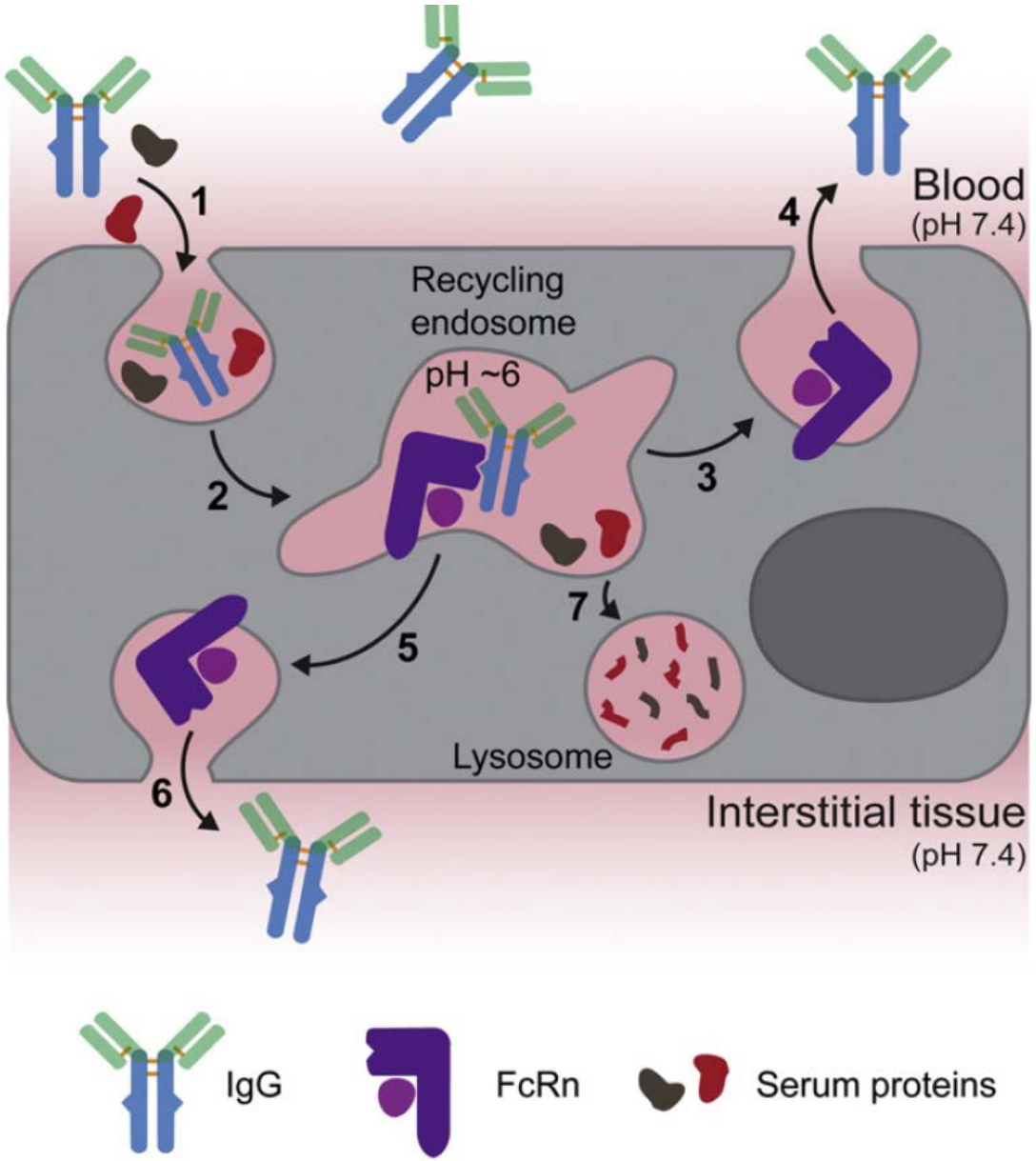
- 28 CIDP pts with associated autoimmune or hematological disorder
- 75% were responders to rituximab
- 48% reduced need for IVIg or corticosteroids

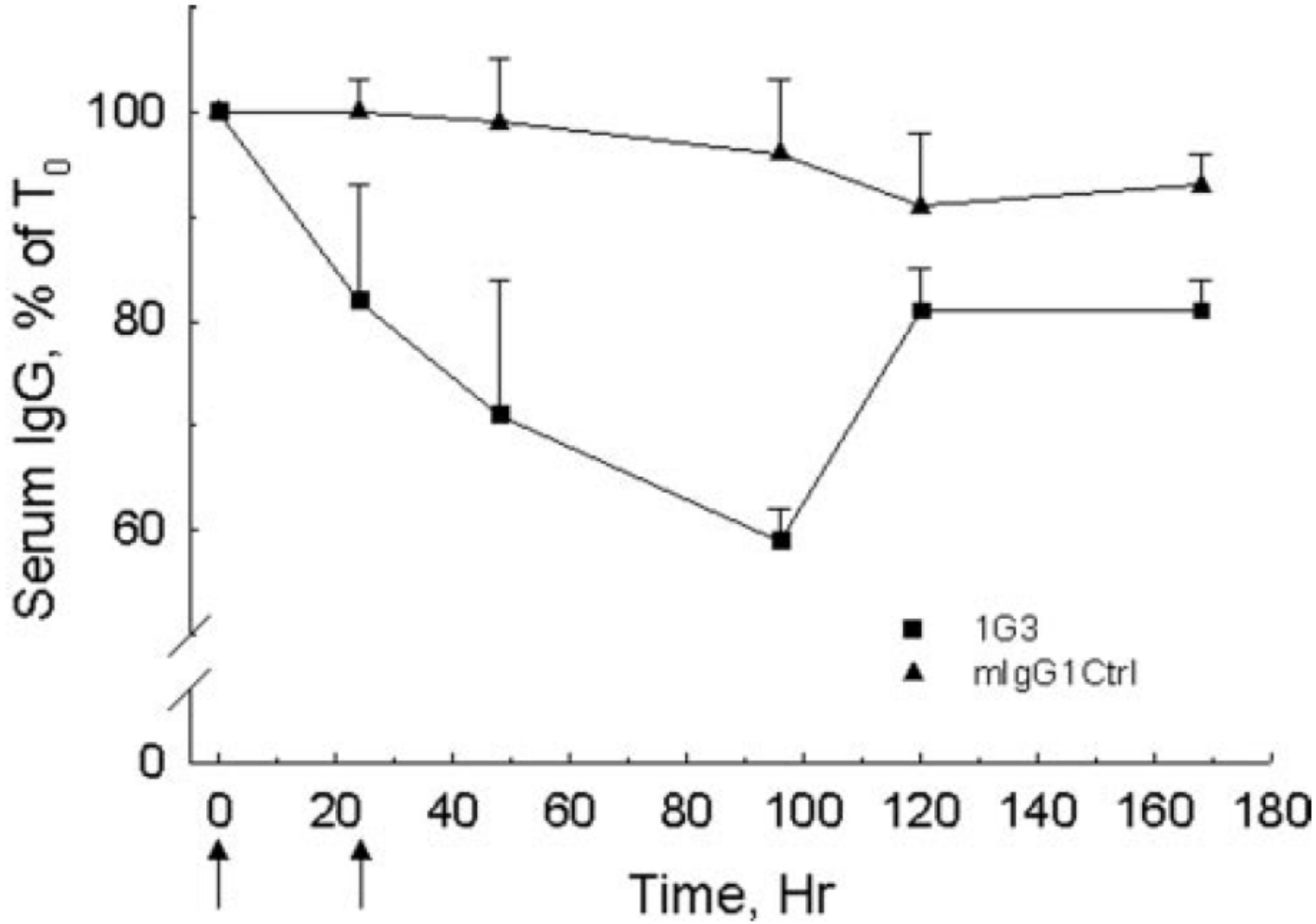
What is the Role of Rutuximab in “Regular” CIDP

- Unclear
- Currently the subject of an Italian study

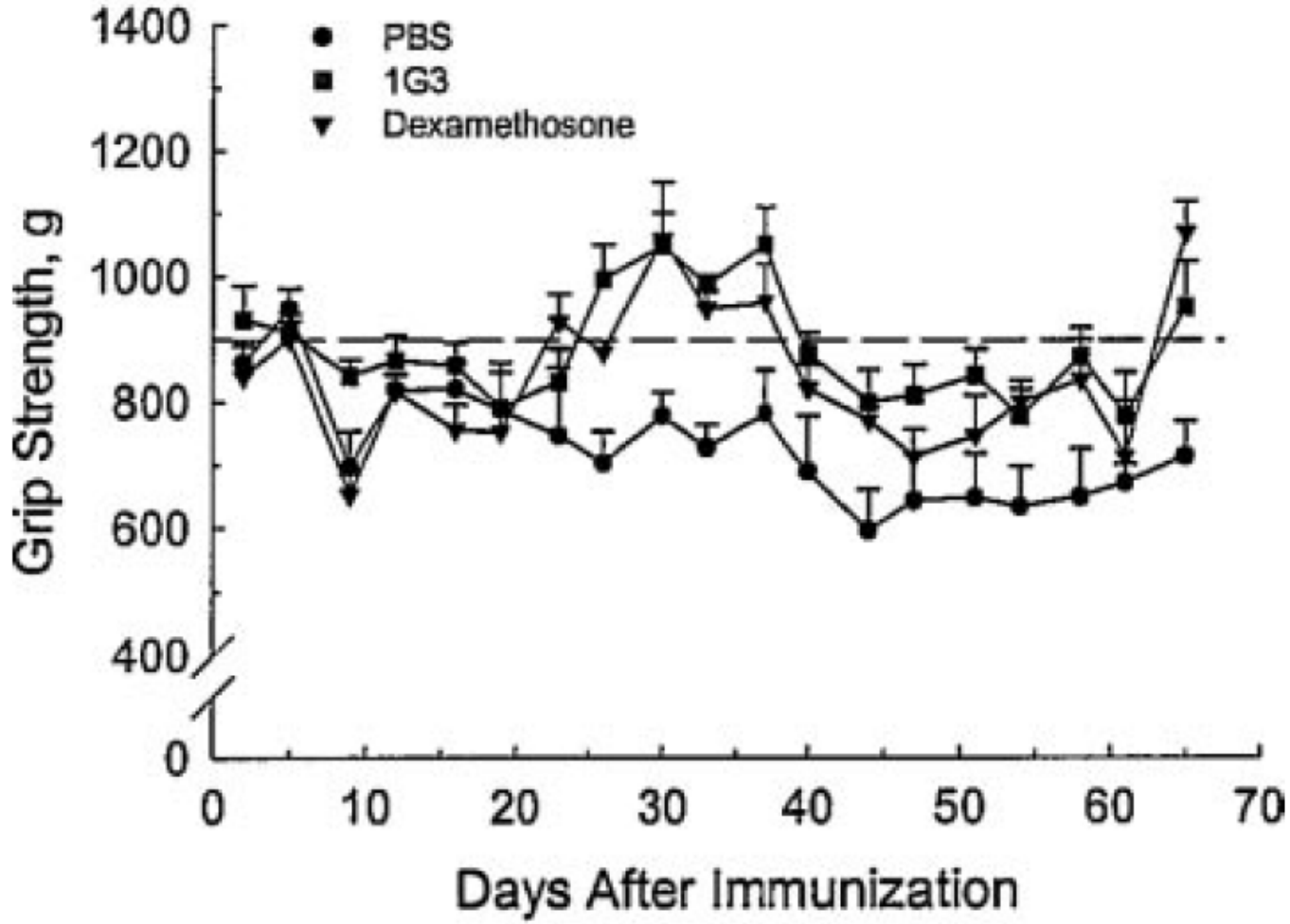
Manipulation of the Neonatal Fc Receptor

- Rozanolixizumab
- Efgartigimod


1
2
3
4
5
6
7
Blood
(pH 7.4)
Recycling
endosome
pH ~6
Lysosome
Interstitial tissue
(pH 7.4)
IgG
FcRn
Serum proteins


Serum IgG, % of T_0
100
80
60
0
0
20
40
60
80
100
120
140
160
180
Time, Hr
1G3
mIgG1Ctrl

B


PBS
1G3
Dexamethosone
Grip Strength, g
1400
1200
1000
800
600
400
0
0
10
20
30
40
50
60
70
Days After Immunization

Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (PATH): a randomised, double-blind, placebo-controlled, phase 3 trial

Ivo N van Schaik, Vera Bril, Nan van Geloven, Hans-Peter Hartung, Richard A Lewis, Gen Sobue, John-Philip Lawo, Michaela Praus, Orell Mielke, Billie L Dunn, David R Cornblath, Ingemar S J Merkies, on behalf of the PATH study group*

Summary

Background Approximately two-thirds of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) need long-term intravenous immunoglobulin. Subcutaneous immunoglobulin (SCIg) is an alternative option for immunoglobulin delivery, but has not previously been investigated in a large trial of CIDP. The PATH study compared relapse rates in patients given SCIg versus placebo.

Methods Between March 12, 2012, and Sept 20, 2016, we studied patients from 69 neuromuscular centres in North America, Europe, Israel, Australia, and Japan. Adults with definite or probable CIDP who responded to intravenous immunoglobulin treatment were eligible. We randomly allocated participants to 0·2 g/kg or 0·4 g/kg of a 20% SCIg solution (IgPro20) weekly versus placebo (2% human albumin solution) for maintenance treatment for 24 weeks. We did randomisation in a 1:1:1 ratio with an interactive voice and web response system with a block size of six, stratified by region (Japan or non-Japan). The primary outcome was the proportion of patients with a CIDP relapse or who were withdrawn for any other reason during 24 weeks of treatment. Patients, caregivers, and study personnel, including those assessing outcomes, were masked to treatment assignment. Analyses were done in the intention-to-treat and per-protocol sets. This trial is registered with ClinicalTrials.gov, number NCT01545076.

Findings In this randomised, double-blind, placebo-controlled trial, we randomly allocated 172 patients: 57 (33%) to the placebo group, 57 (33%) to the low-dose group, and 58 (34%) to the high-dose group. In the intention-to-treat set, 36 (63% [95% CI 50–74]) patients on placebo, 22 (39% [27–52]) on low-dose SCIg, and 19 (33% [22–46]) on high-dose SCIg had a relapse or were withdrawn from the study for other reasons (p=0·0007). Absolute risk reductions were 25% (95% CI 6–41) for low-dose versus placebo (p=0·007), 30% (12–46) for high-dose versus placebo (p=0·001), and 6% (–11 to 23) for high-dose versus low-dose (p=0·32). Causally related adverse events occurred in 47 (27%) patients (ten [18%] in the placebo group, 17 [30%] in the low-dose group, and 20 [34%] in the high-dose group). Six (3%) patients had 11 serious adverse events: one (2%) patient in the placebo group, three (5%) in the low-dose group, and two (3%) in the high-dose group; only one (an acute allergic skin reaction in the low-dose group) was assessed to be causally related.

Interpretation This study, which is to our knowledge, the largest trial of CIDP to date and the first to study two administrations of immunoglobulins and two doses, showed that both doses of SCIg IgPro20 were efficacious and well tolerated, suggesting that SCIg can be used as a maintenance treatment for CIDP.

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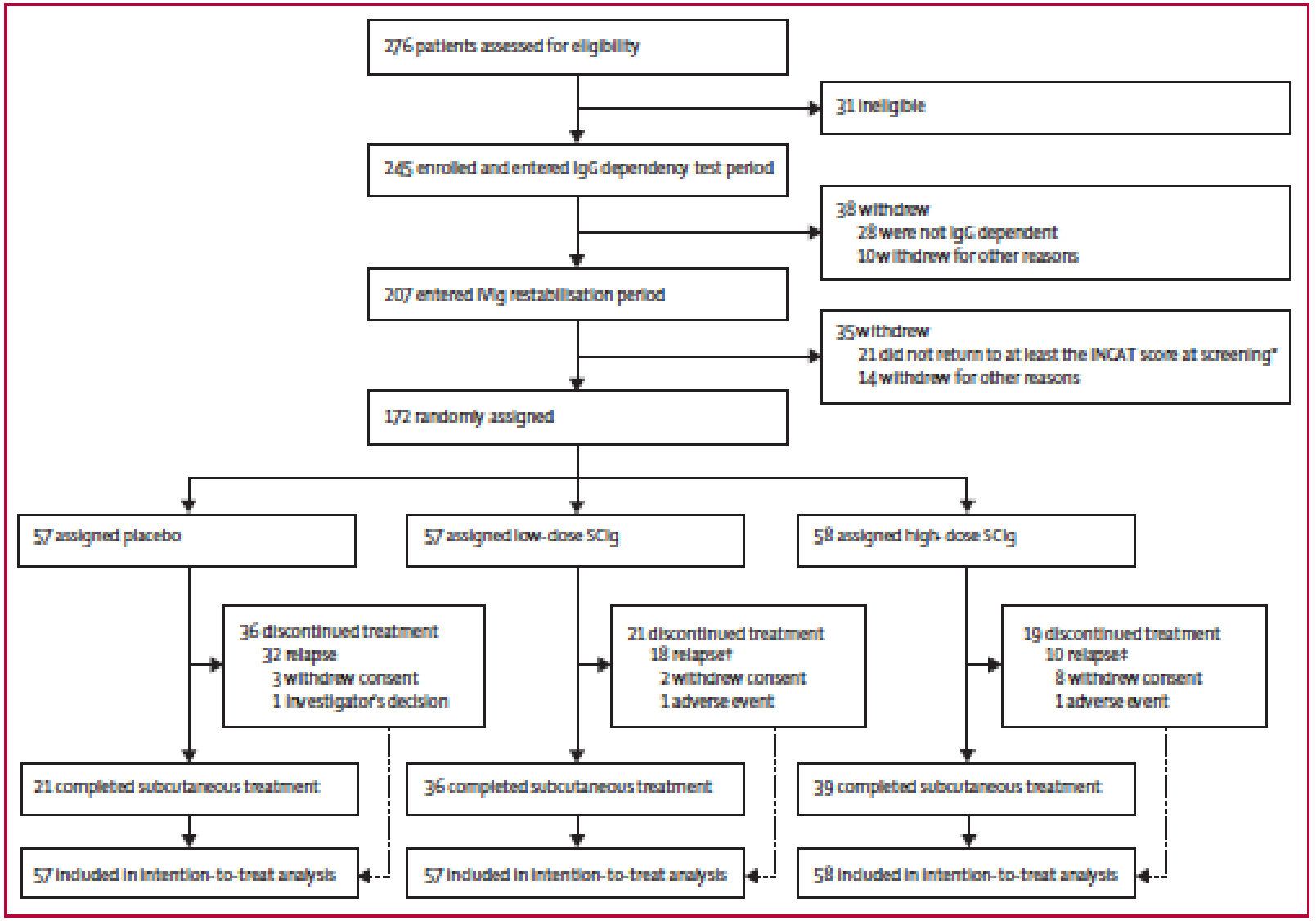

24 weeks of SCIG treatment

	Placebo	Low-dose SCIg 0.2 g/kg/wk	High-dose SCIg 0.4 g/kg/wk	Overall p value*
Primary outcome	63·2% (50·9–75·4)	39·0% (27·7–53·1)	33·7% (22·8–47·8)	0·0002
Relapse	58·8% (46·1–72·0)	35·0% (23·9–49·3);	22·4% (12·9–37·2)	<0·0001

Treatment Specifics

- Subjects performed treatments 2 days/week
- Subjects generally used 4 injection sites (max 9)
- Average treatment duration 1 hour

Other Details

- 90% of subjects rated the SCIG injection process as being easy to learn.
- 53% of subjects receiving SCIG preferred this treatment to IVIG, citing increased independence and less side effects.

SCIG: Remaining Questions

- What dose?
- How to start?
- Use as first-line treatment?