Efficacia, sicurezza e tollerabilità dei Mabs
CIDP

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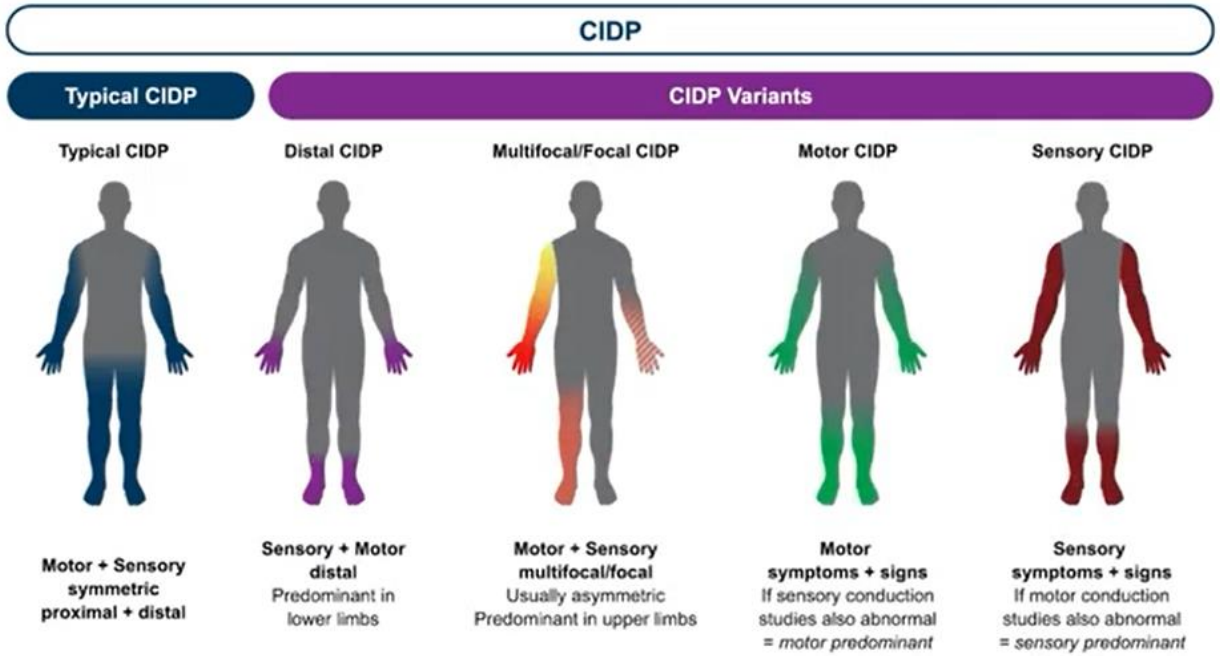
European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force—Second revision

…"the diagnosis of CIDP rests upon a combination of clinical, electrodiagnostic, and laboratory features with exclusions to eliminate other disorders that may mimic CIDP"

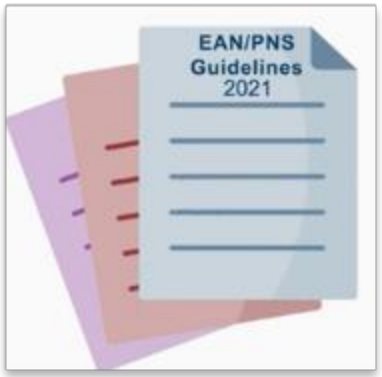


Typical CIDP

All the following:

- Progressive or relapsing, symmetric, proximal and distal muscle weakness of upper and lower limbs, and sensory involvement of at least two limbs
- Developing over at least 8 weeks
- Absent or reduced tendon reflexes in all limbs

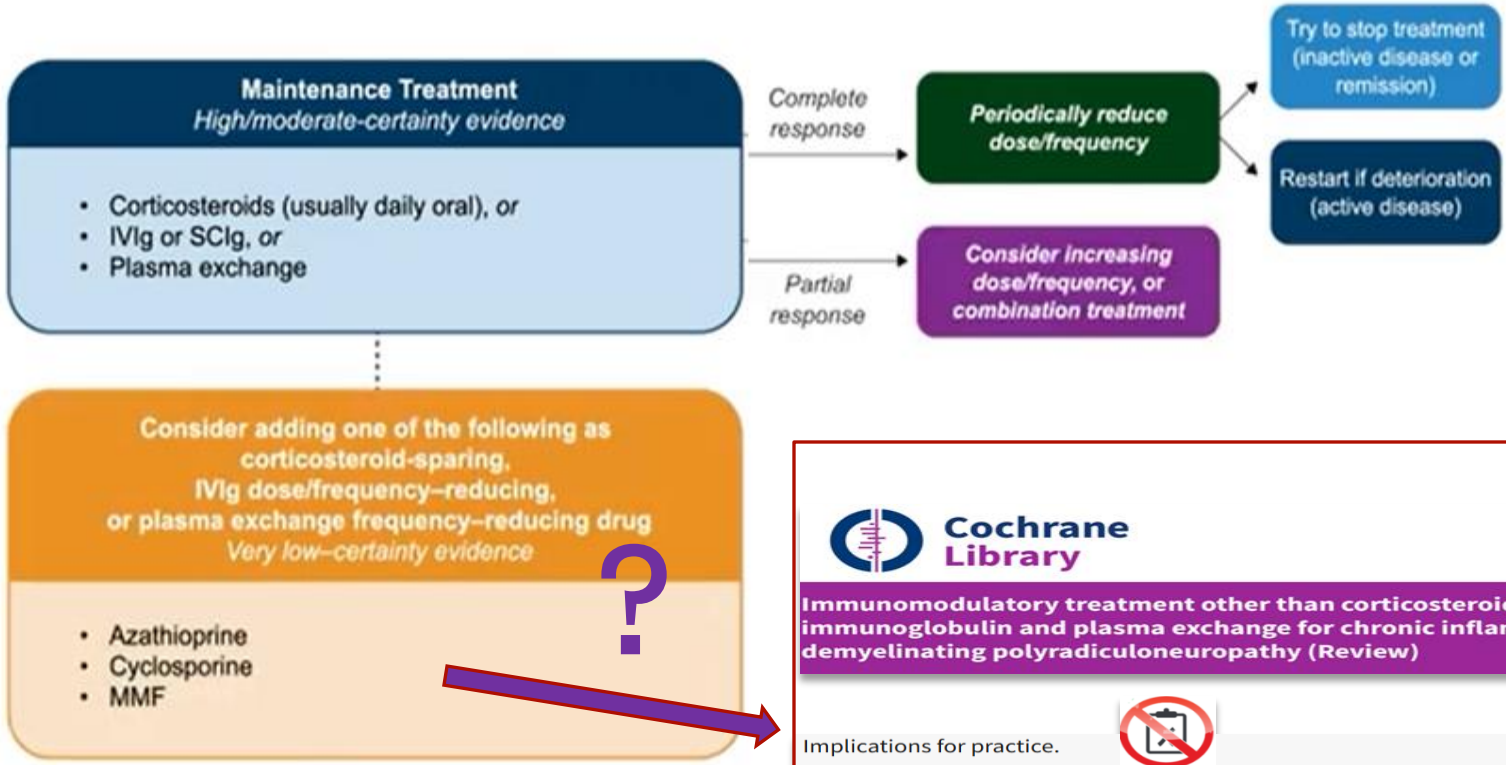
Incidenza: 3-4 casi /100.000
Maggior frequenza: 5° decade



PROVEN EFFECTIVE TREATMENT

INDUCTION

- Corticosteroids (daily oral/pulse) or
- IVIg or
- Plasma exchange



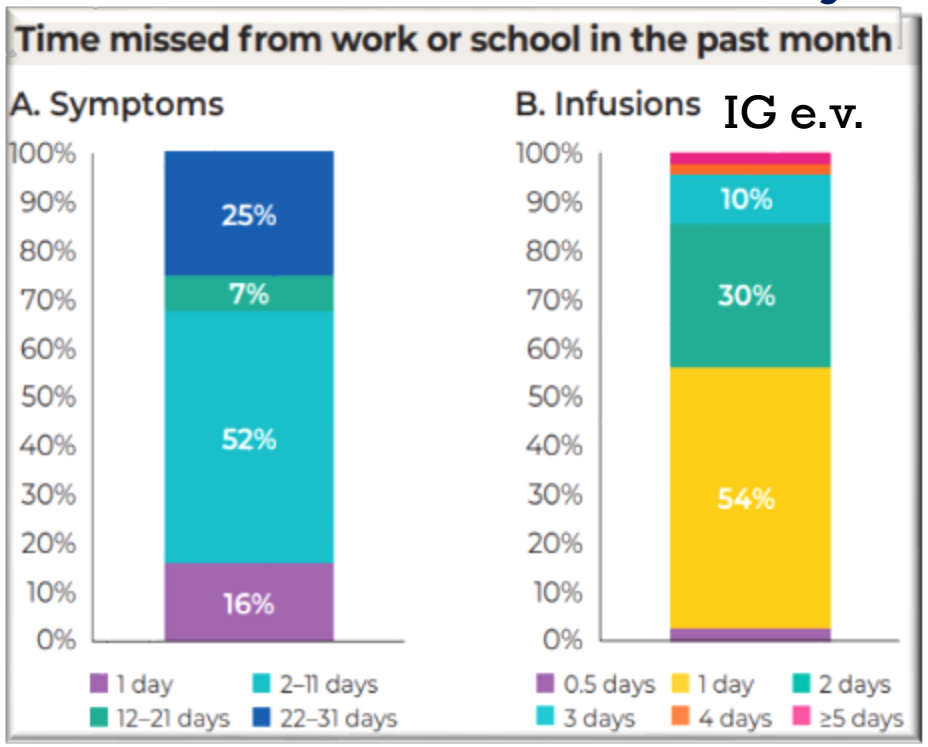
Cochrane Library

Immunomodulatory treatment other than corticosteroids, immunoglobulin and plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy (Review)

Implications for practice.

One randomised controlled trial of azathioprine, two of interferon beta-1a (IFN beta-1a) and one of methotrexate have been performed in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). None showed a significant effect but none were adequate to support or refute mild or moderate benefit or harm. Small numbers of case reports and case series described the use of other immunosuppressant drugs, especially cyclophosphamide, ciclosporin and rituximab, but none consistently produced sufficient improvement to recommend their use without further research.

CIDP Disease Burden — Results of a US Nationwide Patient Survey



Summary of general CIDP disease burden

- 47% of patients stopped working due to CIDP
- Another 14% changed their way of working (e.g., changed job, reduced hours)

- 24% moved to a new home due to CIDP (14% for unlikely CIDP patients)
- 40% made changes to their current residence (e.g., installing ramps, chair lifts)

- 29% cannot go up and down stairs at a normal pace
- 32% currently use a cane (61% have ever used one)

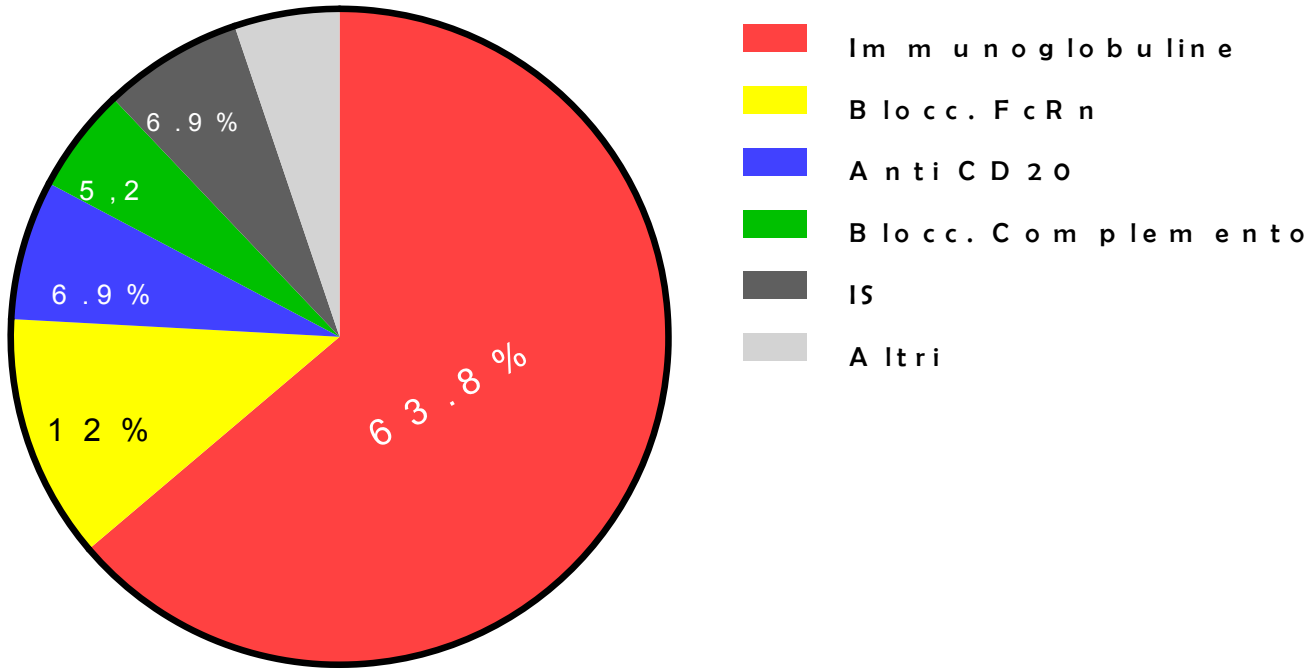
- 48% experienced all 10 symptoms queried, and on average, patients felt some degree of pain at all times, even at their best

Conclusion

- The results from this US nationwide survey demonstrate that both CIDP and commonly prescribed CIDP treatments are associated with disease and treatment burdens that impact school, work. and home activities

NIH U.S. National Library of Medicine
ClinicalTrials.gov

96 trial totali su CIDP

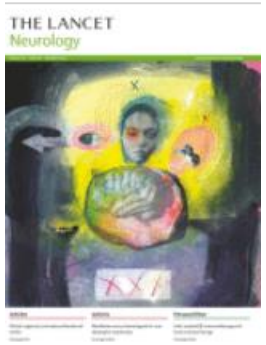


EFGARTIGIMOD

Giugno 2024

APPROVED FDA APPROVED

European Commission



Lancet Neurol. 2024 Oct;23

Safety, tolerability, and efficacy of subcutaneous efgartigimod in patients with chronic inflammatory demyelinating polyradiculoneuropathy (ADHERE): a multicentre, randomised-withdrawal, double-blind, placebo-controlled, phase 2 trial

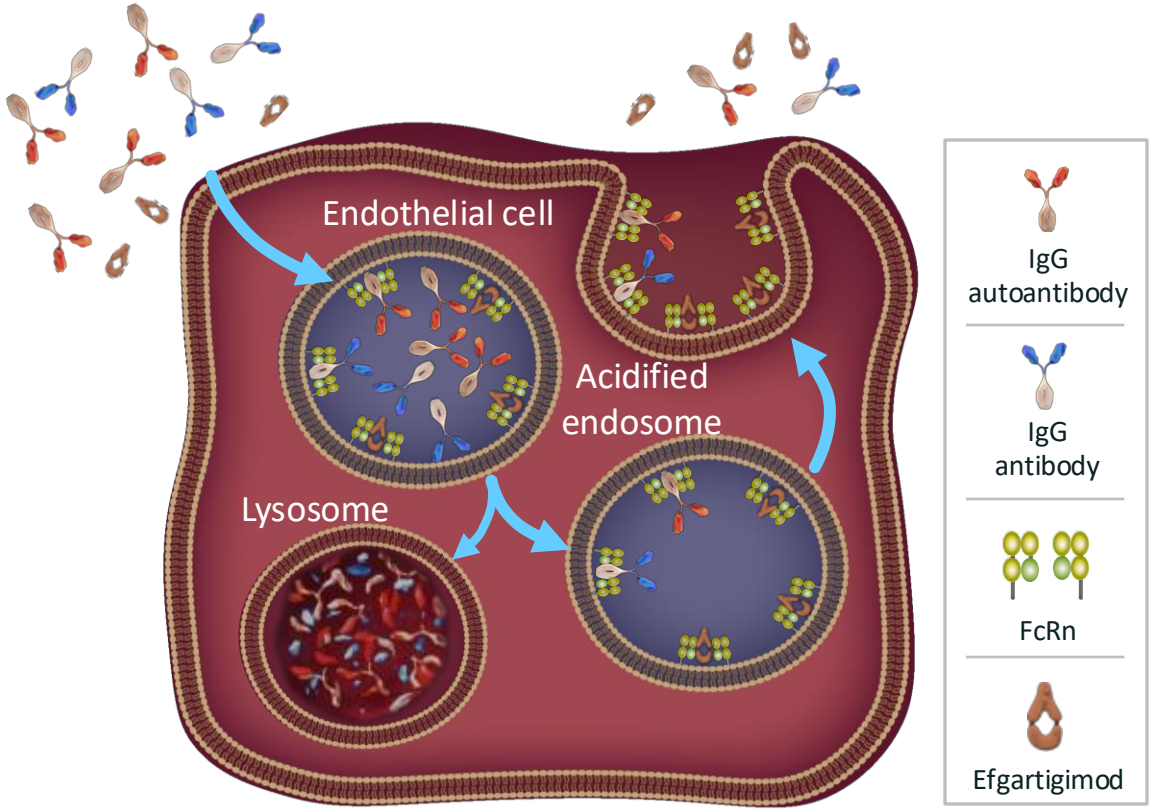
AIFA AGENZIA ITALIANA DEL FARMACO

Farmaci a uso compassionevole

Fondo Nazionale AIFA ("Fondo 5%")

Efgartigimod blocks FcRn and reduces IgG levels

- FcRn recycles IgG, extending its half-life and maintaining serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting IgG lysosomal degradation without directly impacting its production[2–6]
  - **Targeted reduction of all IgG subtypes**
  - **No impact on IgM, IgA, IgE, and IgD**
  - **No reduction in albumin or increase in cholesterol levels**



ADHERE: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

adhere
chronic inflammatory demyelinating polyneuropathy study

Identify patients with active CIDP

Screening
≤4 weeks
CIDP diagnosis confirmed by external expert committee

Run-in period
≤12 weeks
Patients need to demonstrate disease worsening (based on INCAT, I-RODS, grip strength) after current treatment discontinued

Evaluate clinical improvement
Assess efficacy and safety

Stage A: Open-label
Stage B: Randomized-withdrawal, double-blind, placebo-controlled

Stage A
≤12 weeks
Efgartigimod PH20 SC weekly

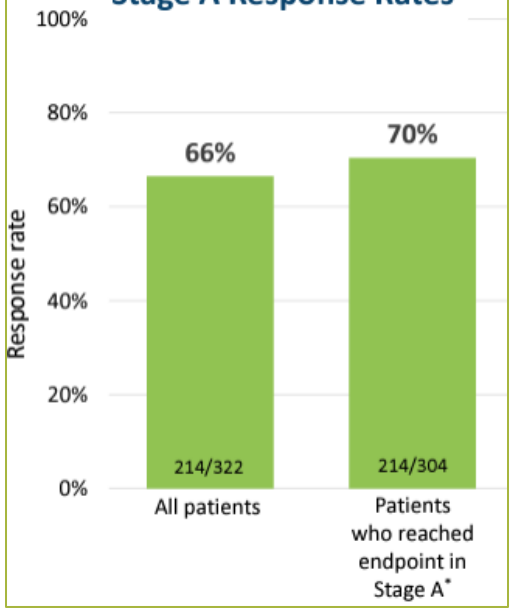
Stage B
≤48 weeks
Placebo PH20 SC weekly
Efgartigimod PH20 SC weekly

Only treatment responders advance to Stage B

Stage A: Primary Endpoint
Percentage confirmed evidence of clinical improvement

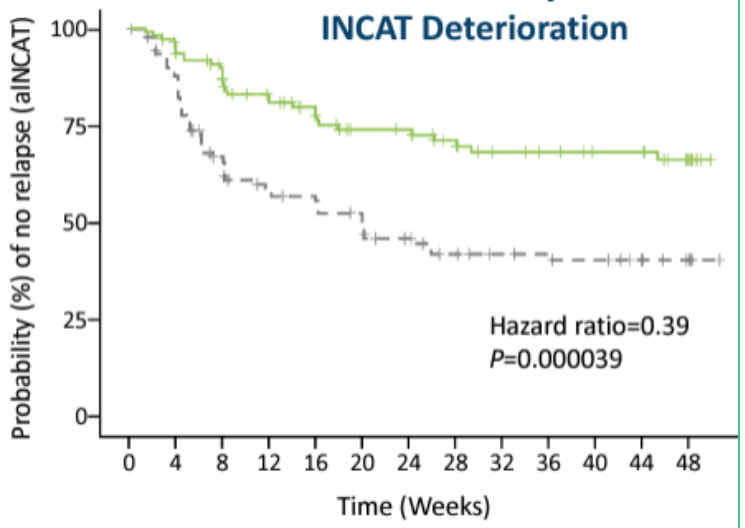
Stage B: Primary Endpoint
Time to first adjusted INCAT deterioration compared to Stage B baseline

Stage A Response Rates



Stage B Efficacy

Time to First Adjusted INCAT Deterioration



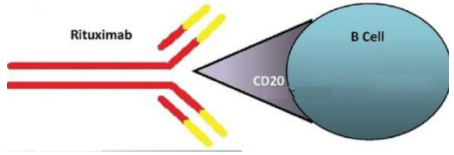
Efgartigimod PH20 SC reduced the risk of relapse versus placebo based on time to first adjusted INCAT deterioration (hazard ratio=0.39; *P*=0.000039)

Highlights from the ADHERE study:

- ADHERE met its primary endpoint (p<0.0001) demonstrating a 61% reduction (HR: 0.39 95% CI: 0.25; 0.61) in the risk of relapse versus placebo
- 69% (221/322) of patients treated with VYVGART Hytrulo, regardless of prior treatment, demonstrated evidence of clinical improvement, including improvements in mobility, function and strength
- 99% of trial participants elected to participate in the ADHERE open-label extension
- VYVGART Hytrulo was well-tolerated and safety results were consistent with the known safety profile of VYVGART in previous clinical studies and real-world use

Rapid onset of action: the median estimate was 22.0 days (15.0-23.0).

RITUXIMAB



Journal of Neurology (2022) 269:1250–1263
https://doi.org/10.1007/s00415-021-10646-y Jianian Hu et 1

REVIEW

Efficacy of rituximab treatment in chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review and meta-analysis

- 13 studi; 96 pazienti; durata media malattia 4.5 anni
- 40.3% positivi per gli Ab anti-CNTN1/NF155 (IgG4)
- 11/13 studi, RTX ripetuto in media dopo 6-7 mesi
- Efficacia in 75% paz

JPNS JOURNAL OF THE PERIPHERAL NERVOUS SYSTEM
PNS PERIPHERAL NERVE SOCIETY

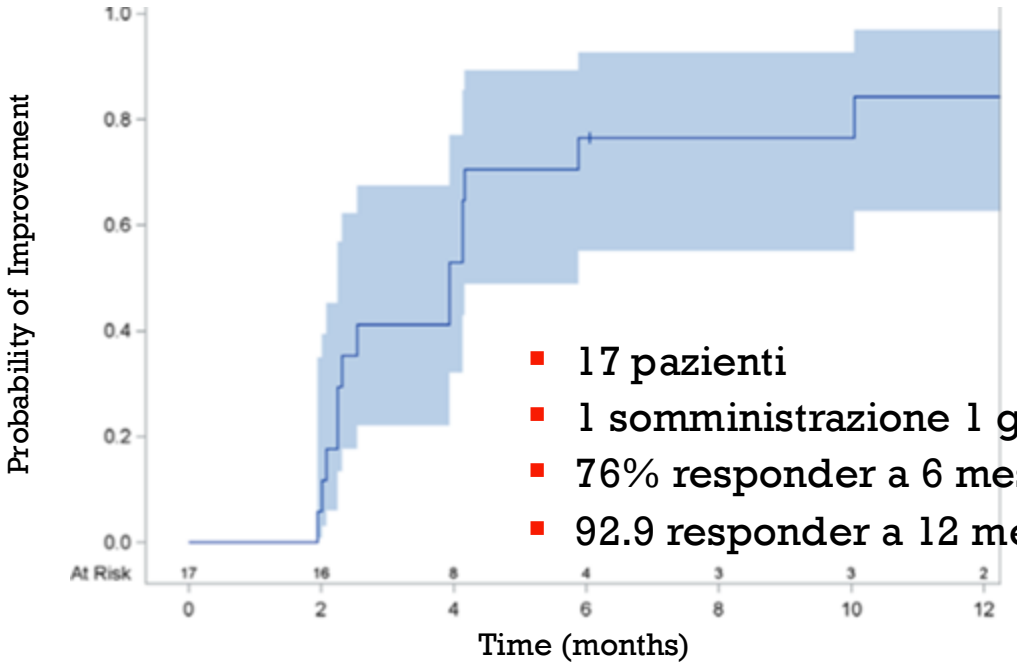
Long-term and low-dose rituximab treatment for chronic inflammatory demyelinating polyneuropathy

Yongsheng Zheng, Chong Sun, Yanyin Zhao, Quanhua Meng, Jianian Hu, Kai Qiao, Jian Sun, Jianying

- 15 paz. refrattari, trattati ad 1 e 6 mesi
- 60% responder a 6 mesi
- 50% responder a 12 mesi

Clinical Trial > J Neurol Neurosurg Psychiatry. 2024 Aug 16;95(9):838-844. Doneddu et al

Prospective open-label trial with rituximab in patients with chronic inflammatory demyelinating polyradiculoneuropathy not responding to conventional immune therapies



- 17 pazienti
- 1 somministrazione 1 gr x 2
- 76% responder a 6 mesi
- 92.9 responder a 12 mesi

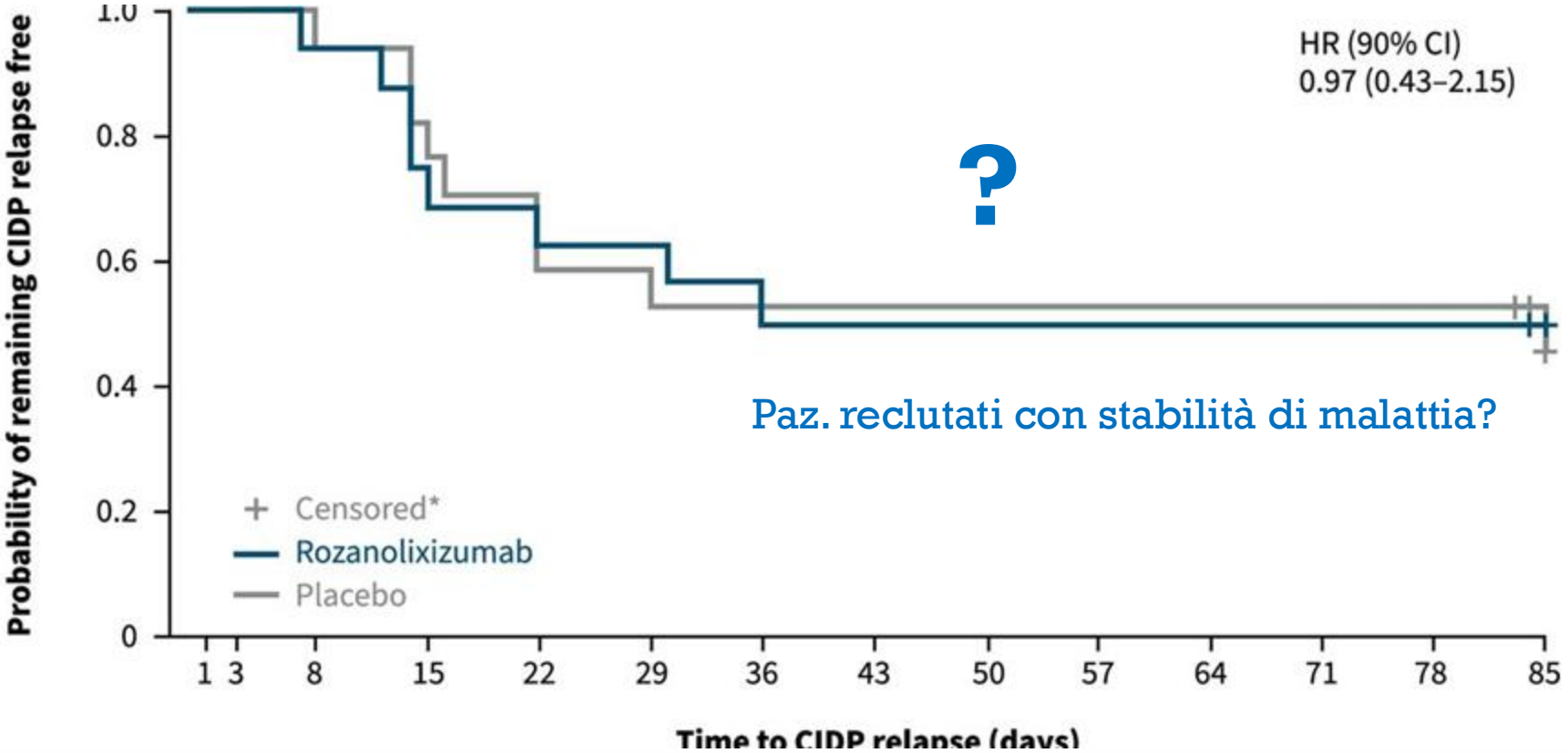
ROZANOLIXIZUMAB

Efficacy, safety and tolerability of **rozanolixizumab** in patients with **chronic inflammatory demyelinating polyradiculoneuropathy**: a randomised, subject-blind, investigator-blind, placebo-controlled, phase 2a trial and open-label extension study.

Luis Querol et al. J Neurol Neurosurg Psychiatry 2024;95:845-854

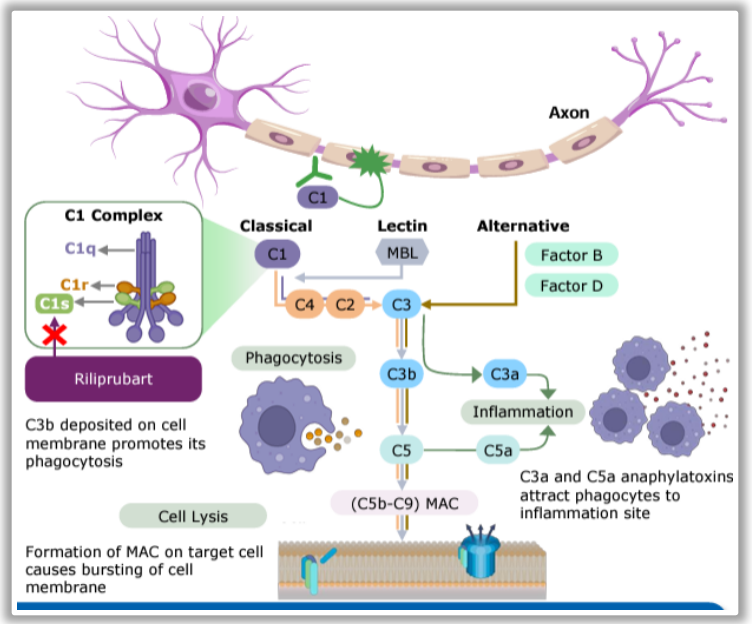
Anticorpo monoclonale IgG4 che blocca il recettore FcRn

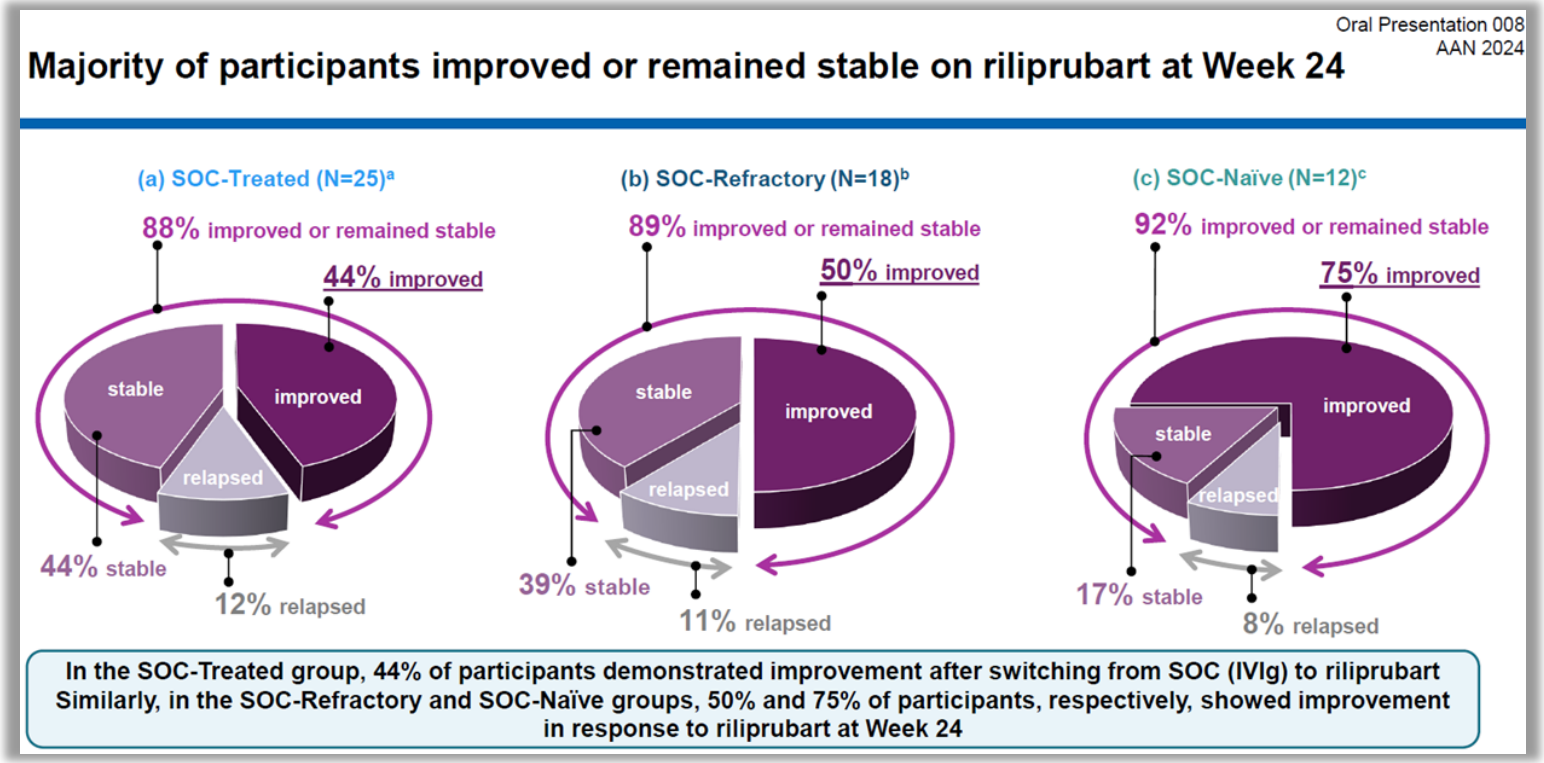
SC 10 or 7 mg(KG/week
IvIG or ScIG responders

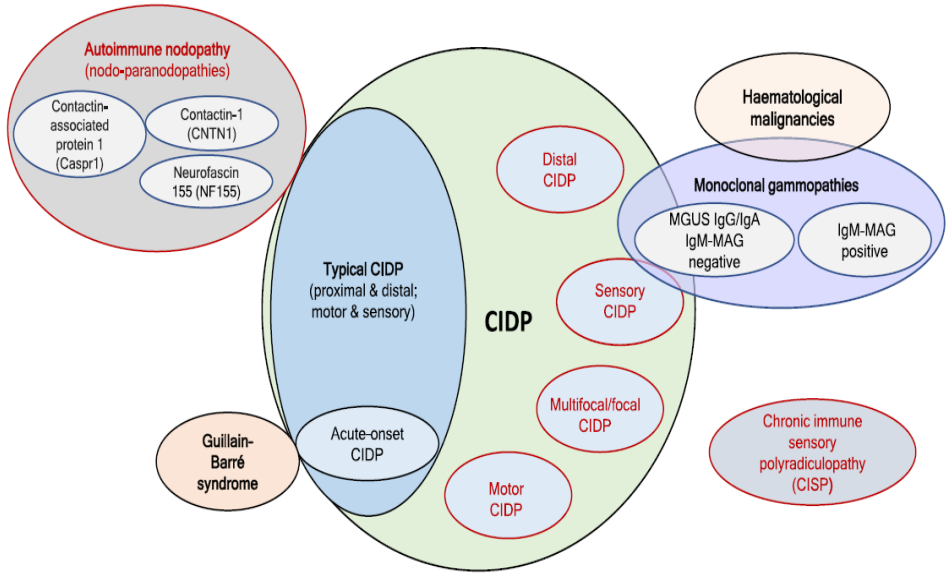


Paz. reclutati con stabilità di malattia?

Preliminary Efficacy and Safety Data from the Phase 2 Trial of Riliprubart (SAR445088), a Humanized Monoclonal Antibody Targeting Complement C1s, in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)







Obbiettivi di trattamento incentrati sul paziente