GBS | CIDP Foundation International

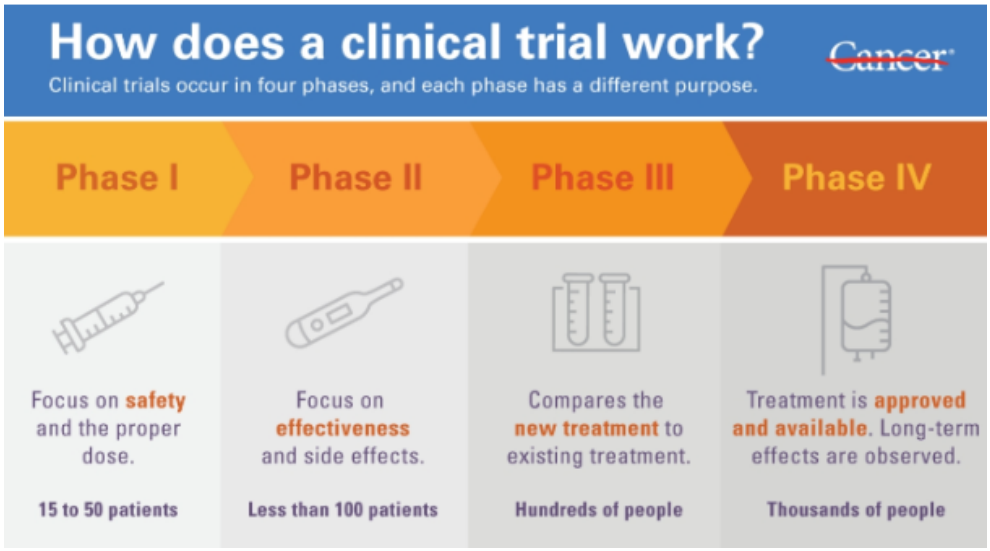
Speaker Series Summary Episode 12: Current Treatments and Emerging Trials for GBS, CIDP, and MMN

Overview

In this Speaker Series episode, Dr. Jeffery Allen educates us about the current treatments for GBS, CIDP, and MMN as well as explain current trials and their findings. Dr. Allen is an associate professor of neurology at the University of Minnesota, adjunct faculty at Northwestern University, and the chairman of out global advisory board.

Summary

Key Terms	**FDA Regulated** signifies that a drug's category is regulated under the FDA; it does not mean that a product is approved or indicated for use for a specific condition. ◦ Example, the FDA regulates the safety and effectiveness of medicines, but does not regulate medical practice and how physician prescribe medications **FDA Approval** signifies that a product has been reviewed and deemed safe and effective ◦ Example, IVIg is an FDA approved medicine used to treat many conditions, including some for which IVIg is indicated. **FDA Indication** signifies that a product has been determined to be safe and effective by the FDA for a specific condition ◦ Example, Certain brands of IVIg are indicated to treat CIDP. **Open label administration** means that a drug in a clinical trial is given to every participant, and they know that they are taking the clinical trial drug **Treatment naive patients** are patients who have not received any treatment for their specific condition

The Phases of a clincal trials	 *University of Texas MD Anderson Cancer Center
Standard Treatments known to improve symptoms	**CIDP** 1. IVIg 2. Coricosteroids 3. SCig (subcutaneous) for maintenance **MMN** 1. IVIg is the only officially approved medicine for MMN **GBS** 1. IVIg 2. Plasma-exchange or plasmapheresis
What trials strive to understand	• Best Dosage of treatment • Best Frequency of treatment • What combination of therapies work • Duration of treatment • How to personalize maintenance • Other treatment options
The knowledge gained from clincal trials over the past 10 years	1. IVIg overtreatment in CIDP (IOC) trial *Adrichem et. A. Brain 2022* ▪ **30-40% of CIDP patients on IVIg do not need treatment as much or at all** 2. Efficacy and safety of 3 different doses of IVIg in CIDP (ProCID trial) Cornblath DR et al. JPNS. 2018 ▪ **The standard dose of IVIg is fine for some but others may need a higher dose to get the same results**

Continued	3. Dose Response of IVIg in CIDP (DRIP) *Kuitwaard K et al. Eur J Neurol 2021* i. **High Doses should be taken less frequently whereas smaller doses should be taken more frequently** ii. **Infusions should occur every 2-4 weeks** iii. **The efficacy of IVIg treatment is dependent on the timing and amount of dosage a patient receives; each patient is different with different needs** 4. IVIg Treatment-Related Fluctuations (GRIPPER) *Allen JA and Lewis R. Neurology 2016* i. **This study quantified the changes patients experience with treatment to understand the importance of infusion rates and how to avoid IVIg wear off**
Completed trial for SCIg	Hyqvia (sponsered by Takeda) • Combines Hyaluronidase + SCIg for CIDP treatment ◦ Hyaluronidase is a compound that lives in the subcutaneous tissue that prevents diffusion of anything that penetrated the subcutaneous tissue • **This combination of hyaluronidase a + SCIg allows patients to take a high dose with less frequency by expanding the tissue to allow more product to be injected and then diffused** ◦ For example: standard SCIg may be taken once a week or more but this combination drug might increase the treatment interval to every 3-4 weeks. Results: • Those who took this combination drug had significantly less of a relapse rate of 10% than the placebo group who had a relapse rate of 30% • The relapse rate was at 6 months • Patients on this combination drug only needed infusions once a month for 2 hours; it only requires with 2 needles What we learned: SCIg + Hyaluronidase is a safe and effective drug that allows patients to take a high dosage of SCIg at a lesser frequency.
FcRn Antagonist	FcRn receptor is a receptor that lives in a cell called endothelial cells • This receptor is the gateway receptor to determine what proteins are friendly and should be recirculated and what needs to be destroyed.

Continued	• Protein or immunoglobulins try to flow down the vasculature and try to bind with the FcRn receptor
	  ▪ Those that bind get kicked back into the body's circulation
	  ▪ Those that don't bind get destroyed by the body or metabolized by that cell
	  • antibodies or proteins that cause damage will be destroyed
	• This does diminish the levels of normal Ig!

In the past 7 years, 4 clinical trials have researched FcRn Receptors	**Completed trials**
	1. Rozanolixizumab (sponsored by UCB Pharma)
	  a. A clinical trial that attempted to find a treatment using FcRn receptors but was stopped because its results were unsubstantiated
	2. Efgartigimod (sponsored by Argenx)
	  a. This clinical trial was completed and the drug studied was granted FDA approval and indicated to treat CIDP in June 2024
	
	Ongoing Trials
	1. Nipocalimab (sponsored by Janssen)
	2. Batoclimab (sponsored by Immunovant)
	
	Visit https:clinicaltrials.gov for a complete list of enrolling sites

Efgartigimod (sponsored by Argenx)	**Vyvgart Hytrulo** • A phase II trial with CIDP patients where patients were asked to stop their normal treatments so that their condition would relapse for a little and then take Vyygart to see if there were any improvements in patients. Those whose condition did improve were randomly assigned to continue taking Vyvgart or completely stop treatment in the placebo group. • Patients were studied to determine a relapse rate at 48 weeks with weekly 1–2-minute subcutaneous injections. Results • Compared to the placebo group, patients on Vyvgart had a 61% reduction in risk of relapse • Now Vyvgart is FDA approved!

Rituximab	• An Immunosupressant that uses monoclonal antibodies to target and deplete B-cells that carry a CD20 marker. Two completed studies 1.Study conducted in Japan Purpose: Is rituximab effective in patients with and without IgG4 auto-antibodies? a. Weekly retreatment 4 times versus placebo b. Outcome: Patients improved at 26 and 52 weeks c. Awaiting full results 2. Study conducted in Italy Purpose: Does rituximab induce remission? a. Retreatment at 6 months; full year study b. Outcome: i. Patients worsened after IVIg treatment stopped ii. Relapse rates at 12 months were similar for both rituximab and placebo patients iii. **Those on rituximab has a longer interval between infusion and relapse than placebo patients but in the end the results were the same** Take away: Based on the Italian study, rituximab is not for everyone with CIDP. The more we learn about rituximab, we will understand if there is a group of patients who are specifically good candidates for CIDP. We need to study rituximab more to learn the best way to use rituximab.
Complement System	Part of the Immune System that enhances the ability of antibodies to: • Attack cells • Promote inflammation • Clear debris or dead tissue • In auto-immune diseases, complements destroy healthy and “friendly” cells and in our community’s case: the peripheral nervous system
Complement Clinical Trials	**Riliprubart (sponsored by Sanofi)** • Phase II trial of patients with CIDP in an open label administration for 52 weeks • Outcome was measured during the trial: Relapse rate or response rate at 52 Week

continued	Results: • 87% of standard of care patients improved or remained stable at 24 weeks • 50% of Refractory patients showed improvement • 71% of treatment naive patients improved and sustained response at 1 year Sanofi is developing two phase III trials • Mobilize: For patients with failure or inadequate response to standard treatments • Vitalize: For patients receiving maintenance treatments with IVIg **Empasiprubart (sponsored by Argenx)** Trial name: "ARDA" • Phase II trial of patients with MMN that were randomized to transition from IVIg to Argenx's treatment or be a part of the placebo group • Outcome: Time to IVIg retreatment in 52 weeks Results: • The study drug reduced the risk of IVIg retreatment by 91% • Demonstrated improvement of grip and muscle strength • Improved patients' ability to perform daily activities • Now it will go into global phase III studies to determine its safety and efficacy in adults with MMN **ANX 005 (sponsored by Annexon)** • Phase III trial of patients with GBS that randomized patients to the study drug or placebo group • Outcome: GBS disability score at day 56 and how long recover took Results: • 2.4 improved disability assessment at week 8 (idk what he means by 2.4 he doesn't say tbh) • Improved muscle strength at day 8 and week 8 • Fewer days on artificial ventilation • Faster time to regain walking ability • **Earlier treatment results in getting better faster**
CIDP Diagnostic Criteria	A new CIDP guideline was published in 2021 by members on our GMAB board! You can access it here: https://pubmed.ncbi.nlm.nih.gov/3408574

IncBase (2021)	**A CIDP patient registry in efforts to***
	• Define CIDP phenotypes
	• Improve diagnostic criteria
	• Develop prediction models
	• Studies on biomarkers
	• Clinimetrics development
	• Clinical trial platform
	
	*This is an epidemiological study does not require CIDP patients who are currently taking treatment for CIDP
	
	If you would like to participate:
	• Currently enrolling:
	  ◦ University of Minnesota
	  ◦ Johns Hopkins University
	  ◦ Kansas University
	  ◦ University of Michigan
	  ◦ Duke University
	  ◦ NeuroMD Center in Dallas, Texas
	• Coming Soon:
	  ◦ Yale University
	  ◦ Lahey Clinic
	• Looking Ahead:
	  ◦ Scottsdale, Arizona
	  ◦ Washington University

Relevant Resources

Treatments and Access Portal

PubMed GBS Publications

PubMed CIDP Publications

PubMed MMN Publications

Clincal Trials that are currently enrolling