ΣΥΓΧΡΟΝΕΣ ΘΕΡΑΠΕΥΤΙΚΕΣ ΕΞΕΛΙΞΕΙΣ ΣΤΗ ΧΡΟΝΙΑ ΦΛΕΓΜΟΝΩΔΗ ΑΠΟΜΥΕΛΙΝΩΤΙΚΗ ΠΟΛΥΝΕΥΡΟΠΑΘΕΙΑ

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Περίληψη

Η Χρόνια Φλεγμονώδης Απομυελινωτική Πολυνευροπάθεια είναι μία αυτοάνοση νόσος η οποία παρότι δύναται να προκαλέσει αναπηρία, είναι αντιμετωπίσιμη με πολλαπλές θεραπευτικές επιλογές. Παρά την καλή ανταπόκρισή της στη θεραπεία, συχνά λανθασμένες διαγνώσεις περιπλέκουν την αποτελεσματική διαχείριση τέτοιων περιστατικών. Διάφορες θεραπείες μπορούν να χρησιμοποιηθούν ως πρώτης και δεύτερης γραμμής. Οι επιλογές πρώτης γραμμής είναι η ενδοφλέβια ανοσοσφαιρίνη, τα κορτικοστεροειδή και η πλασμαφαίρεση. Οι θεραπείες δεύτερης γραμμής, όπως τα ανοσοκατασταλτικά, μπορούν να χρησιμοποιηθούν είτε ως εναλλακτικές λύσεις στα στεροειδή είτε ως βελτιωμένες στρατηγικές θεραπείας για πιο σοβαρές περιπτώσεις. Οι πρόσφατες μελέτες έχουν εισαγάγει νέους θεραπευτικούς στόχους, όπως οι αναστολείς του υποδοχέα Fc, οι οποίοι έχουν πλέον λάβει έγκριση σε κράτη του εξωτερικού και είναι διαθέσιμοι, επεκτείνοντας σημαντικά τις θεραπευτικές δυνατότητες. Αυτό το διαρκώς μεταβαλλόμενο τοπίο καταδεικνύει την ανάγκη προς την προσωποποιημένη ιατρική στη διαχείριση της χρόνιας φλεγμονώδους απομυελινωτικής πολυνευροπάθειας, υποσχόμενο βελτιωμένα αποτελέσματα μέσω προσαρμοσμένων θεραπευτικών προσεγγίσεων στο ατομικό προφίλ του κάθε ασθενούς.

Λέξεις Ευρετηρίου: Χρόνια Φλεγμονώδης Απομυελινωτική Πολυνευροπάθεια (CIDP), Θεραπεία, Ανοσοθεραπεία, Ενδοφλέβια Ανοσοσφαιρίνη (IVIg), Υποδόρια Ανοσοσφαιρίνη (SCIg), Κορτικοστεροειδή.

CONTEMPORARY THERAPEUTIC DEVELOPMENTS IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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Abstract

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a debilitating autoimmune disorder that is treatable with multiple therapeutic options. Despite its responsiveness to treatment, frequent misdiagnoses complicate effective management. Various agents can be utilized as first and second-line. First-line options are intravenous immunoglobulin, corticosteroids and plasma exchange. Second-line therapies, often immunosuppressants, are employed either as alternatives to steroids or as enhanced treatment strategies for more severe cases. Recent advancements have introduced new therapeutic targets, such as Fc receptor blockers, that are now approved and available, significantly expanding treatment possibilities. This evolving landscape highlights the shift towards personalized medicine in CIDP management, promising improved outcomes through tailored therapeutic approaches that are specifically adapted to individual patient profile

Keywords: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Therapy, Intravenous immunoglobulins (IVIg), subcutaneous immunoglobulins (SCIg), corticosteroids.

Introduction

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is characterized as a rare, autoimmune-based peripheral nerve disorder that is amenable to treatment.[1] The reported incidence of CIDP is about 1 per 100,000.[2] The clinical presentation of CIDP commonly involves symmetrical weakness in both the proximal and distal regions of all four limbs, although several atypical forms are recognized.[3] These clinical variants, such as the pure motor, pure sensory, focal, or multifocal types, exhibit a prevalence similar to that of the classic presentation.[4,5] Typically, the progression of the disease spans more than eight weeks, though instances of a more rapid onset have been observed.

In light of these complexities, the European Academy of Neurology (EAN) and the Peripheral Nerve Society (PNS) updated their guidelines in 2021, emphasizing the diagnosis and management of CIDP.[6] Despite enhancements in diagnostic standards and methodologies, substantial obstacles persist in differentiating CIDP from other types of demyelinating neuropathies.[7,8] The diagnostic framework relies extensively on a comprehensive understanding of differential diagnoses and employs various diagnostic tools including nerve conduction studies, cerebrospinal fluid (CSF) protein analysis, nerve ultrasonography, and magnetic resonance (MR) neurography, as well as assessments of patient responses to therapeutic interventions.[6]

Management strategies for CIDP primarily involve first-line treatments such as immunoglobulins, corticosteroids, and plasma exchanges (PLEx).[9,10] IVIg and corticosteroids are equally effective as induction therapy but there is no consensus between the two options on optimum long-term treatment modality.[11,12] In scenarios requiring long-term management to preserve clinical stability or to address suboptimal responses to initial treatments, several immunosuppressive agents are employed to potentially minimize dependency on steroids or IVIg.[13] Additionally, advanced treatments like Hematopoietic Autologous Stem Cell Transplant (ASCT) are considered as viable options for severe, treatment-resistant cases.[14] In 2024, innovative therapies incorporating monoclonal antibodies that target the neonatal Fc receptor (FcRn) were approved by the Food and Drug Administration (FDA). These treatments represent a significant advancement in CIDP management, offering potential shifts in the disease trajectory through novel mechanisms of action.

The scope of this review is to meticulously assess the contemporary approaches to therapy in CIDP, focusing on treatment modalities, optimal dosages, side effects, costs, and accessibility. It will also scrutinize the influence of emerging treatments, such as FcRn-targeted therapies and complement pathway inhibitors, on the therapeutic landscape of CIDP.

Methods

We performed a narrative review of the literature on all articles published until 31st of July 2024 with the search MeSH terms ("Chronic Inflammatory Demyelinating Polyradiculoneuropathy" OR "CIDP "OR "Demyelinating Polyneuropathies") AND ("Glucocorticoids" OR "corticosteroids" OR "steroids") OR "Immunoglobulins, Intravenous" OR "IVIg" OR "Intravenous immunoglobulins" OR "SCIg" OR "Subcutaneous Immunoglobulin" OR "Immunotherapy" OR "immunotherapy") AND ("Plasma Exchange" OR "plasmapheresis" OR "Haematopoietic Autologous Stem Cell Transplant" OR "ASCT" OR "FcR blockers" OR " Complement Pathway Inhibitors" OR "Immunosuppressive Agents" OR "immunosuppressants" OR "immunosuppressive drugs" OR "Therapy" OR "Therapeutic approach "OR" Therapeutic Development") in Pubmed and Scopus . No restrictions were imposed on the search for published articles because we aimed to include all available evidence on available treatments. We reviewed all search titles and abstracts obtained to identify the relevant articles for the review. Full texts of the identified articles that met our review requirement were included for the analysis. In addition, we describe experiences in the clinical practice at our neuromuscular units in relation to therapy for CIDP.

Results

Immunoglobulins

The efficacy of IVIg was validated through five randomized, placebo-controlled trials conducted from 1993 to 2008, employing either parallel group or crossover designs (Table 1).[15–19] These studies provide high-quality evidence supporting the safety and effectiveness of IVIg for both induction and maintenance treatment of CIDP.[15–19] Each trial administered a standard IVIg dose of 2 g/kg over 2 to 5 days.[15–19] One long-term study also employed this initial dose, followed by a maintenance dose of 1 g/kg every three weeks.[19] The primary outcome in all trials was the improvement of disability, assessed using various scales.[15–19] Specifically, Vermeulen et al. established the MRC scale as the primary endpoint.[15] In contrast, Hahn et al. conducted serial quantitative assessments of neurological function, monitoring the Neurological Disability Score (NDS), Clinical Grade (CG), grip strength (GS), and conducting electrophysiological studies before and after each treatment period.[16] Thompson et al. employed the 10-meter walk test, the Nine-Hole Peg Test, the Hammersmith Motor Ability Score, and myometry as alternative measures, all of which are valid, reliable, and sensitive.[17] Mendel et al. defined the primary outcome measure as the change in muscle strength from baseline to day 42, using the Average Muscle Score (AMS).[18] Hughes et al. set the primary endpoint as the percentage of patients who maintained an improvement from baseline in the adjusted INCAT disability score of 1 point or more through week 24.[19] IVIg demonstrated significant efficacy compared to placebo in the short term, with notable improvements within six weeks of initiation and sustained efficacy at 24 weeks. Among these trials, only the ICE study confirmed the long-term efficacy of IVIg over a 48-week period.[19]

Regarding the induction regimen, an initial cycle of 2 g/kg divided over 2-5 days is suggested. The maximum improvement is approximately two weeks post-administration after each cycle. The majority of IVIg-responsive patients will exhibit improvement after two treatment cycles.[20] Nevertheless, some patients may require more than 1 g/kg per cycle to achieve a response, and the full benefit of the initial cycle may not be evident by three weeks.[20]

The PRIMA and PRISM studies demonstrated that IVIg, administered with an induction dose of 2 g/kg followed by maintenance doses of 1 g/kg every three weeks, achieved response rates of 60.7% and 76.2%, respectively.[20,21] Both studies indicated that patients who do not exhibit a response within six weeks of IVIg treatment may still respond at a later stage.[20,21] The PRISM study recommended that CIDP patients should continue IVIg treatment for six months before considering alternative therapies, noting that the median time to response was 15 weeks, with 29% of patients responding after six weeks.[21]

Suspending further treatment, after the induction dose and first maintenance dose, allows for assessment of ongoing disease activity, indicated by re-deterioration following a period of improvement and/or stability, and enables individualized optimization of subsequent dosing intervals.[22]

Body weight is not associated with long-term dosage requirements. Standardized doses (e.g., 1 g/kg every three weeks) are sometimes employed.[23] However, ideal dosage requirements vary among individuals. Therefore, it is advocated for the individual optimization of both the dose per cycle and the treatment interval. Notably, multiple studies have shown that up to 25-50% of patients undergoing treatment for CIDP ultimately achieve remission.[24] This remission might remain unnoticed if the treatment regimen is not modified.[24]

In recent years, subcutaneous immunoglobulin (SCIg) has emerged as a widely used maintenance treatment following successful induction with IVIg. A specific study conducted over 12 weeks between 2010 and 2011 involving 30 Danish participants who had previously responded to IVIg, demonstrated notable efficacy of SCIg.[25] This trial showed significant enhancements in isokinetic strength, Medical

Research Council (MRC) scores, grip strength, and overall disability reduction in the group treated with SCIg compared to those receiving a placebo.[25] Furthermore, the treatment was well-received, indicating good tolerability.[25] Supporting these results, a subsequent, more extensive international randomized controlled trial (RCT), the PATH study, utilizing human SCIg(Hizentra) , encompassed 172 participants across 69 centers (Figure1).[26] This study validated the effectiveness of a 0.2 g/kg weekly dosage of SCIg in preventing relapse among CIDP patients responsive to IVIg, with no further benefits at a higher dosage of 0.4 g/kg weekly.[26] A substantial RCT involving 132 participants, known as ADVANCE-CIDP, assessed the effectiveness of hyaluronidase-facilitated fSCIg (Hyqvia) at 10% concentration (Figure1) [27]. This trial confirmed its efficacy in reducing the relapse rate by more than 20% compared to placebo among subjects with CIDP who were previously responsive to IVIg.[27] However, an IVIg-dependency test was not conducted before inclusion, suggesting that some participants might have been in remission at the time of recruitment.[27] The primary advantage of using hyaluronidase-facilitated SCIg over conventional SCIg lies in its ability to address the limitation of the maximum volume that can be infused into the subcutaneous space.[28] Hyaluronidase aids the dispersion and absorption of SCIg into the lymphatics, thereby allowing for less frequent infusions—potentially as infrequent as every four weeks, instead of weekly.[28] This method also reduces the duration of each infusion and the number of needlesticks required, enhancing patient comfort and compliance.[28]

At our clinic, we have had significant success with the use of fSCIg therapy in CIDP. Over the course of the last two years, we administered fSCIg to 21 patients. Remarkably, 19 of these patients responded positively to the therapy based on MRC scale, demonstrating a high efficacy rate of approximately 90.5%.The treatment protocol included dosage of 60 g every two weeks and a mean treatment duration of three months. Our findings contribute to the growing body of evidence supporting SCIg as a viable and effective option of maintenance treatment for CIDP, underscoring the potential of this treatment in improving patient outcomes

Corticosteroids

The anti-inflammatory and immunosuppressive properties of corticosteroids are mediated through genomic pathways that enhance the production of anti-inflammatory proteins while decreasing the synthesis of pro-inflammatory proteins.[29] Additionally, corticosteroids exhibit rapid, direct non-genomic effects, likely facilitated by a variety of receptors and signaling pathways, resulting in a range of impacts.[30]

Corticosteroids were first identified as an effective treatment for CIDP by Austin in 1958, particularly notable in patients experiencing relapses post-treatment cessation.[31] Despite their long-standing use, there is scant RCT evidence supporting corticosteroid use in CIDP. A seminal study by Dyck et al. in 1982, which was a RCT comparing high-dose alternate-day prednisone (120 mg) with placebo in 28 CIDP patients, confirmed the superiority of prednisone over placebo (Figure1).[32] Nevertheless, this study was compromised by several methodological flaws, including non-concealed allocation, lack of blinding, absence of intention-to-treat analysis, and a significant dropout rate.

Comparative studies between IVIg and corticosteroids are limited. The first comparative RCT, conducted in 2001, involved 32 participants and demonstrated that oral corticosteroids were not inferior to IVIg over a 6-week treatment duration.[33] A subsequent multicenter crossover RCT, the IMC Trial, assessed the efficacy and tolerability of pulsed intravenous methylprednisolone (IVMP) against IVIg in CIDP patients, employing a smaller dose and shorter treatment duration of IVMP (500 mg daily for four consecutive days) compared with IVIg (0.5 g/kg per day for four consecutive days), administered monthly over six months.[34] The primary outcome was not only the discontinuation but the efficacy as well. Steroids performed better in the latter. The proportion of patients with adverse events did not differ between the intravenous methylprednisolone group (14 [67%] of 21) and the IVIg group (11 [46%] of 24; p=0·1606). After therapy discontinuation, more patients on IVIg worsened and required further therapy (eight [38%] of 21) than did those on methylprednisolone (none of ten; p=0·0317).[34] Thus, these RCTs did not conclusively demonstrate the superiority of IVIg over corticosteroids in improving disability.[33,34] However, it is noteworthy that corticosteroids may facilitate longer durations of therapy-free remission or higher remission rates compared to IVIg, supporting their use as a first-line treatment in patients without contraindications.[35,36]

The PREDICT study, another RCT, compared daily oral prednisolone with monthly pulse oral dexamethasone, focusing on the proportion of patients achieving remission without treatment at 12 months (Figure2).[37] While no significant differences were found in the primary or multiple secondary outcomes, monthly dexamethasone showed a faster onset of improvement.[37] Additionally, side effects such as insomnia, cushingoid features, and significant weight gain (>3 kg) were more common with daily prednisolone (Figure2).[37] Evidence from the PREDICT study suggests that pulse therapy with corticosteroids might offer faster action and fewer side effects than daily administration.[37] Oral dexamethasone also has the advantage of not requiring hospital visits.

Current guidelines for daily oral corticosteroid regimens recommend initiating treatment with prednisone or prednisolone at a dosage of 60 mg, equivalent to 48 mg of methylprednisolone.[6] This dosage should be gradually reduced over a period of 6 to 8 months, contingent upon the patient's clinical response and the manifestation of adverse effects.[6] Although some treatment centers advocate commencing therapy with a daily dose of 1 to 2 mg/kg of prednisolone, there lacks empirical evidence to suggest that this generally higher dosage provides superior outcomes.[6] Additionally, the protocol for oral dexamethasone treatment involves administering 40 mg for four consecutive days per month over a duration of six months.[6] The potential adverse effects of corticosteroids, including osteoporosis, gastric ulceration, diabetes, cataracts, avascular necrosis of long bones, and arterial hypertension, may exceed the therapeutic benefits in cases of low-disability diseases.[6] In such instances, clinicians should consider alternative therapeutic strategies.[6]

In addition to the conventional risks associated with steroid therapy, particular caution is warranted in cases of CIDP with pure motor and multifocal presentations. In these specific subtypes, a 'paradoxical' exacerbation of symptoms may occur following the administration of corticosteroids.[38]

Finally, the multicenter OPTIC study aimed to explore the combined benefits of IVIg and corticosteroids, specifically the immediate effect of IVIg and the prolonged remission associated with corticosteroids, was initiated but unfortunately recently suspended.[39] Further publication of details is anticipated.

Plasmapheresis

PLEx serves as an effective and relatively safe therapeutic option for treating CIDP in the short term, despite facing several logistical challenges that restrict its widespread implementation.[40]

Support for plasma exchange in CIDP is derived from two RCTs involving a total of 52 participants.[41,42] The first trial involved 29 patients undergoing plasma versus sham exchange twice weekly for three weeks.[43] The second trial had a smaller cohort, with only 15 participants completing the study, receiving either 10 plasma or sham exchanges over a four-week period.[42] After a five-week washout period, patients switched treatments.[42] Neuropathy Impairment Score (NIS) was utilized by both trials a secondary outcome and demonstrated significant benefits of PLEx in improving disability scores and nerve conduction metrics compared to sham procedures.[41-42] Prior observational studies have also noted positive short-term effects.[40] These findings suggest that concurrent treatments might be necessary alongside plasma exchange, with corticosteroids frequently employed, although the need for systematic integration of these therapies remains unproven.[40] Thus, plasma exchanges are validated as a beneficial treatment for CIDP, particularly useful for patients who are refractory to corticosteroids and immunoglobulins or those heavily reliant on high doses of corticosteroids, which can lead to severe side effects.

No evidence-based protocol for PLEx in CIDP has been established; however, an initial regimen typically involves five daily exchanges, over two weeks, with further treatment tailored based on clinical response.[6] Maintenance PLEx is often administered at intervals of four to six weeks, involving three to five exchanges per cycle, depending on individual patient response.[44]

While PLEx is generally well-tolerated, the safety and tolerability data are limited and primarily based on small case series.[45] Common risks associated with PLEx include vasovagal episodes, fluid overload, under-replacement, and hypotension due to rapid fluid shifts. Less commonly, allergic or anaphylactic reactions to plasma or human albumin solution (HAS) infusions occur.[45] If central or large bore vascular access is needed, complications related to line insertion and usage may also arise.[46] Notably, PLEx with albumin or saline leads to a temporary decrease in blood-clotting factors and a mild prolongation of prothrombin time and activated partial thromboplastin time, typically normalizing within 4 to 24 hours.[45] Clinically significant bleeding is rare.[45]

Immunosuppressive therapy

When first-line treatments are effective yet require sustained administration to maintain clinical stability in CIDP, various immunosuppressive agents may be employed to minimize dependency on steroids or IVIg.[6] The literature provides limited support for the efficacy of methotrexate, fingolimod, and interferon beta-1a.[47-50] However, azathioprine, mycophenolate mofetil, and ciclosporin are considered viable options for reducing the need for ongoing immunoglobulin or corticosteroid therapy.[51-53] The use of azathioprine is backed by a single trial of modest quality and brief duration. Cyclosporine and mycophenolate mofetil are also frequently used in clinical settings, although support primarily stems from case series and individual case reports.[10]

Rituximab has shown promise in treating CIDP, particularly in cases of autoimmune neuropathy with paranodal antibodies, which are now recognized as distinct from the CIDP spectrum.[54] Although evidence is scant and predominantly retrospective, one report highlighted a 70% response rate within approximately two months in CIDP case series, some refractory and others with high demands for IVIg or plasma exchange, with effects lasting up to a year.[55] Rituximab is administered in CIDP either as

a total of 2 grams over two weeks or 375 mg/m_2 weekly for four weeks. Repeat treatments may be considered but are not always necessary, particularly for patients who achieve complete or near-complete remission, as further courses might increase the risk of adverse effects.

Cyclophosphamide has been identified as an alternative therapeutic option for non-responder patients to conventional treatments.[6] In a cohort study involving 15 subjects who were refractory to first-line therapies, improvement was noted within an average of four months, with complete remission achieved in 73.3% of the cases.[56] Similar outcomes have been reported in other studies and supported by systematic reviews and meta-analyses. Cyclophosphamide is typically administered intravenously at a dose of 1 g/m_2, continued monthly for up to six months, unless significant improvement occurs sooner. The routine use of concurrent high-dose corticosteroids is common in many treatment centers.

Haematopoietic Autologous Stem Cell Transplant

ASCT represents an advanced immunosuppressive therapy for CIDP.[14,57] A recent meta-analysis of 11 studies encompassing 89 cases with an average age of 42.1 years reported a response rate of 86%, a remission rate of 85%, and a post-ASCT treatment-free rate of 81%.[58] Of these subjects, only 19 had received cyclophosphamide as a second-line treatment prior to ASCT, and only 18 had been treated with rituximab, representing less than half of the cohort for these agents.[58]

In the most extensive case series to date, 66 CIDP patients who were either dependent on or unresponsive IVIg or PLEX underwent ASCT in a prospective open-label study, with follow-up extending to 5 years post-treatment.[59] Nearly all patients who initially required assistance for ambulation regained and sustained independent mobility, and 83% were free from immunotherapy at the 5-year mark.[59]

Despite these encouraging outcomes, the evidence supporting the use of ASCT in refractory or treatment-dependent severely affected CIDP patients remains insufficient. The procedure carries significant risks of morbidity and mortality, predominantly due to infections and prolonged immunodeficiency. Therefore, ASCT should be reserved as a last-resort treatment option in specialized CIDP centers**.**

FcRn Blockers

The neonatal Fc receptor (FcRn) emerges as a potential therapeutic target in immune-mediated polyneuropathies due to its role in promoting IgG recycling and safeguarding against degradation, thereby prolonging the serum half-life of IgG molecules.[60,61] Therapeutic interventions utilizing monoclonal antibodies targeting FcRn could potentially diminish the levels of pathogenic IgG autoantibodies while sparing other circulating immune components.[62]

Vyvgart Hytrulo, a pharmacological compound comprising efgartigimod alfa, an inhibitor of the neonatal Fc receptor, combined with hyaluronidase to enhance subcutaneous tissue permeability, received approval from the Food and Drug Administration (FDA) in 2024.[63] This approval was for the treatment of adults diagnosed with CIDP, based on outcomes from the phase 3 ADHERE trial. ADHERE was structured as a two-part, multicenter, randomized, double-blind, placebo-controlled study involving treatment-naive adults or those previously on standard therapies, which were withdrawn during a ≤12-week preparatory period. The initial open-label phase (Stage A) involved weekly subcutaneous injections of Vyvgart Hytrulo for a maximum of 12 weeks. Responders from this phase were subsequently randomized to continue receiving weekly doses of Vyvgart Hytrulo or a placebo for up to 48 weeks (Stage B). Among the 221 respondents in Stage B, Vyvgart Hytrulo demonstrated a 61% reduction in CIDP relapse risk (defined by a ≥1 point increment in the adjusted Inflammatory Neuropathy Cause and Treatment score; the primary endpoint) at 48 weeks compared to placebo (hazard ratio, 0.39 [95% CI, 0.25-0.61]; P<.0001). Common adverse reactions included injection site bruising and erythema.

Furthermore, rozanolixizumab, a high-affinity human anti-FcRn IgG4 monoclonal antibody, was evaluated in a RCT for CIDP, which concluded in March 2021 without meeting its primary endpoints.[64] Additionally, nipocalimab, an aglycosylated IgG1 monoclonal antibody against FcRn, is presently under investigation in a multicenter RCT (ARISE Study), following a similar design to the ADHERE trial.[65] Batoclimab, another fully human anti-FcRn monoclonal antibody, is also undergoing evaluation in a concurrent RCT.[66]

Complement Pathway Inhibitors

Additionally, the potential pathogenic involvement of the complement system in chronic autoimmune neuropathies suggests new therapeutic possibilities through agents that inhibit complement activation.[67-69] Riliprubart, a pioneering humanized IgG4 monoclonal antibody, exemplifies this approach by selectively targeting activated C1s within the classical complement pathway. Its formulation allows for subcutaneous administration, enhancing its clinical utility.[70]

Currently, riliprubart is being assessed in an ongoing Phase 2, open-label clinical trial (NCT04658472), which encompasses three distinct patient groups: those receiving Standard-of-Care (SOC) treatments including immunoglobulins and corticosteroids, those who are refractory to SOC, and SOC-naïve patients.[71] The trial is structured into a 24-week initial treatment phase (Part-A), followed by an optional 52-week extension phase (Part-B) for further assessment. Data from this trial will be analyzed using Bayesian statistical methods, which will incorporate predefined efficacy thresholds and leverage historical data-based placebo assumptions to facilitate informed decision-making within the program.[71] This structured approach aims to rigorously evaluate the efficacy and safety of riliprubart, potentially establishing it as a viable treatment option for ratients with chronic autoimmune neuropathies.

Conclusions

CIDP is a potentially disabling neurological disorder; however, it remains highly treatable with significant response rates to established first-line therapies. Current evidence-based treatments include corticosteroids, IVIg, and plasma exchange, each tailored to patient-specific needs based on efficacy and tolerance profiles. Historically, steroids served as the primary treatment, yet in regions where available and cost-effective, IVIg is often favored.[72] This preference persists despite its higher cost, due to perceptions of greater efficacy and safety compared to corticosteroids, although literature reviews suggest that clear superiority of IVIg over steroids is not conclusively established.

Choosing the appropriate administration method of immunoglobulins—SCIg versus IVIg—is a critical decision for clinicians, influenced by factors such as patient comfort, accessibility of venous access, and side-effect profiles. SCIg and fSCIg may be preferred for patients facing challenges with IV access or those who experience severe systemic side effects like headaches. It also offers the flexibility of self-administered, home-based treatment.[25,73-75] Conversely, IVIg might be more suitable for patients with a needle aversion or those who find the handling of subcutaneous pumps and supplies challenging, or for those who suffer from severe local reactions to SCIg.

For patients in remission or those non-responsive to first-line therapies, targeted immunosuppressive treatments become crucial. Moreover, the advent of novel treatments such as FcRn blockers, highlighted by the recent FDA approval of efgartigimod, opens new avenues for managing CIDP more effectively.[63] Ongoing and future clinical trials involving complement pathway inhibitors and BTK inhibitors, already under study for other neurological disorders like multiple sclerosis and neuromyelitis optica (NMO)-spectrum disorders, promise to expand the therapeutic armamentarium for CIDP.[76,77]

The future of CIDP treatment is poised at the edge of significant advancements. Our growing understanding of the disease's pathophysiology holds the promise of personalized medicine approaches, potentially allowing clinicians to identify and target the underlying mechanisms specific to each patient. This precision medicine approach could revolutionize treatment paradigms, offering more effective and tailored therapeutic strategies that directly address the individual pathways involved in CIDP.

Disclosures
None**.**

Conflict of Interest
The authors declare no conflict of interest.

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Table 1: Overview of Randomized Controlled Trial Evidence for Non-Comparative Therapies in CIDP

Therapeutic Intervention	Key Studies	Overall Results	Potential Side Effects
Corticosteroids	- Dyck et al. 1982	Positive effect; superiority to non-treatment	Weight gain, hypertension, diabetes, increased risk of infections
IVIg	-Vermeulen et al. 1993 -Hahn et al. 1996 -Thompson et al. 1996 -Mendell et al. 2001 -Hughes et al. 2008	Demonstrates advantages over placebo	Headaches, fever, chills, rash, nausea, renal dysfunction
SCIg	Markvardsen et al. 2013 -van Schaik et al. 2018 -ADVANCE CIDP-1, 2023	Beneficial effects observed against placebo	Local reactions at injection site, headaches, fatigue
Plasma Exchange	-Dyck et al. 1986 -Hahn et al. 1996	Shows efficacy against sham procedure	Hypotension, citrate toxicity (causing hypocalcemia), bleeding
Efgartigimod alpha and hyaluronidase-qvfc (VYVGART Hytrulo)	-ADHERE, 2023	Efficacy in favor of VYVGART Hytrulo over placebo	Potential infusion reactions, headache, nausea

Abbreviations: IVIg: intravenous immunoglobulin; **SCIg:** subcutaneous immunoglobulin.

Table 2: Overview of Corticosteroid Protocols for CIDP Treatment

Regimen	Route	Dosing Schedule	Potential Side Effects
Tapered Daily Prednisolone	PO	60 mg per day, reduced by 10 mg monthly	Weight gain, mood swings, increased risk of infections, hypertension
Pulsed Dexamethasone	PO	40 mg daily for 4 consecutive days, repeated every four weeks for six cycles	Insomnia, increased appetite, gastric irritation, mood changes
Pulsed Methylprednisolone	IV/PO	1 g every three weeks, completing 8 cycles	Elevated blood sugar, mood alterations, fluid retention, hypertension

Abbreviations: PO: per os; IV: intravenous.