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REVIEW

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Customizing subcutaneous immunoglobulin administration in primary antibody deficiency: patient-centric care perspectives

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ABSTRACT

This report delves into the challenges and potential solutions associated with flexible, customized subcutaneous immunoglobulin (SCIG) infusion regimens for patients with primary antibody deficiency disease (PAD). Advances in the treatment of inborn errors of immunity, particularly PAD, have converted fatal diseases into chronic, complex, long-term conditions that make adherence to treatment a critical issue. Conventional SCIG infusion regimens, while clinically effective, may not always align with the varied lifestyles, changing lifestyles and commitments of patients which can lead to missed doses, diminishing adherence thus posing potential health risks and compromising the overall effectiveness of treatment. For these reasons, it's important to develop flexible infusion regimens tailored to meet individual patient needs. Patient-centric strategies that promote shared decision-making and awareness of patient status not only promote medical efficacy but also enhance the overall patient experience. The authors of this report call attention for a need to shift toward more adaptable and individualized SCIG treatment plans for PAD patients whose needs may change over the long-term course of treatment.

PLAIN LANGUAGE SUMMARY

Primary antibody deficiency (PAD) is a condition where the immune system doesn't work properly, making it hard for the body to fight infections. To stay healthy, people with PAD need regular doses of a medication called immunoglobulin (IgG), which helps strengthen the immune system. This medication can be given in two main ways: through a vein (intravenously, or IVIG) or under the skin (subcutaneously, or SCIG). SCIG has some important benefits. It can be given at home, making it easier for patients to fit treatment into their daily lives. SCIG also causes fewer side effects compared to IVIG. Patients can choose when to take SCIG, making it more flexible and convenient. This article explains how doctors and patients can work together to make SCIG fit into each person's lifestyle. Flexibility can make treatment less stressful and help patients stick to their treatment plan. One type of SCIG, called SCIG 16.5%, can be taken daily, weekly, every 2 weeks, or multiple times a week as long as the total monthly dose stays the same. Flexible ways to use SCIG are safe and effective and can help people manage their treatment leading to better health over time.

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Immunoglobulin replacement therapy; patient-centric; primary antibody deficiency disease; shared decision-making; subcutaneous immunoglobulin; Cutaquig

1. Introduction

1.1. Understanding the burden of treatment

The treatment of primary antibody deficiency disease (PAD) requires regular and frequent replacement of immunoglobulin (IgRT) over a period of years, if not a lifetime, to prevent infections and other complications [1]. Immunoglobulins, including intravenous (IVIG) and subcutaneous (SCIG) formulations, are fundamental to the management of PAD. These polyclonal antibody preparations, derived from pooled human plasma, contain a broad spectrum of antibodies that support immune function through both effector and regulatory mechanisms [2]. In addition to providing replacement immunoglobulin (IgG) for patients with absent or abnormal

antibody function, these therapies also modulate immune responses through interactions with Fc receptors, regulation of cytokine production, and facilitation of regulatory T cell expansion [2].

The necessity of lifelong IgRT creates formidable obstacles with compliance and adherence. An area of investigation which has assumed greater importance looks at convenience and adaptability. The adoption of SCIG infusion has revolutionized the treatment of PAD, providing an effective, convenient, and well-tolerated alternative to IVIG therapy [3–6]. However, while SCIG therapy offers significant benefits including more stable IgG levels, reduced systemic adverse effects, and improved quality of life, there are notable barriers to its adoption as a home treatment option [7]. Patients may face

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Article highlights

- Primary immunodeficiency/inborn errors of immunity were uniformly fatal diseases prior to remarkable advances in therapy. However, these advances have converted fatal illnesses into chronic diseases with enormous, underappreciated consequences.
- Living with a chronic illness such as primary antibody deficiency disease (PAD) is problematic, and coupled with the potential need for lifetime treatment with immunoglobulin replacement therapy (IgRT), these challenges can become formidable tasks requiring long-term compliance.
- Involvement of the patient in the treatment process (patient-centric care) and shared decision-making to develop individual, customized, flexible treatment regimens is critical for adherence and facilitating optimal medical outcomes and quality of life for PAD patients in need of IgRT treatment.
- Understanding the difference between patient compliance and adherence is crucial; while compliance implies passively following instructions, adherence emphasizes active patient engagement and partnership, both of which are essential for long-term treatment success.
- Patient involvement and choices, along with enhancing flexibility and convenience, may minimize barriers which impair adherence, thus playing a pivotal role in insuring the successful management of this rapidly growing group [long-term treatment patients].
- A key tactic in minimizing barriers to adherence may include flexibility in dosing volumes, rates, and frequency.
- Ongoing, regular monitoring is essential to ensure a patient's dosing regimen remains effective, and modifications may be necessary depending upon the circumstances and changes in the needs of the patient over the long term.

challenges such as discomfort with frequent needle insertions, local injection site reactions, and apprehension about self-administration [7]. Psychological factors, such as anxiety and a lack of confidence in managing and maintaining infusion schedules independently, may also influence adherence to SCIG treatment. Living with a chronic illness such as PAD creates a substantial burden, and coupled with the lifelong need for treatment with IgRT, the challenges are amplified [8–12]. Treatment for a month or a year is often burdensome, but when it continues for decades, adherence is, certainly, an issue. In the words of one patient with PAD on IgRT, “I think it’s just because I’ve been doing it for like 32 or 33 years, and that’s quite a big commitment isn’t it? I really wish I could have a break ... but I know I can’t” [11]

1.2. Subcutaneous immunoglobulin replacement therapy in primary antibody deficiency disease

Improved quality of life, a decrease in systemic adverse effects, and increased patient satisfaction are all advantages of SCIG therapy [6,8,13,14]. In individuals with immunodeficiency diseases, SCIG therapy has generally lowered systemic adverse events and hospitalization rates without affecting its efficacy [6,14,15]. Currently, a variety of SCIG preparations are available to cater to the diverse needs of patients with PAD. These include high-concentration SCIG products, such as Cutaquig (16.5% IgG), Hizentra, Cuvitru, and Xembify (all 20% IgG) [13,16]. High-concentration SCIG allows for the administration of smaller infusion volumes, which can reduce the infusion time and improve patient comfort [13]. Additionally, facilitated SCIG (fSCIG; Hyqvia) combines immune globulin with

recombinant human hyaluronidase (rHuPH20) [17]. This enzyme temporarily increases tissue permeability, enabling larger infusion volumes at fewer infusion sites and longer intervals between infusions [17].

A study focusing on the patient experience with IVIG and SCIG found that patients using SCIG reported greater satisfaction in terms of effectiveness and had a higher proportion of respondents with disease symptoms that were considered well managed compared to those using IVIG [18]. This suggests that the mode of IgRT administration can significantly impact patient satisfaction and overall treatment experience, which is a crucial factor in patient-centric care. However, the large range of alternatives available and the individual heterogeneity in patient demands and preferences make it challenging to choose the best IgRT regimen.

SCIG therapy, while offering the convenience of home administration and greater autonomy compared to IVIG, requires frequent and repetitive procedures that may feel burdensome to patients, particularly younger individuals or those with active lifestyles [19]. In elderly or physically impaired patients, some special considerations may be necessary as these patients may have reduced physical strength and mobility, cognitive skills, and diminished incentive after prolonged treatment and illness, making the self-administration of SCIG more challenging [20–22]. The long-term, frequent nature of SCIG therapy in PAD demands sustained engagement with the treatment regimen.

Clinicians must be cognizant and proactive in discussing these aspects with their patients, ensuring that the treatment plan is not only effective but also psychologically sustainable and realistically achievable [23]. This may include incorporating variety in treatment routines, providing psychological support, and exploring new advancements in treatment that may offer more convenience [11,12]. For example, equipment and protocols that facilitate infusion rate, volume, and calculation devices simplify the process and, therefore, may help with treatment adherence [19]. Physicians adopting a proactive and anticipatory approach to care can significantly mitigate the feeling of isolation for patients living with chronic illnesses. By actively engaging patients and reinforcing their ongoing support, physicians ensure that patients genuinely feel and understand that they are not facing their condition alone. This proactive provider involvement reassures patients of their support network. The physician also must be acutely aware of the recipient's ability and motivation to carry out protracted IgRT therapy, further recognizing that this is a dynamic situation.

2. Patient-centric care and shared decision making

In recent years, there has been a growing recognition of the importance of patient-centric care which involves engaging patients as active partners and taking their individual needs and preferences into account (Table 1) [9,15,23–32]. To make treatment decisions that take into account the patient's preferences and goals, the clinician and the patient must engage in shared decision-making which has been demonstrated to improve patient satisfaction, treatment adherence, and health outcomes [24–26,30]. This method places significant emphasis

Table 1. Patient-centric care and shared decision-making in SCIG therapy for PAD.

Aspect	Description	Significance in SCIG Therapy
Patient Autonomy	Emphasizing the patient's role in managing their treatment.	Patients can self-administer SCIG at home, offering control over their treatment schedule [27].
Individualized Treatment Plans	Tailoring therapy to meet individual patient needs and preferences.	SCIG dosages and schedules can be adjusted based on patient response, lifestyles, and preferences [23,28].
Patient Education	Providing comprehensive information about disease and treatment options.	Educated patients are more confident in self-administration and management of SCIG [29].
Shared Decision-Making	Collaborative process between clinician and patient in choosing the best treatment approach.	Involving patients in decisions about switching to SCIG or adjusting dosages enhances satisfaction and adherence [30].
Quality of Life Considerations	Assessing the impact of treatment on patients' daily lives.	SCIG is associated with fewer systemic side effects and less impact on daily activities compared with IVIG [15,31].
Monitoring and Follow-up	Regular assessment of treatment effectiveness and patient well-being.	Continuous monitoring ensures optimal SCIG dosing and early identification of potential complications [32].
Access to Support Services	Providing resources for psychological, financial, and logistical support.	Support services facilitate the transition to home-based SCIG therapy and ongoing management [15].

Abbreviations: IVIG: intravenous immunoglobulin; PAD: primary antibody deficiency; SCIG: subcutaneous immunoglobulin.

on empowering patients to develop a comprehensive understanding of their disease, enabling them to actively participate in healthcare decision-making alongside healthcare providers.

When it comes to IgRT, shared decision-making includes informing patients about the various treatment options and their advantages and disadvantages, as well as taking into account the patient's lifestyle, treatment objectives, and preferences when choosing an IgRT regimen [25,33]. In this context, it's also important to understand the subtle difference between the terms, "compliance" and "adherence." Traditionally, compliance has been defined as the extent to which a patient follows medical instructions. This term often implies a passive role on the part of the patient, who is seen as simply executing a plan laid out by healthcare providers. While compliance ensures that a patient meets the requirements of their prescribed therapy, it does not account for the patient's understanding, engagement, or agreement with the treatment regimen.

Adherence, by contrast, conveys a more collaborative approach. It emphasizes the patient's active participation in their care, highlighting the importance of mutual understanding and agreement between the patient and healthcare provider. Adherence implies that patients are not just following orders but are actively engaged in shared decision-making with their providers. This shift from compliance to adherence is particularly significant in the management of chronic conditions like PAD where commitment and motivation are crucial for optimal outcomes. Further, patient adherence is critical when life-saving treatment [IgRT] is required. It is one thing to comply for a year, it is another thing to comply for decades or a lifetime.

Clinicians must also consider that patients need quality infusion education and educational resources to ensure long-term success [34,35]. Multiple resources are available online, in print, and in specialized SCIG infusion apps [36–38].

3. Benefits of flexible infusion regimens

Flexible IgRT regimens have emerged as an effective approach to enhancing patient-centric care in the management of PAD [9,23]. Flexible regimens allow patients to adjust the timing, dose, and administration route of IgRT to suit

their individual needs and preferences [28,39]. The goal of a specific treatment regimen should be to provide optimal medical outcomes and quality of life by adapting the volume, rate, and frequency of treatments for suitability to each patient's clinical requirements including body weight and baseline serum IgG levels, as well as their lifestyle and comorbidity profile [8,40]. The ability to deliver larger volumes of SCIG over shorter periods of time, on a daily, weekly, or every other week basis, may enhance convenience and patient adherence as well as optimize dosing to accommodate individual patient needs [28,41].

It's also important to choose the right product rather than prescribing IgRT as a generic drug. Patients requiring ongoing IgRT should be maintained on a consistent product that is well tolerated. Product administration should also be considered. In general, SCIG is delivered using small needles attached to the tubing and a syringe which is placed in a pump [5]. A variety of SCIG infusion pumps are available ranging from simple, portable mechanical pumps to more complicated electronic, programmable pumps [5].

In addition to conventional SCIG, it is important to highlight alternative methods that may suit specific patient needs, such as fSCIG and less commonly a "manual push" technique for high-concentration SCIG (e.g., 16.5% and 20% formulations). As mentioned, fSCIG incorporates recombinant human hyaluronidase to temporarily increase tissue permeability, allowing for larger infusion volumes and higher rates. This approach can be especially beneficial for patients requiring larger doses or those who desire less frequent infusions. The rapid push or rapid technique for high-concentration SCIG allows patients to infuse using a syringe without a pump, providing an option for faster administration and greater control over the process [42]. However, it is important to note that physical or cognitive limitations, combined with the complexity of various infusion procedures, may inhibit the ability to infuse IgRT on a regular and prolonged basis. Another consideration is that the high viscosity of some SCIG solutions can make it difficult to accommodate the manual push technique [42]. Biennu and colleagues demonstrated that manual push of SCIG 16.5% was a safe, easy-to-learn method that was well accepted by patients and manual push infusions were five- to six-fold faster but more than threefold more frequent than pump infusions [42].

The paradigm of patient-centric care involves awareness and attention related to patient wants, preferences, and values. Adherence to therapy and positive overall clinical outcomes may be encouraged when patients have greater control over their treatment, particularly if it is a lifelong regimen-like IgRT [40,43].

4. Patient selection and customized subcutaneous immunoglobulin treatment regimens

4.1. Patient selection

For the best possible therapeutic results, it is essential to choose the patients who are well suited to SCIG therapy and ensure they can manage the procedure and adapt their treatments, as needed, over time. Additionally, it is vital to instruct and educate patients on appropriate infusion techniques. Emphasizing the necessity of adhering to a regular infusion schedule, as well as the importance of consistent follow-ups and reviews, positively impacting long-term outcomes [44]. Missed doses of IgRT do not result in immediate adverse consequences and, therefore, it is not unexpected that rigid compliance could be an issue. Long term, complex treatment is an ongoing, dynamic process that requires periodic reassessment to accommodate changes and adapt to new circumstances, ensuring the therapy remains effective and aligned with the patient's evolving needs.

An obvious benefit of SCIG is the convenience it offers to patients. Instead of having to travel to a clinic or hospital to receive their medication, patients can administer the medication themselves at home or while traveling. This can also be particularly beneficial for patients who live in or are traveling to remote areas where access to medical facilities may be limited. Patients can also choose to administer the medication at a time that is convenient for them, which can help them to better manage their schedule and maintain a sense of control over their treatment.

Another benefit of SCIG is that it can be less disruptive to a patient's daily life. Traditional IVIG therapy can require

patients to spend hours at a time in a hospital, clinic, or home setting under the care of a healthcare provider. This can be mentally and physically taxing and can make it difficult for patients to manage their work or other responsibilities. On the other hand, it is obvious that confirmation of adherence to rigorous, regular infusions is less scrutinized, and combined with lack of immediate consequences of noncompliance, one can appreciate that patient adherence is pivotal to home infusion.

In an effort to gain more inclusion within the healthcare system, the motto of the PAD patient community is, "Nothing about us without us." [45] This motto was first developed by disability rights activists to convey the idea that no policy should be reached without patient participation. Results from a study conducted by Lamb and Wang [25] suggest that patient-centric care is the best method for physicians to most effectively increase patient participation for the care of PAD.

Patient wants, preferences, and values are given top priority in all facets of health management under the perspective of patient-centric care. It entails a cooperative relationship and shared decision-making between the patient, their family, and the healthcare professionals, where the patient's goals and priorities are at the center of all health-related decisions [24]. Instead of focusing on a patient's illness, this method of treatment emphasizes the value of patients as individuals with their own specific needs and circumstances. In other words, the patient's care is aligned with their lifestyle and preferences and the physician develops a more holistic picture of the patient, taking into account their physical, emotional, and social well-being.

In a survey developed by Lamb and colleagues [43], it was demonstrated that physicians treating patients with PAD with a patient-centric approach and shared decision-making enhanced patient participation. Choices available to patients and physicians related to IgRT include treatment schedules, administration methods (volume, rate, and location), and products best suited to these needs [25].

To ensure a patient's needs are met, a thorough evaluation and examination should be undertaken to ensure the patient

Table 2. Patient selection for SCIG therapy for PAD.

Factor	Description	Considerations
Diagnostic Criteria of PAD Requiring IgRT	Presence of PAD.	PAD requiring IgRT.
Venous Access	Accessibility and condition of venous access.	SCIG is preferable to IVIG in patients with difficult venous access.
Previous IVIG Intolerance	Patients with a history of IVIG intolerance.	History of adverse reactions to IVIG, intolerances, or contraindications.
Patient Preference and Lifestyle	Patient's preference and ability to manage therapy at home or while traveling.	Willingness and ability to self-administer (including physical dexterity and visual acuity), or have caregivers who can provide assistance as well as lifestyle compatibility.
Burden of Care	Evaluation of the impact of therapy on a patient's life.	Consideration of the frequency, duration, and location of infusions, as well as the patient's ability to manage these aspects.
Dosage Requirements	Assessment of the required IgRT dose for effective treatment.	Feasibility of administering the required dose subcutaneously.
Comorbidities	Other existing medical conditions.	Cardiac, renal, or systemic conditions (e.g., diabetes, coagulopathies) that may affect therapy choice.
Age and Body Weight	Patient's age and body weight.	Suitability and dosage adjustments based on age and body weight.
Insurance Coverage and Cost	Financial aspects of therapy.	Insurance coverage and cost-effectiveness as compared with IVIG.
Clinical Monitoring Capability	Ability to monitor treatment efficacy and safety.	Access to healthcare professionals and facilities for regular monitoring and management of efficacy and potential adverse effects.

Abbreviations: IgRT: immunoglobulin replacement therapy; IVIG: intravenous immunoglobulin; PAD: primary antibody deficiency disease; SCIG: subcutaneous immunoglobulin.

is a good candidate for SCIG therapy (Table 2). Medical and social history should be taken as well as laboratory evaluations performed, including hematologic/inflammatory, renal, and liver function tests [13,46]. Once it has been determined that the patient is a good candidate, the SCIG dosage is calculated based on the patient's weight, age, and baseline/desired immunoglobulin levels. It should be noted that the effect of body mass index (BMI) on serum trough levels is unclear [5]. In a meta-analysis published in 2023 by Zhou and colleagues, they found no compelling evidence to justify a reconsideration of a patient's current dosing strategy based on total body weight for PAD [47]. Therefore, titration of dosing should be based on the serum trough levels as well as the clinical response. The infusion schedule should be chosen in close coordination with the patient and in accordance with their preferences, lifestyle, age, and socioeconomic circumstances. Ongoing monitoring is essential to ensure the dosing regimen is appropriate and may need to be modified as the circumstances dictate.

4.2. Subcutaneous immunoglobulin treatment administration and clinical evidence

SCIG infusions utilize aseptic technique with the choice of ancillary supplies, infusion site, and injection technique taking into consideration the patient's age, body habitus, physical and cognitive limitations, and preference [5,48].

A recent study evaluating safety, efficacy, and flexibility utilized an SCIG 16.5% product in managing PAD with enhanced treatment regimens [28]. The primary objective of the SCGAM-06 trial was to assess the efficacy of enhanced infusion regimens in terms of providing greater flexibility in administration. Three distinct cohorts were administered to SCIG 16.5% with different infusion regimens to assess the effects of varying volume, infusion rate, and frequency of administration (Table 3) [28]. The dosing regimens included the following: 1) volume assessment per site; 2) infusion flow rate per site; 3) infusion frequency: every other week at the equivalent of twice the patient's body-weight dependent [mg/

kg] weekly dose. Sixty-four patients were enrolled in the study and 55 (85.9%) completed the study. All the SCIG infusions ($n = 1,338$) were completed at home.

In Cohort 1 (increased infusion volume), the mean (standard deviation [SD]) maximum volume per site was 69.43 (23.47) mL/site ranging from 36.0 to 108.0 mL/site [28]. The mean (SD) volume administered per infusion was 83.38 (21.82) mL over a mean of 2.3 infusion sites which reduced the number of infusion sites, a potential convenience. In Cohort 2 (increased infusion flow rates), the mean (SD) maximum realized flow rate per site was 42.06 (13.02) mL/h/site ranging from 17.1 to 67.5 mL/h/site [28]. Due to the increased flow rate, the mean infusion duration was decreased by >57% as compared with the other cohorts, again a potential convenience. In Cohort 3 (dosing every other week with no increases to flow rate or volume), the mean (SD) volume administered per infusion was 117.61 (57.84) mL (range: 7.0 to 252.0 mL) over a mean of 3.9 infusion sites, and the maximum realized mean (SD) flow rate per site was 19.25 (7.01) mL/h/site [28].

Implementing these infusion variables resulted in no serious bacterial infections reported during the study [28]. The majority of adverse events were mild (23.4%) or moderate (56.3%). Results of the satisfaction questionnaire completed at the Termination Visit indicated that a majority of patients (67.3%) found the new infusion regimen to be better or somewhat better than their previous regimen and that switching from their previous SCIG product to SCIG 16.5% was very easy.

4.3. Customized subcutaneous immunoglobulin treatment regimens

Customizing the infusion experience for patients receiving SCIG involves considering several factors. These factors include SCIG product choice/concentration, dose, number of infusion sites/volumes per site, rate/speed of infusion, tubing, needles, and the type of pump used (Figure 1) [28,49,50]. The ancillary supplies associated with SCIG infusions can have a major impact on the overall patient experience with SCIG [49,50].

Table 3. SCGAM-06: summary of demographic and baseline characteristics (full analysis set).

Characteristic	Cohort 1: Increased Volume (N = 15) n (%)	Cohort 2: Increased Rate (N = 15) n (%)	Cohort 3: Every Other Week (N = 34) n (%)	Total (N = 64) n (%)
Age (years)^a, n	15	15	34	64
Mean (SD)	51.20 (17.27)	47.88 (20.53)	50.81 (18.54)	50.21 (18.49)
Median	49.72	56.52	58.37	55.71
Min, Max	17.2, 74.2	10.5, 67.2	5.7, 71.0	5.7, 74.2
Sex				
Female	10 (66.7)	11 (73.3)	27 (79.4)	48 (75.0)
Male	5 (33.3)	4 (26.7)	7 (20.6)	16 (25.0)
Type of PI Disease				
CVID	14 (93.3)	13 (86.7)	30 (88.2)	57 (89.1)
Other ^b	1 (6.7)	1 (6.7)	4 (11.8)	6 (9.4)
XLA	0	1 (6.7)	0	1 (1.6)
BMI (kg/m²), n	15	15	34	64
Mean (SD)	35.17 (8.99)	28.20 (4.56)	27.98 (5.97)	29.72 (7.11)
Median	32.70	28.20	26.05	28.90
Min, Max	22.5, 49.0	20.6, 34.9	16.5, 38.5	16.5, 49.0

Abbreviations: BMI = body mass index; CVID = common variable immunodeficiency; Max = maximum; Min = minimum; N = number of patients; PI=primary immunodeficiency; SD = standard deviation; XLA = X-linked agammaglobulinemia.

^aPediatric patients included young children (>2 and <6 years), children (≥6 and <12 years), and adolescents (≥12 and <17 years).

^b"Other" included 5 cases of hypogammaglobulinemia with antibody deficiency and 1 case of hereditary hypogammaglobulinemia.

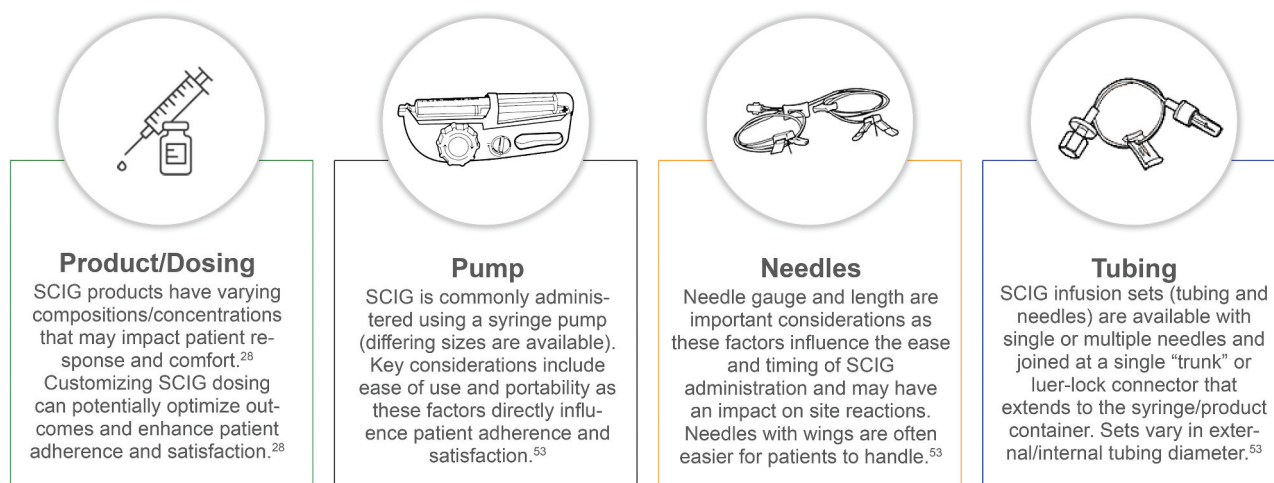


Figure 1. Key factors for optimization of subcutaneous immunoglobulin (SCIG) therapy for primary antibody deficiency disease (PAD).

The typical replacement dose for PAD patients is 400–600 mg/kg of IgG per month [1]. For SCIG, this monthly dose is administered in several different ways, and in different anatomical sites, depending on individual tolerance. Some patients may choose to dose weekly, every other week, or even prefer daily infusions of SCIG. In the case of fSCIG, the infusions can be given once a month. Flexibility is paramount in devising an optimal, personalized SCIG therapy plan. A detailed dialogue with the patient should be conducted to determine their preferred frequency of infusion, the volume to be administered, and the preferred number of infusion sites. Subsequently, a customized infusion regimen that aligns seamlessly with their daily routine, capabilities, and support system ensuring greater adherence and effectiveness should be developed [50].

The choice of infusion equipment and supplies plays a key role in facilitating SCIG infusions. Any procedure or device which simplifies or makes a treatment procedure such as IgRT more convenient may facilitate near and long-term adherence. In today's digital age, the availability of websites and applications plays a pivotal role in enhancing healthcare delivery, especially for patients requiring specialized treatment modalities. This information may facilitate patient flexibility, convenience, simplicity, and efficacy. Digital resources, specifically, online rate calculators for SCIG pump systems, such as examples, the Koru Freedom Flow Rate Calculator (KORU Medical Systems, available at: <https://korucalculator.com/>) and the EMED Flow Rate Calculator (EMED technologies, available at: <https://www.versarate.com/calculator>) are helpful for healthcare providers managing patients with PAD requiring SCIG IgRT (please note these are examples only, with no endorsement of any specific platform)(Figure 2). These tools aid in optimizing SCIG administration by assisting in the selection of the appropriate tubing and needle set combinations for a desired flow rate and infusion time. Digital tools offer a systematic way to determine the most efficient and patient-compatible infusion setup. The calculator has been used for years by pharmacists and infusion nurses to choose the appropriate tubing sets for patients. Since the treating prescriber and their clinical staff are, typically, the healthcare professionals who will follow-up with

PAD patients, these may be helpful tools when a patient is looking to customize their infusion regimen.

Customization can be crucial as it directly impacts patient comfort, infusion efficiency, and overall treatment effectiveness. These tools simplify the process of calculating infusion parameters and developing a personalized therapy plan. The calculators are user-friendly, requiring only a few simple steps to obtain the desired infusion setup. Users choose the device, input the medication and dose, select the flow-rate tubing and needle set, and ensure that the flow rate per site and total infusion time are within the range of the prescribed IgRT.

The use of calculators may aid in tailoring the infusion parameters to the individual needs of each patient, which is critical in managing PAD where one-size-fits-all approaches are often suboptimal. By adapting the infusion regimen for comfort and convenience, patients are more likely to adhere to their treatment plans. This is particularly important in PAD, where regular and lifelong therapy is often necessary. Proper selection of infusion parameters reduces the risk of complications such as site reactions or inadequate dosing, thus enhancing the overall safety of SCIG therapy as adverse effects could potentially impact adherence.

The use of flow-rate calculators simplifies and enhances patient-centric care, allowing for adjustments based on patient-specific factors such as body weight, total SCIG dose, and individual response to therapy. It empowers clinicians to make informed decisions that take into account the unique characteristics and preferences of each patient, leading to more personalized and effective care. A clinician can use these tools as part of the shared decision-making processes, where patients are involved in their care plan. This involvement can lead to better understanding, greater satisfaction, and improved adherence to therapy. These tools may also facilitate education for both healthcare providers and patients, enhancing understanding of the intricacies of the SCIG administration.

It should be noted that while routine, annual monitoring of IgG serum levels is crucial [or more frequently if the clinical situation demands it and further emphasizing that over the long-term, frequency monitoring can change], it is equally

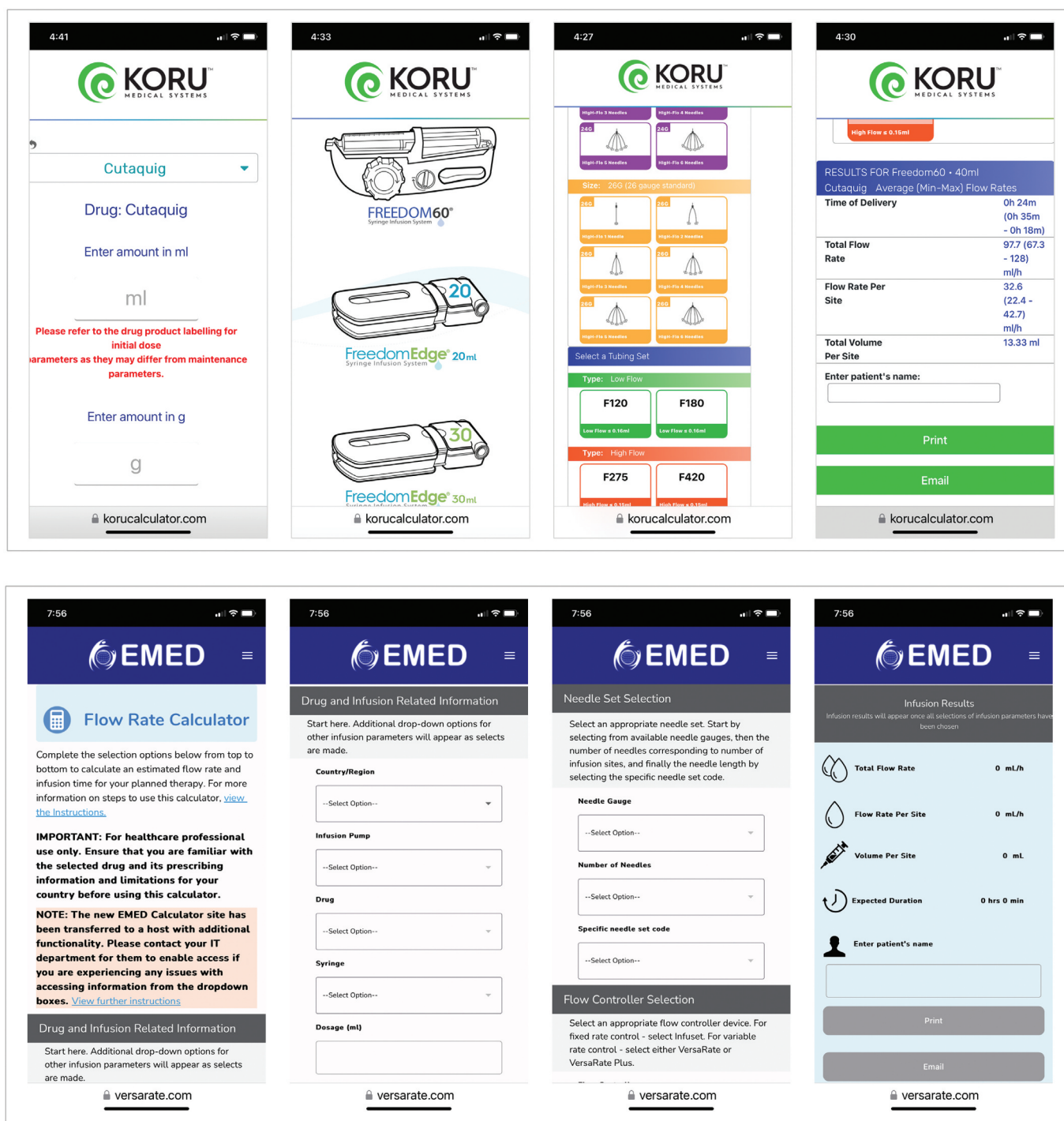


Figure 2. Sample screens from: (upper) KORU freedom flow rate calculator (KORU medical systems, available at: <https://korucalculator.com/>); (lower) EMED flow rate calculator (EMED technologies, available at: <https://www.versarate.com/calculator>).

important to conduct additional assessments when significant alterations to infusion protocols are made to ensure optimal levels are maintained, offering reassurance to both the patient and the physician regarding the effectiveness of the treatment plan. As a crucial reminder, assessment of the patient's clinical status, most importantly infections, complications associated with PAD, and comorbid diseases (especially heart, kidney, liver, neurological, musculoskeletal diseases) must be carefully monitored.

As SCIG is often administered at home, these calculators may play a significant role in assisting home-based care. They may promote a regimen that is manageable for patients or caregivers, fostering independence and reducing the need for frequent healthcare facility visits. This aspect is particularly beneficial during times where minimizing hospital visits is crucial. To better illustrate the development of flexible, individualized dosing regimens, example case studies are provided below.

4.3.1. Example patient 1: a teacher and mother of four

- **Background:**
 - Age: 35
 - Occupation: High school teacher
 - Family: Married with four children (ages 6–13)
 - Medical History: Diagnosed with common variable immunodeficiency (CVID) at 20
- **Lifestyle and Challenges:**
 - Active lifestyle with frequent hiking and family trips to national parks
 - Busy schedule during the school year due to work and children's sports
- **Initial Infusion Schedule:**
 - Infusing every other week during the summer with extra time available
 - Difficulty adhering to the longer infusion schedule during the school year
- **Consultation and Adjustments:**
 - Admitted to missing infusions due to time constraints
 - Physician highlighted the importance of adherence, especially with bi-weekly infusions
 - Collaborated with an experienced infusion nurse to find a feasible solution
- **New Infusion Plan:**
 - Daily infusion schedule integrated into morning routine (30 minutes spent on hair/makeup)
 - Plan: 10 g weekly dose split into 5 daily doses of 2 g each
 - Equipment: Single 26-gauge needle, specific flow-rate tubing
 - Infusion time: 16 minutes per day
- **Outcome:**
 - No adverse events reported
 - Improved adherence and no missed doses since switching
 - Gained time on events and weekends for family activities

4.3.3. Example patient 3: an active college student

- **Background:**
 - Age: 19
 - Occupation: College student studying paleontology
 - Medical History: Diagnosed with X-linked agammaglobulinemia at age 3
 - Known for: Laughter, intelligence, dedication to paleontology and the study of dinosaurs
- **Lifestyle and Challenges:**
 - Childhood Infusion Experience: Enjoyed educational infusion times with parents reading stories or watching dinosaur movies
 - Current Situation: Busy college schedule and first time living independently, leading to challenges finding time for infusions
- **Initial Infusion Schedule:**
 - Struggled to maintain adherence due to a demanding academic schedule
- **Consultation and Adjustments:**
 - Consulted with his physician, who acknowledged the adherence risks in young adult patients
 - Decided on a regimen of SCIG 16.5% infusions every other week, aiming for less than an hour per session
- **New Infusion Plan:**
 - Dose: 22 g every other week
 - Equipment: 3, 24-gauge needles and appropriate tubing
 - Infusion time: Completed in 44 minutes
- **Outcome:**
 - Adapted well to the new bi-weekly infusion schedule
 - No missed doses over the past 6 months
 - Feels more confident in self-managing his condition with guidance from his prescriber
 - Demonstrated the importance of patient engagement and active participation for sustained adherence in long-term treatment

4.3.2. Example patient 2: a retired traveler

- **Background:**
 - Age: 78
 - Occupation: Retired architect
 - Medical History: Diagnosed with CVID at age 60
 - Previous Treatment: 15 years on IVIG, switched to SCIG 3 years ago
- **Lifestyle and Challenges:**
 - Enjoys traveling across North America with his wife in their recreational vehicle
 - Adversely affected by late CVID diagnosis (multiple infections and hospitalizations)
 - Concerned about maintaining IgG trough levels to prevent recurrent infections
- **Initial Infusion Schedule:**
 - Twice-weekly infusions of SCIG 16.5% (8 infusions per month)
 - Found the schedule manageable but expressed interest in less frequent dosing
- **Consultation and Adjustments:**
 - Discussed potential for infusing every other week with his doctor
 - Doctor suggested revised plan with monitoring IgG trough levels to ensure effectiveness
 - Plan: New regimen of 26 g every other week, with a higher volume per site and increased infusion rate
- **New Infusion Plan:**
 - Infusion rate: 29 mL/hr/site
 - Infusion time: Completed in under 2 hours using 4 infusion sites
 - Equipment: 26-gauge needles, suitable tubing
- **Outcome:**
 - Tolerated the new regimen without issues
 - Maintained IgG trough levels over 2 months
 - Clinically effective and allowed flexibility to accommodate travel plans

5. Conclusions

The discussion included herein underscores the importance of personalized infusion schedules and ongoing support for patients with PAD. It is practical and reasonable to allow adjustments in rate, volume, and frequency as long as the total monthly number of grams of IgG and IgG serum blood levels are maintained, infections are avoided, and careful monitoring for complications is assiduously followed. This paper also provides tools and examples for the development and maintenance of flexible regimens. Rigidity in relation to SCIG infusion regimens may ultimately impair long-term treatment for PAD patients where faithful IgRT infusions are essential for well-being and outcomes. Traditional regimens with little or no flexibility, while effective and conventional, may be contrary to the diverse lifestyles and commitments of patients, leading to missed doses and potential health risks. By taking into account and adapting to individual routines, shared decision-making and active, ongoing support can help patients achieve better adherence to their treatment without compromising their quality of life.

Furthermore, examples from the SCGAM-06 trial emphasize that changes in the infusion rate, volume, and frequency are well tolerated by patients [28]. The quality of life data from that study also indicate that these adjustments do not result in any deterioration of the patient's well-being [28]. As the medical community continues to advance in its understanding and treatment of PAD, it's imperative to prioritize patient-centric

approaches that not only ensure medical efficacy but also enhance the overall patient experience.

6. Future perspective

It needs to be emphasized that more and more PAD patients will be treated for decades and adherence and compliance over the long term is critical. As IgRT for PAD continues to evolve, future research is increasingly focusing on the optimization of SCIG therapy to enhance both efficacy and patient quality of life. Personalized dosing strategies that account for individual pharmacokinetic variations are seen as a critical development [51,52]. By tailoring dosages more precisely, it may be possible to maintain more stable serum IgG levels, which could help reduce the frequency of infections and improve overall health outcomes [18].

Additionally, technological advancements in the devices used for SCIG administration present significant opportunities for improving patient outcomes. Emphasis on infusion procedures must make it easier and more convenient to administer, particularly as the IgRT population ages and with more physical, mental, and accessibility considerations. Innovations in pump technology that allow for more controlled and comfortable infusion experiences are on the horizon. These improvements could lead to better adherence to treatment regimens, especially among younger patients or those new to lifelong therapies. Future studies could focus on the integration of smart technology in infusion devices, which could provide real-time feedback to patients and healthcare providers, ensuring that the therapy is optimally delivered.

The future of SCIG therapy also involves expanding the understanding of its long-term effects on patient health beyond just infection control. Research into how sustained SCIG therapy affects quality of life, including physical, psychological, and social health domains, will be essential. This comprehensive approach will help to refine treatment protocols and support services to address the full scope of patient needs in managing PAD.

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