Facilitated Immunoglobulin Administration Registry and Outcomes Study (FIGARO): Interim Results in Patients With Secondary Immunodeficiency Diseases (SID)

P071

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Introduction

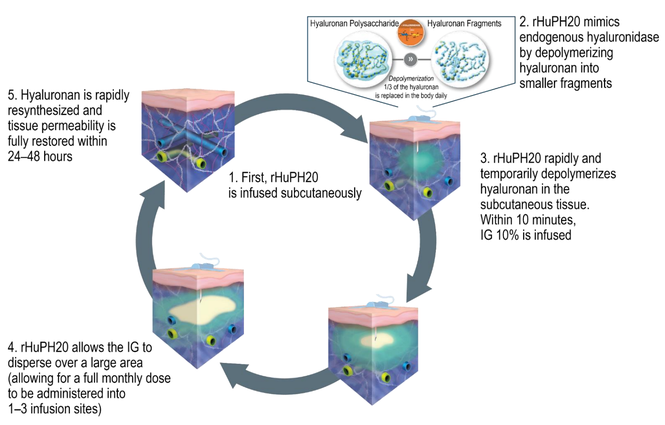
Background

- Secondary immunodeficiency diseases (SID) are a frequent complication of hematologic malignancies such as chronic lymphocytic leukemia (CLL) or multiple myeloma (MM) and associated treatments[1]
  - Patients who have SID are at an increased risk of infections, which are a major cause of morbidity and mortality[2]
- Several national guidelines recommend the use of immunoglobulin replacement therapy (IGRT) to reduce the incidence of infections among patients who have SID and repeated infections despite using prophylactic antibiotic therapy[1]
  - IGRT can be administered intravenously (IVIG) or subcutaneously (SCIG). Unlike IVIG, conventional SCIG (cSCIG) allows for self-administration at home with better systemic tolerability
  - However, SCIG is limited by the volume that can be infused, necessitating more frequent infusions and multiple infusion sites[3,4]

Facilitated Subcutaneous Immunoglobulin

- Facilitated SCIG (fSCIG; Baxalta US Inc., a Takeda company) is a dual-vial unit of immunoglobulin G (IgG) 10% and recombinant human hyaluronidase (rHuPH20)[5]
  - rHuPH20 depolymerizes hyaluronan in the extracellular matrix, resulting in a transient and local increase in subcutaneous tissue permeability, allowing for larger volumes / infusion site relative to cSCIG[4] (**Figure 1**)

Figure 1. rHuPH20 Mechanism of Action Allows Increased Volume and Flow Rate of IG Infusion Into the Subcutaneous Tissue



IG, immunoglobulin; rHuPH20, recombinant human hyaluronidase.

- fSCIG is approved in Europe for the treatment of primary immunodeficiency diseases (PID) and SID[a5]
  - In a pivotal phase 3 study of patients with PID (NCT00814320), fSCIG was effective, safe, and bioequivalent to IVIG at the same administration intervals, with fewer systemic reactions. Annual overall infection rates during treatment with IVIG and fSCIG were 4.51 and 2.97 events / patient-years, respectively[6]
- Additional data on fSCIG use in patients with SID are needed

Objective

- The objective of this analysis is to assess the use of fSCIG in routine clinical practice in patients with SID

Methods

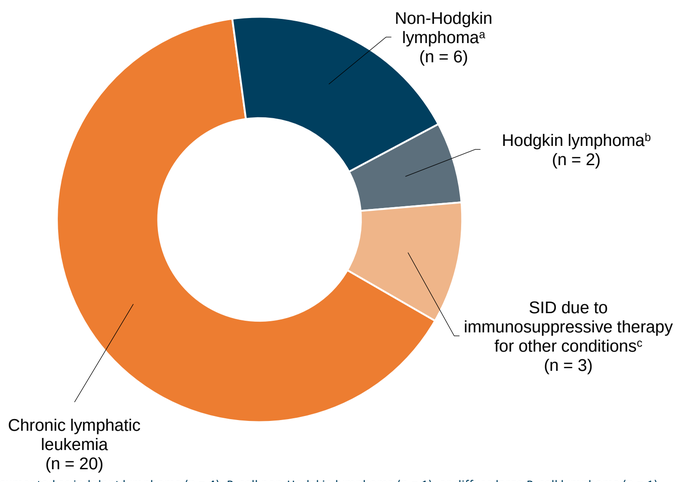
- FIGARO (NCT03054181) is a multicenter, prospective observational study conducted in Europe under the auspices of the European Society for Immunodeficiencies
- Patients are eligible for inclusion if they:
  - Received ≥ 1 fSCIG infusion for PID or SID
  - Provide informed consent
- An interim analysis (data cut-off 12 March 2020) was conducted on data collected at inclusion visits in the subset of patients with SID
  - Parameters assessed included:
    - Patient characteristics and medical history
    - fSCIG utilization patterns at inclusion visit
    - IgG trough levels at inclusion visit
    - fSCIG tolerability (local or systemic adverse drug reactions [ADRs])
- Patients will be followed for up to 3 years

Results

Patients and Baseline Characteristics

- Of the 154 patients enrolled at the data cutoff date, 31 received fSCIG for SID and were included in the analysis
  - Nineteen (61.3%) patients were male, and 29 (93.5%) were Caucasian / White
  - The mean (standard deviation; SD) age was 61.4 (17.8) years (range: 3–88 years)
  - The most common SID diagnoses were CLL (64.5%) and non-Hodgkin lymphoma (19.4%) (**Figure 2**)

Figure 2. SID Diagnoses at Baseline (Number of Patients)

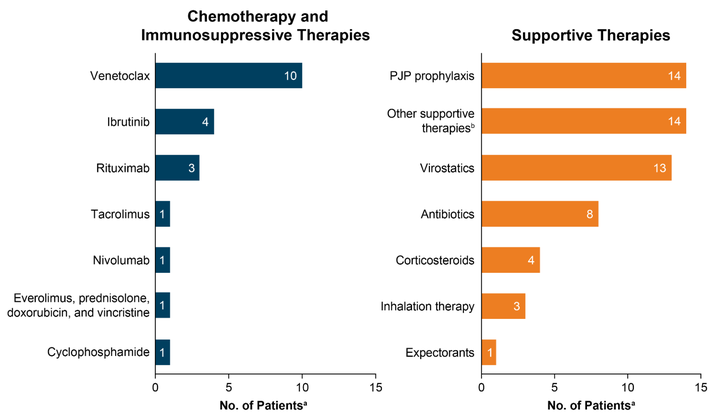


[a]Documented as indolent lymphoma (n = 4), B-cell non-Hodgkin lymphoma (n = 1), or diffuse large B-cell lymphoma (n = 1).
[b]Documented as Hodgkin lymphoma (n = 1) or Hodgkin lymphoma after autologous transplantation (n = 1).
[c]Documented as lung transplantation with rituximab therapy (n = 1), rheumatoid arthritis with sulfasalazine therapy (n = 1), and liver disease with corticosteroids and tacrolimus therapy (n = 1).

SID, secondary immunodeficiency diseases.

- At baseline, 28 (90.3%) patients were receiving chemotherapy and/or immunosuppressive or supportive therapy (**Figure 3**)
  - The most common chemotherapy / immunosuppressive therapies were venetoclax and ibrutinib
  - The most common supportive therapies were *Pneumocystis jiroveci* pneumonia prophylaxis, virostatics, and antibiotics

Figure 3. Concomitant Chemotherapies, Immunosuppressive Therapies, and Supportive Therapies at Baseline (Number of Patients)



[a]Patients could have received > 1 therapy.
[b]Other supportive therapies reported in > 1 patient were allopurinol (n = 7) and aciclovir (n = 5).
PJP, *Pneumocystis jiroveci* pneumonia.

Infusion Parameters / fSCIG Administration

- Infusion parameters at inclusion visit are described in **Table 1** and **Figure 4**
  - Mean (SD) monthly fSCIG dose was 26.6 (6.1) g
  - Most patients self-administered fSCIG (58.1%) and infused at home (61.3%)
  - Patients predominantly (67.7%) received fSCIG treatment every 4 weeks
  - All but 1 patient (96.3%) used a single infusion site
  - Only 1 of 31 patients required premedication
  - No technical problems were reported, and all patients received the full fSCIG dose as planned on the scheduled date (93.1%) or within ±1–3 days of the scheduled date (6.9%)

Table 1. fSCIG Infusion Parameters (Inclusion Visit)

Parameter[a]	
Monthly fSCIG dose, mean (SD), g	26.6 (6.1)
Infusion volume, median (range), mL	300.0 (100.0–300.0)
Maximum infusion rate, median (range), mL/hr	290.0 (180.0–300.0)

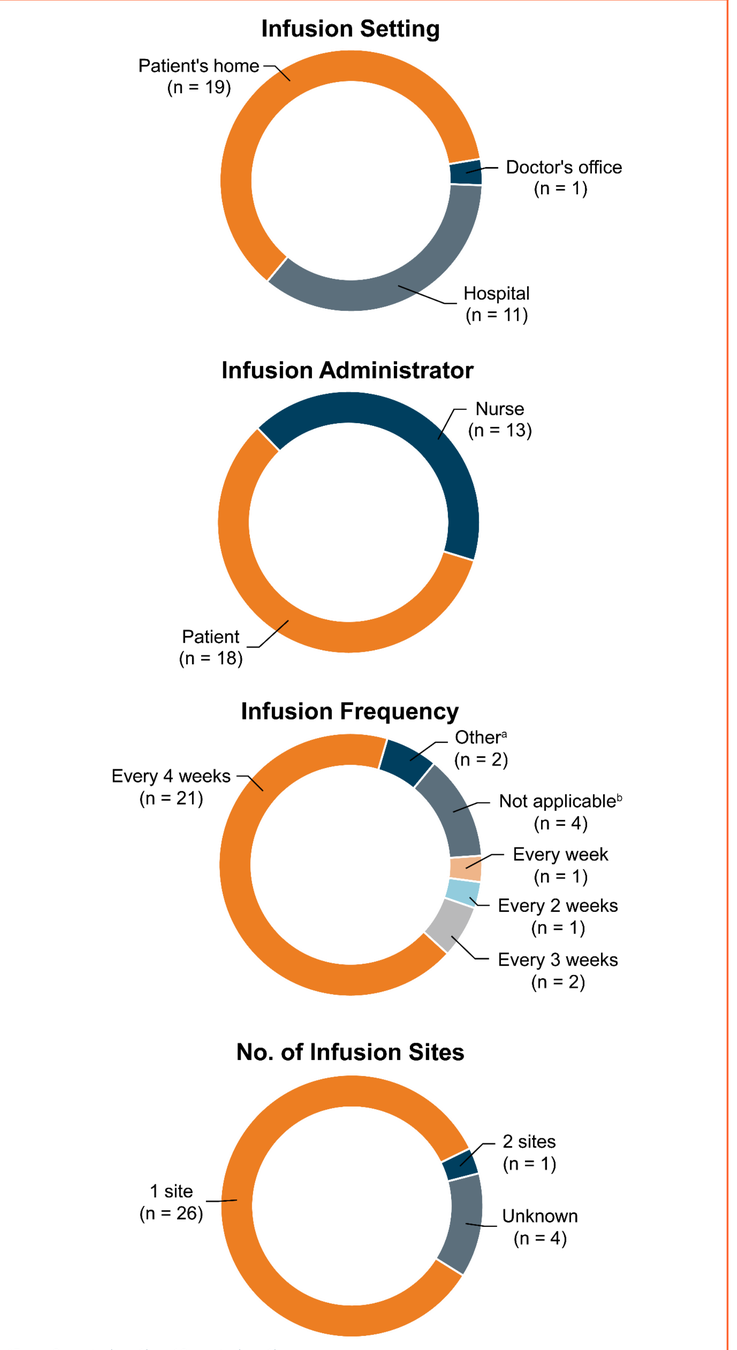
[a]Of patients with available data.
fSCIG, facilitated subcutaneous immunoglobulin; SD, standard deviation.

- The mean (SD) IgG serum trough level at the inclusion visit was 5.9 (1.9) g/L

Tolerability

- One patient reported a local ADR (erythema), and 1 patient had a systemic ADR (severe headache) at the inclusion visit

Figure 4. fSCIG Administration (Number of Patients; Inclusion Visit)



[a]Every 8 weeks (n = 1) or 12 weeks (n = 1).
[b]Patients had received only 1 fSCIG infusion to date.
fSCIG, facilitated subcutaneous immunoglobulin.

Conclusions

- **In patients with SID primarily due to hematologic malignancies, fSCIG provided the flexibility for subcutaneous infusion at home or in the hospital setting or doctor's office, either by the patient or a nurse**
- **The dosing schedule similarly allowed for flexibility, although most infusions were administered every 4 weeks, with > 95% of patients using 1 infusion site**
- **fSCIG tolerability for patients with SID in clinical practice was consistent with previous observations in patients with PID**
- **Patient observation is ongoing**

[a]In patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure[b] or serum IgG level of <4 g/L

[b]Defined as failure to mount at least a 2-fold rise in IgG antibody titer to pneumococcal polysaccharide and polypeptide antigen vaccines

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