

HEALTHCARE RESOURCE UTILIZATION AND DIRECT MEDICAL COSTS IN FRENCH PATIENTS RECEIVING TREATMENT FOR HYPOGAMMAGLOBULINEMIA: A NATIONAL COHORT STUDY

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BACKGROUND

- Subcutaneous immunoglobulin (SCiG) replacement therapy is recommended for patients with hypogammaglobulinemia caused by primary (PID) and secondary immunodeficiency (SID) for example in the context of chronic lymphocytic leukemia, multiple myeloma, or patients pre- and post-allogeneic hematopoietic stem-cell transplantation¹.
- Conventional SCiGs (cSCiGs) can be self-administered at home but are limited by the administration volume, leading to multiple injection sites and frequent infusions².
- Hyaluronidase-facilitated SCiG (fSCiG) associates a therapeutically effective human type G (IgG) immunoglobulin with recombinant human hyaluronidase, which results in increased permeability of connective tissue and enhanced uptake of IgG. As a result, fSCiG can be administered at a high rate, increased volume, and low frequency (once every 3–4 weeks), implying improved patient care, treatment adherence, and reduced healthcare costs^{4,5}.

OBJECTIVES

- Describe and compare the healthcare resource utilization (HCRU) and direct medical costs in French patients receiving SCiGs for hypogammaglobulinemia, either weekly cSCiG or monthly fSCiG.

METHODS

Study design and study population

- Retrospective observational cohort study conducted from November 1, 2015 to December 31, 2018 in adult and pediatric French patients treated with fSCiG or cSCiG for the management of PID and SID (Figure 1), using the French National Healthcare database (SNDS).
- This study included newly treated patients (no Ig-administration during the previous 6 months) with SID and receiving SCiGs during the study period.
- PID patients were identified based on the presence of specific ICD-10 codes. SID patients were identified by excluding patient with PID-related code from the population of patients treated with an a SCiG. All potential SID patients, regardless of the indication were included in the study including hypogammaglobulinemia situations with chronic lymphocytic leukemia, multiple myeloma, or patients pre- and post-allogeneic hematopoietic stem-cell transplantation.

Data sources

- The SNDS collates and pseudonymizes health datasets from the following:
 - The SNIRAM, a hospital/retail database⁵ containing anonymous individual-level data for all healthcare claims, covering more than 99% of residents in France (i.e., approximately 65 million people) regardless of the insurance scheme, sourced from DCIR (outpatient healthcare consumption data).
 - The PMSI, a hospital database containing medical and administrative data managed by the Agence Technique de l'Information sur l'Hospitalisation, collected from Médecine-Chirurgie-Obstétrique (MCO), Soins de Suite et de Réadaptation (SSR), Hospitalisation à Domicile (HAD), and psychiatric institutions (Psy).
 - Both databases are linked with a unique, anonymous identifier, the social security number (NIR).

Variables of interest, HCRU and their costs (2019 €) related to SCiG administration considered in the study were:

- At-home administration:** 1) Through service providers: All services from a provider responsible for home perfusion pump installation (PPV) and regular use ; and 2) Through private nurses (NV): Private nursing procedures reimbursable by health insurance.
- In-hospital administration:** All hospital stays for an SCiG administration (HO).
- At-home and in-hospital:** SCiG doses (≥ 8 g/month) delivered at home and in the hospital (DO).

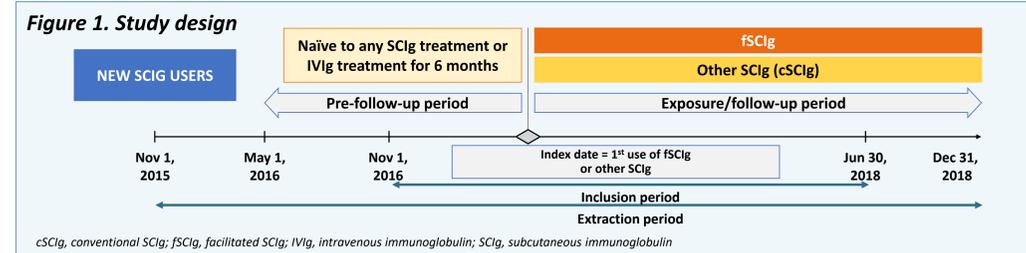
Data analyses

- Mean (standard deviation [SD]) monthly rates of each HCRU were calculated for the entire follow-up period available.

CONCLUSIONS

- This study provides real-world evidence on patient characteristics and HCRU in PID and SID patients in France, confirming the known clinical profile of these patients including comorbidities.
- Regardless of the indication, fSCiG-treated patients had lower HCRU related costs for SCiG-administration versus cSCiG-treated patients.
- The hospitalizations rates without stayover in fSCiG subgroup can be explained by the dose adjustment necessary during treatment initiation.

- Across the SCiG subgroups, patient characteristics and monthly rates of HCRU variables (e.g. hospitalizations, nurse and pump provider visits at home, treatment doses...), were described. Sensitivity analyses were performed for hospitalizations by type (with or without stayover) and by timing of occurrence (first month or rest of the follow-up).
- Poisson models adjusted for patient characteristics were used to compare HCRU endpoints between each treatment group (fSCiG and cSCiG [Hizentra[®] and Gammanorm[®] pooled data]); the relative risk (RR and 95%CI) reported is the ratio of the mean value of each HCRU endpoint in the fSCiG vs cSCiG groups.
- Linear regression models were used to quantify the additive difference (95% CI) between the mean dose in the fSCiG vs cSCiG groups. Only covariates with P <0.05 in the univariate analysis were retained in the final Poisson model (age, gender, affiliation to the CMUC [supplementary universal health coverage], co-treatments at inclusion by Anatomical Therapeutic Chemical (ATC) class, expert center for PID patients, presence of comorbidities, beneficiary of Long-Term Disease (ALD) status for SID).



RESULTS

- Overall, 2,012 patients (534 PIDs; 1,478 SIDs) were analyzed.

Figure 2. Study inclusion flowchart

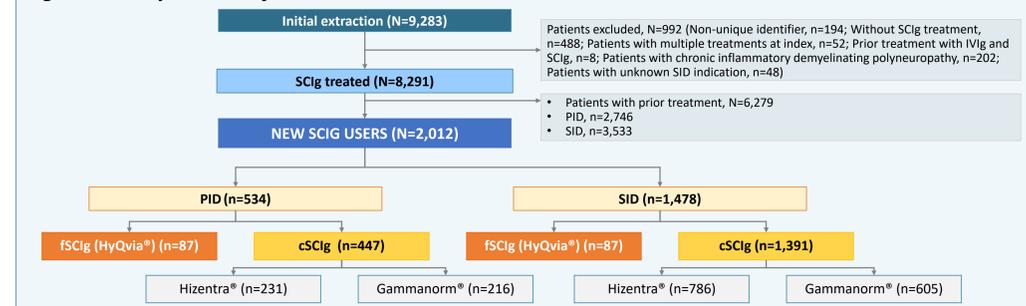


Table 1. Main demographics and baseline patient characteristics of each patient cohort.

Variables of interest	PID			SID		
	All patients N=534	fSCiG n=87	cSCiG n=447	All patients N=1,478	fSCiG n=87	cSCiG n=1,391
Age at index date, years, mean (SD)	53.6 (21.8)	53.7 (16.9)	53.6 (22.6)	65.1 (16.1)	68.1 (12.8)	64.9 (16.3)
Gender (female), n (%)	308 (57.7)	48 (55.2)	260 (58.2)	717 (48.5)	40 (46.0)	677 (48.7)
Comorbidities, n (%)						
Cancer	209 (39.1)	27 (31.0)	182 (40.7)	1,169 (79.1)	73 (83.9)	1,096 (78.8)
Cardiovascular disorders	88 (16.5)	10 (11.5)	78 (17.5)	392 (26.5)	18 (20.7)	374 (26.9)
Diabetes	49 (9.2)	5 (5.8)	44 (9.8)	220 (14.9)	12 (13.8)	208 (15.0)
Hypertension	118 (22.1)	13 (15.0)	105 (23.5)	453 (30.7)	20 (23.0)	433 (31.1)
Respiratory disorders	248 (46.4)	32 (36.8)	216 (48.3)	508 (34.4)	38 (43.7)	470 (33.8)
Number of comedications, ^a mean (SD)	1.5 (1.6)	1.24 (1.3)	1.59 (1.7)	2.02 (1.9)	1.99 (1.8)	2.02 (1.9)
Length of follow-up, months, mean (SD)	8.5 (6.8)	7.72 (5.3)	8.65 (7.0)	8.34 (6.6)	7.53 (4.6)	8.39 (6.7)

^aTreatment with ATC A* or M* or L01* or L03* or L04* or H02* or J01* or J02A* or J07BB* or P01* or R03* ATC, Anatomical Therapeutic Chemical classification system. fSCiG, facilitated subcutaneous immunoglobulin; cSCiG, conventional subcutaneous immunoglobulin; PID, primary immunodeficiency; SID, secondary immunodeficiency; SD, standard deviation.

- Patient characteristics of each patient cohort are reported on Table 1. On average, SCiG treated patients with SID were older than those with PID. There were more females in the PID patient population vs SID population. Respiratory disorders and cancer were the most frequently observed comorbidities in PID and SID populations, respectively.

HCRU and related costs

- NV & PPV:** Compared to fSCiG-subgroups, monthly mean rates of NV and PPV were respectively 2.5 and 3.1 times higher in PID cSCiG-treated patients, and 1.6 and 3.1 times higher in SID cSCiG-treated patients, leading to NV+PPV costs 2.6 and 2.3 times higher, both in PIDs and SIDs (Table 2).
- Hospitalizations (HO):** Monthly mean costs for all hospitalizations (with and without stayover) were 1.6 times and 1.8 times higher for cSCiG versus fSCiG -treated patients, in PIDs and SIDs, respectively. Such differences are related to the observed hospitalizations types, fSCiG-treated patients had more frequent but less costly hospitalizations (without stayover) versus cSCiG-treated patients.
- The total HCRU costs** related to SCiG-administration was estimated to be 575€ and 1,851€ lower with fSCiG versus cSCiG, in PIDs and SIDs respectively.

Table 2. HCRU and costs related to SCiG administration

Variables of interest	PID				SID				
	Descriptive, non-adjusted results (mean±SD)			Adjusted results*, (95% CI)	Descriptive, non-adjusted results (mean±SD)			Adjusted results*, (95% CI)	
	All N=534	fSCiG N=87	cSCiG N=447	cSCiG vs fSCiG, N=534	All N=1,478	fSCiG N=87	cSCiG N=1,391	cSCiG vs fSCiG, N=1,478	
HCRU	PPV	5.8±3.6	2.6±2.6	6.4±3.4	3.1 [2.9;3.2]	5.4±3.9	2.1±1.7	5.6±3.9	3.1 [2.9;3.3]
	NV	3.1±4.5	1.3±1.9	3.4±4.8	2.5 [2.3;2.6]	4.3±5.4	3.1±5.1	4.4±5.4	1.6 [1.5;1.6]
	HO	0.4±0.7	0.6±0.8	0.3±0.7	0.5 [0.4;0.6]	0.3±0.7	0.5±0.8	0.3±0.7	0.4 [0.4;0.5]
	DO	23.7±11.9 (N=414)	26.8±9.7 (N=81)	23.0±12.3 (N=333)	-4.0 [-6.9;-1.2]	23.1±15.7 (N=1,054)	23.4±8.4 (N=75)	23.1±16.1 (N=979)	-0.7 [-4.4; 3.0]
Costs (€)	PPV	526.1±328.2	261.2±361.8	577.7±295.2	2.4 [1.9;3.0]	497.2±359.3	226.5±264.1	514.1±358	2.2 [1.8;2.8]
	NV	119.8±204.2	42.0±69.9	134.9±217.9	2.6 [2.0;3.3]	152.0±159.7	60.4±64.6	157.7±162.2	2.6 [2.1;3.3]
	HO	522.7±2,751.7	242.7±432.2	577.2±2,999.1	1.6 [1.3;2.1]	1,664.1±17,126.2	474.5±1,661.5	1,738.5±17,647.1	1.8 [1.4;2.2]
	DO	1,108.0±554.8	1,245.2±449.7	1,079.4±573.1	0.7 [0.6;0.9]	1,074.0±7345.0	1,089.6±392.0	1,072.8±755.0	0.8 [0.7;1.0]

*Adjusted results for PPV, NV and HO are expressed as relative ratios, and those for DO are average differences. HCRU, health care resource utilization; fSCiG, facilitated subcutaneous immunoglobulin; cSCiG, conventional subcutaneous immunoglobulin; PID, primary immunodeficiency; SID, secondary immunodeficiency; PPV, pump provider visit; NV, nurse visit; HO, hospitalization; DO, SCiG dose delivered at home and in hospital; SD, standard deviation; CI, confidence interval.

Table 3. Sensitivity analyses according to hospitalization types

HCRU for the Ig administration in hospital (monthly mean number, ±SD)	PID			SID		
	All N=534	fSCiG n=87	cSCiG n=447	All N=1,478	fSCiG n=87	cSCiG n=1,391
Hospitalizations according to length of stay						
Without stayover (HDI)	0.3 (±0.7)	0.5 (±0.8)	0.2 (±0.6)	0.2 (±0.5)	0.4 (±0.7)	0.2 (±0.5)
With stayover	0.1 (±0.2)	0.0 (±0.0)	0.1 (±0.2)	0.1 (±0.5)	0.1 (±0.5)	0.1 (±0.5)
Hospitalizations according to occurrence timing during FU						
Occurring within the 1 st month	1.0 (±1.0)	1.6 (±1.1)	0.9 (±0.1)	0.8 (±0.9)	1.9 (±1.0)	0.7 (±0.8)
Occurring after the 1 st month of follow-up	0.0 (±0.3)	0.1 (±0.2)	0.0 (±0.3)	0.0 (±0.2)	0.0 (±0.1)	0.0 (±0.2)

HCRU, health care resource utilization; fSCiG, facilitated subcutaneous immunoglobulin; cSCiG, conventional subcutaneous immunoglobulin; PID, primary immunodeficiency; SID, secondary immunodeficiency; FU, follow-up; HDI, hospitalization without stayover; SD, standard deviation.

- Given fSCiGs are administered in hospital in first month for dose adjustments, we conducted sensitivity analysis on types of hospital-stays. These analyses confirmed that hospitalizations for fSCiG administration occurred mainly during hospitalizations without stayover (outpatient care); and within the first month of follow-up versus during the rest of the follow-up (Table 3).