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ORIGINAL RESEARCH

An evaluation of the budget impact of a new 20% subcutaneous immunoglobulin (Ig20Gly) for the management of primary immunodeficiency diseases in Switzerland

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Introduction: While most individual primary immunodeficiency diseases (PID) are rare, the collective prevalence of PID results in a substantial economic and clinical burden. The aim of this study was to evaluate the budgetary implications of Ig20Gly (Immune Globulin Subcutaneous [human] 20% solution; CUVITRU®, Baxalta US Inc, now part of Shire Plc, Westlake Village, CA, USA) as a treatment for PID relative to intravenous immunoglobulin (IVIG) and other subcutaneous immunoglobulin (SCIG) formulations in the Swiss health care setting.

Materials and methods: A budget impact model was developed in Microsoft Excel to capture the estimated prevalence of PID in Switzerland, the proportion of patients treated in different health care settings, and the costs of administering SCIG and IVIG in each setting. Unit costs were based on a recent cost-minimization analysis of SCIG in Lausanne, and drug costs were taken from the Spezialitätenliste. All costs were reported in 2016 Swiss Francs (CHF), and future costs were not discounted.

Results: The total cost of treating PID in Switzerland was estimated to be CHF 11.16 m over 3 years, comprising CHF 9.28 m of drug costs and CHF 1.87 m of ancillary costs, including health care professional time and other administration costs, such as pumps and needle sets. The analysis showed that using Ig20Gly in place of other SCIG formulations would be cost neutral, while using Ig20Gly in place of IVIG would result in savings of 4.0%.

Conclusion: Ig20Gly would be cost neutral relative to existing SCIG products and would result in cost savings relative to IVIG in patients with PID in Switzerland, even with modest uptake.

Keywords: costs and cost analysis, immune system diseases, immunoglobulin, Switzerland

Background and aims

Primary immunodeficiency diseases (PID) are a heterogeneous group of >300 congenital disorders characterized by a genetic defect in either the adaptive or innate immune system.[1] The prevalence and incidence of these disorders vary geographically; however, it has been estimated from registry data and epidemiologic surveys that ~6 million individuals worldwide may have PID.[2] PID may affect one or more components of the immune system, including humoral B-cells, T-cells, or combined (T- and B-cell) defects, in addition to phagocytic cell disorders and complement protein dysfunction.[3] The most common PID are antibody deficiency conditions such as common variable immunodeficiency, X-linked agammaglobulinemia, and specific antibody deficiencies.[4]

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Treatment of PID varies by the type of disorder, but with the exception of selective immunoglobulin (Ig)A deficiency, Ig replacement therapy is the first-line treatment for antibody deficiency conditions.[4] Ig replacement therapy is administered via intravenous infusion (IVIG) treatment or subcutaneous Ig (SCIG) infusion. SCIG formulations are typically administered in the home setting, as distinct from IVIG, which is typically administered every 3–4 weeks in the hospital or clinic setting. SCIG formulations allow for dosing daily to every other week, although weekly dosing is most common.[5]

Recently, a new ready-to-use 20% liquid SCIG formulation, Ig20Gly (Immune Globulin Subcutaneous [human]; CUVITRU®, Baxalta US Inc, now part of Shire Plc, Westlake Village, CA, USA) was approved for use in several countries, including Switzerland, the USA, and Germany. No serious or severe nonserious adverse events related to Ig20Gly treatment have been observed in clinical studies.[6,7] In the clinical studies, Ig20Gly demonstrated annual rates of validated acute serious bacterial infections that meet the European Medicines Agency (EMA)-recommended primary endpoint of <1.0 infection/patient/year.[6–8]

The aim of this study was to evaluate the budgetary implications of using Ig20Gly, a 20% SCIG formulation, relative to IVIG and other existing SCIG 20% formulations, in pediatric and adult patients with PID treated with Ig in Switzerland, the first European country to approve Ig20Gly.

Materials and methods

A budget impact model was developed in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) to evaluate the budgetary implications of using Ig20Gly relative to other SCIG 20% formulations and IVIG (Figure 1). The analysis was conducted in a target population including both children and adolescents (0–18 years) and adults with a diagnosis of PID who required Ig.

The prevalence of all PID in Switzerland was estimated to be 0.004% based on Swiss PID registry data from 2014, which included 338 patients with PID, and the 2015 Bundesamt für Statistik Swiss population estimate of 8.327 million.[9,10] This prevalence estimate represents a "minimal estimate" as it was based exclusively on patients enrolled at 17 medical centers with experience with PID rather than epidemiological methods such as random or multistage sampling.[10] Based on the data from the European Society for Immunodeficiencies database, it was assumed that 42.1% (142 patients) would be treated with Ig.[11] This population was, in turn, assumed to consist of 31.6% pediatric (<18 years of age) patients and 68.4% adult (≥18 years of age) patients, based on the Swiss PID registry, resulting in a population of 97 adult and 45 pediatric patients in total.[10] Adult patients were assumed to weigh 75 kg on average, in line with another analysis of Ig therapies in Switzerland.[12] Patients under 18 years were assumed to weigh 30 kg on average.

The treatment mix in the base case analysis assumed that patients treated with Ig would be treated with IVIG, Ig20Gly, or other SCIG products. The most common SCIG product in Switzerland is IgPro20 (Immune Globulin Subcutaneous [human]), 20% solution (Hizentra®, CSL Behring AG, Bern, Switzerland). In the scenario without Ig20Gly, the distributions of IVIG and SCIG were assumed to change over time

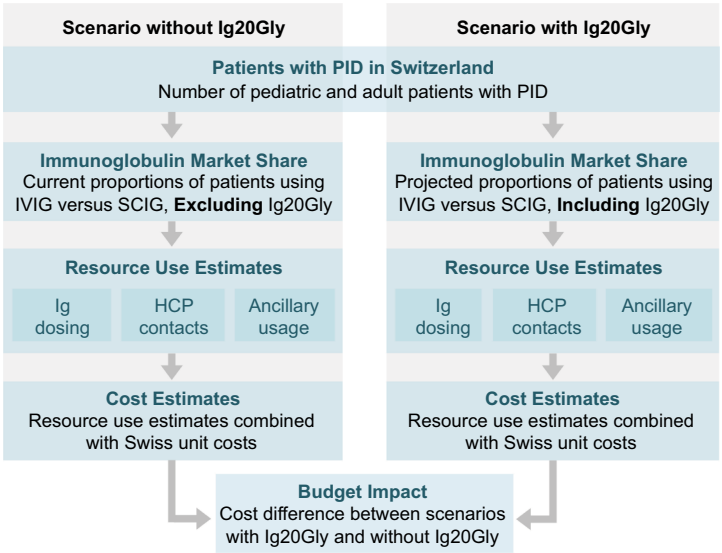

Figure 1 Budget impact model schematic.
Abbreviations: HCP, health care professional; Ig, immunoglobulin; IVIG, intravenous immunoglobulin; PID, primary immunodeficiency diseases; SCIG, subcutaneous immunoglobulin.

based on current changes in Swiss Ig treatment patterns. Specifically, SCIG use was assumed to increase by ~4% per year, starting at 37% of SCIG use in Year 1 and increasing to 45% by Year 3 (Figure 2), based on the observation of increasing SCIG use over time.[13] In the Ig20Gly scenario, it was assumed that there would be a faster increase in SCIG use relative to IVIG use. The baseline (Year 1) SCIG proportion for the Ig20Gly scenario was the same as in the no Ig20Gly scenario (37%), but increased to 47% by the third year (Figure 2). In the Ig20Gly scenario, Ig20Gly's proportion of the treatment mix increased to 40% of the SCIG proportion of Ig use by the end of the third year of the analysis. The overall size of the Ig-treated population was assumed to remain constant over the 3-year period of the analysis.

This analysis was conducted from the perspective of a Swiss health insurance provider. Cost data were based primarily on costs utilized in a 2016 Swiss cost-minimization analysis (CMA), including costs from a study on home care, hospitalizations, and doctor visits in Switzerland published by the Université de Genève (Table 1).[12,14] Drug costs were taken from the Spezialitätenliste in February 2017 (Table 1),[15] with the cost of "other SCIGs" based on IgPro20, as it is currently the most commonly used SCIG in the Swiss market. Future costs (i.e., those beyond the first year of the analysis) were not discounted, following guidelines from the International Society for Pharmacoeconomic and Outcomes Research.[16]

Ig dosing was assumed to be 0.4 g/kg/month for both SCIG and IVIG based on the European consensus proposal for Ig therapies.[17] Dose equivalence between SCIG and IVIG was based on the EMA assessment that the reduced area under the curve (of serum IgG versus time) for an equivalent dose of SCIG relative to IVIG is not relevant for clinical

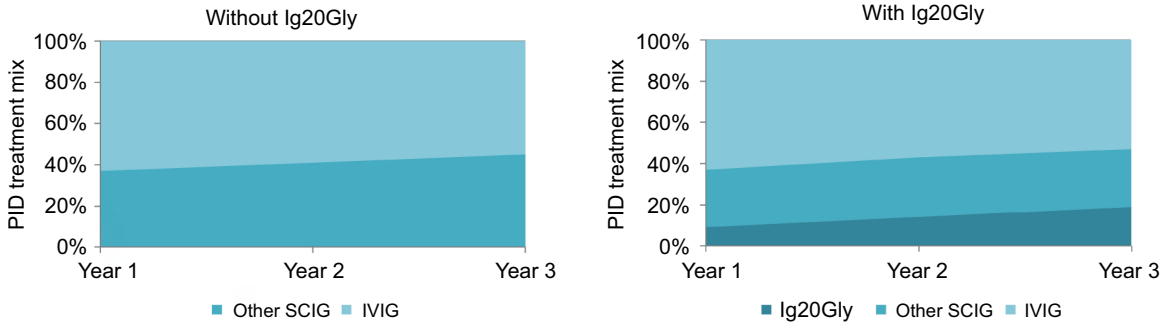

Figure 2 Treatment mix scenarios.
Abbreviations: IVIG, intravenous immunoglobulin; PID, primary immunodeficiency diseases; SCIG, subcutaneous immunoglobulin.

Table 1 Unit cost estimates in the base case analysis

Model input	Cost (CHF)	Cost basis	Reference
Hospital outpatient SCIG (per administration)	265.00	Hospital overheads, 1 hour of nurse time	Perraudin et al[12]
Physician office SCIG (per administration)	117.10	One GP visit	Gonçalves and Weaver[14]
Home visit SCIG (per administration)	282.00	One hour of round-trip travel time (30 km), 2 hours of community pharmacist time	Perraudin et al[12]
Pump	2,840	One-off pump cost (per patient)	Spezialitätenliste[15]
Other supplies, per administration	1.40	Alcohol wipes, hand sanitizer, gauze, tape, sharps container	Perraudin et al[12]
Needle set	59.30	Needle, infusion tubing, and syringe	Perraudin et al[12]
Hospital outpatient IVIG (per administration)	402.00	Hospital overheads, 2 hours of nurse time, and IVIG materials	Perraudin et al[12]
Physician office IVIG (per administration)	174.10	One GP visit and IVIG materials	Perraudin et al[12] and Gonçalves and Weaver[14]
Home visit IVIG (per administration)	426.00	One hour of travel time (30 km), 3 hours of community pharmacist time, and IVIG materials	Perraudin et al[12]
IVIG (per mg)	0.076	IVIG 10% (CSL Behring AG, Bern, Switzerland) 40 g/400 mL at CHF 3,034.00 per vial	Spezialitätenliste[15]
Other SCIG (per mg)	0.073	IgPro20 (CSL Behring AG, Bern, Switzerland) 10 g/50 mL at CHF 730.45 per vial	Spezialitätenliste[15]
Ig20Gly (per mg)	0.073	Ig20Gly (Baxalta US Inc, now part of Shire Plc, Westlake Village, CA, USA) 8 g/40 mL at CHF 587.65 per vial	Spezialitätenliste[15]

Abbreviations: CHF, Swiss Francs; GP, general practitioner; IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

response.[18] Dosing frequencies were assumed to be once monthly with IVIG and four times monthly with SCIG, and the setting of administration for SCIG and IVIG was based on recent data from the Immune Deficiency Foundation (Table 2).[19] All SCIG products were assumed to be administered using a pump; rapid push was not considered to be sufficiently widely used to warrant inclusion in the analysis. IVIG in the home setting was not included as it is quite rare in Switzerland.

Several sensitivity and scenario analyses were conducted to evaluate the impact of changing assumptions around Ig dosing and IVIG dosing frequency, treatment setting, the proportion of patients treated with IVIG, PID prevalence, and age groups. The dose scenario analysis evaluated a higher monthly dose of Ig 0.6 g/kg/month (base case 0.4 g/kg/month). The dose frequency analysis was conducted to establish the impact of a once-every-3-weeks IVIG dosing schedule (base case once monthly dosing). The treatment setting was analyzed with assumptions of 100% hospital outpatient for IVIG and 100% self-administered for SCIG. A sensitivity analysis of the route of administration parameters evaluated an alternative assumption that the proportion of IVIG and SCIG treatment would not change between the Ig20Gly and no Ig20Gly scenarios. A sensitivity analysis of the PID prevalence estimate was conducted reflecting the highest European country-level prevalence estimate from the 2014 European Society for Immunodeficiencies database.[20] The PID prevalence in France was utilized for this purpose (6.164 per 100,000 patients), resulting in an estimated population of 515 patients with PID in the Swiss population, of which 216 would be receiving Ig treatment. Finally, subgroup analyses were conducted for pediatric and adult patients.

Results

The model projected average total annual costs (including Ig therapies, ancillaries, and labor) for a single patient treated with either Ig20Gly or other SCIGs of CHF 27,502 in the first year and CHF 24,662 in subsequent years, for a 3-year total cost of CHF 76,826. Because the drug costs of Ig20Gly and IgPro20 are the same and the ancillary and pump costs are the same for all SCIG products, there was no difference in Ig treatment costs for treating a patient with IgPro20 or Ig20Gly in this analysis. The higher first year costs for SCIG were driven by pump acquisition costs, which only accrue in the first year. For SCIG patients, Ig costs accounted for 83.3% of total costs, with labor and ancillary costs comprising 1.7% and 15.0%, respectively, over the 3-year time horizon.

For patients treated with IVIG therapy, the estimated total cost for a single patient was CHF 26,681 annually for a total cost of CHF 80,042 per patient over 3 years. For patients receiving IVIG, Ig costs accounted for 82.9% of total costs, with labor and ancillary costs comprising 17.1% of the total cost over the 3-year time horizon. The total estimated cost of treating a single patient with SCIG compared to treatment with IVIG was lower by CHF 3,216, a reduction of 4.0%.

The model estimated that the introduction of Ig20Gly would result in total savings of CHF 11,467 over 3 years, based on the assumed changes in the treatment mix of IVIG and SCIG in the Swiss PID population (Table 3). The overall cost reduced from CHF 11.163 m in the scenario without Ig20Gly to CHF 11.151 m in the scenario with Ig20Gly. The cost estimates were based on a population of 142 patients with PID in Switzerland, consisting of 97 adults and 45 children, with 63% of all patients using IVIG and 37% using SCIG in Year 1, transitioning to 53% using IVIG and 47% using SCIG in Year 3.

Several sensitivity and scenario analyses were run to evaluate the impact of assumptions on the results (Table 4). The model results were relatively insensitive to changes in individual model parameters. Increasing the Ig dose per kilogram body weight to 0.6 g/kg/month increased the cost savings with Ig20Gly to CHF 13,745 over the whole population, from a cost of CHF 15.8 m in the scenario without Ig20Gly. Increasing the frequency of IVIG administration to once every 3 weeks from once monthly increased the cost savings with Ig20Gly to CHF 23,090 from a cost of CHF 11.7 m without Ig20Gly. If the introduction of Ig20Gly does not increase the proportion of patients treated with SCIG, then introducing Ig20Gly would have no effect on the overall PID treatment budget. When the PID prevalence estimate was changed to the highest reported prevalence in Europe, the resulting savings increased to CHF 17,443. The age subgroup analysis demonstrated that adult patients (n=97) represented CHF 9.1 m of the Ig treatment costs and pediatric

Table 2 Treatment settings for patients using IVIG versus SCIG

Treatment setting	IVIG therapy, %	SCIG therapy, %
Hospital outpatient	89	2
Physician office	10	3
Home visit	1	0
Self-administered	0	95

Note: Treatment setting data based on Immune Deficiency Foundation 2008 National Survey of Patients.[19]
Abbreviations: IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Table 3 Projected cumulative costs of PID treatment over time

Year	Cumulative costs without Ig20Gly (CHF)		Cumulative costs with Ig20Gly (CHF)		Cumulative difference (CHF)	
	Total	Drug costs	Total	Drug costs	Total	Drug costs
1	3.832 m	3.100 m	3.832 m	3.100 m	0	0
2	7.503 m	6.195 m	7.497 m	6.193 m	–5,733	–2,278
3	11.163 m	9.286 m	11.151 m	9.282 m	–11,467	–4,557

Note: Cost estimates based on a population of 142 patients with PID in Switzerland.
Abbreviations: CHF, Swiss Francs; PID, primary immunodeficiency diseases.

Table 4 One-way sensitivity analysis results over 3 years

Analysis	Cumulative costs without Ig20Gly (CHF)	Cumulative costs with Ig20Gly (CHF)	Cumulative difference (CHF)
Base case	11.163 m	11.151 m	–11,467
0.6 g/kg/month Ig dose	15.806 m	15.792 m	–13,745
Once-every-3-weeks IVIG dosing	11.677 m	11.654 m	–23,090
High PID prevalence estimate	16.980 m	16.962 m	–17,443
Adults only	9.116 m	9.107 m	–8,564
Pediatrics only	2.047 m	2.044 m	–2,903
Treatment settings (100% hospital IVIG, 100% self-administered SCIG)	11.157 m	11.141 m	–15,407
Equivalent IVIG usage share in both scenarios	11.163 m	11.163 m	0

Abbreviations: CHF, Swiss Francs; IVIG, intravenous immunoglobulin; PID, primary immunodeficiency diseases; SCIG, subcutaneous immunoglobulin.

patient costs accounted for the remaining CHF 2.0 m (18%) in both scenarios. In the Ig20Gly scenario, adults contributed CHF 8,564 (75%) of savings and pediatric patients contributed the remaining CHF 2,903 (25%) in savings.

Discussion

This analysis showed that the introduction of Ig20Gly would be cost neutral relative to existing SCIG formulations, such as IgPro20, and cost saving relative to IVIG over a 3-year time horizon in patients with PID in Switzerland. This budget impact analysis was conducted in the Swiss context because Switzerland was the first European country to approve Ig20Gly. Ig20Gly is currently approved and available in several countries including USA and Germany.

A recent CMA in the Swiss setting reported an SCIG cost of CHF 35,862 per patient during the first year and CHF 30,309 in subsequent years versus CHF 35,370 per year for IVIG.[12] These estimates are similar to the estimates in this analysis; however, the CMA cost estimates for both SCIG and IVIG were slightly higher than the current study estimates of CHF 27,502 and CHF 26,681, respectively, primarily due to the inclusion of pediatric patients in this analysis (lowering the average dose and, therefore, the costs of Ig) and the inclusion of transport and indirect costs in the CMA.

This budget impact analysis has a number of limitations that should be acknowledged when interpreting the results. First, data on the average Ig dose were not available in the Swiss setting. The European consensus statement recommendation of 0.4 g/kg/month was, therefore, utilized across the whole population for the base case analysis.[17] It is unclear, however, whether this dose reflects the clinical practice in Switzerland; thus, a sensitivity analysis was conducted, which demonstrated that higher doses resulted in greater cost savings with Ig20Gly relative to IVIG. While the assumption of dose equivalence between SCIG and IVIG is based on EMA recommendations,[18] the approach is not universal and dosing may differ by administration route depending on the implementation of recommendations in routine practice.[21]

There was also substantial uncertainty as to the prevalence of patients with PID in Switzerland. The base case prevalence was taken from the Swiss PID registry, which is almost certainly an underestimate of the Swiss prevalence of PID. However, in the sensitivity analysis evaluating the impact of the higher French prevalence, the introduction of Ig20Gly increased the absolute savings for the Ig treatment budget. One further limitation that may have resulted in inaccurate estimates of the costs of SCIG relative to IVIG was the inclusion of 100% of pump costs in Year 1 of the analysis. Pump replacement frequencies >3 years would render the current analysis conservative with regard to the cost of SCIG, while pump replacement frequencies shorter than 3 years would have resulted in an underestimate of SCIG costs. Finally,

the model did not account for any changes in costs over the 3 years, including drug costs, health care professional time, and pump and needle set costs, all of which may change within the 3-year time horizon, thereby affecting the estimated budgetary consequences.

Many factors should be considered when choosing Ig therapies, including the side effects, tolerability, burden of treatment, and patient preferences, in addition to cost. This analysis demonstrates the cost savings of SCIG relative to IVIG for PID treatment and may be considered alongside improvements in satisfaction and patient preferences in patients switching to SCIG from IVIG therapy.[6,7]

Conclusion

According to this analysis, converting patients from IVIG to SCIG would likely result in savings of ~4% per patient over a 3-year period, with potential improvements in patient's quality of life, reductions in hospital outpatient visits, and no detriment to treatment efficacy. The introduction of Ig20Gly would increase the options available to treat PID in Switzerland with no increase in expenditure relative to existing SCIG formulations.

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Disclosure

Richard F Pollock is a full-time employee of Ossian Health Economics and Communications GmbH, which received consultancy fees from Shire to conduct the analyses and write the manuscript. Lisa M Meckley is an employee and shareholder of Shire Plc, the manufacturer and marketing authorization holder for Ig20Gly. The authors report no other conflicts of interest in this work.

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