Use of intravenous immunoglobulins (5% and 10%) for the treatment of patients with primary or secondary antibody deficiencies – An interim analysis of a non-interventional study

Habier A, Jansen M, Lietz C, Muenster U

Octapharma GmbH, Business Unit Immunology, Langenfeld, Germany

Background

Intravenous immunoglobulin (IVIG) is generally used for replacement therapy in primary or secondary immunodeficiencies and for immunomodulation in the treatment of different autoimmune diseases.

Patients with antibody deficiencies need long-term substitution with immunoglobulins to prevent recurrent infections and irreversible complications. In addition to the efficacy, the tolerability of the immunoglobulin product is a critical factor for the treatment of these patients.

In 2014 a multicentre, non-interventional study (NIS) was started in Germany to evaluate the tolerability of a 5% and a 10% IVIG preparation in daily routine practice. All data received between January 1st 2014 to December 31th 2017 were included in this interim analysis. Presented is a subgroup analysis in patients with primary or secondary immunodeficiencies (PID or SID).

Methods

Patients of all age groups were enrolled in this study, who received at least one dose of the IVIG product (octagam® 5% or octagam®10%) as prescribed by the treating physician.

The participating centres documented data by using detailed case report forms (CRFs). For the reporting of an adverse drug reaction (ADR), separate ADR report forms were used.

The patients' health-related quality of life during the IVIG treatment was measured with the patient self-reporting Short Form-36 Health Survey (SF-36) questionnaire on a voluntary basis.

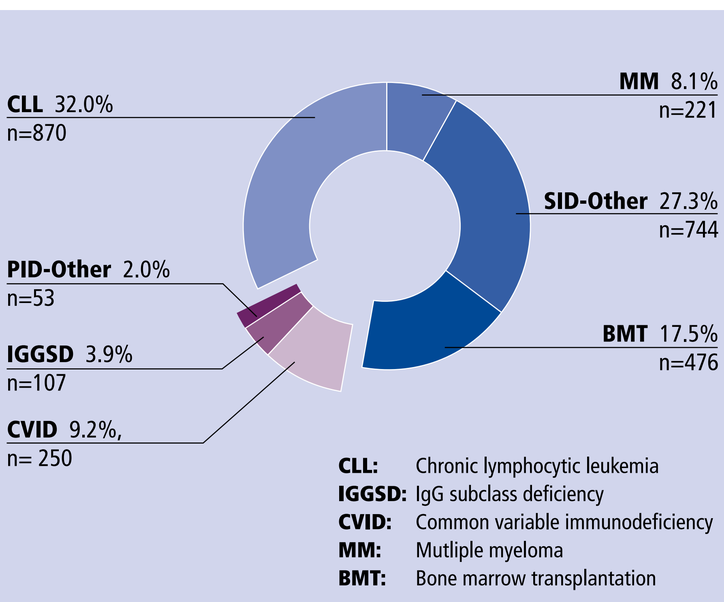
Results

Patients

A total of 2,721 patients with antibody deficiencies receiving 43,677 infusions were enclosed in the study. Of these, 410 patients were treated with IVIG for primary (15.1%) and 2,311 patients for secondary (84.9%) antibody deficiencies **(Figure 1).**

The most common disease within the PID group was common variable immunodeficiencies (CVID) and within the SID group chronic lymphocytic leukemias (CLL). The other SID patients (n=744) were primarily patients with various Non-Hodgkin lymphomas (NHL), furthermore patients with other leukemias or solid tumors.

Figure 1 Most common indications



The patient characteristics for the two indication groups were summarized in **Table 1.**

In total 53.2% of the patients received the 5% und 46.8% the 10% IVIG product. The 10% IVIG product was preferably administered to PID patients while the 5% product was mainly applied to SID patient.

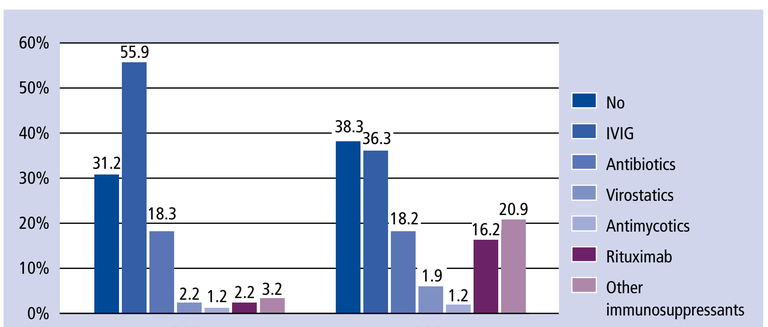
Table 1 Patient characteristics, demographic data by indication group

		PID	SID
Patients (n), total		410	2,311
treated with IVIG 5% (n)		172 (42%)	1,275 (55%)
treated with IVIG 10% (n)		238 (58%)	1,036 (45%)
Age (at start, years)	Mean Min – Max	52 7 – 87	66 18 – 91
Male / Female (n)		245 / 165	1,115 / 1,196
Time in study (days)	Median Min – Max	512 1 – 1,445	292 1 – 1,457

The mean diagnostic delay between first symptoms and diagnosis of PID was 11.9 months. In SID patients the mean time between diagnosis of the primary disease and diagnosis of the SID were 48.7 months.

31.2% of the PID and 38.3% of the SID patients were previously untreated. 55.9% of the PID and 36.3% of the SID patients received immunoglobulin therapy prior to inclusion into the study. 37.1% of the SID patients were pretreated with Rituximab or other immunosuppressants **(Figure 2).**

Figure 2 Pretreatment of the included patients*



* Multiple answers were possible

Treatment and therapy regimes

The therapy regime for the two products und indication groups was more or less identical **(Table 2).**

Table 2 Dosage, infusion rates, treatment intervals

		PID	SID
Infusions (n)		9,383	34,294
Infusions per patient (n)	Mean Min – Max	22.9 1 – 144.0	14.8 1 – 162.0
Dose / infusion (g/kg)	Median Min – Max	0.2 0.04 – 1.05	0.17 0.04 – 1.00
Treatment interval (weeks)	Median Min – Max	4.2 0.3 – 56.9	4.2 0.2 – 47.1
Infusion rate (ml/kg/h)	Median Min – Max	1.9 0.4 – 9.5	1.7 0.3 – 77.2

Tolerability

ADRs occurred in 0.68% of infusions in PID and 0.57% of infusions in SID patients **(Table 3).** The majority of ADRs were non-serious (98.5% for PID, 99.0% for SID). The ADR rates were similar in all age groups.

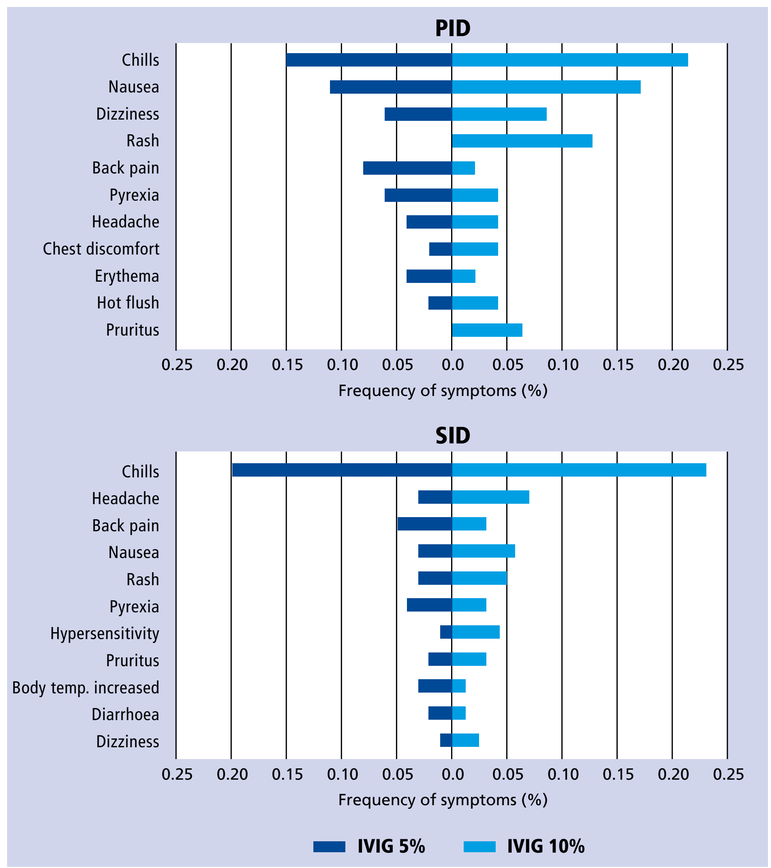
The most frequent ADR symptoms are summarized in **Figure 4.**

Premedication was used in 9.9% of the PID infusions and 10.2% of the SID infusions.

Table 3 Infusions and ADRs

	PID		SID	
	Infusions (n)	with ADRs (n)	Infusions (n)	with ADRs (n)
IVIG 5%	4,718	29 (0.61%)	18,762	95 (0.51%)
IVIG 10%	4,665	35 (0.75%)	15,532	101 (0.65%)
Total	9,383	64 (0.68%)	34,294	196 (0.57%)

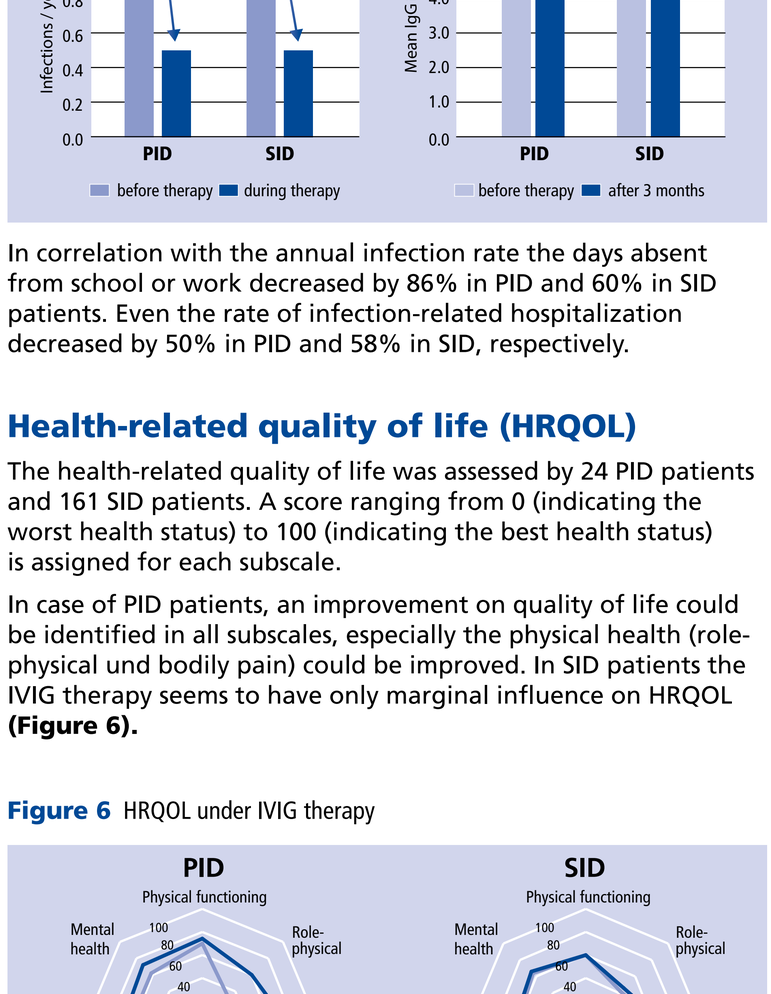
Figure 4 Most frequent ADR symptoms



Efficacy

Efficacy was assessed in PID and SID patients by analysing the mean annual infection rate and IgG trough levels before and during IVIG treatment. The infection rate for all infections decreased in both indication groups during treatment, with a slightly stronger effect in PID patients compared to SID **(Figure 5).** The IgG level increased within the first 3 months and remained stable during IVIG treatment.

Figure 5 Infections and IgG levels



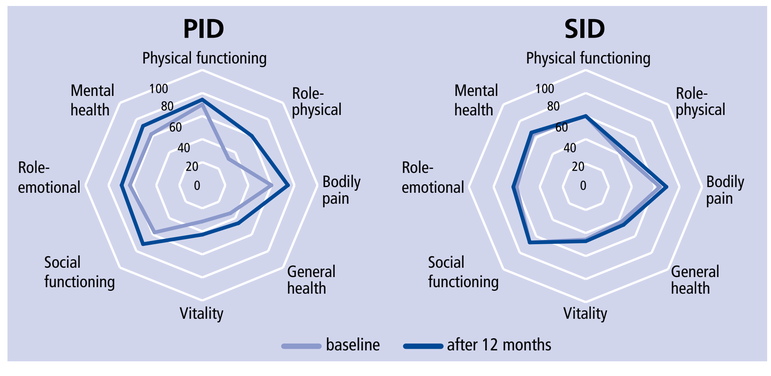
In correlation with the annual infection rate the days absent from school or work decreased by 86% in PID and 60% in SID patients. Even the rate of infection-related hospitalization decreased by 50% in PID and 58% in SID, respectively.

Health-related quality of life (HRQOL)

The health-related quality of life was assessed by 24 PID patients and 161 SID patients. A score ranging from 0 (indicating the worst health status) to 100 (indicating the best health status) is assigned for each subscale.

In case of PID patients, an improvement on quality of life could be identified in all subscales, especially the physical health (role-physical und bodily pain) could be improved. In SID patients the IVIG therapy seems to have only marginal influence on HRQOL **(Figure 6).**

Figure 6 HRQOL under IVIG therapy



Conclusions

- Both IVIG products (5% and 10%) are well tolerated in PID and SID patients
- The kind of ADR symptoms differed between the indications groups and the products
- In PID and SID patients IVIG therapy increased the IgG levels and reduced the infection rate

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