A multicenter observational study on the efficacy and tolerability of Privigen® (intravenous immunoglobulin preparation) – Interim analysis with focus on immune thrombocytopenia (ITP)

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Corrected Abstract

Introduction: Privigen® is a 10% liquid preparation of polyvalent human IgG for intravenous administration. The use of a novel stabiliser, L-proline, fully preserves IgG functional activity without refrigeration, making Privigen® ready-to-use. Privigen® is licenced as a maintenance therapy in primary or secondary immunodeficiencies and as an immunomodulatory therapy in autoimmune or inflammatory diseases. **Methods:** This is an interim analysis of an ongoing multicenter observational study started in 2008 to evaluate the efficacy and tolerability of Privigen®. In April 2009, a revision of the case report form (CRF) was implemented, capturing additional efficacy data in most of the registered indications including ITP. Only treatment courses documented with the revised CRF were included in this interim analysis. The cut-off date was Dec 13, 2010. **Results:** 313 patients (143 m, 170 f, mean age 60 years) received a total of 1,586 Privigen® infusions with a mean dose of 15 g. The indications were primary immunodeficiency (n=36), secondary immunodeficiency (n=175), ITP (n=26), multiple sclerosis (n=43), chronic inflammatory demyelinating polyneuropathy (n=10), other polyneuropathies (n=10), other autoimmune diseases (n=10), and others (n=3). Across all indications, the efficacy of Privigen® was judged by the physicians as very good or good in 91%, as moderate in 2% and as insufficient in 1% of the cases; 5% of the patients were judged as not evaluable for efficacy; in 1%, data are missing. 26 patients with ITP received a total of 128 Privigen® infusions with a mean dose of 22 g; the efficacy was judged as very good or good in 22 cases, as moderate in 1 case and as insufficient in 3 cases. Over all patients, the tolerability of Privigen® was judged by the physicians as very good or good in 92%, as moderate in 3%, and as insufficient in 3% of the cases; in 2%, data are missing. Adverse events possibly or probably related to Privigen® were reported for only 43 of the 1,586 infusions (2.7%); 2 of them (0.1%) were serious (both patients recovered completely). Among the 128 infusions in ITP patients, only 3 (2%) were associated with non-serious adverse reactions. **Conclusion:** Privigen® demonstrated very good or good efficacy and tolerability in >90% of 313 patients receiving 1,586 infusions.

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Introduction

Privigen® is a 10% liquid preparation of polyvalent human IgG for intravenous administration formulated with the novel stabilizer L-proline, which preserves IgG functional activity without refrigeration for up to 36 months, [1] rendering Privigen® ready-to-use.

Previous clinical studies have shown very good efficacy and tolerability of Privigen® in both children and adults with primary immunodeficiency and immune thrombocytopenia.[2-4] Immunoglobulin therapy has been successfully used in a number of other autoimmune diseases including multiple sclerosis, dermatomyositis and various polyneuropathies, as well as in transplantation.

A multicenter, observational study performed in Germany was designed to evaluate the efficacy and tolerability of Privigen® in patients with primary or secondary immunodeficiencies and different autoimmune diseases in the clinical practice.

Methods

This is an interim analysis of an ongoing, multicenter, observational study of Privigen® in patients with immunodeficiencies and autoimmune disorders. The study started in September 2008. In April 2009, a revision of the case report form (CRF) was implemented, capturing additional efficacy data in most of the registered indications including ITP. Only treatment courses documented with the revised CRF were included in this interim analysis. The cut-off date was Dec 13, 2010.

The study was approved by an independent ethics committee.

Results

Patients

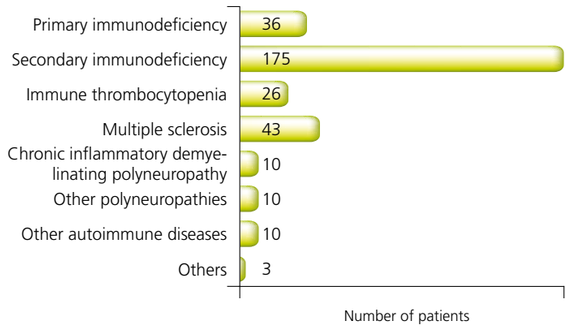
77 sites in Germany included 313 patients. Demographic characteristics are summarized in **Table 1**.

Table 1. Demographic characteristics of patients (n=313)

Gender	
Female	170 (54%)
Male	143 (46%)
Age (mean)	60 years
Weight (mean)	74 kg

Indications for immunoglobulin therapy are summarized in **Figure 1**.

Figure 1. Indications for Privigen® therapy (n=313)



Patients treated for secondary immunodeficiencies were diagnosed with the following indications (multiple diagnoses per patient possible): chronic lymphocytic leukemia (n=98), myeloma (n=24), non-Hodgkin lymphoma (n=31), solid tumor (n=9), other (n=12), missing (n=3).

Treatment

For each patient, a maximum of 6 Privigen® administrations could be documented in the case report form.

In total, the 313 patients received 1,586 Privigen® infusions; on average, 5.1 administrations per patient were recorded. The mean single dose was 15 g.

2 patients (1%) discontinued treatment because of inadequate clinical response, and 13 patients (4%) discontinued because of treatment-related AEs.

Efficacy outcomes

At the final visit, the efficacy of Privigen® was judged as very good or good in 91% of the patients **(Figure 2)**. Similar efficacy results were observed by indication **(Table 2)**.

In the 211 patients with immunodeficiencies, the efficacy was assessed as very good or good in 91% of patients, moderate in 1% and insufficient in 0%; 8% of the patients were not evaluable for efficacy or had missing data. In the 99 patients with autoimmune disorders, the efficacy was assessed as very good or good in 90% of patients, moderate in 4% and insufficient in 3%; 3% of the patients were not evaluable for efficacy or had missing data.

Figure 2. Evaluation of overall efficacy by investigators – all indications

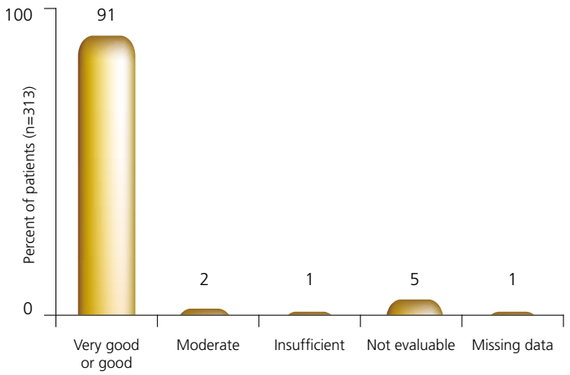


Table 2. Evaluation of overall efficacy by investigators – summary by indication

Indication (Number of patients)	Assessment of efficacy: Very good or good	Moderate	Insufficient
Primary immunodeficiency (n=36, 32 evaluable)	31	1	
Secondary immunodeficiency (n=175, 163 evaluable)	161	2	
Immune thrombocytopenia (n=26)	22	1	3
Multiple sclerosis (n=43, 41 evaluable)	39	2	
Chronic inflammatory demyelinating polyneuropathy (n=10)	10		
Other polyneuropathies (n=10)	9	1	
Other autoimmune diseases (n=10, 9 evaluable)	9		
Others (n=3)	3		

Safety outcomes

Adverse events (AEs) possibly or probably related to Privigen® were reported for only 43 (2.7%) of the 1,586 infusions; in two cases, the AEs were serious (0.1% of all infusions).

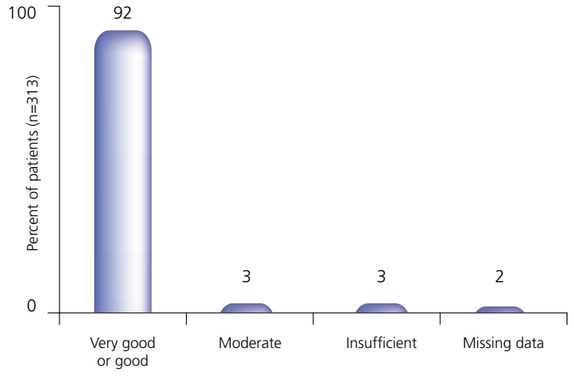
AEs with occurrence >2 events were chills (20 events), nausea (11), headache (9), increased temperature (6), reddening of the face (6), increased blood pressure (5), back pain (4), urticaria (4), dyspnea (3), feeling cold (3), feeling hot (3) and pruritus (3).

One patient had a serious adverse drug reaction with chills, increased temperature and increased blood pressure, and another patient had a serious adverse drug reaction with chills and increased blood pressure.

All AEs were resolved by the cut-off date of this interim analysis.

At the final visit, the overall tolerability of Privigen® was judged as very good or good in 92% of the patients **(Figure 3)**.

Figure 3. Evaluation of overall tolerability by investigators



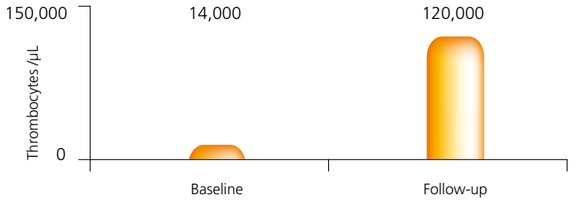
Results in Immune Thrombocytopenia (ITP)

26 patients (17 male, 9 female) were treated with Privigen® for ITP. Mean age was 57 years; mean weight was 81 kg.

5 ITP patients received maintenance treatment with an average monthly dose of 11 g Privigen® (mean treatment interval: 30 d; mean number of documented infusions: 5.4). The average „trough" thrombocyte count (measured immediately before a Privigen® infusion) in these patients was 82,000 /µL (4.2 measurements per patient on average). No bleedings were reported during the observation period (662 patient days). The efficacy was judged as very good in 4 cases and as insufficient in 1 case.

In 21 ITP patients, the physicians documented short-term treatment courses with Privigen®. 17 of these patients were evaluable for the analysis of the thrombocyte counts; for 4 patients, baseline or follow-up thrombocyte counts were missing. The 17 patients evaluable for this analysis received treatment courses over 2 to 8 days (average 4.5 days; resumed infusions after a delay were not considered for this analysis). The mean number of infusions was 3.8, the mean total dose was 85 g (average single dose: 22 g). The median thrombocyte count rose from 14,000 /µL at baseline to 120,000 /µL at follow-up **(Figure 4)**. 14 of the 17 patients (82%) had a thrombocyte count >50,000 /µL at follow-up. At the final visit, the efficacy of Privigen® was judged as very good or good in 18 of 21 patients (86%), as moderate in 1 patient (5%) and as insufficient in 2 patient (10%). One patient was prepared for splenectomy by the Privigen® treatment (thrombocyte count >400.000 /µL before surgery).

Figure 4. Median thrombocyte counts before and after a short-term treatment course with Privigen® in ITP patients (n=17)



Over all patients with ITP (n=26), the tolerability of Privigen® was judged by the physicians as very good or good in 96% and as moderate in 4%. Among the 128 infusions in ITP patients, only 3 (2%) were associated with adverse reactions (all non-serious).

Summary

The results demonstrate very good or good efficacy and tolerability of Privigen® in the vast majority of patients across several indications in which immunoglobulin treatment is recommended as a key therapy.

Efficacy of Privigen® was judged as very good or good in 91% of patients.

A short treatment course of Privigen® in ITP patients led to an increase of the median thrombocyte count by 106.000 /µL. In ITP patients on maintenance therapy, the average thrombocyte count was 82.000 /µL; no bleedings were observed.

Overall tolerability of Privigen® was judged as very good or good in 92% of patients.

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Conflicts of interest

Barbara Tschechne: Financing of scientific research by CSL Behring
Dietmar Pfründer: Employment with CSL Behring.