

Feasibility of Subcutaneous IgPro20 Administration Via Manual Push at High Flow Rates in Patients With Primary Immunodeficiency: Findings of the HILO Study

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Introduction

- IgPro20 (Hizentra[®], CSL Behring, King of Prussia, PA, USA) is a ready-to-use 20% subcutaneous immunoglobulin G (SCIG) approved for treatment of primary immunodeficiency (PID)^{1,2}
- Infusion of IgPro20 via manual push (also known as rapid push) is used in clinical practice but has not been approved by the US Food and Drug Administration¹
- The safety and tolerability of IgPro20 manual push flow rates of 0.5–2.0 mL/min/injection site have not been systematically evaluated
- Assessment of increasing flow rates is important, as higher flow rates allow shorter infusion times^{3,4}

Objectives

- The Hizentra[®] Label Optimization (HILO) study aimed to evaluate the safety and tolerability of IgPro20 flow rates of 0.5–2.0 mL/min/injection site administered via manual push in patients with PID

Methods

- The HILO study was a multicenter open-label trial (NCT03033745) using a forced upward titration design
- Patients with PID and previous experience with frequent manual push IgPro20 infusions at ~0.5 mL/min were eligible for inclusion in the manual push study cohort
- IgPro20 was administered in 2–7 manual push infusions/week at 0.5, 1.0, and 2.0 mL/min/site (or 30, 60, and 120 mL/h/site, respectively) over 12 weeks
 - Each flow rate was tested for 4 weeks
- Responder rates (percentage of patients who administered the minimum number of valid infusions) were evaluated for each flow rate
 - Valid infusions were those with ≥95% of planned volume/day and infusion duration not 1 minute or 10% longer than the calculated infusion duration (whichever was higher)
 - Only responders switched to the next flow rate after 4 weeks; non-responders continued at the highest tolerated rate
 - Flow rates were considered successful if the responder rate was ≥33%
- Treatment-emergent adverse events (TEAEs) up to a patient's non-response were summarized and tolerability under forced upward titration was evaluated (number of infusions without severe local reactions divided by total number of infusions)
- Infusion compliance and serum IgG levels were assessed

Results

Patient disposition and demographics

- 16 patients were enrolled in this cohort, and 14 completed the study
 - 2 patients (12.5%) discontinued at the 1.0-mL/min infusion rate: 1 owing to an AE unrelated to study drug and 1 owing to a protocol deviation
 - Patient baseline demographics are reported in **Poster 097**

Responder analysis

- The percentage of responders at 0.5-, 1.0-, and 2.0-mL/min flow rates was 100%, 100%, and 87.5%, respectively (**Figure 1**)
- Mean weekly duration of infusions decreased compared with Week 1 as flow rates increased (**Figure 2**)
- Infusion compliance was high for all flow rates, with most patients achieving >90% compliance (**Table 1**)

Figure 1. Responder analysis of increasing manual push flow rates (safety analysis set)

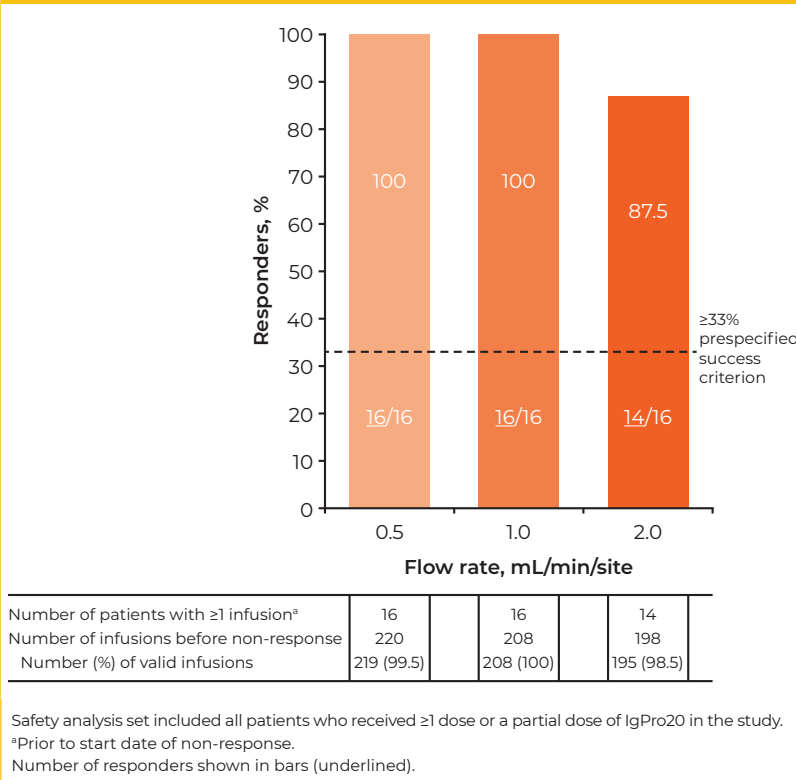


Figure 2. Mean weekly infusion duration with increasing manual push flow rates

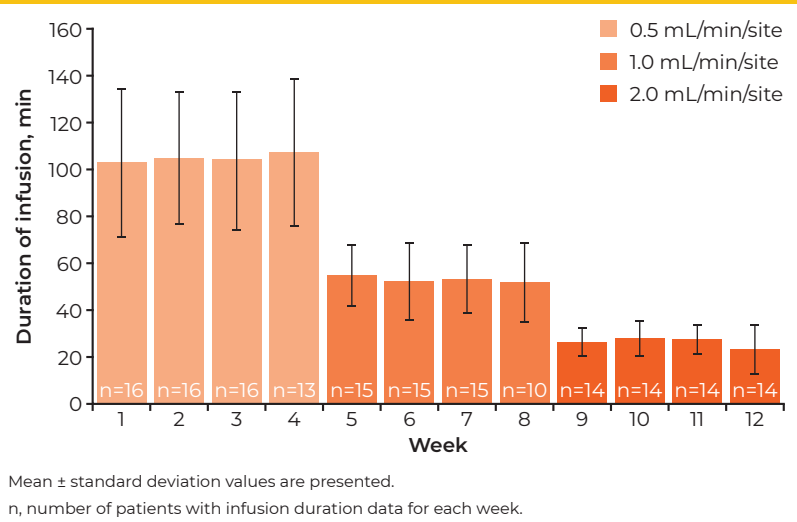


Table 1. Infusion compliance (safety analysis set)

Flow rate	0.5 mL/min/site (N=16)	1.0 mL/min/site (N=16)	2.0 mL/min/site (N=14)
Overall compliance (administered dose/planned dose), %			
Mean (SD)	99.5 (10.1)	93.7 (11.8)	98.5 (3.5)
Median (min, max)	100.0 (82.9, 131.7)	99.8 (60.7, 100.5)	100.0 (90.0, 100.5)
Compliance level, n (%)			
<90%	2 (12.5) ^a	4 (25.0) ^b	0
≥90%	14 (87.5)	12 (75.0)	14 (100.0)

Safety analysis set included all patients who received ≥1 dose or a partial dose of IgPro20 in the study.
^a2 patients had missing data records for some infusions at the 0.5-mL/min rate; therefore, compliance was <90%; ^bat the 1.0-mL/min rate, 1 patient received 9 of 12 planned infusions (to compensate for additional infusions at the 0.5-mL/min rate), 2 patients missed doses (one owing to a natural disaster and the other for an unknown reason), and 1 patient discontinued owing to an unrelated serious AE (suicide attempt) after receiving 5 of 8 planned infusions.
AE, adverse event; max, maximum; min, minimum; N, total number of patients per cohort; n, number of patients; SD, standard deviation.

Tolerability under forced upward titration conditions

- TEAE rates were low, with mostly mild local reactions, and were comparable across flow rates (**Table 2**)
- Tolerability was 100% for all flow rates
- Detailed safety and tolerability are reported in **Poster 097**

Table 2. Summary of TEAEs under forced upward titration conditions (safety analysis set)

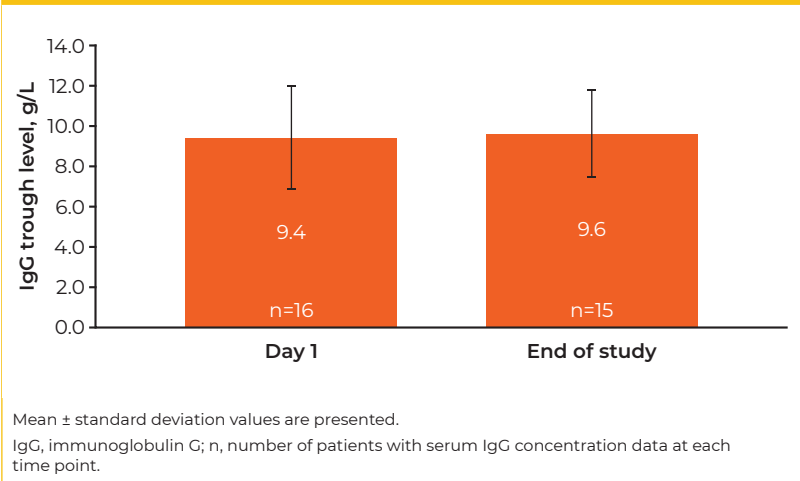
	Manual Push Flow Rate Cohort (N=16; Inf=626)	
	n (%)	E (rate)
Any TEAE	12 (75.0)	53 (0.085)
Treatment-related	6 (37.5)	33 (0.053)
Intensity of TEAEs		
Mild	11 (68.8)	49 (0.078)
Moderate	3 (18.8)	3 (0.005)
Severe	1 (6.3) ^a	1 (0.002)
Serious TEAEs	1 (6.3) ^a	1 (0.002)
Deaths	0	0
Study discontinuation due to TEAE	1 (6.3) ^a	1 (0.002)
Treatment-related	0	0
Local TEAEs	7 (43.8)	28 (0.045)
Treatment-related	6 (37.5)	27 (0.043)

Safety analysis set included all patients who received ≥1 dose or a partial dose of IgPro20 in the study.
^a1 patient reported a severe, unrelated, serious TEAE (suicide attempt), which led to discontinuation.
E, number of events; inf, number of infusions; N, total number of patients per cohort; n, number of patients; rate, TEAE rate per infusion; TEAE, treatment-emergent adverse event.

Serum IgG trough levels

- Patient serum IgG concentrations were similar between the start and end of study (**Figure 3**)

Figure 3. Serum IgG trough levels at start and end of study



Conclusions

- IgPro20 infusions via manual push at flow rates up to 2.0 mL/min/site were well tolerated in treatment-experienced PID patients
- Responder rates exceeded the prespecified success criterion at all flow rates
- Increasing flow rates did not impact the tolerability of IgPro20 manual push infusions
- Manual push IgPro20 administration at flow rates of 0.5–2.0 mL/min/site allows patients to individualize SCIG therapy by reducing infusion time

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