Pegloticase Monotherapy Response Rates: A Retrospective Database Study

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Background

- Pegloticase is a recombinant DNA-produced porcine-like uricase enzyme which metabolizes relatively insoluble urate to highly soluble allantoin. It is used in the treatment of refractory gout which has failed maximal medical management.
- Studies have shown a complete responder rate of 42% when defined as repeat serum uric acid levels (sUA) <6.0mg/dL for >80% of the time during months 3 and 6 of treatment.[1]
- Incomplete responders are presumed to have developed anti-drug antibodies which rapidly clear the pegloticase molecule and are associated with an increased risk of infusion reactions, as high as 26% in clinical trials.[1]
- The aim of the current study was compare the real-world experience with the previously published response and infusion reaction rates in patients treated with pegloticase monotherapy from randomized controlled trials.

Methods

- In this retrospective, observational cohort study, anonymized medical data was collected from a single outpatient facility on adult patients who received at least 2 doses of pegloticase.
- Exclusion criteria included concomitant immunomodulatory treatment[2,3] at any time during the pegloticase treatment course.
- A pre-treatment sUA level was obtained before each pegloticase infusion.
- Responders were defined as any patient able to maintain sUA <6.0 mg/dL between 3 and 6 months of treatment or able to receive at least 6 doses of pegloticase before treatment discontinuation because of clinical disease resolution as determined by the treating provider.
- Patients with at least 2 consecutive sUA >6.0 mg/dL were considered to be incomplete responders, even if additional infusions were received.
- Any patient that experienced an infusion reaction was noted.
- At the conclusion of the study, the observed response rate between months 3 and 6 of treatment and the overall infusion reaction rate were compared to previously published rates (known to be 42% and 26%, respectively)[1] for pegloticase monotherapy.

References

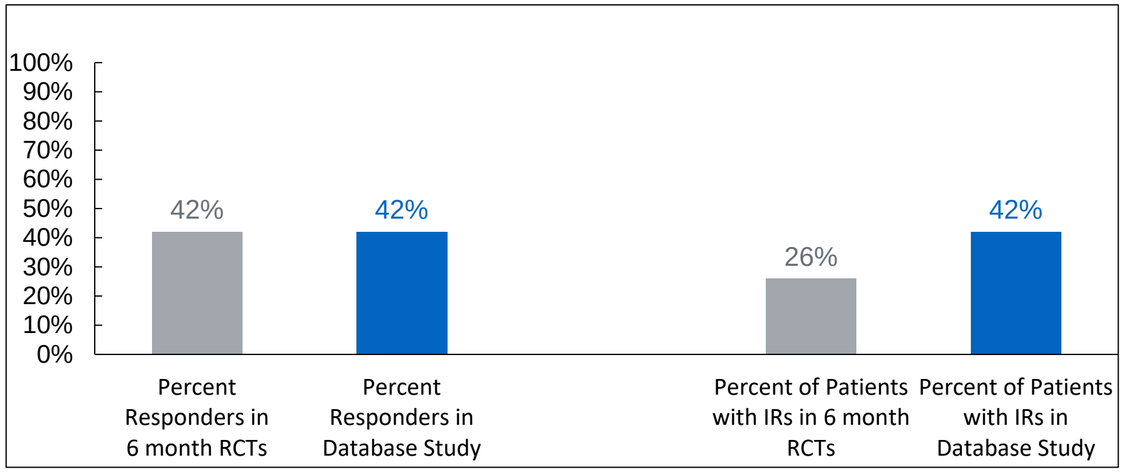
1. Sundy JS, et al. JAMA. 2011;306:711-20.
2. Botson J, Peterson J. Ann Rheum Dis 2019;78:A1289
3. Albert JA et al. Arthritis and Rheumatology 2019;71(S10):A1236.

Table 1: Patient Baseline Characteristics and Treatment Documentation

Patient	Sex	Age	Comorbidities	Baseline sUA	Total Number of Infusions	Responder	Infusion Reaction
1	M	51	Renal Insufficiency, Hypertension, Hyperlipidemia	9.6 mg/dL	21	Yes	No
2	M	38	None	10.8 mg/dL	23	No (2nd Infusion)	Yes/Hives
3	M	43	Renal Insufficiency, Hypertension, Hyperlipidemia, Congestive Heart Failure	11.3 mg/dL	13	Yes	No
4	F	50	Renal Transplant, Lupus, Hypertension, Hyperlipidemia	11.5 mg/dL	41	[1]Yes	No
5	M	58	Renal Insufficiency, Hypertension	10.3 mg/dL	28	Yes	No
6	M	40	Hypertension	8.1 mg/dL	6	No (4th Infusion)	Yes/Hives
7	M	47	Coronary Artery Disease, Diabetes, Congestive Heart Failure	10.1 mg/dL	6	Yes	No
8	M	72	Hypertension, Anxiety	9.1 mg/dL	12	Yes	No
9	M	34	Hypertension, Hypothyroidism	10.4 mg/dL	4	No (2nd Infusion)	Yes/Flushing/ Tachycardia/ Chest Pain
10	F	69	Hypertension, Congestive Heart Failure, Atrial Fibrillation	8.2 mg/dL	7	No (3rd Infusion)	Yes/Hives
11	M	48	Rheumatoid Arthritis, Diabetes, Hypertension	9.7 mg/dL	1	[2]Unknown	No
12	F	64	Pancreas Transplant, Hypertension, Diabetes, Hyperlipidemia	11.3 mg/dL	12	[3]Yes	No
13	F	59	Psoriatic Arthritis, Hypertension, Fibromyalgia	8.8 mg/dL	4	No (2nd Infusion)	No
14	M	39	Renal Insufficiency, Hypertension	10.0 mg/dL	4	[4]No (1st Infusion)	No
15	M	49	None	8.2 mg/dL	3	No (2nd Infusion)	Yes/Pruritis

[1] Patient 4 excluded due to concomitant immunomodulatory treatment with cyclosporine.
[2] Patient 11 was not included as only received a single dose of pegloticase.
[3] Patient 12 excluded due to concomitant immunomodulatory treatment with azathioprine.
[4] Patient 14 had received >10 previous infusions at another clinic (unknown treatment response).

Figure 1: Percentage of Pegloticase Responders and Percentage of Patients with an Infusion Reaction (IR) from Database Compared to Results of Randomized Controlled Trials (RCT) of Pegloticase Every 2 Weeks[1]



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Results

- Fifteen patients ranging in age from 34-69 were identified as having received pegloticase treatment.
- One patient received only a single infusion and did not meet inclusion criteria.
- Two patients were excluded due to concomitant immunomodulatory treatment (1 azathioprine and 1 cyclosporine).
- Of the 12 patients included, there were five (5/12 = 42%) complete responders and seven (7/12 = 58%) incomplete responders.
- Loss of response to pegloticase monotherapy occurred in 1 patient after the first infusion, 4 patients after the second, 1 patient after the third and 1 patient after the fourth.
- Five of the incomplete responders (5/7 = 71%) experienced an infusion reaction while no infusion reactions were seen in the complete responders (0/5 = 0%).
- The overall rate of infusion reactions was 5/12 = 42%.

Conclusion

- In this retrospective, observational cohort study of 12 patients, pegloticase monotherapy was associated with a 42% response rate and a 42% overall infusion reaction rate.
- Both the response and overall infusion reaction rates corroborated results from previously published data.
- Loss of response was also associated with a high (71%) rate of infusion reactions.
- Although additional studies are needed to further validate these results, these data continue to illustrate challenges in the treatment of refractory gout with pegloticase monotherapy.

Clinical Implications

- The study supports the previous data that Pegloticase is highly immunogenic and over half of the patients treated with monotherapy will eventually become non-responders to treatment.
- Patients that become non-responders have a high risk of infusion reactions.
- In this population of patients with refractory gout, there remains a large unmet need.

Disclosures

John Botson is a speaker and consultant for Horizon Therapeutics; however, research was entirely sponsored by the Alaska Rheumatology Alliance.