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An Increased Failure Rate Of Asparaginase Desensitization With Calaspargase Pegol

Jillian Fry
Children's Mercy Kansas City

Erin Guest
Children's Mercy Kansas City

Keith August
Children's Mercy Kansas City

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Jillian Fry, MD[1], Erin Guest, MD[1] and Keith August, MD, MS[1]

[1]Children's Mercy Kansas City, Division of Hematology/Oncology/BMT

Introduction

In late 2022, pegaspargase (SS-PEG) became unavailable to patients younger than 22 years in the United States, leaving calaspargase pegol (SC-PEG) as the only available long-acting asparaginase formulation. SC-PEG has been compared to SS-PEG in two randomized, pediatric clinical trials and found to have similar rates of adverse events with comparable rates of event-free survival. Our institution uses a desensitization protocol for patients who experience a hypersensitivity reaction to asparaginase. Here we review our experience with desensitization since the transition to SC-PEG from SS-PEG, comparing the rates of hypersensitivity reactions, success of desensitization protocols, and need for alternative asparaginase preparations between patients receiving SC-PEG and SS-PEG at our institution.

Methods

This is a retrospective, single center study of 26 patients with acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LLy) who received at least two doses of SC-PEG between November 2022 and December 2023. Serum asparaginase activity (SAA) was measured 7 days following dosing. Ten patients underwent SC-PEG desensitization using a protocol that was identical to our previously published protocol using SS-PEG. In the desensitization protocol, patients were premedicated with prednisone, cetirizine, famotidine, and montelukast. SC-PEG 2500 IU/m2 was divided into three fractions of 1:100, 1:10, and 1:1 dilution. Each fraction was infused over approximately 60 minutes, increasing the rate every 15 minutes.

Results

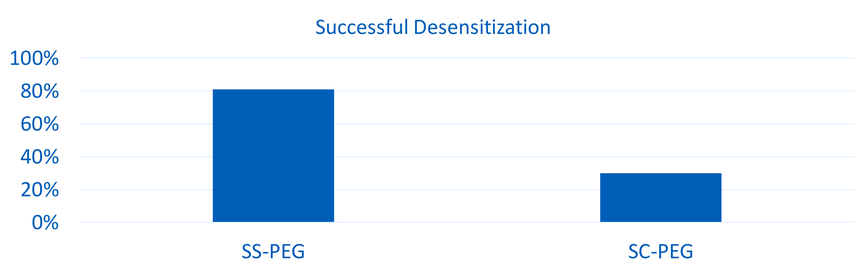
- The frequency of a grade 2 or higher clinical hypersensitivity reaction in those who received SC-PEG was 42.3% (n=11).
- Silent inactivation, defined as SAA <0.1 IU/mL measured seven days following dosing, occurred in an additional 7.8% (n=2).
- Ten patients underwent SC-PEG desensitization, which was tolerated with appropriate SAA levels (0.1 IU/mL) in 30% (n=3) of patients, 60% tolerated the infusion but had inappropriately low AA levels (n=6), and one patient did not complete the infusion due to an adverse event.
- Seven patients received Rylaze following SC-PEG hypersensitivity, silent inactivation, or unsuccessful desensitization.
- Compared to our prior experience with SS-PEG desensitization where 17 out of 21 attempts were successful with appropriate SAA levels, our success rate using SC-PEG (7 failures out of 10 attempts) is significantly less (p=0.013), leading to an increase in the use of an alternative asparaginase preparation.

Cases

Patient	Age (Years)	Diagnosis	Successful SC-PEG Infusions	SC-PEG Hypersensitivity Reaction (≥ Grade 2)	SC-PEG Silent Inactivation (SAA <0.1 IU/mL)	Underwent SC-PEG Desensitization	Successful SC-PEG Desensitization	Switched to Alternative Preparation
1	2	B-ALL (SR)	5	--	--	--	--	--
2	3	B-ALL (SR)	1	Yes	--	--	--	Yes
3	11	B-ALL (HR)	6	--	--	--	--	--
4	3	B-ALL (SR)	1	Yes	--	Yes	No (Silent Inactivation)	Yes
5	2	B-ALL (SR)	2	--	--	--	--	--
6	2	B-ALL (HR)	5	--	--	--	--	--
7	2	B-ALL (SR)	1	Yes	--	Yes	No (Silent Inactivation)	--
8	4	B-ALL (SR)	1	Yes	--	Yes	Yes	--
9	13	B-ALL (HR)	2	Yes	--	Yes	No (Adverse Event)	Yes
10	7	B-ALL (SR)	2	--	--	--	--	--
11	15	T-ALL	1	--	Yes	--	--	Yes
12	14	B-ALL (HR)	2	Yes	--	Yes	Yes	--
13	14	B-ALL (HR)	3	--	--	--	--	--
14	16	B-ALL (HR)	2	Yes	--	Yes	No (Silent Inactivation)	--
15	7	B-ALL (SR)	2	--	--	--	--	--
16	10	B-ALL (HR)	1	--	Yes	--	--	Yes
17	14	B-ALL (HR)	3	--	--	--	--	--
18	4	B-ALL (SR)	2	--	--	--	--	--
19	3	B-ALL (SR)	2	--	--	--	--	--
20	2	B-ALL (SR)	1	Yes	--	Yes	Yes	--
21	2	B-ALL (SR)	3	--	--	--	--	--
22	3	B-LLy	1	Yes	--	Yes	No (Silent Inactivation)	Yes
23	9	B-ALL (SR)	1	Yes	--	Yes	No (Silent Inactivation)	Yes
24	11	B-ALL (HR)	3	--	--	--	--	--
25	12	T-LLy	4	--	--	--	--	--
26	2	B-ALL (SR)	1	Yes	--	Yes	No (Silent Inactivation)	--
Total	--	--	--	11 (42.3%)	2 (7.8%)	10 (38.5%)	3 (30%)	7 (26.9%)

SR: Standard Risk; HR: High Risk; SAA: Serum Asparaginase Activity

SS-PEG vs. SC-PEG



Conclusion

Our single institution experience with SC-PEG shows a higher rate of hypersensitivity reactions than expected, a higher likelihood of failure of to asparaginase desensitization compared to our historical experience, and a switch to an alternative asparaginase preparation in 26.9% of all patients.

Contact Information:
Jillian Fry, MD
Children's Mercy Kansas City
jkfry@cmh.edu
(816) 302-6808

UMKC School of Medicine
KU School of Medicine, The University of Kansas
Children's Mercy Kansas City | Research Institute