Intravenous and Intramuscular Administration of Asparaginase in Pediatric Patients With Acute Lymphoblastic Leukemia: Treatment Patterns and Perceptions

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Background

- Asparaginase is an important component of therapy for acute lymphoblastic leukemia (ALL)[1,2]
- Asparaginase may be administered as a course of intramuscular (IM) injections, which can be painful and cause anxiety[3,4]
- Intravenous (IV) administration may offer a less painful option; however, concerns may exist over a perceived increased incidence of infusion-related reactions[5-7]
  - In the United States and the European Union, asparaginase derived from *Erwinia chrysanthemi* can be given IM or IV and is specifically indicated for patients with ALL who have developed hypersensitivity to *Escherichia coli*–derived asparaginase[8,9]
  - A study of pharmacokinetic simulations for 1- versus 2-hour IV asparaginase *Erwinia chrysanthemi* showed similar mean 48-hour trough serum asparaginase activity (SAA) levels, as well as similar proportions of patients having therapeutic 48-hour trough SAA ≥0.1 IU/mL[10]
    - This study led to recent changes to the product label of Erwinaze® (asparaginase *Erwinia chrysanthemi*; Jazz Pharmaceuticals, Palo Alto, CA USA; Erwinaze is a registered trademark of Porton Biopharma Limited used by Jazz Pharmaceuticals under license) allowing for IV administration over a 1- to 2-hour period[8]
- The goal of this online survey was to assess practices and attitudes of physicians regarding their treatment of pediatric patients with ALL, including the preferred route of administration and the infusion rate of asparaginase *Erwinia chrysanthemi*

Methods

- This was an online survey developed by Jazz Pharmaceuticals and conducted by Cognizant Analytics from May 20, 2015, to June 16, 2015
- Physician participants were recruited from a Jazz Pharmaceuticals list and Cognizant Analytics opt-in panel

KEY ELIGIBILITY CRITERIA

- US board-certified pediatric hematologists/oncologists, pediatric oncologists, hematologists/oncologists, or medical oncologists with 2 to 30 years in practice who treat pediatric patients (aged ≤21 years) with ALL
- Eligible physicians should have spent ≥75% of their time in direct patient care
- Monthly patient volume of ≥30 patients for any condition
  - Eligible physicians had to have personally treated ≥5 patients aged ≤21 years with ALL monthly
- In the past year, physicians used Children's Oncology Group (COG), Dana Farber, or the St. Jude Protocols for ≥80% of their patients with ALL

SURVEY INSTRUMENT

- Data included in this analysis were obtained from a subsection of a 30-minute, online, quantitative survey. Participants who indicated that they currently prescribe asparaginase *Erwinia chrysanthemi* (Erwinaze) were asked the following questions:

1. What is your standard route of administration for asparaginase?
   - IV; IM; Preference determined by patient characteristics and situation
2. How long has this been your standard practice for Erwinaze?
   - Under 6 months; 6–18 months; Over 18 months
3. Why is IV/IM your preferred route of administration for Erwinaze?
   - Open response

If participant answered ≥6 months to question #2, they were asked the following:

4. When administered IV, what is the typical infusion duration for Erwinaze in your practice?
   - Less than 60 minutes; 60 minutes; 90 minutes; 120 minutes; More than 120 minutes; Other
5. Please provide the main reason(s) why you choose to administer Erwinaze IV over this duration.
   - Consistent with the product label; Patient preference; Standard infusion time for IV asparaginase administration at my institution; Reduce the risk of infusion reaction; Other
6. When administering Erwinaze IV, do you typically start the infusion gradually (at a lower drug-delivery rate) before ramping up delivery of the remaining dose?
   - Yes; No; I do not know

If participant answered Yes to question #6, they were asked question #7:

7. Please explain why you choose to deliver Erwinaze gradually rather than equally from the very start to the end of infusion time.
   - Open response
8. If applicable, please tell us how you typically premedicate your patients when administering the asparaginase.
   - Antiemetic; Antihistamine; Steroids; Acetaminophen; Other; None

Results

RESPONDENTS

- A total of 74 responding physicians were recruited for this survey (**Table 1**)
  - On average, responding physicians treated 95% of their patients with ALL with a COG, Dana Farber, or St. Jude ALL treatment protocol
  - Sixty-seven of 74 (90.5%) responding physicians indicated that they currently prescribed asparaginase *Erwinia chrysanthemi*

Table 1. Demographic and Practice Characteristics of Responding Physicians

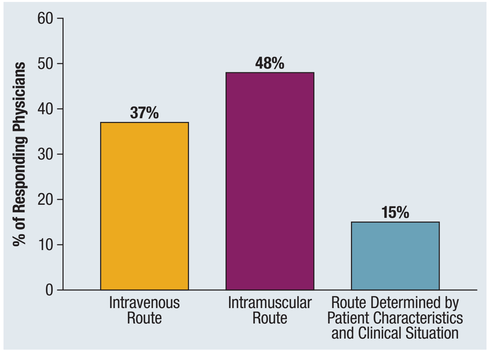
Characteristic	Responding Physicians (N=74)
Mean years in practice	13.1
Medical specialty, n (%)	
Pediatric hematology/oncology	56 (76)
Pediatric oncology	10 (14)
Hematology/oncology	6 (8)
Medical oncology	2 (3)
Practice setting, (%)	
Community hospital or oncology practice	24
Comprehensive cancer center	23
NCCN/NCI facility	14
Other academic or teaching hospital	38
Mean % time spent in direct patient care	87
Mean % of patients on COG, Dana Faber, or St. Jude protocols	95

COG, Children's Oncology Group; NCI, National Cancer Institute; NCCN, National Comprehensive Cancer Network.

ROUTE AND RATE OF ADMINISTRATION

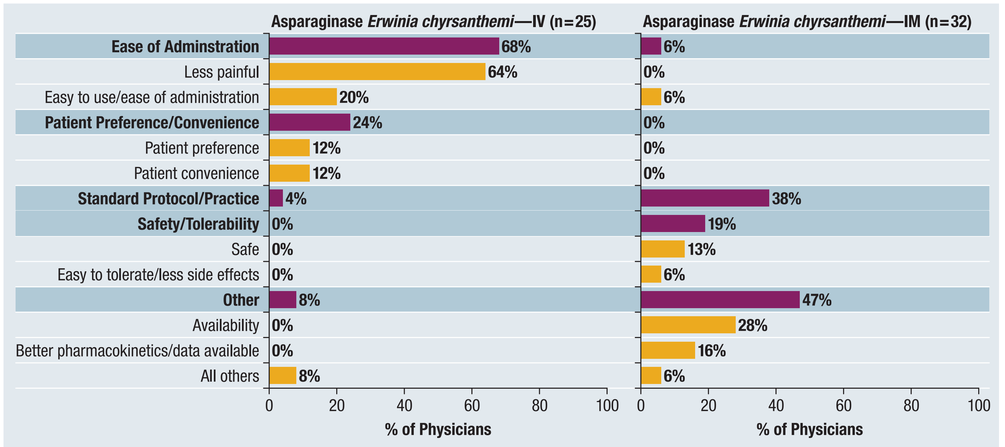
- Of the respondents currently prescribing asparaginase *Erwinia chrysanthemi*, nearly half, 48% (32/67), reported IM as their preferred route of administration; and 37% (25/67) reported a preference for IV administration (**Figure 1**)
- The remaining respondents, 15% (10/67), selected the route of administration based on patient and medical factors

Figure 1. What is Your Standard Route of Administration for Asparaginase *Erwinia chrysanthemi*? (n=67)



- Among respondents preferring IM administration, the most commonly cited reasons were standard of practice and/or protocol (38%, 12/32; **Figure 2**)

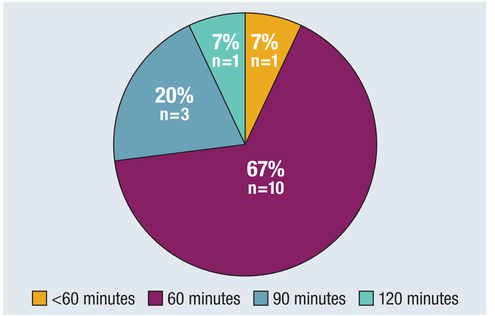
Figure 2. Why do you Prefer the Intravenous (IV) or Intramuscular (IM) Route?[a] (n=57)



[a]Lighter bars under the darker bars represent subcategories contributing to the darker bar category.

- Ease of administration (68%, 17/25) was the most commonly cited reason for preferring IV administration
- Of 25 respondents who reported using IV administration of asparaginase *Erwinia chrysanthemi*, 15 were experienced and had used the route of administration for ≥6 months
  - The majority of experienced IV responders (10/15) reported a typical infusion duration of 60 minutes for asparaginase *Erwinia chrysanthemi* (**Figure 3**)
  - A typical infusion duration of ≥90 minutes was reported by 3/15 responders

Figure 3. Typical Infusion Duration for Asparaginase *Erwinia chrysanthemi*[a] (n=15)



[a]Physicians using intravenous asparaginase *Erwinia chrysanthemi* for ≥6 months and who reported the infusion rates selected.

- The most common reasons reported for adhering to a 60-minute infusion duration were that it was consistent with the product label (n=6) and that it was the institutional standard (n=7; **Table 2**)

Table 2. Reasons for Using Intravenous (IV) Infusion Rates Among Responding Physicians Using Asparaginase *Erwinia chrysanthemi* ≥6 Months (n=15)

Rate of Infusion	Respondent-Reported Reasons for Preferred Rate[a] (n=15)
<60 minutes	Standard infusion time at my institution (n=1)
60 minutes	Consistent with product label (n=6) Patient preference (n=1) Standard infusion time for IV asparaginase administration at my institution (n=7) Reduces the risk of infusion reaction (n=3) Other (n=1)
90 minutes	Consistent with product label (n=1) Patient preference (n=1) Standard infusion time for IV asparaginase administration at my institution (n=1) Reduces the risk of infusion reaction (n=1)
120 minutes	Reduces the risk of infusion reaction (n=1)

[a]Responding physicians could cite more than 1 reason.

- The practice of starting the infusion gradually before ramping up delivery of the remaining dose was reported by 40% (6/15) of respondents
  - Reasons for a gradual infusion rate focused on:
    - Hospital policy (n=1)
    - Perception of improved tolerance/ability to better monitor patients for side effects (n=5)

Conclusion

- The majority of respondents using asparaginase *Erwinia chrysanthemi* preferred using IM administration, most commonly citing institutional preference/standard of practice
- Among physicians experienced with IV asparaginase *Erwinia chrysanthemi* administration, two thirds adhered to a 60-minute infusion, while one third adhered to a ≥90-minute infusion

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