

Intensive Asparaginase Therapy in Young-Adult Patients With Acute Lymphoblastic Leukemia: Treatment Patterns and Barriers to Asparaginase Use

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Background

- Long-term survival of pediatric patients with acute lymphoblastic leukemia (ALL) currently exceeds 80%¹; however, the prognosis for adolescent, young-adult (YA), and adult patients remains poor, with only 30% to 45% of patients achieving long-term survival^{2,3}
- Several studies suggest that when compared with traditional adult protocols, YA patients (aged 18–40 years) have superior overall survival with manageable toxicity when treated with intensive “pediatric-inspired” regimens that include asparaginase^{4–9}
- Despite these results, many YA patients with ALL continue to be treated with regimens that include little or no asparaginase¹⁰
- The goal of this study was to assess the views and practices of hematologists/oncologists with respect to asparaginase use in YA patients with ALL

Methods

- An online survey was developed by Jazz Pharmaceuticals and conducted by AlphaImpactRx from May 14 to June 22, 2015
- Survey participants were recruited from the AlphaImpactRx opt-in panel
- The study had 2 parts: a 10-minute quantitative survey and a 10-minute per-patient chart-audit component for up to 4 charts provided by each participating physician
 - The quantitative portion consisted of general and attitudinal questions (asked once)
 - Each patient chart review lasted 10 minutes; for example, if physicians were willing to share data from 4 different patient charts, they spent a total of about 50 minutes online
 - Questions in the chart audit were aimed at understanding the treatment dynamics for YA (ages 18–40 years) ALL patients in the United States, and in confirming (from claims data) the proportion of YA patients with ALL treated with any asparaginase, as well as what proportion of these ever received asparaginase *Erwinia chrysanthemi*

- Patient records were handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA)

KEY ELIGIBILITY CRITERIA

- United States board-certified physicians with 2–30 years experience treating YA patients with ALL were eligible
- Eligible physicians:
 - Spent ≥75% of their time in direct patient care and ≥20% of their time in an academic setting
 - ALL patient volume (patients aged ≥18 years) included >5 patients over the previous 2 years
 - Had to have personally treated ≥1 YA patient with ALL during the past 2 years

ANALYSIS

- Responses were analyzed using descriptive statistics

Results

- A total of 63 practicing physicians met eligibility criteria and agreed to participate. The physician sample is described in **Table 1**

Table 1. Physician Practice Sample Profile

Criteria	Physician Sample (N=63)
Time in practice, mean, years	12
Time spent in direct patient care, mean, %	89
Number of patients by cancer type treated in previous 2 years, median	ALL: 20 CLL: 40 AML: 30 CML: 25
YA patients with ALL treated over the previous 2 years, median, (% of ALL patients)	15 (75)
Newly diagnosed patients with ALL treated over the previous 2 years, median (% of YA ALL patients) ^a	10 (67)
Specialty, n (%)	
Hematology/oncology	52 (82.5)
Oncology	11 (17.5)
Primary academic affiliation, %	
Academic or teaching hospital	71
National Comprehensive Cancer Network/	22
National Cancer Institute	6
Both	6

^aFrom the quantitative survey; see Table 2 for the newly diagnosed proportion of chart-audit patients.

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CLL, chronic lymphoblastic leukemia; CML, chronic myeloid leukemia; YA, young adult.

- Charts for 189 YA patients with ALL were provided by participating physicians
 - Patient demographic information is presented in **Table 2**

Table 2. Patient Demographic and Disease Characteristics

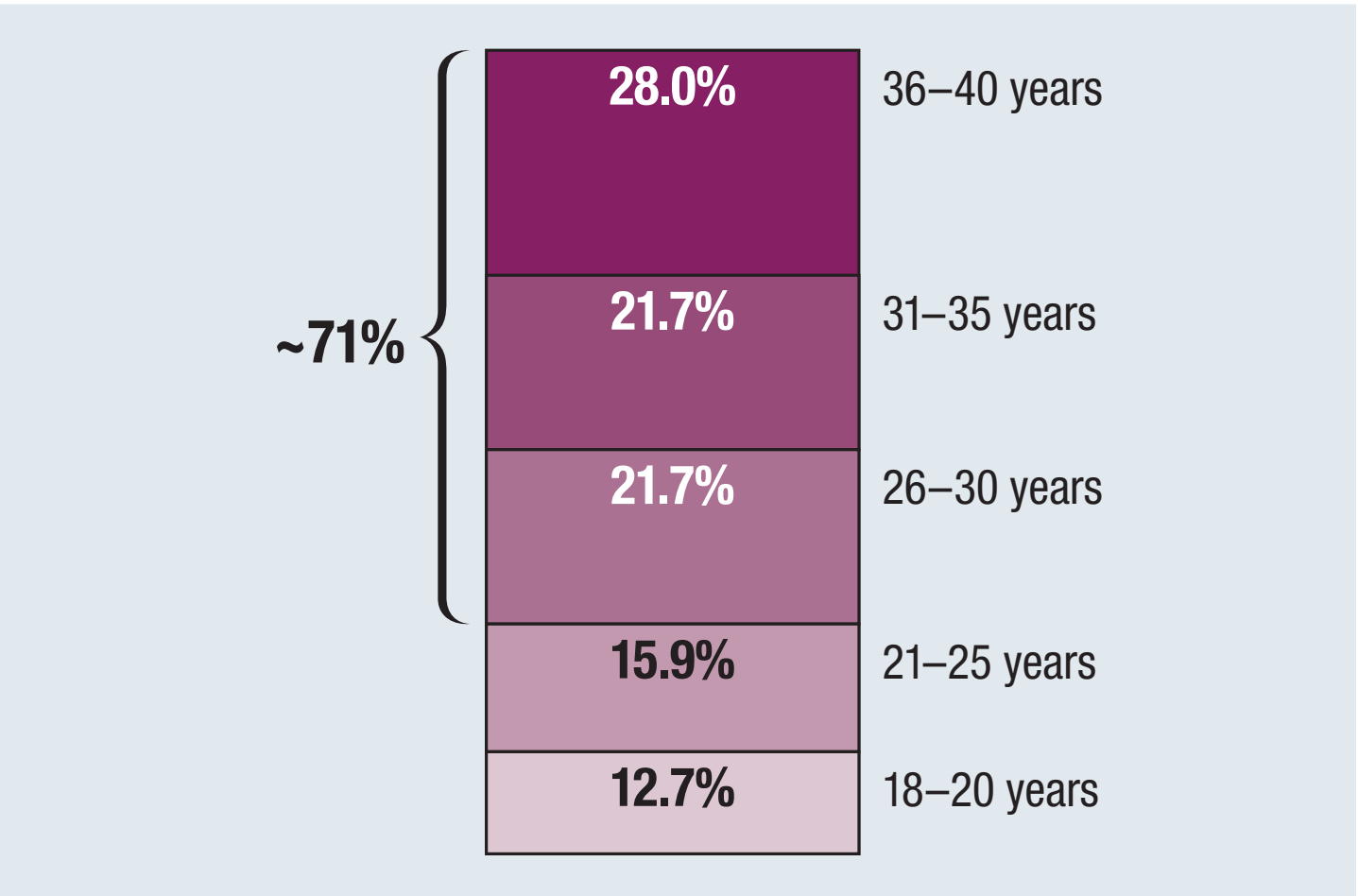
Characteristic		Patient Sample (N=189)
Gender, n (%)	Male	123 (65)
	Female	66 (35)
Age, median, years		30
Patient ALL status, n (%)	Newly diagnosed ^a	174 (92)
	Relapsed	15 (8)

^aFrom chart-audit patients; see Table 1 for most recent (ie, within last 2 years) physician-reported proportion of newly diagnosed patients.

ALL, acute lymphoblastic leukemia.

Of the 189 patients, about 71% were between the ages of 26 and 40 years; with approximately 50% between 18 and 30 years and 50% between 31 and 40 years (**Figure 1**)

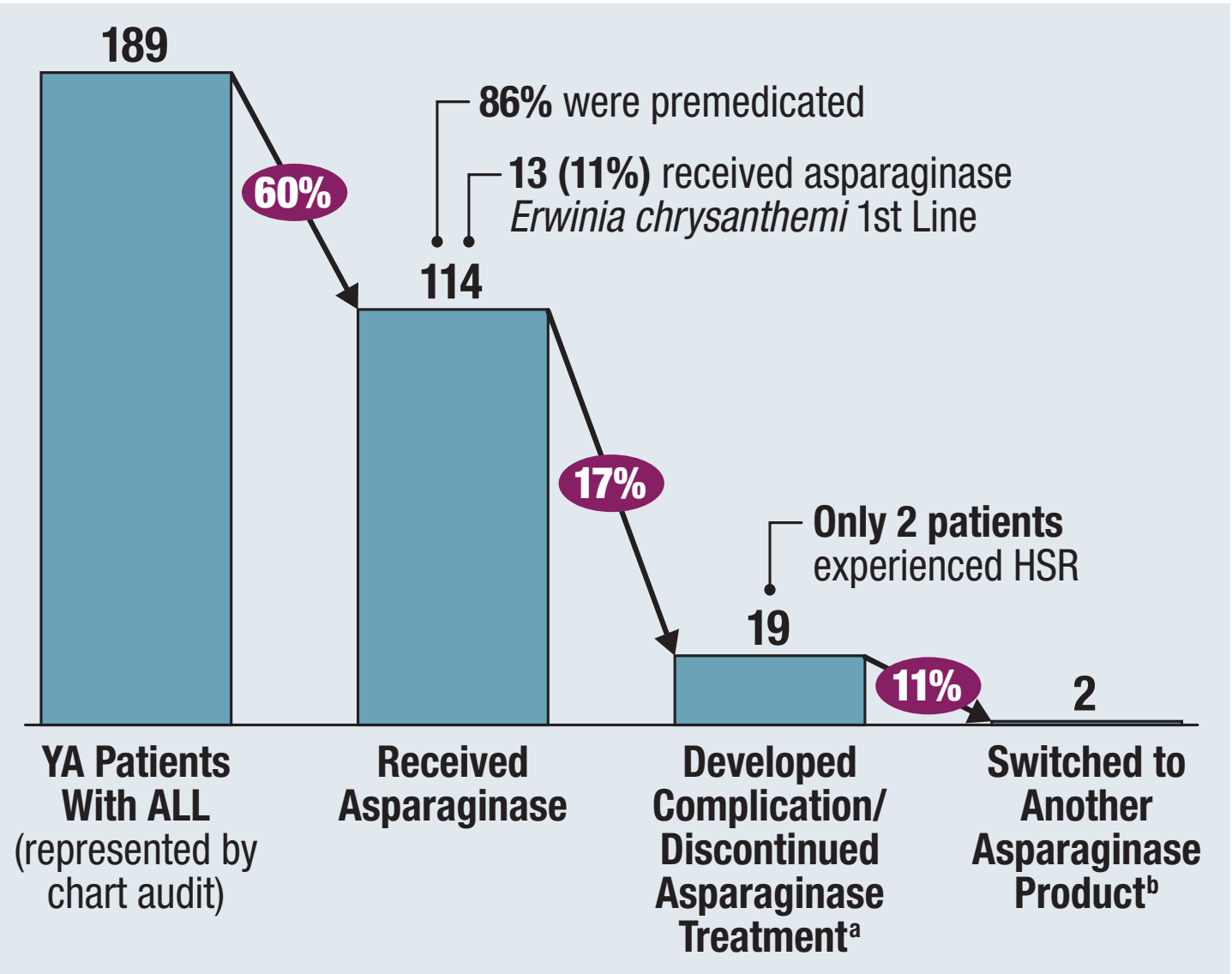
Figure 1. Patients’ Age Distribution



TREATMENTS

- Of 189 YA patients, 60% (n=114) received any asparaginase during treatment (**Figure 2**)

Figure 2. Asparaginase Treatment Snapshot



^aNone of the patients who discontinued treatment were switched to another asparaginase product before discontinuation.

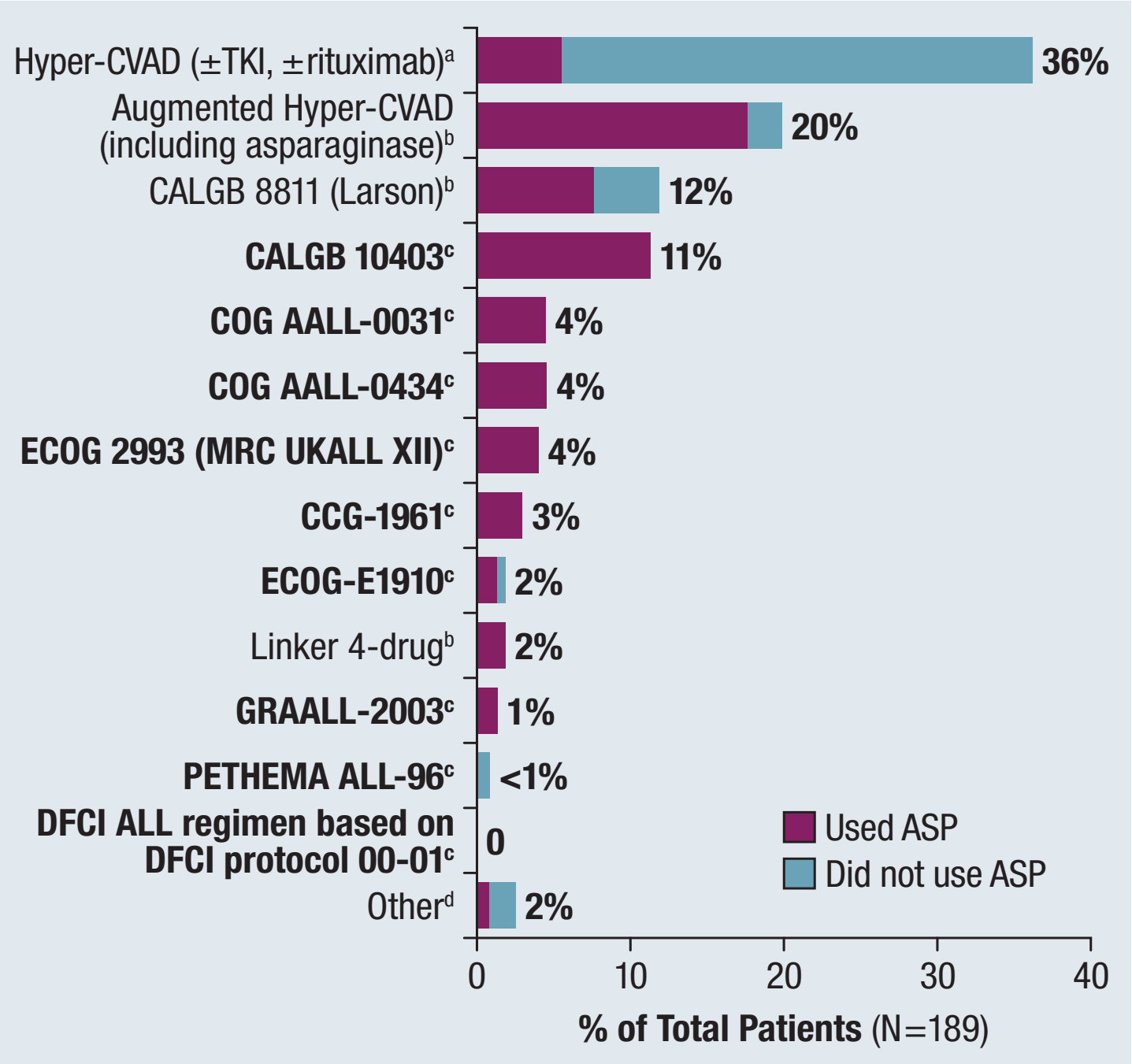
^bBoth patients who switched to other asparaginase products were able to complete treatment.

ALL, acute lymphoblastic leukemia; HSR, hypersensitivity reaction; YA, young adult.

- Fewer than 1 in 3 YA ALL patients were treated on a recommended protocol (**Figure 3**)
 - 29% (55/189) of YA patients were treated with asparaginase-intensive, pediatric-inspired protocols

- The most commonly used treatment regimen was hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyper-CVAD)
 - In contrast to augmented hyper-CVAD, no asparaginase is included in the hyper-CVAD protocol

Figure 3. ALL Treatment Protocols (% of patients)



^aNonasparaginase protocol; ^bNot a recommended protocol for treatment of YA ALL patients; ^cRegimens in bold are recommended by the National Comprehensive Cancer Network for the treatment of Philadelphia-negative YA ALL patients; ^dOther includes TKI+steroids, ALL protocol with dasatinib.

ALL, acute lymphoblastic leukemia; ASP, asparaginase; CALGB, Cancer and Leukemia Group B; CCG, Children's Cancer Group; COG, Children's Oncology Group; DFCI, Dana Farber Cancer Institute; ECOG, Eastern Cooperative Oncology Group; GRAALL, Group for Research in Adult Acute Lymphoblastic Leukemia; Hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; MRC UKALL, Medical Research Council, United Kingdom Acute Lymphoblastic Leukaemia; PETHEMA, Programa para el Tratamiento de Hemopatías Malignas; TKI, tyrosine kinase inhibitor; YA, young adult.

Conclusions

- Participating physicians indicated that 29% of YA patients were treated on a pediatric-inspired regimen, and that 60% of YA patients received some asparaginase during therapy
- 40% of YA patients were treated with protocols not including asparaginase, most commonly hyper-CVAD
- Factors leading to physicians’ decisions to not use asparaginase-intensive treatment regimens were patient specific, treatment related, and physician related

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