

COG AALL07P2 – Limited Institution Study

**Pharmacology and Toxicity of *Erwinia*
Asparaginase Following Allergy to PEG-
Asparaginase in Treatment of Children with
Acute Lymphoblastic Leukemia**

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Available FDA-Approved Asparaginase Formulations

- Native *E. Coli* L-asparaginase
- PEG-asparaginase
- *Erwinia* asparaginase
 - Approved by FDA in Nov 2011 based largely on data from COG AALL07P2

Clinical Allergy - Background

- CCG 1961 (high risk ALL)
 - 54% on intensified arm
 - Native *E. Coli* asparaginase used during induction, with PEG asparaginase for some and *E. Coli* asparaginase for others post induction
- CCG 1991 (standard risk ALL)
 - 16% on the augmented arm
 - PEG-asparaginase used during induction and post-induction phases of therapy

Pharmacology

Formulation	Elimination Half-Life (administered by IM)	Asparagine Depletion (days after dose)
Native <i>E .coli</i> asparaginase	26-30 hours	14-23
PEG-asparaginase	5.5- 7 days	26-34
<i>Erwinia</i> asparaginase	16 hours	7-15

COG AALL07P2 - Objectives

Primary Objectives

- To determine if 48 hour nadir asparaginase activity is ≥ 0.1 IU/mL.
- To determine the frequency of asparaginase related toxicity.
- To characterize the pharmacokinetics of Erwinase® in children with leukemia and allergy to PEG-asparaginase.

Secondary Objectives

- To determine the 72 hour trough serum asparaginase activity.
- To determine if plasma asparagine is depleted pre-dose 6.
- To determine the presence of anti- Erwinase® antibodies.

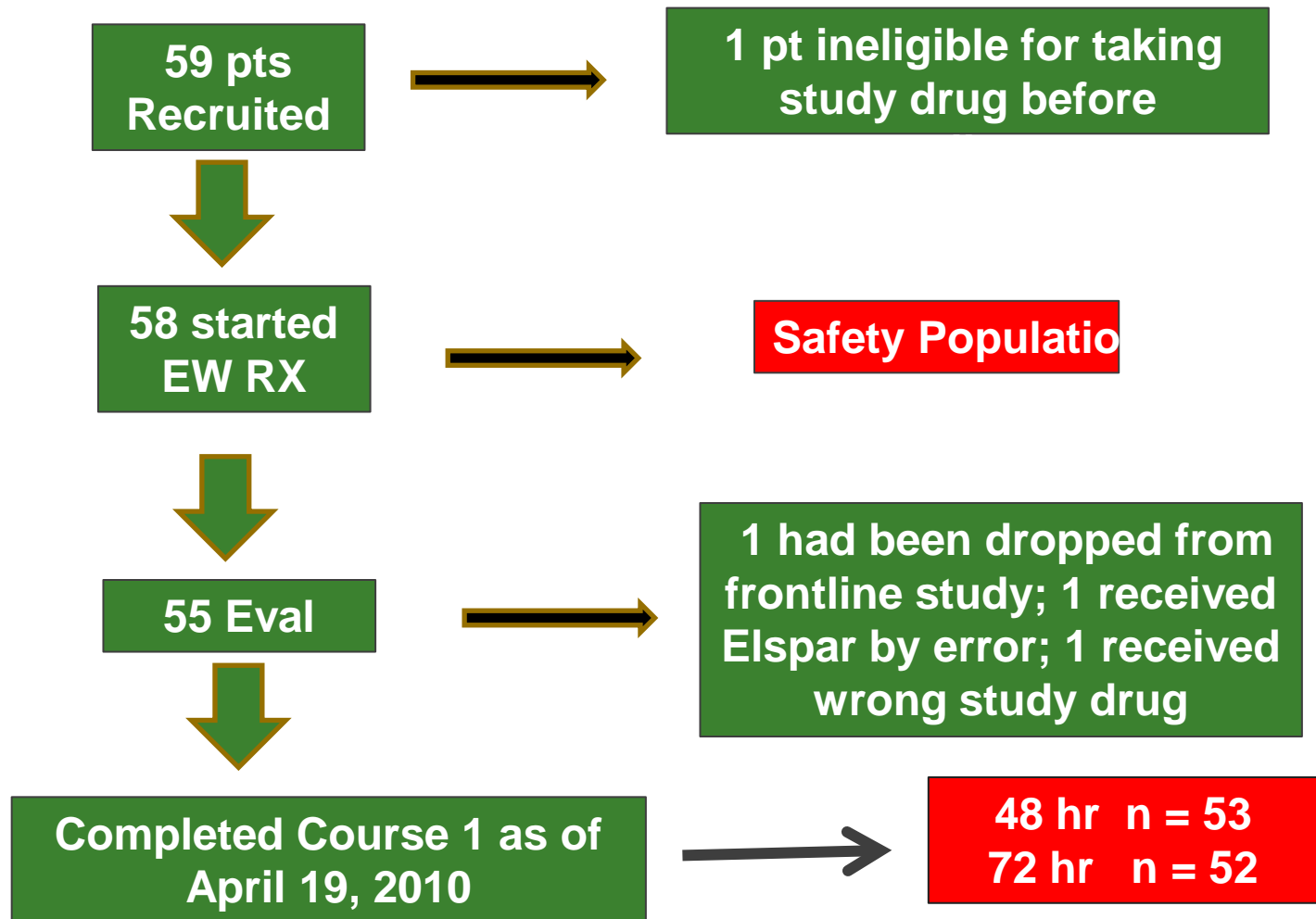
AALL07P2 - Eligibility

- Age > 1 and ≤ 30 years
- Enrolled on frontline COG ALL therapeutic study
- \geq Grade 2 hypersensitivity to PEG-asparaginase
- No exposure to *Erwinia* asparaginase
- No history of \geq grade 2 pancreatitis

AALL07P2 - Design

- Erwinaze™ 25,000 IU/m² x 6 IM
Monday/Wednesday/Friday for each
remaining PEG-asparaginase
- Pharmacokinetic/Pharmacodynamic studies
 - Asparaginase levels
 - Asparagine levels
 - Antibody formation

Patient Disposition



Demographics

N=58

Characteristic	Mean (SD)	Range
Age (years)	9.7 (5.2)	2 - 18
Weight (kg)	44.7 (30)	12 - 117
Height (cm)	140 (30)	87 - 186

Demographics (cont.)

N=58

Gender	34 (58.6%) Male	24 (41.4%) Female	
Race	45 (77.6%) White	6 (10.3%) Black	7 (13.1%) Other
Primary Disease	51 (88%) B-Precursor ALL	7 (12%) T-Cell ALL	
Months Since Diagnosis	0 - 3 months 29 (50%)	4 - 6 months 26 (44.8%)	7 - 9 months 3 (5.2%)

Asparaginase Activity Results

GLA Laboratory Results

Proportion of Patients in AALL07P2 with Sustained Asparaginase Activity

Trough sampling time post Dose 3	Main Outcome Proportion (n/N) and 95% CI with asparaginase activity ≥ 0.1 IU/ml	Exploratory Analysis Proportion (n/N) and 95% CI with asparaginase activity ≥ 0.4 IU/ml
48-hour	100% (35/35) 95% CI: 90%, 100%	80% (28/35) 95% CI: 64%, 90%
72-hour	100% (13/13) 95% CI: 77%, 100%	38% (5/13) 95% CI: 18%, 65%

AALL07P2 - Conclusions

- Erwinaze™ was well tolerated and achieved nadir serum asparaginase activity at both 48 and 72 hours after dosing that was similar to that achieved with PEG-asparaginase.
- Following allergy to PEG-asparaginase, Erwinaze™ 25,000 IU/m² x 6 doses IM on a Monday/Wednesday/Friday schedule can be substituted for a single dose of PEG-asparaginase.