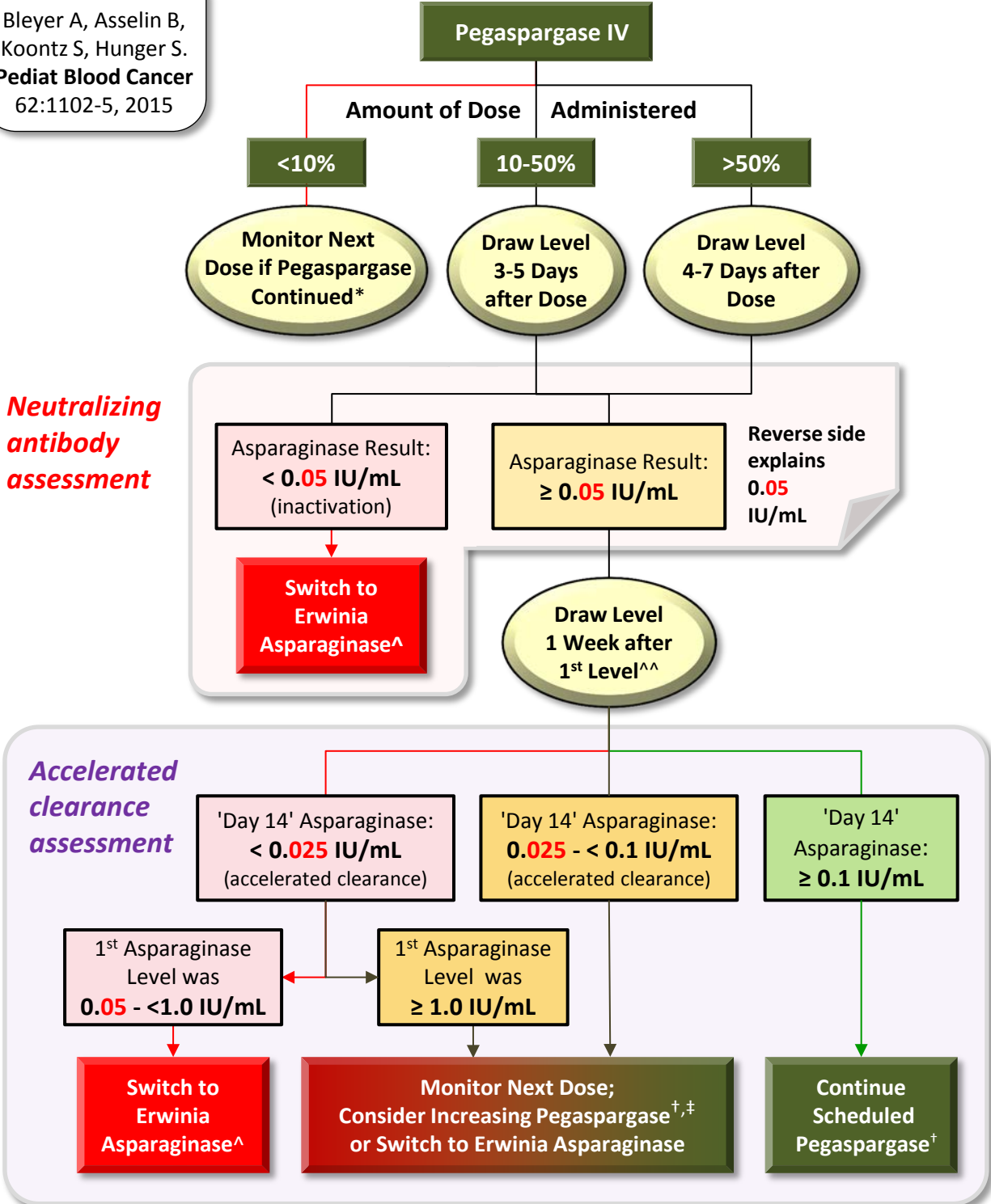


Modified from  
Bleyer A, Asselin B,  
Koontz S, Hunger S.  
*Pediat Blood Cancer*  
62:1102-5, 2015



\* In most instances, the asparaginase preparation would be discontinued      ^^ 7 days after 1st sample  
 ^ 6 doses of Erwinia asparaginase, 25,000 IU/m<sup>2</sup>, IM at 2-3 day intervals for each scheduled dose of pegaspargase  
 † With premedication to prevent a clinical allergic reaction if asparaginase levels monitored  
 ‡ Administering another dose of pegaspargase should be considered, as well as monitoring future doses levels for continued accelerated terminal-phase disappearance

## Why 0.05 IU/mL is the Lower Threshold for Intervention instead of previously-used higher levels

### Excerpt from

Bleyer A, Asselin B, Koontz S, Hunger S.  
Pediatr Blood Cancer . 2015;62:5  
Correspondence online March 2, 2015

“... Not included in our report are unpublished data from Children’s Oncology Group (COG) clinical trial AALL07P4 (cited by the correspondents) that we were provided by Sigma-Tau Pharmaceuticals and COG. Those data allowed us to compare the last detectable asparaginase activity  $\geq 14$  days after 70 doses of pegaspargase, 2,500 IU/m<sup>2</sup>, in 42 patients with concomitant asparagine concentrations, the latter measured under conditions designed to prevent *ex vivo* hydrolysis.<sup>3</sup>

The only samples with detectable asparagine were the two with the lowest asparaginase activities, 0.014 and 0.016 IU/mL (Figure) Asparagine was undetectable after all 68 doses with asparaginase between 0.02 and 0.20 IU/mL.

1) **These data**, 2) **a prior report**,<sup>4</sup> and 3) **a recommendation from the Journal’s manuscript reviewer(s)** led us to select <0.05 IU/mL on days 3\* to 7\* after dose administration as a threshold for switching to Erwinia asparaginase.“

\*depending upon the amount of pegaspargase received  
(see algorithm on reverse side)

- \*\*3. Angiolillo AL, Schore RJ, Devidas M, et al. Pharmacokinetic and pharmacodynamics properties of calaspargase pegol Escherichia coli l-asparaginase in the treatment of patients with acute lymphoblastic leukemia: results from Children’s Oncology Group 98 study AALL07P4. J Clin Oncol 2014. 55:57-63.
- \*\*4. Rizzari C, Citterio M, Zucchetti M, et al. A pharmacological study on pegylated asparaginase used in front-line treatment of children with acute lymphoblastic leukemia, Haematologica 2006; 91:24-31.

\*\*Reference numbers in original publication