

TO: Participating centers  
Neuroblastoma Purging Expanded Access Protocol

FROM: C. Patrick Reynolds, MD, PhD  
Judith Villablanca, MD

DATE: September 3, 2008

RE: Final closure of protocol

The COG A3973 study randomized patients to receive either purged or unpurged peripheral blood hematopoietic stem cells after the same induction and high dose consolidation chemotherapy. An analysis of COG A3973 study data was released by the DSMB to the COG membership at the April 19, 2007 meeting, and was presented at the American Society of Clinical Oncology in June 2008 (SG Kreissman et al: "Outcome for randomized trial of immunomagnetic purged vs unpurged peripheral blood stem cells (PBSC) following myeloablative autologous PBSC transplant (ASCT) for high risk neuroblastoma (HR-NB); a Children's Oncology Group (COG A3973) study" Proc Amer Soc Clin Oncol: 26: 541s (Abstract # 10011) June 2008).

The analysis of the A3973 study showed no significant difference in the two year event-free (EFS) and overall survival (OS) in patients randomized to purged versus unpurged PBSC from the time of study entry, or from the time of transplant (analysis done based on intent to treat). There was also no significant difference in toxicity between the two arms.

Since the A3973 study did not demonstrate a significant benefit for purging peripheral blood stem cells, Dr. Reynolds has withdrawn the FDA Investigational Device Exemption BB-IDE-2259. Therefore the Expanded Access Protocol for Purging of Peripheral Blood Stem Cells or Bone Marrow from Patients with High-Risk Neuroblastoma Prior to Autologous Transplantation was permanently closed effective as of the date of his IDE withdrawal memo (June 13, 2008).

*Note that if your patients have purged stem cells stored at CHLA, they may still be infused, if medically indicated, but to use those stem cells a single patient IND will need to be filed with the FDA.*

#### **SUMMARY OF STUDY DATA:**

A total of 39 patients were registered on study, 36 products were purged. Three patients were collected after registration on study, but the stem cells were not shipped for purging. A total of 27 purged products were infused into patients. Six purged products remain stored at CHLA, and three products were shipped to the collecting institution but have not been infused.

Engraftment data from the 27 patients infused is summarized below. ANC engraftment data was submitted on all 27 patients. One patient died of sepsis prior to platelet engraftment, and one other patient has not submitted platelet engraftment data.

	<b>Median days to engraftment from day of stem cell infusion</b>	<b>Range of days to engraftment</b>
<b>ANC (n=27)</b>	11	9-40
<b>Platelets (n=25)</b>	29.5	8-260

The protocol defined delayed ANC engraftment as > 28 days, and delayed platelet engraftment as > 56 days. One patient had delayed ANC engraftment at 40 days. Four patients had delayed platelet engraftment at 64, 66, 74, and 260 days. No patient required infusion of a backup unpurged stem cell product. There were no serious side effects reported due to delayed engraftment.

Please submit this closure memo to your local IRB. If you have any questions regarding this study, you may contact Dr. Judy Villablanca at 323-361-5687 (jvillablanca@chla.usc.edu).