CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

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Re: Correction in a Children's Oncology Group Scientific Publication

Dear Patients and Families participating in COG Neuroblastoma Studies:

The Children's Oncology Group (COG) is committed to keeping all families who participate in research aware of new developments, including any problems that may arise with the research we conduct. We are writing to inform you about an error that was discovered when analyzing results from a study conducted in children with high risk neuroblastoma during the 1990s, the results of which were first published in 1999 and the follow up results published in 2009. We have found that two statistical tests published in the 2009 article were incorrect, and would like to share details about this finding with you.

In the 1990s we conducted a study, CCG-3891, which evaluated the role of autologous bone marrow transplant (ABMT) and isotretinoin (13-cis-retinoic acid, Accutane®) for the treatment of children with high risk neuroblastoma. The study found that both ABMT and administration of isotretinoin improved the outcome of children with this disease. We published these results in 1999 in *The New England Journal of Medicine*, and since that time these treatments have been recommended as part of treatment for children with high risk neuroblastoma.

Our publication in 2009 in the Journal of Clinical Oncology confirmed the benefit of ABMT for children with high-risk neuroblastoma in terms of the number of children alive without return of cancer (termed event-free survival or EFS). However, although the percentage of patients surviving at 5 years on each of the treatments was reported correctly in our 2009 publication, two statistical tests to compare how many children survived were calculated incorrectly. One calculation related to ABMT was incorrect. The other incorrect calculation related to isotretinoin.

After extensive review of the corrected analyses from the 2009 publication, including review by COG neuroblastoma experts, COG leadership, the independent Data and Safety Monitoring Committee for the COG, and members of the Cancer Therapy Evaluation Program of the National Cancer Institute, we are not recommending any change to the standard treatment for children with high risk neuroblastoma. We continue to recommend that ABMT and administration of isotretinoin be included as part of standard therapy.

The recommendation for continued use of ABMT is based on the confirmed benefit for EFS from the 2009 publication and on results of other randomized clinical trials. For isotretinoin, one factor supporting the recommendation is the low number of side effects in children receiving the agent compared to other drugs used to treat cancer. Another factor is the higher EFS rates that we saw in the 1999 report for patients receiving isotretinoin in CCG-3891, although we are now less certain that the rates are truly higher with the use of isotretinoin.

COG recognizes the importance of reliable reporting of results from our clinical trials and we sincerely regret the two incorrect statistical analyses published in 2009. We have identified how this error occurred and have taken steps to help prevent such statistical analysis errors from occurring in the future. Importantly, over the past twenty years, research conducted by the COG has resulted in doubling the number of children who survive following a diagnosis of high risk neuroblastoma. We still have a long way to go, as too many children still die from neuroblastoma and the side effects children must endure to survive are too great. Advances will only come through research, and participation of children and their families is central to success. We view our research mission as a partnership with children and their families, and assure you that we will take all steps necessary to correct any errors that may occur. This includes sharing information directly with you.

Your pediatric oncologist will be in the best position to answer any additional questions about this matter, or questions about treatment your child has undergone or is undergoing.

Sincerely,

Dr. Peter Adamson, Chair, Children's Oncology Group
Dr. Mini Devidas, Group Statistician, Children's Oncology Group
Dr. Julie Park, Chair, COG Neuroblastoma Disease Committee