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New therapy boosts cure rate by 20 percent in a deadly childhood cancer

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Using immunotherapy—biologic agents that stimulate the body's immune system—pediatric oncologists have achieved the first substantial increase in over a decade in cure rates for the childhood cancer neuroblastoma. A newly released study shows that the new treatment improved two-year survival rates by 20 percent, compared to standard treatment for an aggressive form of neuroblastoma, a cancer of the nervous system.

"We expect these findings will change clinical practice, setting a new gold standard of treatment for this often-deadly disease," said John M. Maris, M.D., a co-author of the study and director of the Center for Childhood Cancer Research at The Children's Hospital of Philadelphia. Maris is the chair of the neuroblastoma committee of the Children's Oncology Group (COG), the cooperative multicenter research organization that sponsored the study.

The study appears in the Sept. 30 issue of the New England Journal of Medicine, along with a separate COG study on intermediate-risk neuroblastoma. The corresponding author of the immunotherapy study is Alice L. Yu, M.D., Ph.D., of the University of California, San Diego.

Neuroblastoma, a cancer of the peripheral nervous system, usually appears as a solid tumor in the chest or abdomen. It accounts for 7 percent of all childhood cancers, but because it frequently occurs in an aggressive form, it causes 15 percent of all childhood cancer deaths. While low-risk forms of neuroblastoma may spontaneously disappear, in

high-risk forms, the cancer tends to return after initial treatment, usually with lethal results.

In the current study, researchers assigned 226 high-risk patients at multiple cancer centers to receive either the standard therapy (the chemotherapy drug isotretinoin) or immunotherapy—three biological agents in combination with isotretinoin. Immunotherapy consisted of the monoclonal antibody ch14.18, plus two cytokines: granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-2. Monoclonal antibodies are molecular "guided missiles" engineered to kill cancer cells by targeting a substance appearing on those cells. Cytokines are naturally occurring signaling proteins that regulate immune responses.

Within two years of follow-up, approximately 54 percent of the neuroblastoma patients receiving standard treatment suffered a disease relapse, which is almost uniformly fatal. In contrast, over the same time period, only 34 percent of patients receiving the experimental immunotherapy regimen had their disease return, resulting in a much higher cure rate. The immunotherapy group of patients did experience pain and other toxic side effects at a higher rate than the standard treatment group. Nonetheless, the evidence of clear benefits from immunotherapy allowed the researchers to halt the trial earlier than expected.

The Cancer Center at The Children's Hospital of Philadelphia has been using this immunotherapy regimen as part of standard treatment for children with high-risk neuroblastoma for more than a year, since preliminary trial results were reported in June 2009. Children have arrived from around the world to receive this treatment at Children's Hospital, which has a long-established research and clinical program in neuroblastoma.

Maris is internationally prominent as a neuroblastoma expert; among many other findings, in 2008, he led the first study that identified the gene location in which neuroblastoma originates. Earlier this year, the New England Journal of Medicine selected Maris to write a review article, “Recent Advances in Neuroblastoma,” describing the current state of the science.

In addition to the current immunotherapy study, Maris also co-authored a second study in the same issue of the journal, reporting on a separate COG phase 3 clinical trial of intermediate-risk neuroblastoma. The corresponding author was Katherine K. Matthay, M.D., of the University of California, San Francisco. That study found that physicians could substantially reduce the dose and duration of chemotherapy used for neuroblastoma, and still achieve very high survival rates of 98 percent among children receiving the treatment. The benefits of lower doses include better quality of life, reduced costs, and an expected reduction in late effects of chemotherapy, which may occur years after treatment.

“Together, these studies report important advances in care for children with this challenging cancer,” said Maris. “We will continue to investigate treatments to further refine the standard of care.”

More information: “Anti-GD2 Antibody with GM-CSF, Interleukin-2 and Isotretinoin for Neuroblastoma,” and “Outcome after Reduced Chemotherapy for Intermediate Risk Neuroblastoma,” New England Journal of Medicine, Sept. 30, 2010.

Provided by Children's Hospital of Philadelphia

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