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## **Improved treatment raises medulloblastoma survival rate**

***Study led by St. Jude finds that adapting intensity of radiation therapy to individual patients and shortening the length of intensive chemotherapy improves outcome***

A team of investigators led by St. Jude Children's Research Hospital has announced that improvements in the treatment of the childhood brain cancer medulloblastoma have significantly increased the rate of survival of children with this disease.

The treatment increased the overall five-year survival for 86 children with average-risk medulloblastoma from the current rate of 70 percent to 85 percent; and raised the rate of survival among the 48 high-risk patients from 55 percent to 70 percent. Patients are considered to be at average risk of treatment failure if their cancer has not spread following initial surgery to remove the tumor, or if the remaining tumor is very small. Patients are considered at high risk of failure if their tumor has spread following surgery or if the remaining tumors are larger than those of low-risk patients.

A report on these results appears in the September 7 issue of *Lancet Oncology*.

The investigators were able to achieve the improved survival rates while reducing the amount of radiation and length of chemotherapy following surgery in average-risk patients from levels used in standard treatments, according to Amar Gajjar, M.D., co-chair of the St. Jude Department of Oncology and director of its Neuro-Oncology Division. The chemotherapy for average-risk patients was completed in 16 weeks, versus the standard treatment, which lasts 48 weeks. The new treatment not only reduced radiation to the brain and spinal cord, but also reduced the level of two chemotherapy drugs by 75 percent and 50 percent, respectively. This reduction in radiation and chemotherapy holds promise for lessening the long-term, troublesome side effects on intellectual development of young patients treated for this cancer, Gajjar said.

In addition to improving overall five-year survival of average-risk patients to 85 percent, this group had an 83 percent rate of event-free survival and a rate of five-year, event-free survival of 70 percent for high-risk patients. Event-free survival means that a child did not have medical complications or relapse that required further treatment.

Moreover, the improved treatment achieved a survival rate of 66 percent as compared to 30-40 percent among children whose cancer had spread.

The results of the current clinical trial, SJMB96, are especially significant because they represent a dramatic change from the 45 percent survival rate achieved two decades ago using just surgery and irradiation, according to Gajjar. The subsequent addition of chemotherapy before or after radiotherapy improved that survival rate to 65 percent for children aged 3 years or older who had medulloblastoma.

"We attribute our very promising results to the early use of high-dose radiotherapy after surgery--rather than waiting until after chemotherapy--in combination with short-term, intense chemotherapy," Gajjar said. "Shorter-term, intense chemotherapy is an especially important component of treatment that contributes to the improved survival of high-risk patients."

The researchers also showed that genetic differences exist in medulloblastoma tissues among children. These differences could be used to differentiate between children whose

tumors are very aggressive and require novel experimental treatment and those children whose tumors are less aggressive and who could benefit from further reduction in treatment.

"These additional studies suggest that we can further reduce the long-term effects of treatment among some children by further reducing the treatment intensity," Gajjar said. The researchers previously reported that medulloblastoma consists of several distinct subgroups of this cancer that can be identified according to specific genetic abnormalities.

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The 134 patients who were enrolled in this clinical trial were treated at St. Jude; Texas Children's Hospital, Baylor College of Medicine (Houston, Texas); Children's Hospital at Westmead (Sydney, Australia); and Royal Children's Hospital (Melbourne, Australia).

The other authors of this paper include Larry Kun, Thomas Merchant, Matthew Krasin, Maryam Fouladi, Alberto Broniscer, Gregory Hale, Clinton Stewart, Robert Sanford, Christine Fuller, James Boyett, Dana Wallace and Richard Gilbertson (St. Jude); Murali Chintagumpala, Shaio Woo, Robert Krance, Robert Dauser and Ching Lau (Baylor); Stewart Kellie and Valerie Ahern (Children's Hospital at Westmead); and David Ashley and Greg Wheeler (Royal Children's Hospital).

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#### **St. Jude Children's Research Hospital**

St. Jude Children's Research Hospital is internationally recognized for its pioneering work in finding cures and saving children with cancer and other catastrophic diseases. Founded by late entertainer Danny Thomas and based in Memphis, Tenn., St. Jude freely shares its discoveries with scientific and medical communities around the world. No family ever pays for treatments not covered by insurance, and families without insurance are never asked to pay. St. Jude is financially supported by ALSAC, its fund-raising organization. For more information, please visit [www.stjude.org](http://www.stjude.org).

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