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New treatment more than doubles survival for high risk childhood leukemia

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Results of a phase two clinical trial published October 5th in the *Journal of Clinical Oncology* show that adding continuous daily doses of a targeted drug called imatinib mesylate to regular chemotherapy more than doubled three-year survival rates for children with a high risk type of blood cancer called Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL).

The Children's Oncology Group performed the study at nearly 20 North American centres under the leadership of Dr. Kirk Schultz, head of childhood cancer research at the Child & Family Research Institute (CFRI) and a pediatric oncologist at BC Children's Hospital, an agency of the Provincial Health Services Authority.

"With conventional chemotherapy, the three-year survival rate for children with this high-risk type of leukemia is between 30-35 per cent," says Dr. Kirk Schultz, professor of pediatrics at the University of British Columbia.

"Adding continuous exposure to imatinib for two-and-a-half years made a big difference and increased the survival rates to 87 per cent. The drug was well tolerated and it didn't have any significant side effects," he says. Survival rate refers to the length of time that a patient survived without a relapse and without developing a new cancer.

There are multiple types of acute lymphoblastic leukemia and each responds differently to treatment. Ph+ ALL involves genetic

abnormalities on two specific chromosomes.

Because traditional chemotherapy doesn't work well for many children with Ph+ ALL, the standard treatment is blood and marrow transplantation, a life-saving procedure that's associated with a risk of complications.

"By using the targeted drug imatinib in combination with traditional chemotherapy, these results suggest that we've been able to improve survival enough that we may no longer have to do blood and marrow transplants for this disease," says Dr. Schultz. "Understanding more about the genetics of cancers allows us to determine the best way to treat each child and be more selective in the appropriate use of expensive medications."

Known commercially as Gleevec®, imatinib is a pill that's used to treat some adult leukemias and gastrointestinal cancers. It binds to a specific protein in cancer cells and prevents the cells from proliferating.

Collaborative networks such as the Children's Oncology Group are crucial for recruiting sufficient numbers of patients to trial new treatments for rare diseases such as Ph+ ALL, which is diagnosed in approximately six children and 90 adults each year in Canada.

For this study, there were 92 children and adolescents between one and 21 years of age with Ph+ ALL. Each received an initial four weeks of standard chemotherapy. They were assigned to five different groups that received imatinib for different lengths of time: either 42, 63, 84, 126, or 280 days. All patients received an additional 336 days of imatinib.

The group that received imatinib for more than 280 continuous days had survival rates of 87 per cent, a dramatic improvement over traditional chemotherapy and blood and marrow transplantation. Groups that

received imatinib for 84 and 126 days showed moderate improvement in survival rates, while groups receiving the drug for 42 and 63 days had the same survival rates as current standard treatments. There were also 21 patients with Ph+ ALL who were treated with blood and marrow transplantation followed by six months of imatinib. This approach didn't affect survival rates.

"Using imatinib plus chemotherapy had a synergistic type of interaction," says Dr. Schultz. "I never expected these results. Although it's very promising, we need to do more follow up to get the five-year survival data and determine the long-term survival. We submitted our study for publication earlier instead of waiting because the data was so exciting and this type of leukemia is such high risk."

The researchers are now looking at setting up a phase three study to validate whether adding imatinib to chemotherapy could replace blood and marrow transplantation as the standard treatment for Ph+ ALL.

"Using other targeted drugs with regular chemotherapy might give results for other types of cancer in children and adults," says Dr. Schultz.

Source: Child & Family Research Institute