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Children with Down syndrome and ALL fare as well as others treated on DFCI ALL protocols

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Despite an elevated risk of toxicity from chemotherapy, children with Down syndrome and acute lymphoblastic leukemia (ALL) did not experience higher rates of relapse or treatment-related mortality compared with other children treated on Dana-Farber Cancer Institute ALL Consortium Protocols, according to research presented at the 58th annual meeting of the American Society of Hematology, December 5, 2016.

"Without dose reductions or modifications, the Down syndrome patients did just as well as the non-Down syndrome patients," said Lewis B. Silverman, MD, senior author of the abstract and clinical director of the Hematologic Malignancy Center at Dana-Farber/Boston Children's Cancer and Blood Disorders Center. "They were able to tolerate full-dose chemotherapy based on their risk group and did well despite biologic differences in their disease compared with other children's disease."

Children with Down syndrome are at increased risk for developing ALL, but the optimal therapy for this group of patients has not been established. Silverman notes that previous studies have shown that children with Down syndrome have an increased risk of complications of treatment. Some studies have also reported that they have higher rates of relapse and/or treatment-related mortality, resulting in lower rates of long-term cure. While the Dana-Farber protocol has never modified

treatment for children with Down syndrome, Silverman added, other protocols have made dose-adjustments to minimize side effects.

"There has been controversy in the field regarding how Down syndrome children do in terms of their prognosis compared with children who don't have Down syndrome," Silverman said. "We found that with our particular treatment approach, we're not running into problems that others have reported."

Researchers studied 1286 diagnosed children and adolescents with ALL treated on the Dana-Farber Consortium protocols between 2000 and 2011 at 11 institutions in the United States, Canada, and Puerto Rico. Of these patients, 38 (3 percent) had Down syndrome. Among the findings:

- There was no difference in the rate at which children achieved complete remission after the first month of treatment (100 percent of children with DS vs 95.2 percent without).
- There were no treatment-related deaths among the DS patients.
- With a median follow-up of 6.2 years, there was no statistically significant difference in five-year rates of event-free survival (90.7 percent vs 83.7 percent), disease-free survival (90.7 percent vs 87.4 percent), or overall survival 91.8 percent vs 91.4 percent).
- Patients with Down syndrome suffered more treatment-related mucositis (mouth sores) (52 percent vs 12 percent), clots or bleeding (18.4 percent vs 8.2 percent), seizure (15.3 percent vs 4.7 percent), and infection (55.3 percent vs 41.3 percent).

As has been reported in other studies, researchers found that the Down syndrome patients were less likely than other patients to present with T-cell ALL (none in the DS group vs 11.7 percent in non-DS patients) and high hyperdiploidy (8.8 percent vs 25.1 percent). The former is considered a higher-risk form of ALL, while the latter is associated with

a more favorable prognosis, Silverman said.

"The target toxicities that one needs to think about are infections and mucositis," Silverman said. "With supportive care to try to prevent these complications, our overall recommendation is that you can treat children with Down syndrome the same as other children with ALL."

Provided by Dana-Farber Cancer Institute

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