Refining treatment for childhood leukemia

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Scientists at St. Jude Children's Research Hospital are working with colleagues in China to develop better therapy for childhood acute lymphoblastic leukemia (ALL). Results from a large phase 3 noninferiority clinical trial definitively showed that vincristine and dexamethasone pulses can be eliminated in patients with low-risk

disease. The findings were published today in *The Lancet Oncology*.

Adding the chemotherapy vincristine plus a steroid (originally prednisone, and later dexamethasone) as pulse therapy for childhood ALL has been part of standard care since the 1970s. This is despite their being associated with neuropsychological side effects, neuropathy and other late effects. However, to date studies about the need for prolonged treatment with pulse therapy have been inconclusive.

"We wanted to study this issue to provide definitive conclusions about whether we can safely omit prolonged pulse therapy with these two drugs to improve quality of life for patients and lessen the burden to their family," said corresponding author Ching-Hon Pui, M.D., St. Jude Department of Oncology chair. "That's why doing this study through the Chinese Children's Cancer Group was key: a definitive noninferiority randomized trial of a disease with a high cure rate such as ALL requires very large numbers of patients all treated consistently."

Clinical trial provides clarity

Between January 2015 and February 2019, children with newly diagnosed ALL joined a randomized, open-label, phase 3 noninferiority study as part of the Chinese Children's Cancer Group ALL-2015 protocol. This clinical trial randomized 6,108 patients, making it the largest clinical trial ever conducted in childhood acute lymphoblastic leukemia.

Patients in continuous remission for one year were stratified and randomized to receive or not receive seven pulses of vincristine plus dexamethasone during the second year of treatment. Using the noninferiority study design, researchers firmly established that pulse therapy can be safely omitted in the second year of care in patients with low-risk disease without affecting their five-year event-free survival or

overall survival.

Omitting vincristine plus dexamethasone pulses after the first year of treatment in these children should reduce many acute and late effects of treatment as well as the burden on their families. Additional studies are needed to confirm whether this is true for patients with intermediate or high-risk ALL.

"These findings are very good news for patients and families because shortening this pulse therapy will substantially reduce neuropsychological side effects, emotional disturbances and many other neurological and metabolic late effects," Pui said.

More information: Wenyu Yang et al, Pulse therapy with vincristine and dexamethasone for childhood acute lymphoblastic leukaemia (CCCG-ALL-2015): an open-label, multicentre, randomised, phase 3, non-inferiority trial, *The Lancet Oncology* (2021). DOI: 10.1016/S1470-2045(21)00328-4

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