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HAEMATOLOGICAL CANCER

Less is more for paediatric patients—it's ALL in the dosing

Although 80% of children and adolescents with acute lymphoblastic leukaemia (ALL) can be cured, osteonecrosis is a severe debilitating complication of treatment that is associated with high morbidity, particularly in adolescents. A previous study by the Children's Oncology Group (COG) indicated that continuous dexamethasone dosing might be the cause of this complication.

This finding led Leonard Mattano Jr and his coauthors to design a multicohort trial to assess whether a novel dexamethasone dosing strategy would safely reduce the incidence of osteonecrosis. Mattano elaborates, "we hypothesized that reducing the dexamethasone exposure during delayed intensification by use of an alternate-week schedule (days 1–7, 15–21) would be less toxic to bone than continuous exposure (days 1–21)."

Newly diagnosed patients with high-risk ALL aged 21 or younger were enrolled in the trial. As Mattano explains, "to preserve therapeutic efficacy, this alternate schedule was only used for patients randomized to two delayed intensification courses, ensuring that all patients would receive a total of at least 3 weeks of dexamethasone as part of their overall therapy." The use of dexamethasone at alternate weeks significantly reduced the 5-year cumulative incidence of osteonecrosis in patients aged 10–21 (8.7% versus 17.0%), especially in those aged 16–21 (11.3% versus 37.5%) and in those on intensified therapy (two 21-day courses; 6.9% versus 21.4%), despite a greater overall exposure to dexamethasone (4 weeks versus 3 weeks).

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"Thus, a simple dexamethasone dose modification successfully reduced osteonecrosis risk, particularly benefitting those who received the most intensive therapy," notes Mattano. As a result of these practice-changing data, alternate-week dexamethasone during delayed intensification has been incorporated into other front-line COG clinical trials in patients with ALL.

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Original article Mattano Jr, L. A. *et al.* Effect of alternate-week versus continuous dexamethasone scheduling on the risk of osteonecrosis in paediatric patients with acute lymphoblastic leukaemia: results from the CCG-1961 randomized cohort trial. *Lancet Oncol.* **13**, 906–915 (2012)