

**Is it ethical to avoid high dose methotrexate (HDMTX) patients with localized high grade osteogenic osteosarcoma ? A macro-analysis of the literature.**

*N. Delepine, G. Delepine, F. Delepine, H. Cornille, S. Alkallaf*

Service d'oncologie pédiatrique

**Backgrounds:** As HDMTX is costly and potentially dangerous, some groups (for example: E.I.O.: European Intergroup for Osteosarcoma) advocate protocols of chemotherapy without HDMTX in high grade osteosarcoma. We present here the results of a comprehensive literature analysis, to assess the comparative results of both approaches.

**Methods:** A computerized literature search encompassing January 1976 to March 2002 was conducted to identify all available published reports on clinical trials for localized primary osteosarcoma. All reports were reviewed to see if they matched the inclusion criteria: stage II limb osteosarcoma, at least 20 patients included, chemotherapy treatment with dosages and schedule clearly specified, clear quantification of 5 year DFS. HDMTX was defined by at least 12 g/m<sup>2</sup>/course for children (< 12), 8 g/m<sup>2</sup>/course for adults and a minimal total dose of MTX of 150 g/m<sup>2</sup>.

**Statistical analysis:** Compared DFS in the group with HDMTX, and without HDMTX using non-parametric test (test U).

**Results:** A total of 56 protocols fulfilled the inclusion criteria. 25 with HDMTX and 31 without HDMTX. The total number of patients included in eligible studies was 3956.

Patients included in protocols without HDMTX had a 5 year average life expectancy of 48 % (min 24- max 61) versus 72 % for patients included in protocols with HDMTX (min. 53 – max. 84).

The difference is significant (p<0.001).

**Conclusion:** Protocols without HDMTX offer a lower cure rate for patients with high-grade osteosarcoma. The conclusions of EOI studies 1 and 2 were inadequate and their application decreased the disease free life expectancy of patients with osteosarcoma.

