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**The comparison of 2 protocols for treatment of osteosarcoma (OS) with or without escalation of HDMTX enhances the high value of MTX individual adaptation**

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**Purpose:** To demonstrate the role of HDMX adaptation in long term survival of patients (p.) with high grade OS, we compared our results in 2 successive OS protocols.

**Methods:** From 85 to 95, 90 p. with primary high grade OS fulfilled the classical criteria: non metastatic, resectable tumor, previously untreated. **Group 1 (G1):** 45 p. received a fixed dose of MTX adapted only to age. **Group 2 (G2):** 45 p. received escalating doses of MTX with PK and clinical monitoring.

**Results:** In G2, a dose escalation was necessary in nearly 70% of cases (32/45) due to low serum concentration (15), or lack of clinical response (9) or both (8). G1 p. received a mean dose of 10.5 g/m<sup>2</sup>/course and G2 p. a mean dose of 13.5 g/m<sup>2</sup>/course (mean seric concentration of respectively 850 µmol/l and 1175 µmol/l). No significant difference in toxicity was observed **Outcome** the overall survival and DFS at 5 (and 10) y. are respectively **71% (69%) for G1** (fixed dose of MTX), **93% (91%) for G2**. **The differences are statistically significant.**

**Conclusion:** **The serum peak and AUC are correlated with the rate of GR. The seric intensity is correlated with the late DFS.** Individual PK of MTX, supplemented by careful examination of the tumoral limb before each course of MTX led to increase the dose of MTX in 70% of p., resulting in more GR and more late survivors without significant increase of toxicity.

