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/m²/course and G2 p. a mean dose of 13.5 g/m²/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.