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# An Analysis of Correlation of MTX Seric Intensity and Long Term Disease Free Survival in Osteosarcoma (OS) in Function of the Infusion Length (4--6 hours) (Meeting abstract).

**Sub-category:**
Pediatric Oncology

**Category:**
Pediatric Oncology

**Meeting:**
1999 ASCO Annual Meeting

**Abstract No:**
2199

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**Abstract:**

Introduction: In 1986, we first described the crucial role of the MTX seric peak at the end of the infusion to improve OS. To optimize the response rate, we observed that the MTX seric peak at the end of a 6 hour-infusion should be attained 1000 mmol/l, combined with a good "hand on" clinical response. Material: Nevertheless, to take into account the intercourse delay and timing, we defined the notion of "seric intensity" (SI) as the sum of seric peaks by time unit in mmol/l/week. The accuracy of SI is becoming evident by analyzing the preoperative histological response of the tumor and DFS. In our series, in DD1 and DD11 protocols (90 pts 4--45 y av 16---1986--1995) the tumor response is correlated with MTX SI, higher SI higher response rate. With a short preoperative monodrug induction (4 weekly HD MTX), SI < 500 mmol/l/wk gave less than 10 % chance to obtain a good response (GR), 700 mmol/l/wk < 25 %. If SI > 1000 mmol/l/wk GR > 66 %. All results are statistically significant. We must insist on the value of the seric peak established for a 6 hour infusion. When authors use a 4 hours infusion, they must study the corresponding seric peak correlated with the AUC of MTX. In COSS protocols (as in Rosen's protocols), the infusion of MTX is done over 4 hours and a 1000 mmol/l seric peak needs average one third less MTX (9.5 g/m2 versus 13 g/m2). At the 1GR in Villejuif, the methodological bias testing the 1000 mmol/l values for a 4 hour-infusion without considering the intercourse delay and including a too small number of patients explains the failure to find a statistical correlation between seric peak and DFS. On the opposite, in the Rizzoli Institute, data available on 382 patients, showed than when the MTX peak at the end of the 6 hour-infusion was below 700 mmol/l the DFS was 56 % compared to 77 % for higher levels ($p < 0.001$). The difference remains significant also using the limit of 1000 mmol/l (67 % versus 80 % $p = 0.02$) (Picci and al-Oslo 1998). In conclusion, these data confirm the high necessity to adjust individually the dose of MTX, to analyze not only the seric peak but the area and the concentration time curve and also the seric intensity and to take into account in these retrospective studies, the length of the infusion (4 versus 6 hours) the length and quantify of overhydration, the delay between the courses of MTX. HDMTX remains the best drug correlated with DFS. Nevertheless no one must forget that even with a pharmacokinetic guidance, the tumoral and patient variability compels doctors "to examine the patient and tumor before every infusion and increase the dose if the response is unclear and the tolerance is good, following the old Rosen's advises.

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