

# LONG TERM FOLLOW UP OF OSTEOSARCOMA TREATED WITH MULTIDISCIPLINARY TREATMENT .

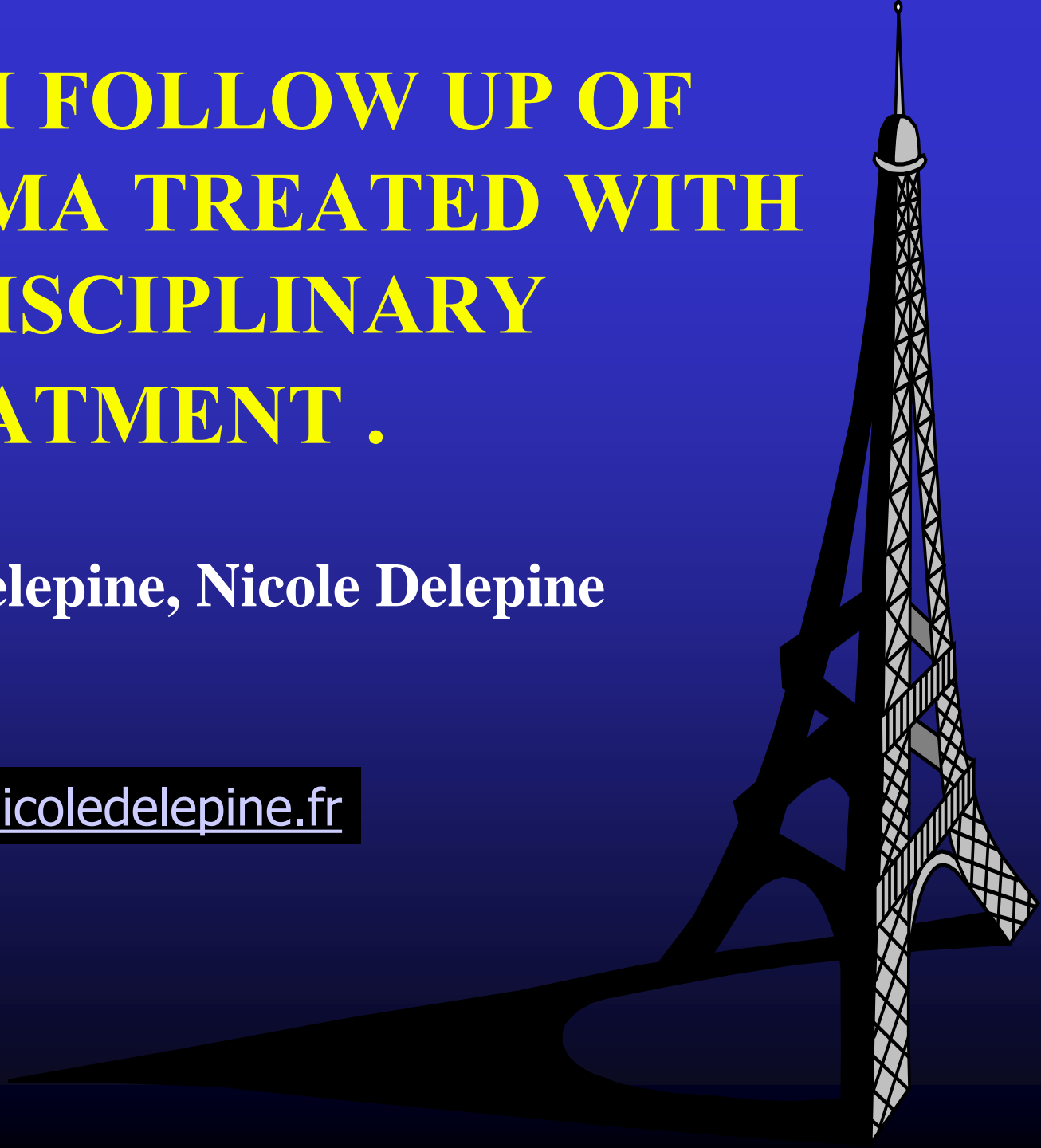
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# Purpose of this study

Evaluation of effects of protocols :

bidrug therapy (Doxo+CCDP) versus HDMTX  
and for MTX evaluation of escalating induction on  
toxicity,  
response of tumours and  
survival of patients with osteosarcoma.

Long term follow up of osteosarcoma (2003)

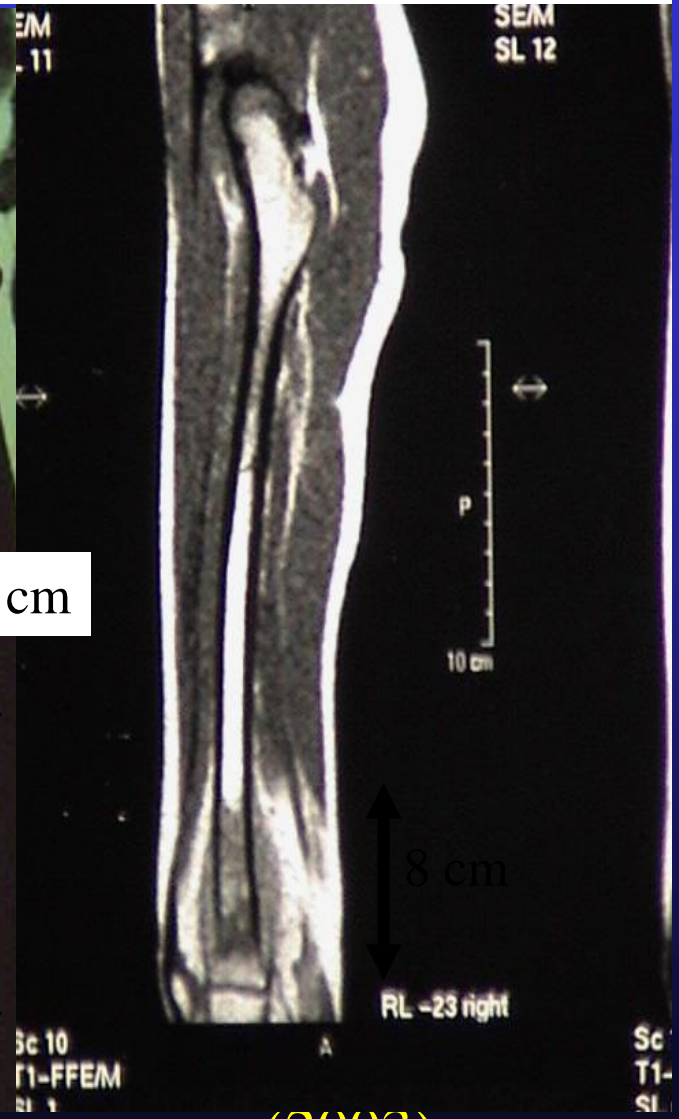
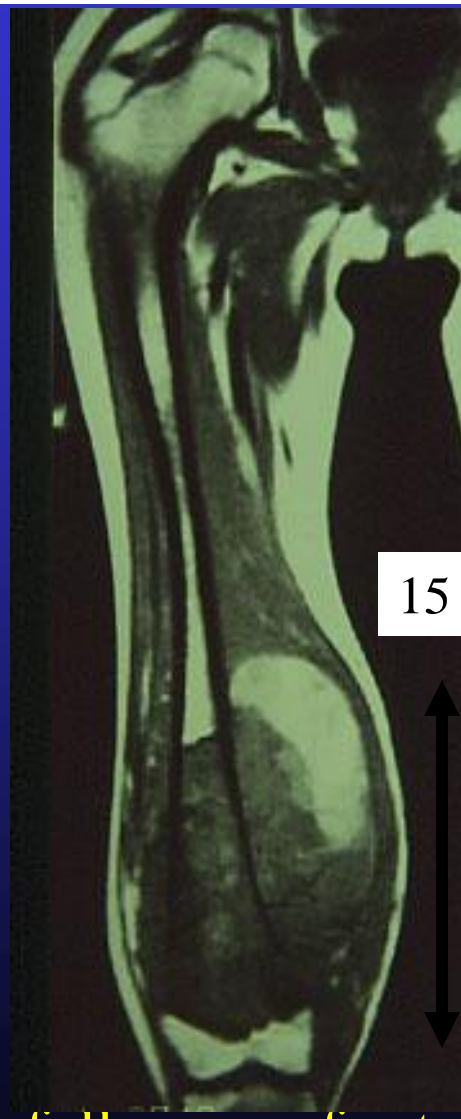
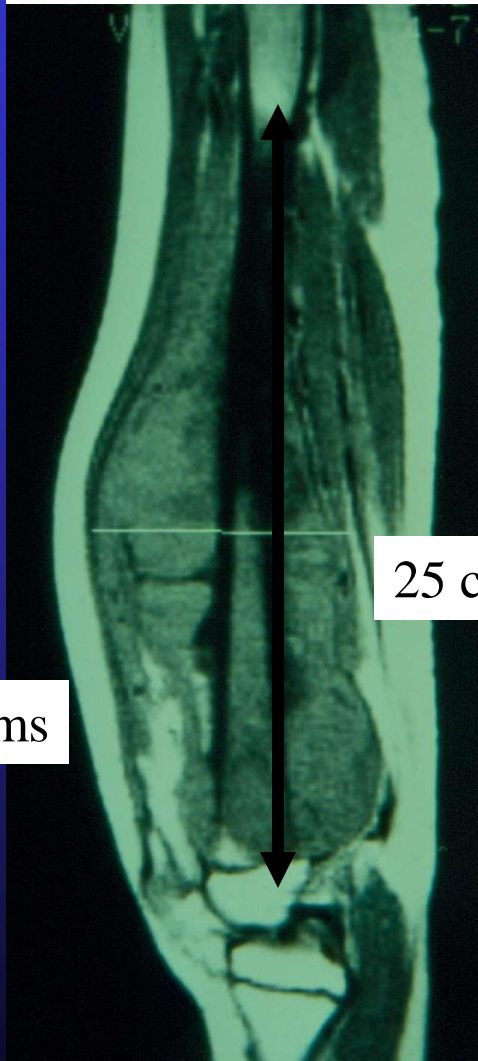
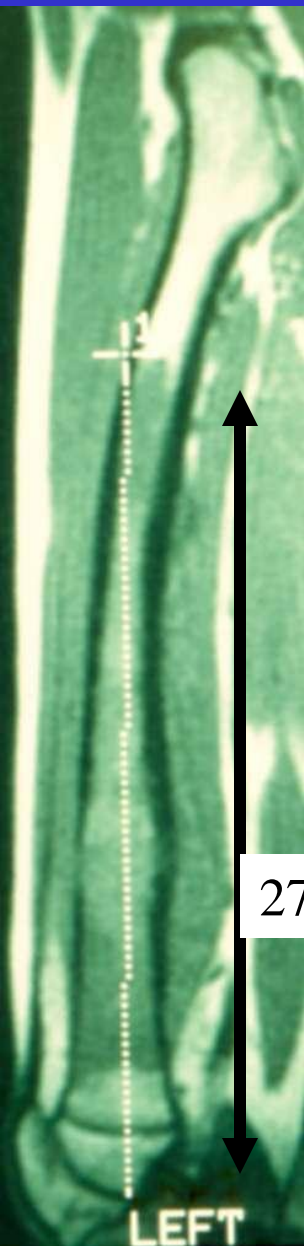
# Patients (1980 to 1995)

- 106 patients with primary high grade OS fulfilled the classical criteria : non metastatic, resectable tumor,
- previously untreated,
- definitive local treatment administered by the team after preoperative chemotherapy.
- 65 men and 41 women (4 to 45 years; median. : 16.8.)
- 12 p. had upper limb lesions (10 humerus and 2 scapula), 93 lower limb locations (54 femoral, 34 tibial, 2 fibula and 2 inonimate bones, one foot) and 1 maxillar.

Long term follow up of osteosarcoma (2003)

# Size of the tumors

The average diameter of tumor was 12 centimeters (5-28)



Long term follow up of osteosarcoma (2003)

# Treatment.

- Group 1 : 16 p. received 6 Doxo-CDDP (total dose 300 mg/m<sup>2</sup> Doxo and 600 mg/m<sup>2</sup> of CDDP) for 20 weeks.
- Group 2 : 45 p. received a fixed dose of MTX adapted only to age. 35 received part of CT in other centers .

## Group 3 (OS DD Protocols)

- 45 p. received escalating doses of MTX.
- The dose of the first course was adapted to age.
- The doses of subsequent courses were adapted to the seric PK of each p.
- and to the response of the tumor in order to reach a serum peak of 1000  $\mu\text{mol/l}$  at the end of the 6 hours infusion and to achieve an objective response.

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# (OS DD) MTX dose of first course

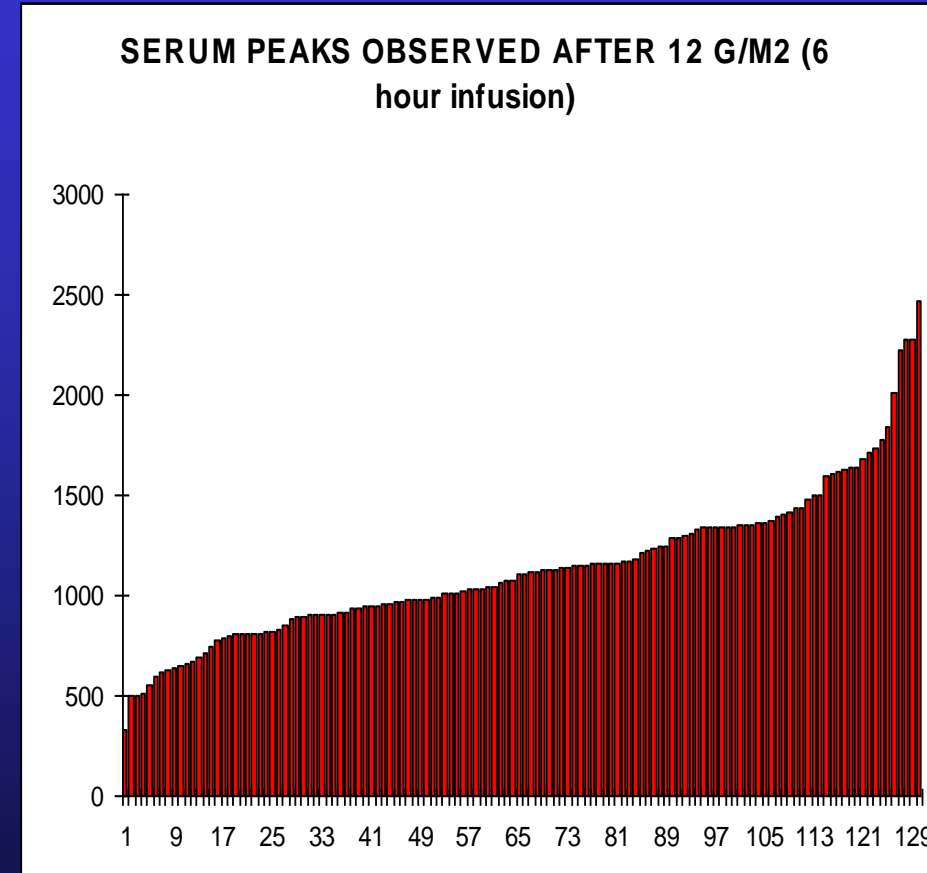
- The dose of the first course was adapted to age.

5-9 y : 18 g/m<sup>2</sup>,

10/15 y : 15 g/m<sup>2</sup>,

> 15 : 12 g/sqm .

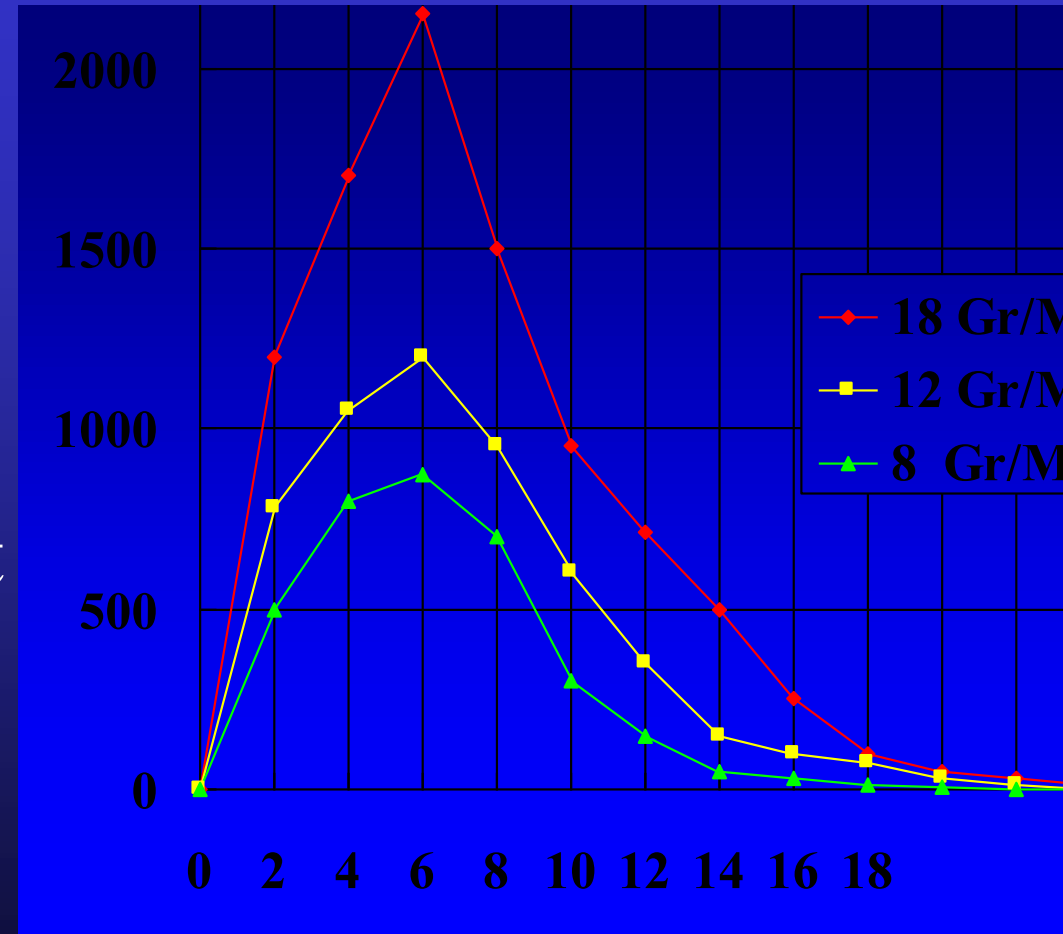
For the same dose inter patient variability of **serum peaks** was high.



Long term follow up of osteosarcoma (2003)

# (OS DD) Dose escalation schedule

- The doses of subsequent courses were adapted to the seric PK of each p.
- and to the response of the tumor in order to reach a serum peak of 1000  $\mu\text{mol/l}$  at the end of the 6 hours infusion and to achieve an objective response.

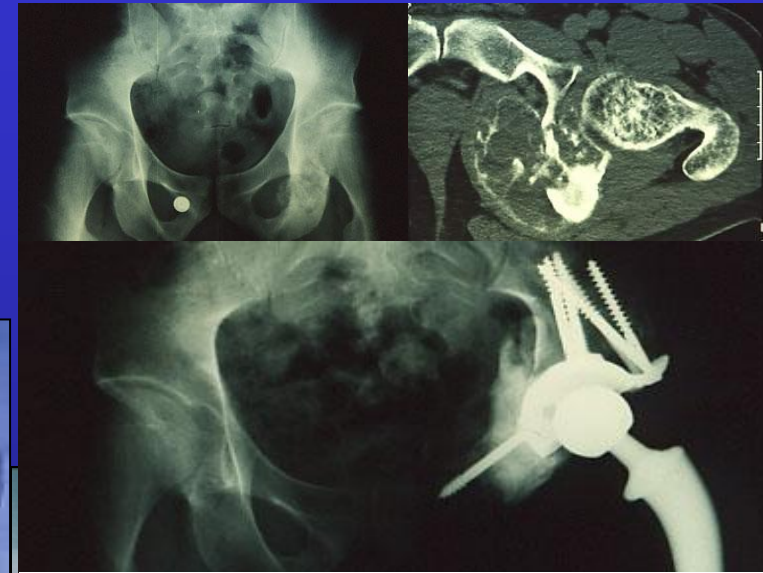


Long term follow up of osteosarcoma (2003)



# Local treatment

- 1 had a radical hip desarticulation
- others underwent limb salvage.
- In 18 bad responders marginal resection received local radiotherapy.



Periacetabular resection +prosthesis



Young child

Long term follow up of osteosarcoma (2003)

# Results

- G2 p. received a mean dose of 10,5 g/m<sup>2</sup>/course and G3 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).
- In G3 a dose escalation was necessary in nearly 70 % of cases (32/45) due to low serum concentration (15), lack of clinical response (9) or both (8). The average dose increase was 35 % of the first given dose.

# Limiting factor of dose escalation

- No significant difference in toxicity of MTX was observed in the p. with escalating dose compared to the p. with a fixed dose

Hepatic toxicity was the main limiting factor of postoperative MTX.

Observed in 7 %) courses of MTX (it resulted in early stopping of MTX in 4 patients.

# LOCAL CONTROL

- 6 local recurrences were observed
- 4 in G2 and 2 in G3.
- All 6 p. had a low seric intensity of MTX (early stopping of MTX
- with drug intensity < 50 % of the planned dose).

# Dose escalation of MTX in group 3

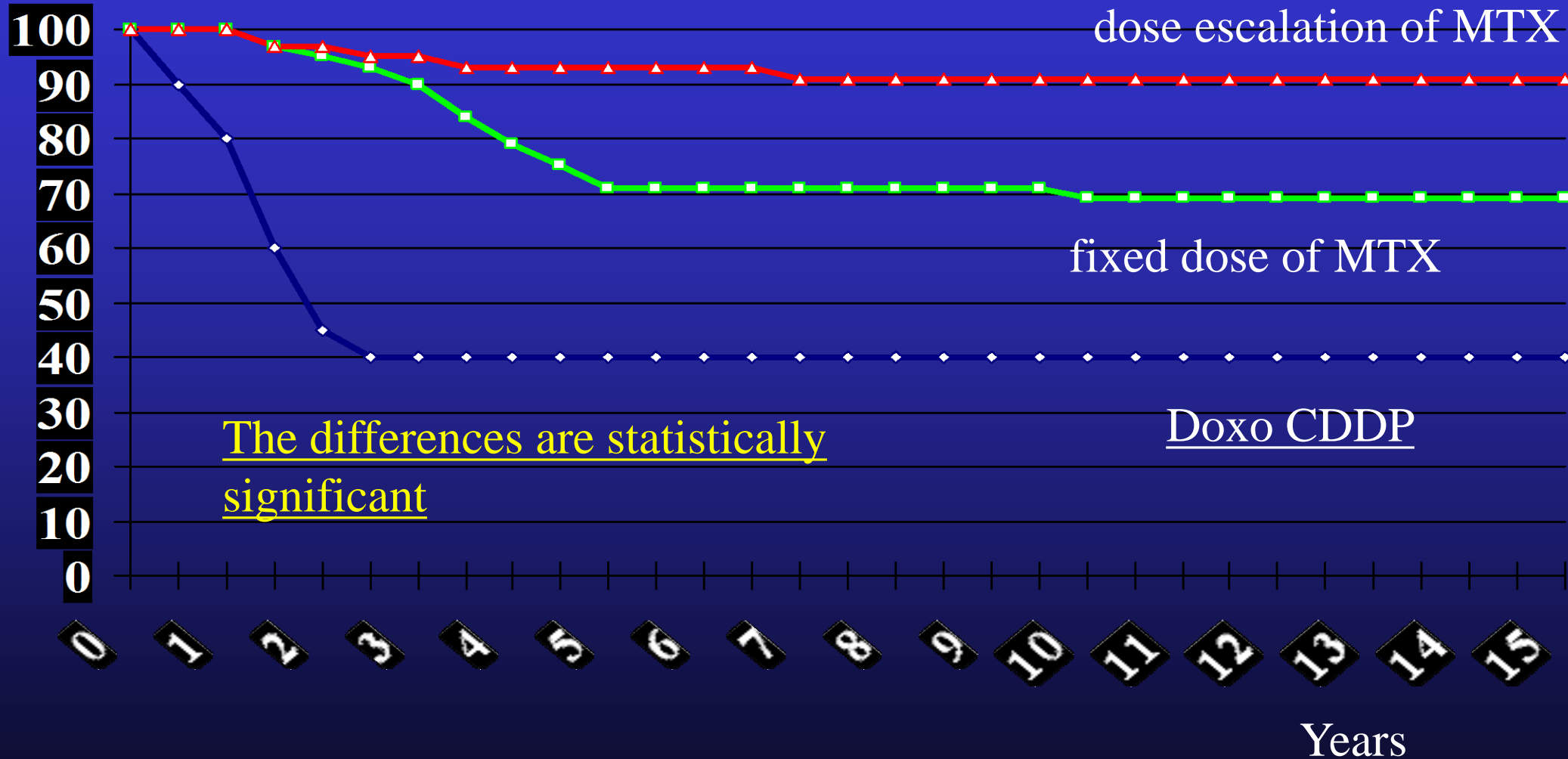
- A dose escalation was necessary in nearly 70 % of cases (32/45) due to low serum concentration (15), lack of clinical response (9) or both (8).
- The average dose increase was 35 % of the first given dose. The mean dose of MTX of 13.5 g/m<sup>2</sup>/course (mean seric concentration of 1175 µmol/l).
- No significant difference in toxicity was observed in the p. with escalating dose compared to the p. with a fixed dose

# Disease free survival.

- At a median F.U. of 13.5 years we observed 38 relapses :
- Lungs 27
- Bone 5
- Local and metastatic 4,
- Local recurrence 2.
- Subsequently 29 p. died,
- 77 p. are still alive, 2 with ED, 6 in 2nd CR and 69 are EFS.

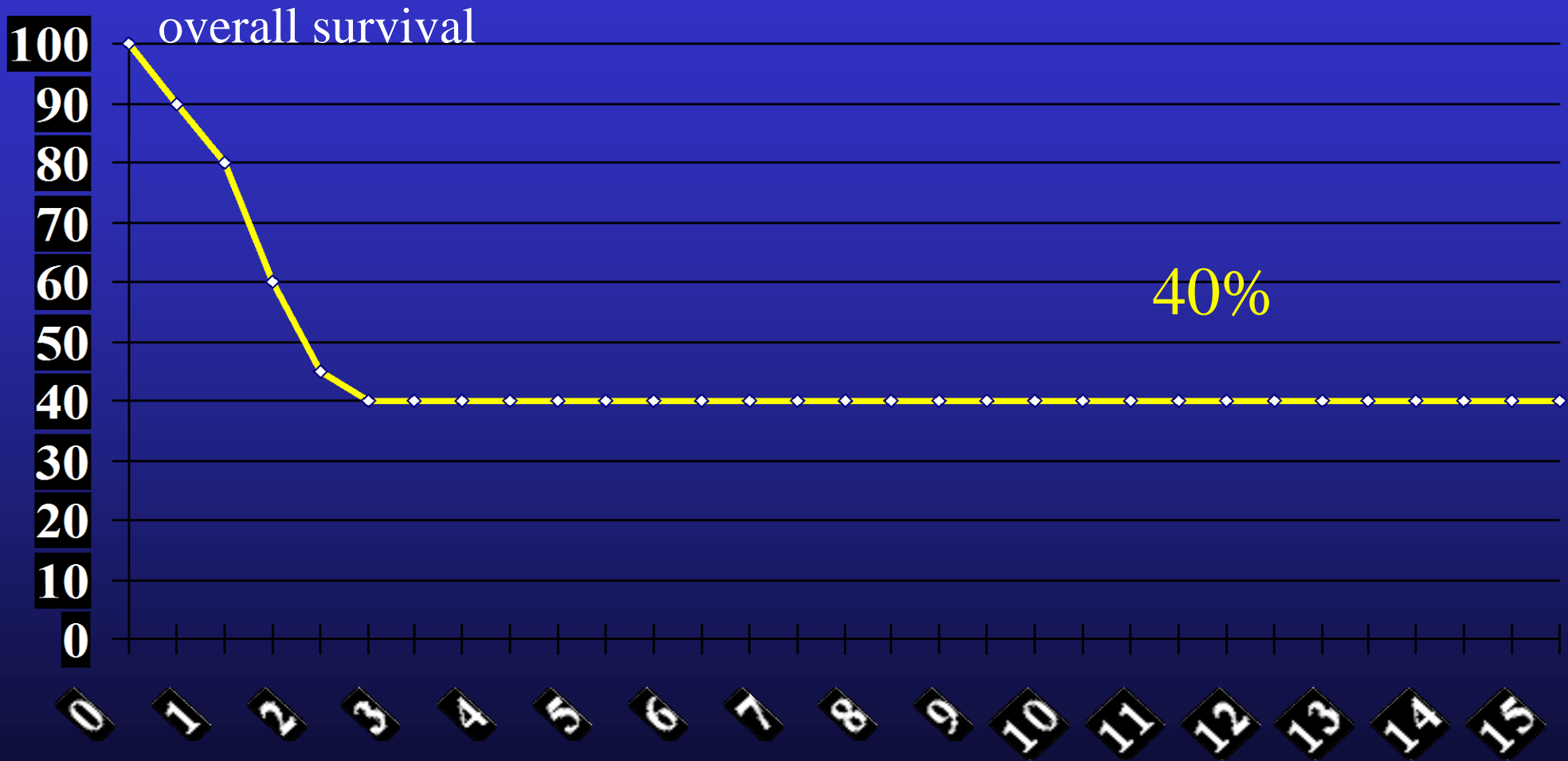
# Results according to protocols

overall survival



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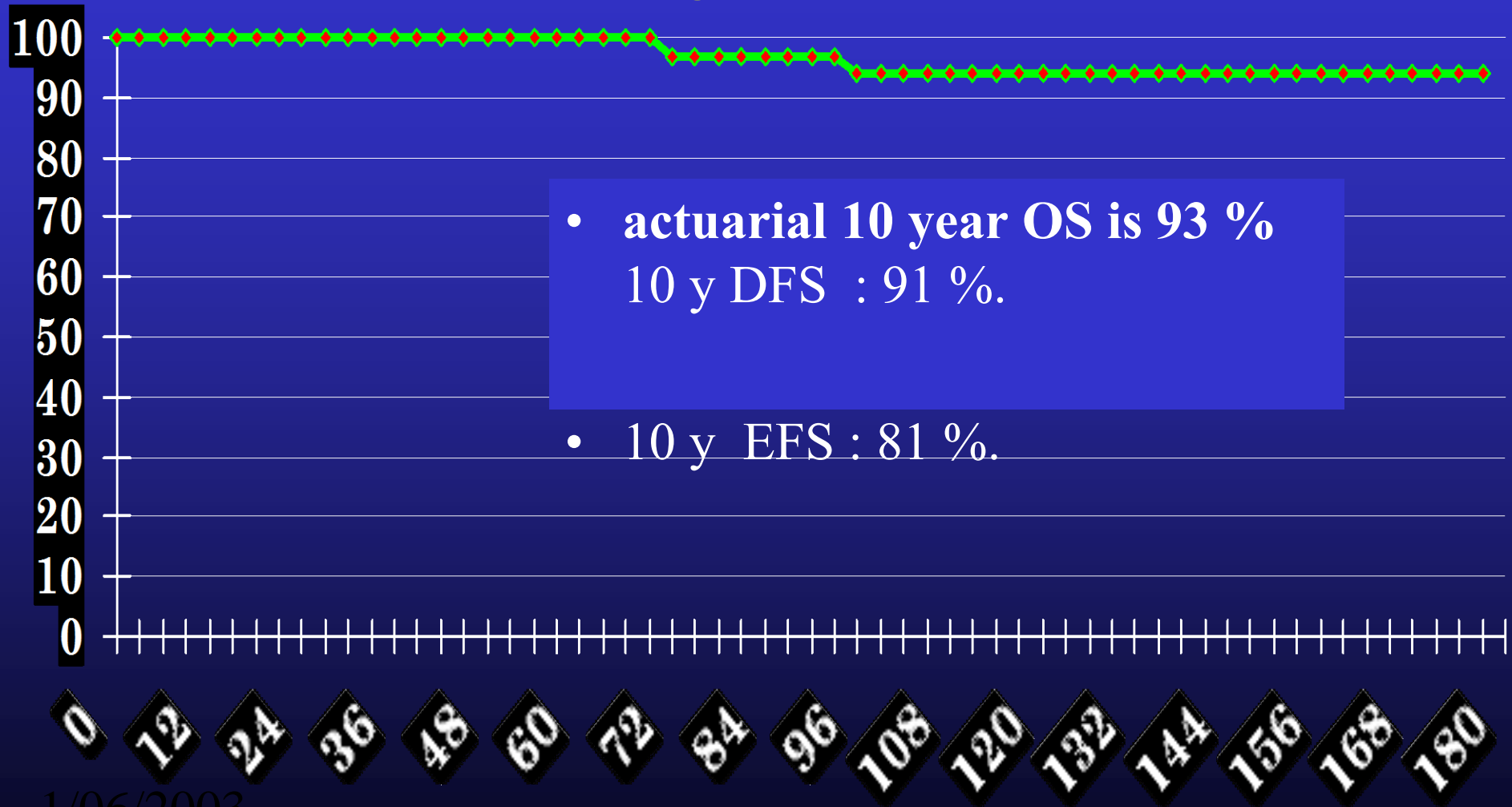
# Conclusion 1 : Bidrug CT with Doxo+Cddp is not effective enough !



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# protocols with dose escalation of MTX give best long term results



1/06/2003

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