

Osteosarcoma: Euramos Study

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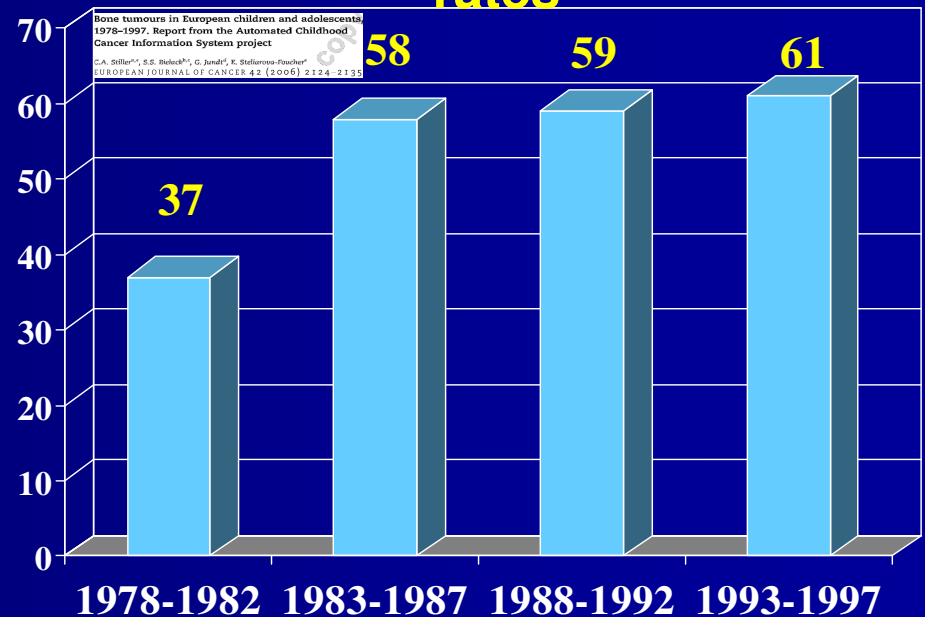
Osteosarcoma: Epidemiology

- Most frequent primary tumor of bone
- 5% of malignant disease in adolescence
- Male:Female 3:2
- 450 – 550 cases in North America per year under 19 years
- 150-200 cases in those 20-29 years of age

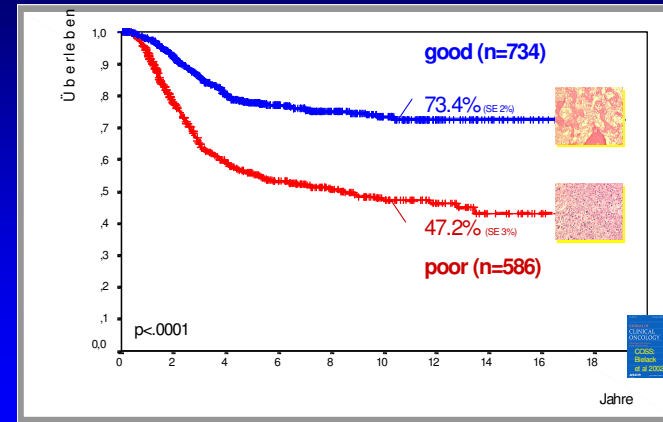
Osteosarcoma: International Studies

- **Similar Regimens**
MAP- MAPI
- **Similar Results**
- **Progress Slow**

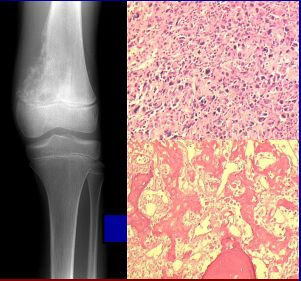
Osteosarcoma: 5-year survival rates



Osteosarcoma: Response & Survival



Salvage of poor responders ?



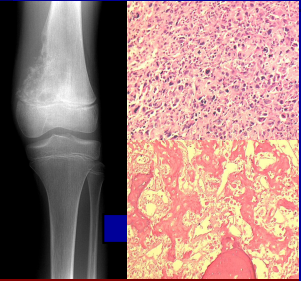
Salvage-Question Statistics

3 year EFS: good $\approx 70\%$
poor $\approx 45\%$

Significance 5%

Power 80%

45% \Rightarrow 55%



Salvage-Question Statistics

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Power 80%

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needed: ± 700 poor responders
 \Rightarrow **± 1400 patients**

Outcome Improvement

- Good responders
- 70 to 80%
- Around 600 randomized patients

Euramos: Study design

- Should post-operative therapy be altered based on histological response?
- Choice influenced by toxicity profile of medications:
 - Ifosfamide, etoposide: bone marrow suppression, fever, sterility, induced leukemia, renal dysfunction
 - Interferon: flu-like syndrome; spasticity in young children, mainly infants: those less than 5 years of age excluded

Osteosarcoma, Euramos

S
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Cisp-Dox-MTX

CDM: cisplatin,
doxorubicin, high-
dose methotrexate

POOR >10% viable
tumor

Good:

R
A
N
D
O
M
I
Z
E

CDM

CDM +
pegintron

POOR

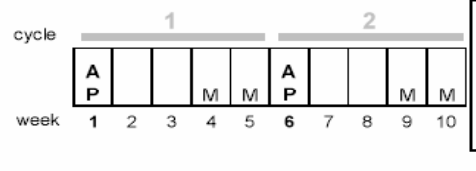
R
A
N
D
O
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E

CDM

CDMIE

EURAMOS: Treatment Schema

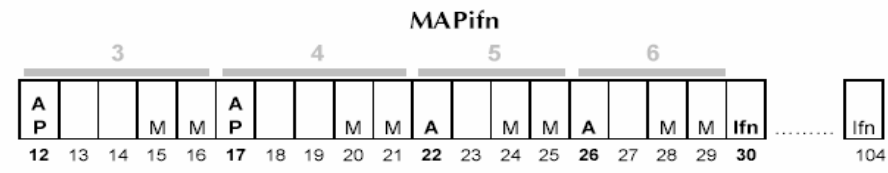
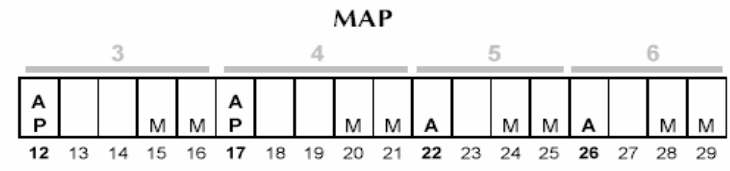
A = Doxorubicin 37.5mg/m²/d d1, d2
 P = Cisplatin 60mg/m²/d d1, d2
 M = Methotrexate 12g/m²
 E = Etoposide 100mg/m²/d
 I = Ifosfamide 2.8g/m²/d
 i = Ifosfamide 1.8g/m²/d
 lfn = Interferon-α 2b 1μg/kg weekly



Evaluation of histological response

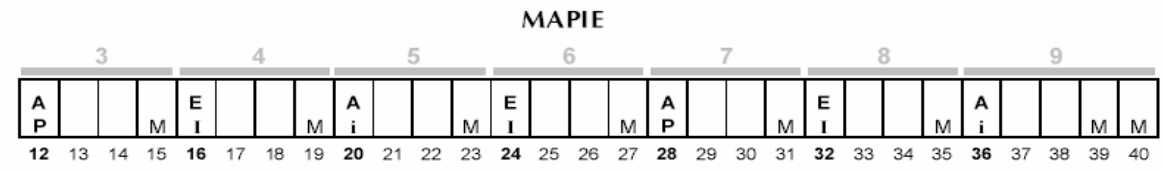
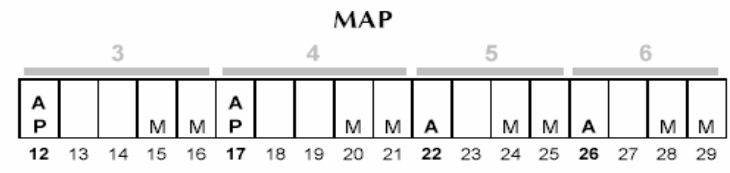
GOOD RESPONSE

RANDOMISE

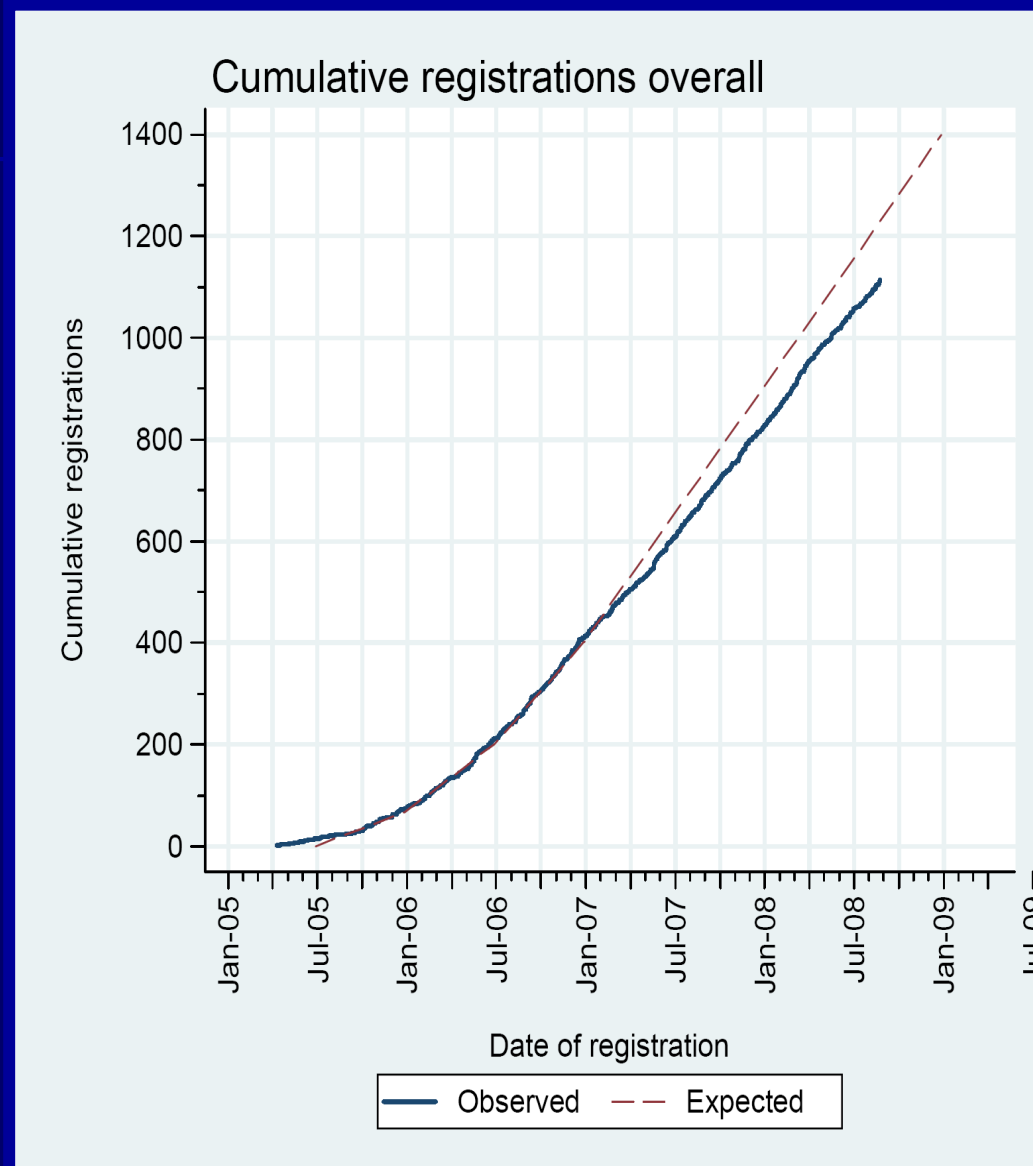


POOR RESPONSE

RANDOMISE

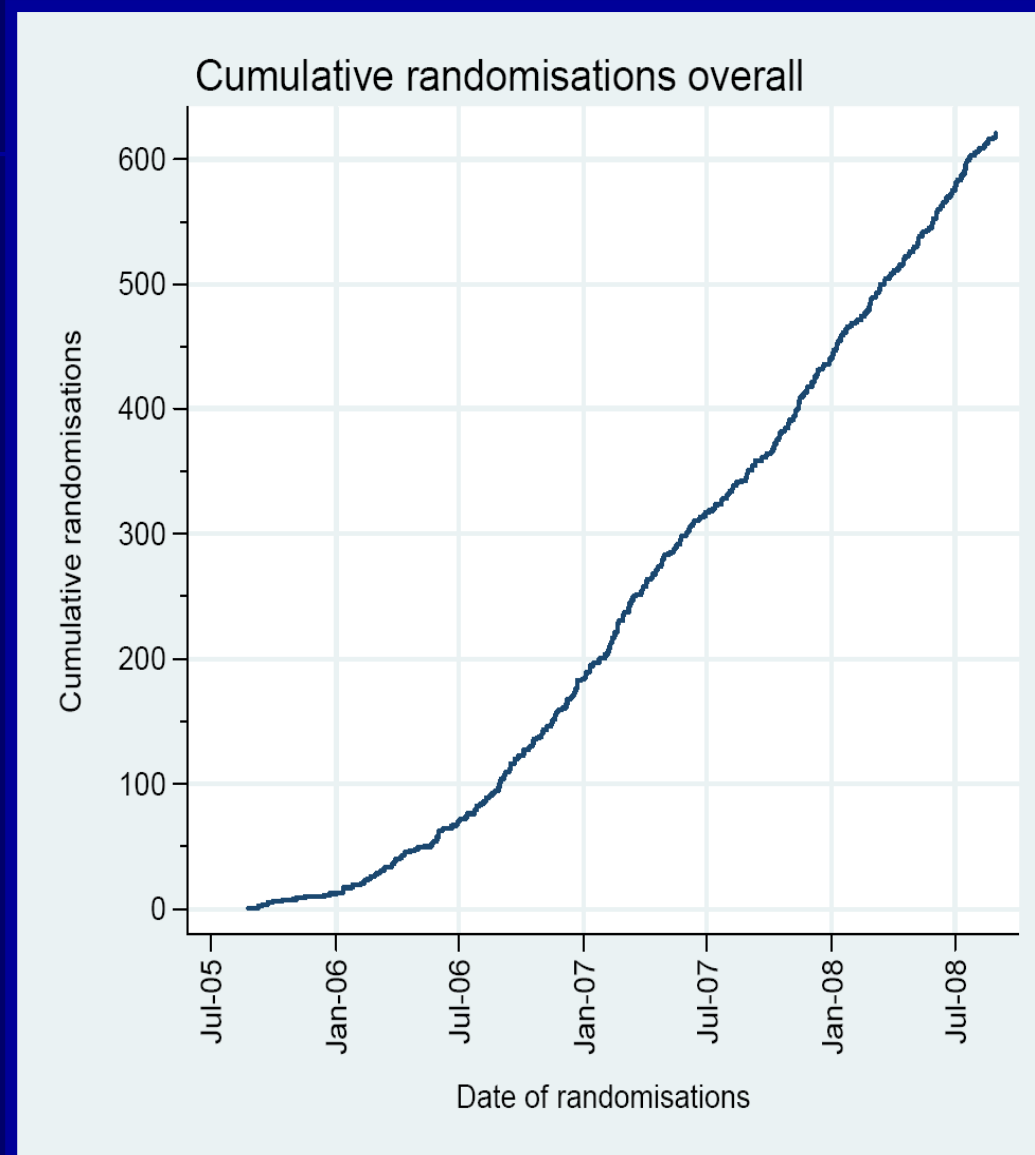


EURAMOS Recruitment as of August 31, 2008



Courtesy of
EURAMOS-CDC,
MRC London

EURAMOS Randomisation as of August 31, 2008



Courtesy of
EURAMOS-CDC,
MRC London

Euramos: Study problems

- Good responder rate higher than predicted
- Randomization rate lower than predicted
 - 65-70%, not 85-90%
 - Late, at week 15-16
- Accrual likely to be extended (to June, 2010)

FAQs

- Is it okay to proceed with my institutional pathologist's assessment or do I have to wait for Dr. Teot?

Answer: It is okay to proceed with your institutional pathologist's assessment. S/he is the pathologist of record. Note: disagreement is relatively uncommon

FAQs

- Is it necessary to send specimens to the BPC for Dr. Teot's review if we decide to proceed with our own institutional pathologist's assessment?
- Answer: yes