ANIMALI E UOMO
ALLEATI CONTRO IL CANCRO:
ATTUALITÀ E NUOVE PROSPETTIVE.

I tumori in medicina comparata:
Oncogenesi spontanea umana ed animale

Giovedì, 21 Marzo 2013

TUMORI PRIMITIVI DELL'OSSO

EPIDEMIOLOGIA

Int J Cancer. 2012 Aug 15;131(4)

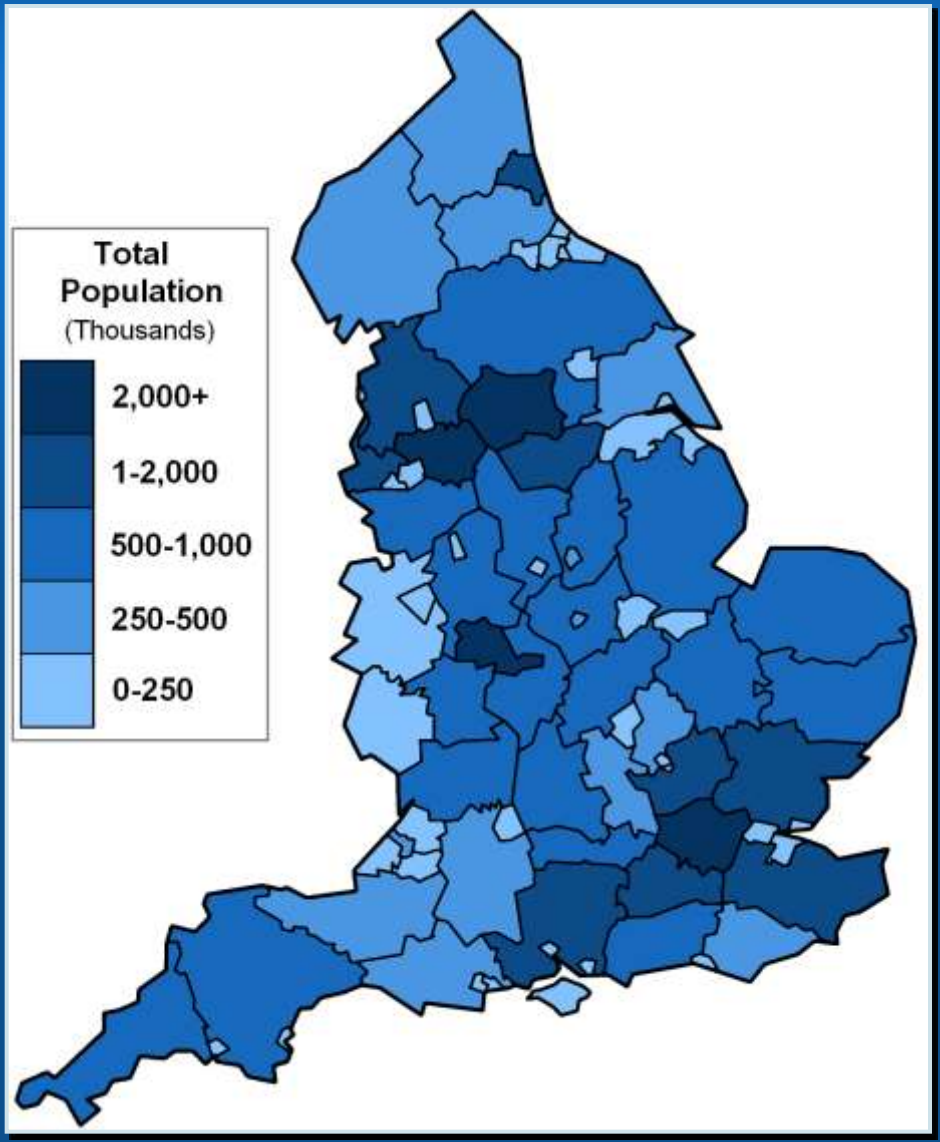
UICC
global cancer control

IJC
International Journal of Cancer

Incidence and survival of malignant bone sarcomas in England 1979–2007

Jeremy Whelan[1], Anne McTiernan[1], Nicola Cooper[2], Yuen K Wong[3], Matthew Francis[3], Sally Vernon[3] and Sandra J. Strauss[1]

[1] London Sarcoma Service, Department of Oncology, University College Hospital, London, United Kingdom
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ENGLAND POPULATION

- 2006 - 50,762,900
- 2007 - 51,092,000
- 2008 - 51,456,400



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global cancer control

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Incidence and survival of malignant bone sarcomas in England 1979–2007

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TUMORI MALIGNI PRIMITIVI DELL'OSSO

media 379 per anno (463 in 2007)

Incidenza 7.5 casi/milione/anno

OSTEOSARCOMA: 34% DEI CASI

media 131 casi per anno

Incidenza 2.5 casi/milione/anno

Tumori maligni primitivi dell'osso

ITALIA: circa 60 milioni di abitanti

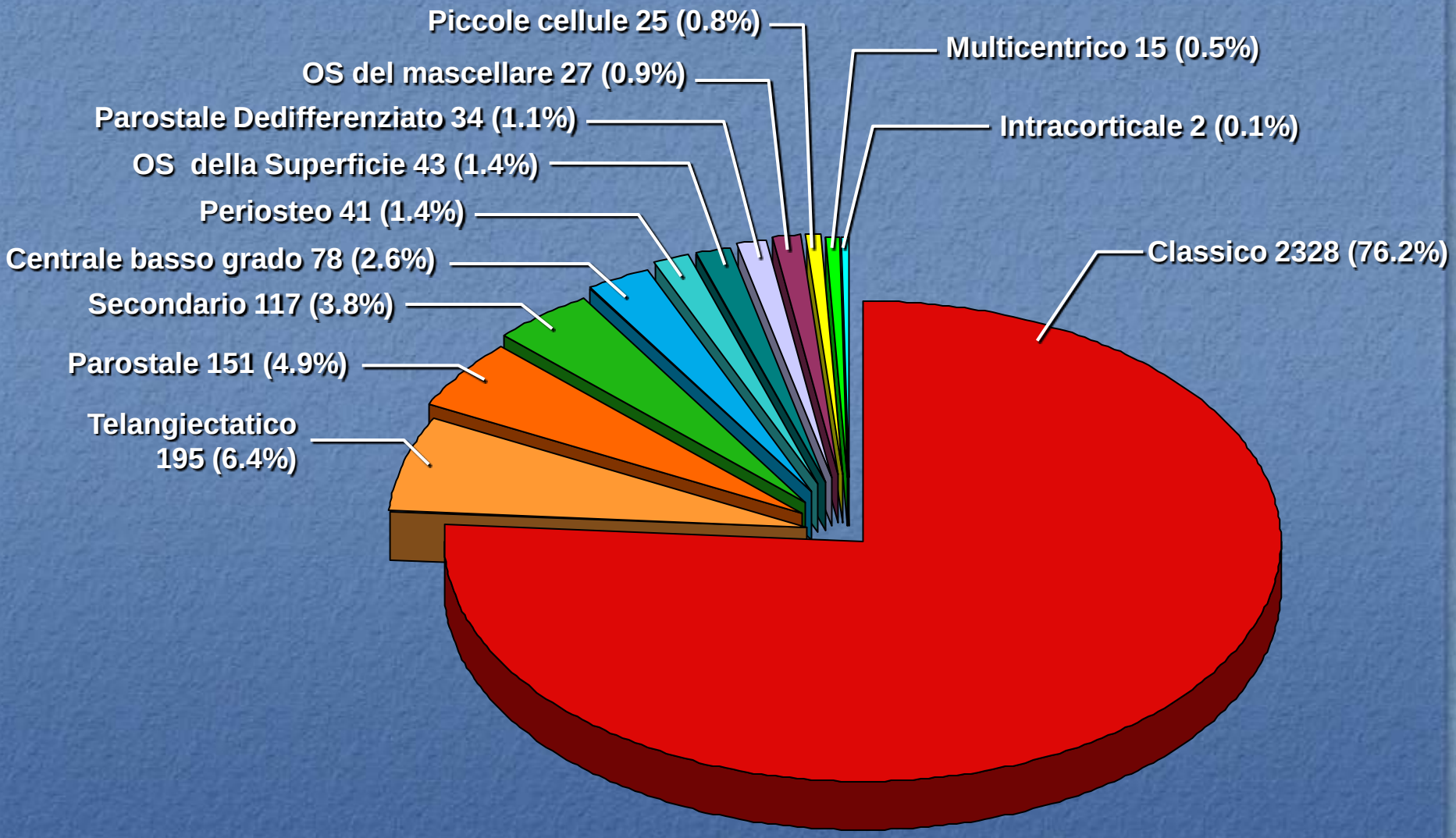
- **0,8 - 1 caso / 100.000 abit.**
- **≅ 500 nuovi casi / anno in Italia**

Osteosarcoma
Più frequente tumore maligno primitivo dell'osso

- ≅ 25-30 % di tutti i casi
- ≅ 120-150 nuovi casi / anno in Italia

Incidenza: 2-2.5 casi/milione/anno

OSTEOSARCOMA
3056 casi

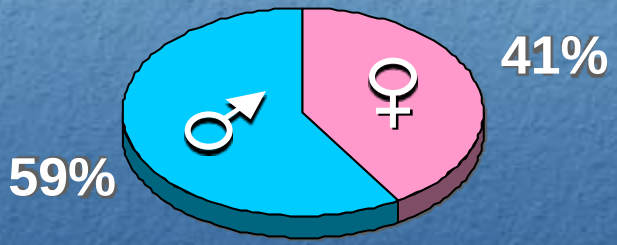


Varietà dell'Osteosarcoma

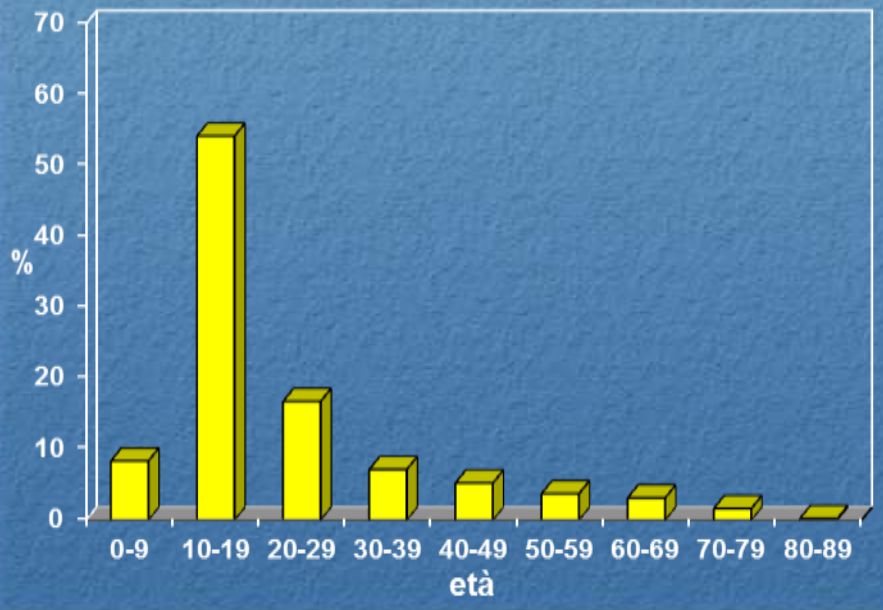
Varietà	*Frequenza*	*Istologia*	*Radiologia*	*Prognosi*
Classico	693 (75.3%)	Classica	Classica	Media
Telangiectatico	73 (7.9%)	Speciale	Classica	Media
Piccole cellule	15 (1.6%)	Speciale	Classica	Scarsa
Secondario	30 (3.3%)	Classica	Classica	Scarsa
Multicentrico	6 (0.7%)	Classica	Speciale	Scarsa
Basso Grado	27 (2.9%)	Speciale	Classica	Buona
Periosteo	23 (2.5%)	Speciale	Speciale	Buona
Parostale	53 (5.8%)	Speciale	Speciale	Buona
Mascellare	- - -	Classica	Speciale	Buona

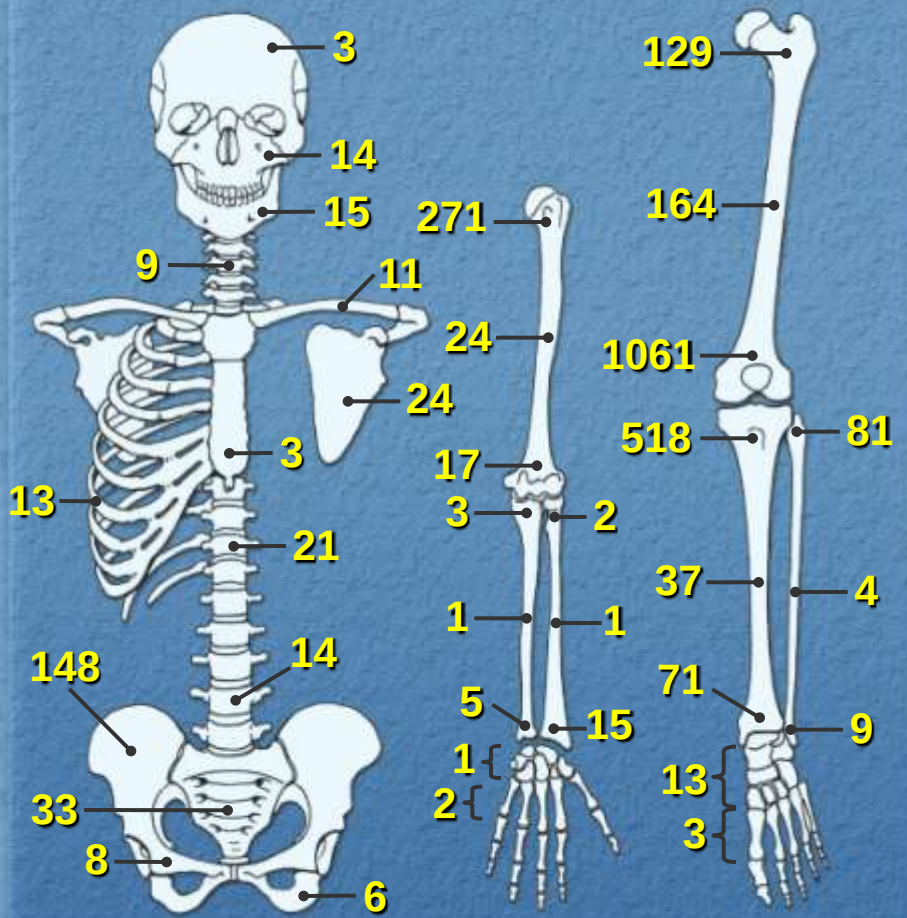
Osteosarcoma ad alto grado
2771 casi

Include:
Classico (2328), Telangiectatico (195), Secondario (117), Classico della superficie (43), Parostale Dedifferenziato (34), OS del mascellare(27), Piccole cellule (25), Intracorticale (2).



Media: 22 - Mediana: 17





BIOPSIA

↓

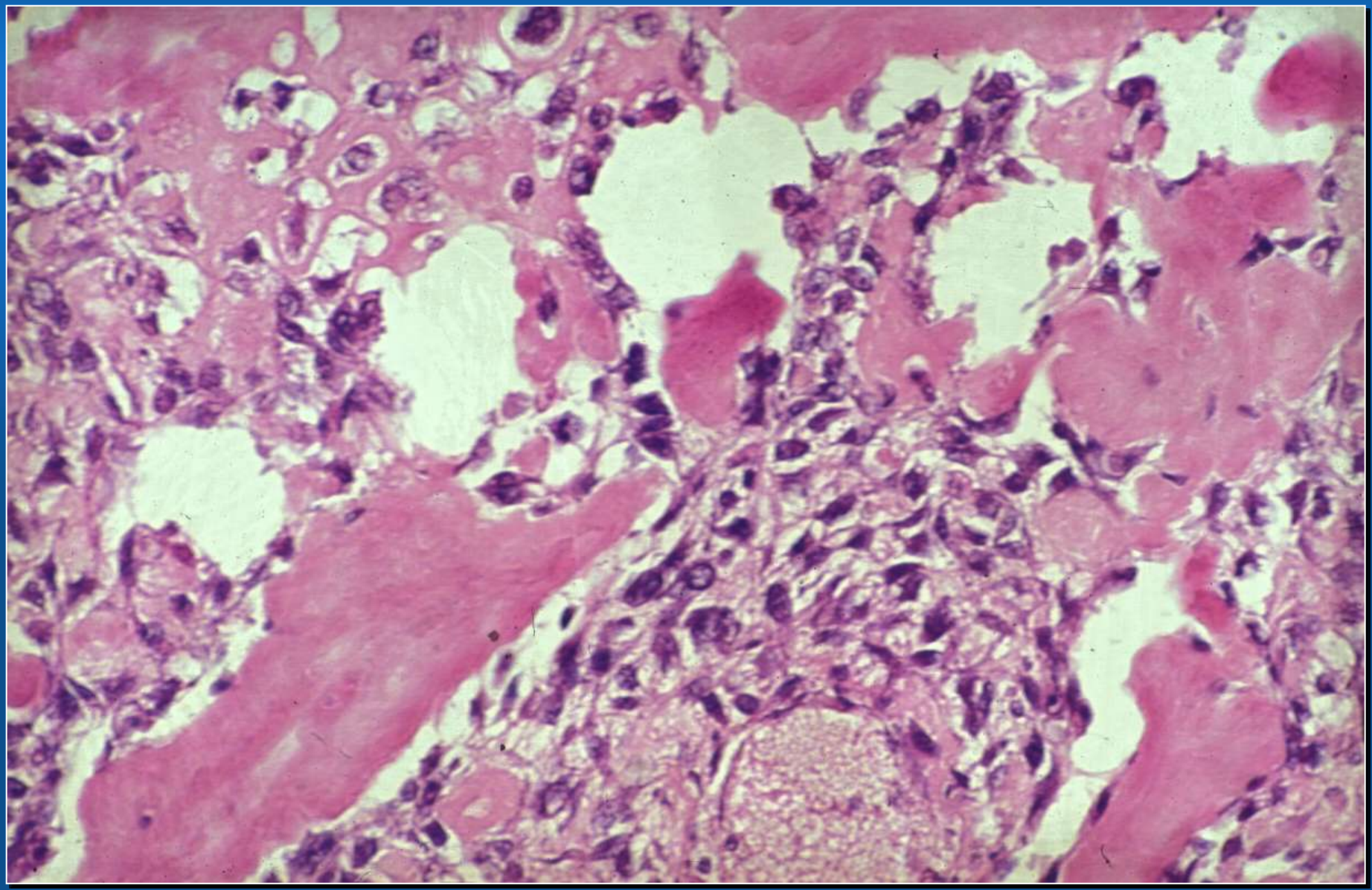
CHEMIOTHERAPIA PRE-OP

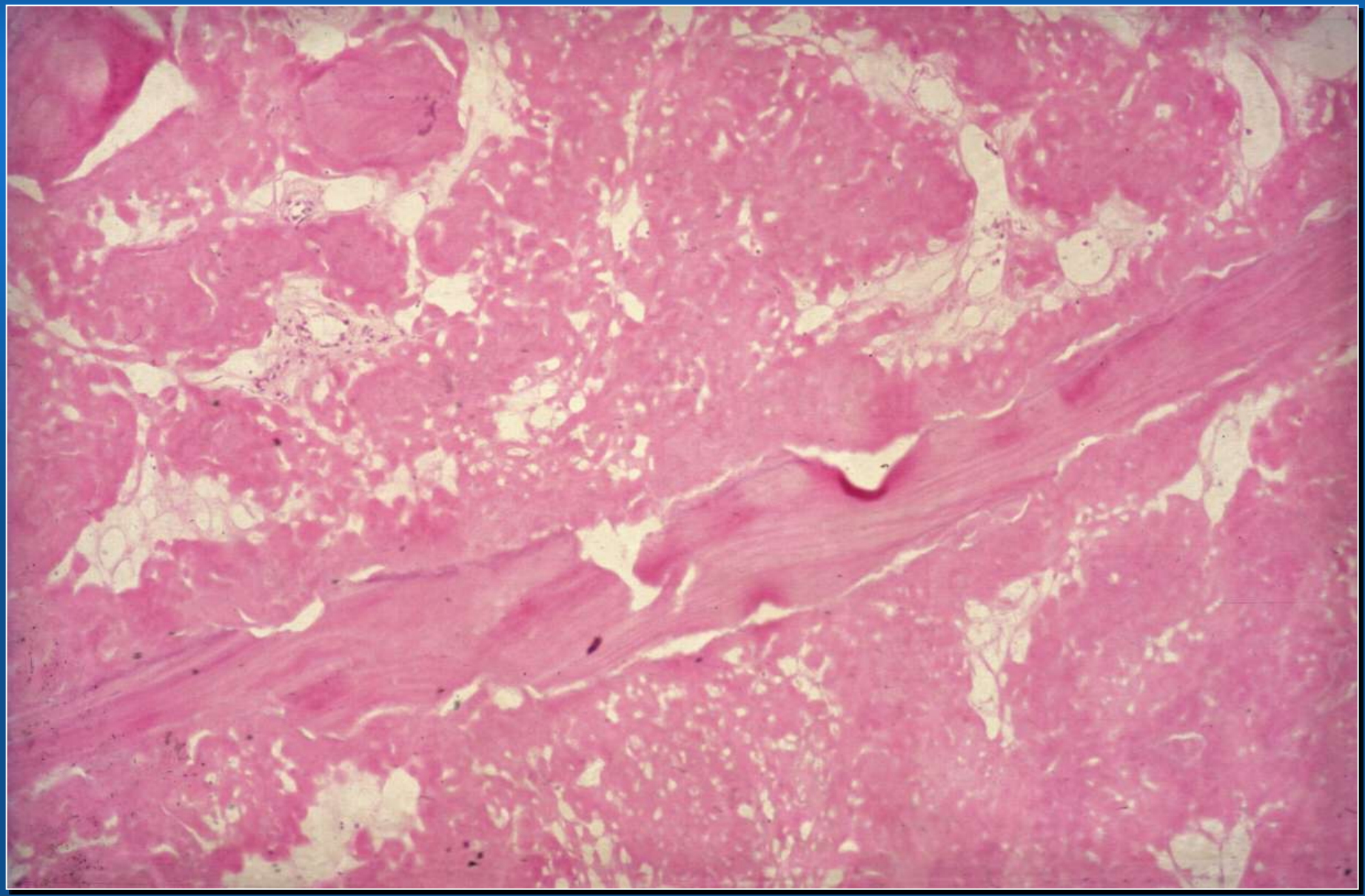
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CHIRURGIA

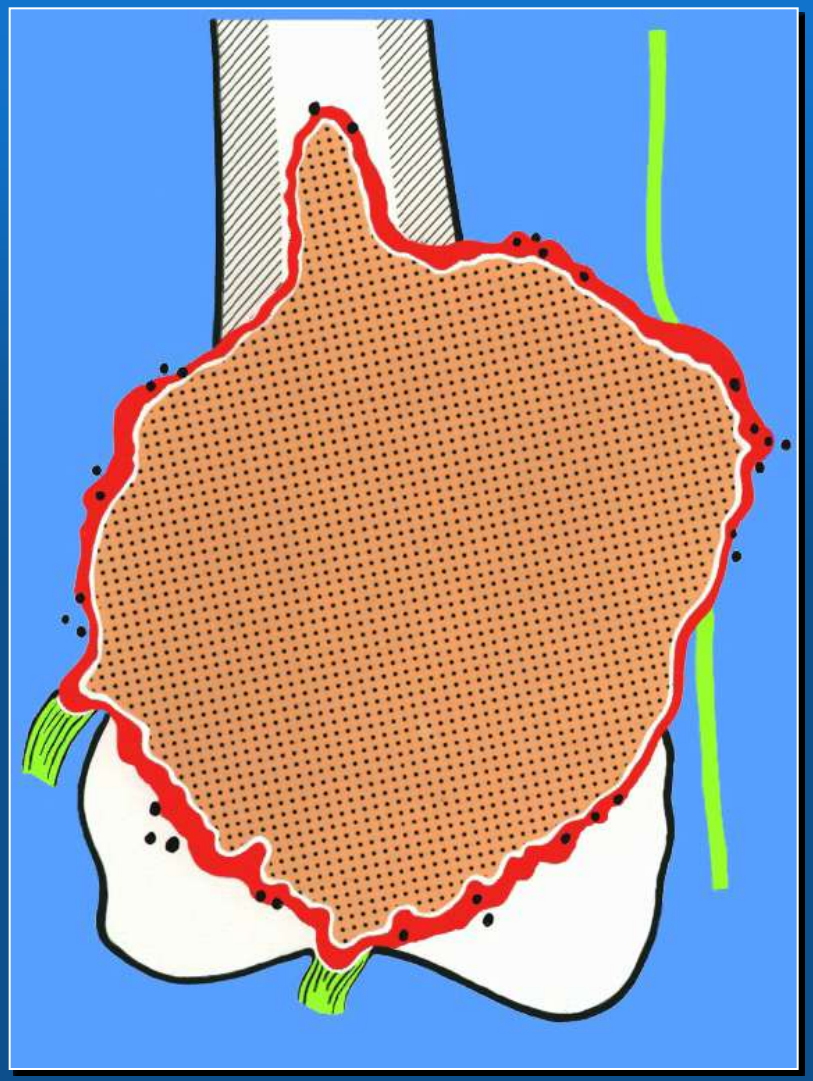
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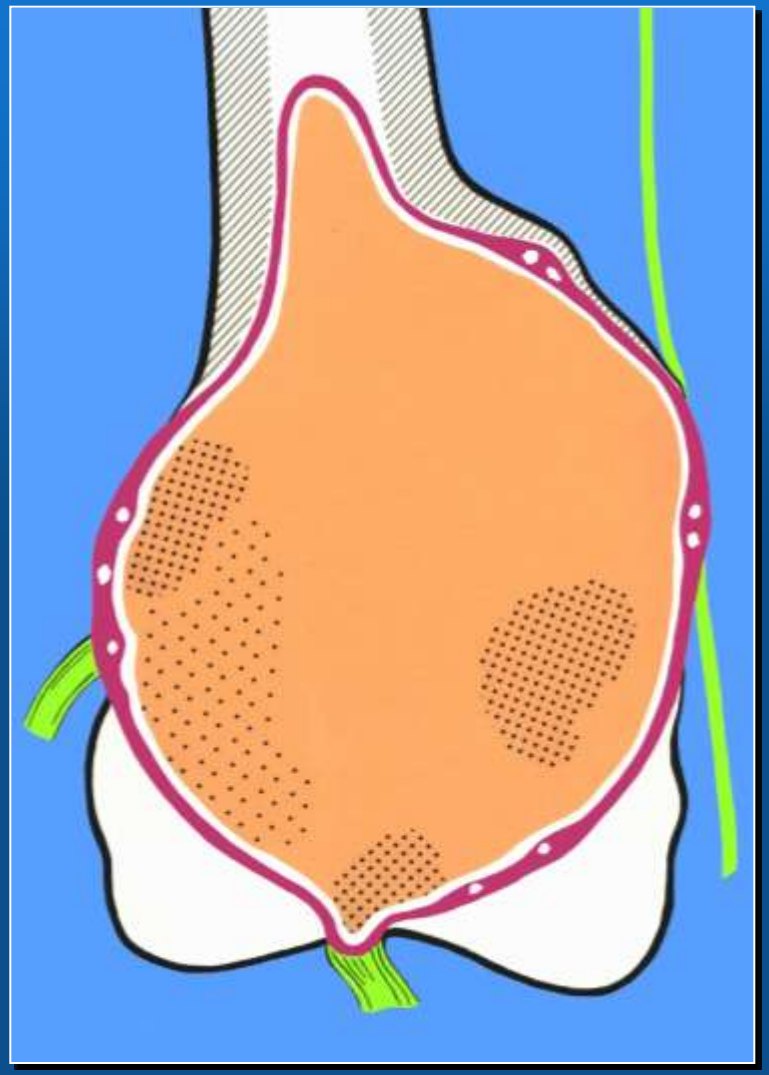
CHEMIOTHERAPIA POST-OP

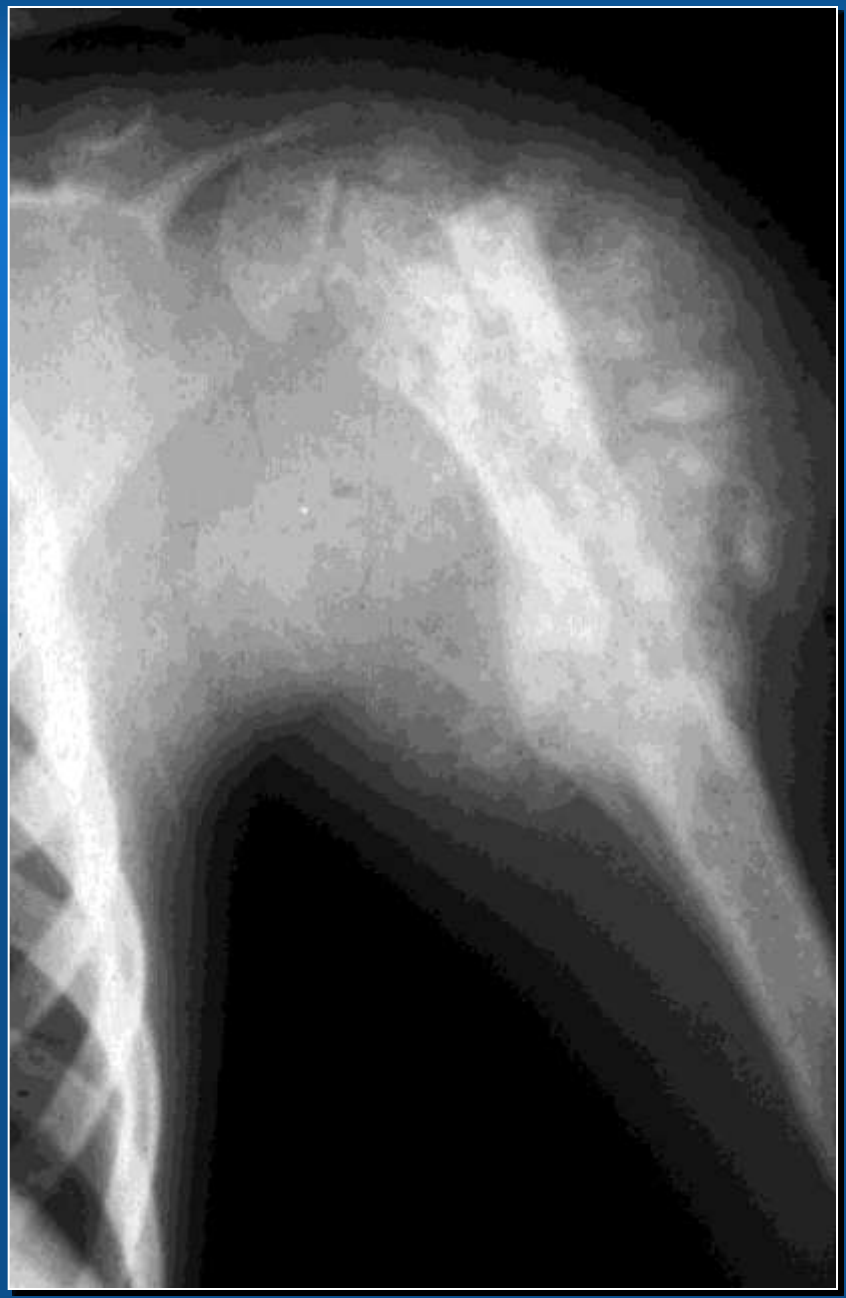




Prima e dopo chemioterapia

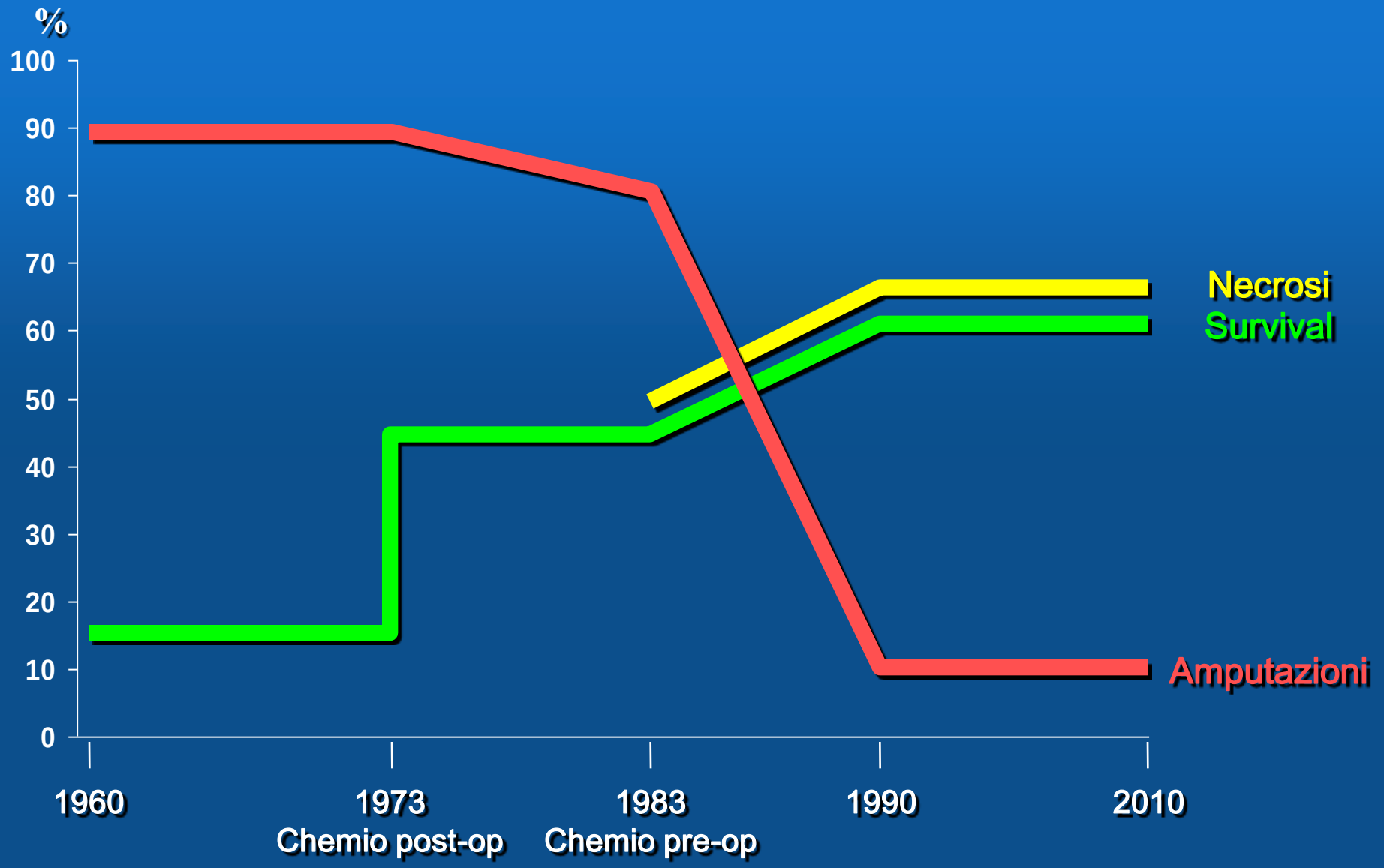








Osteosarcoma – Evoluzione nel trattamento



Criteri di inclusione nei protocolli standard

- Alto grado
- Età 0-40
- Malattia localizzata
- Estremità

Osteosarcomi diagnosticati al Rizzoli negli anni 2001-2010

CASI TOTALI 797

Alto grado

Età 0-40

Malattia Localizzata

Estremità

414 (52%)

Età e Sede

	Estremità	*Assili*
0 - 40	505 (86%)	83 (14%)
> 40	93 (72%)	36 (28%)

P = 0.0002

Età e Stadio

	Localizzati	*Metastatici*
0 - 40	420 (82%)	92 (18%)
> 40	71 (72%)	27 (28%)

P = 0.04

Sede e Stadio

	Localizzati	*Metastatici*
Estremità	**444 (83%)**	**94 (17%)**
Assili	**47 (66%)**	**24 (34%)**

P = 0.003

RISULTATI

Follow-up mediano 12 anni (5-25)

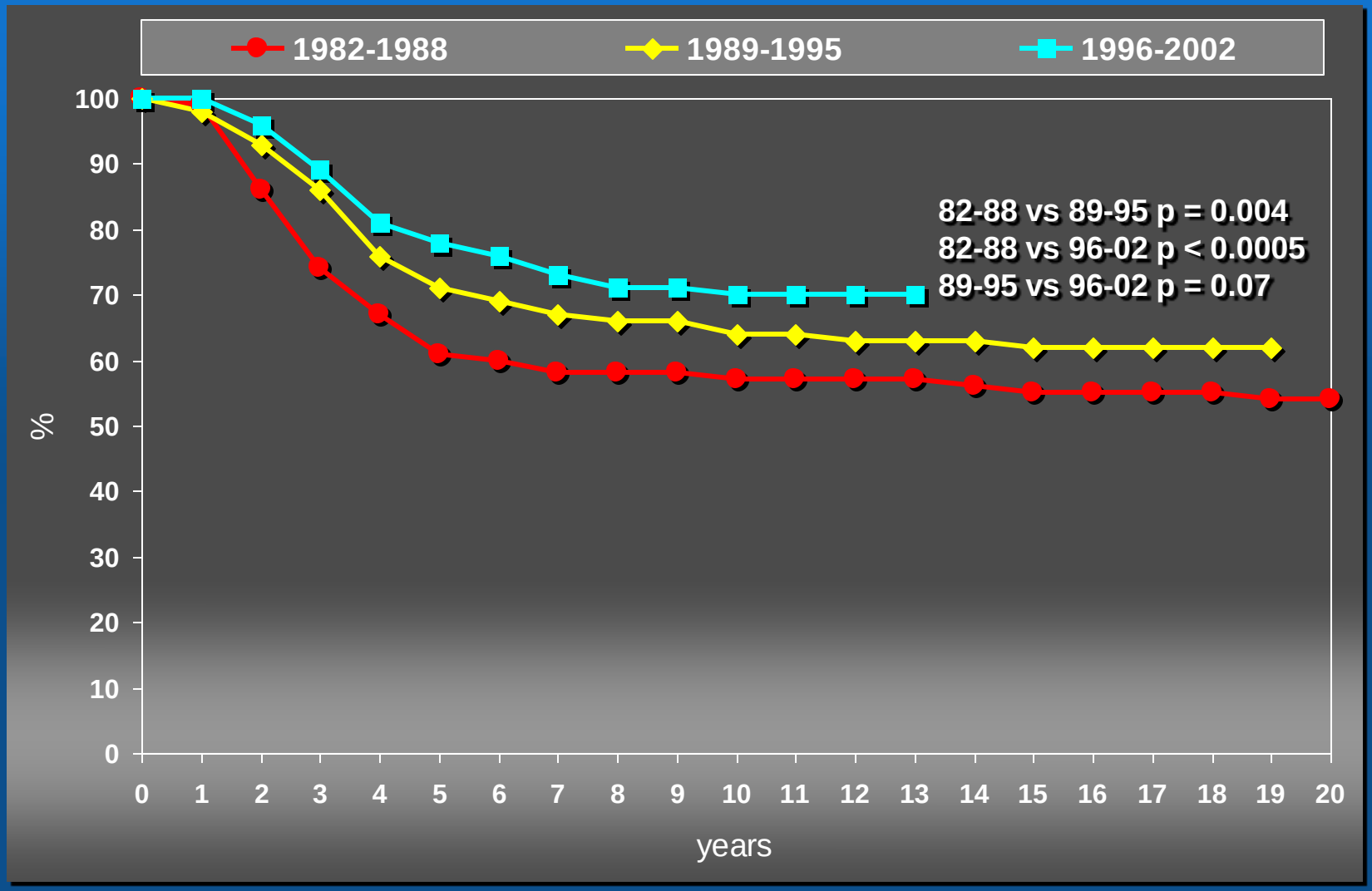
PAZIENTI CANDIDATI AI PROTOCOLLI : 1032

Sopravvivenza a 5 anni: 68%
Sopravvivenza a 10 anni: 64%
Sopravvivenza a 15 anni: 61%

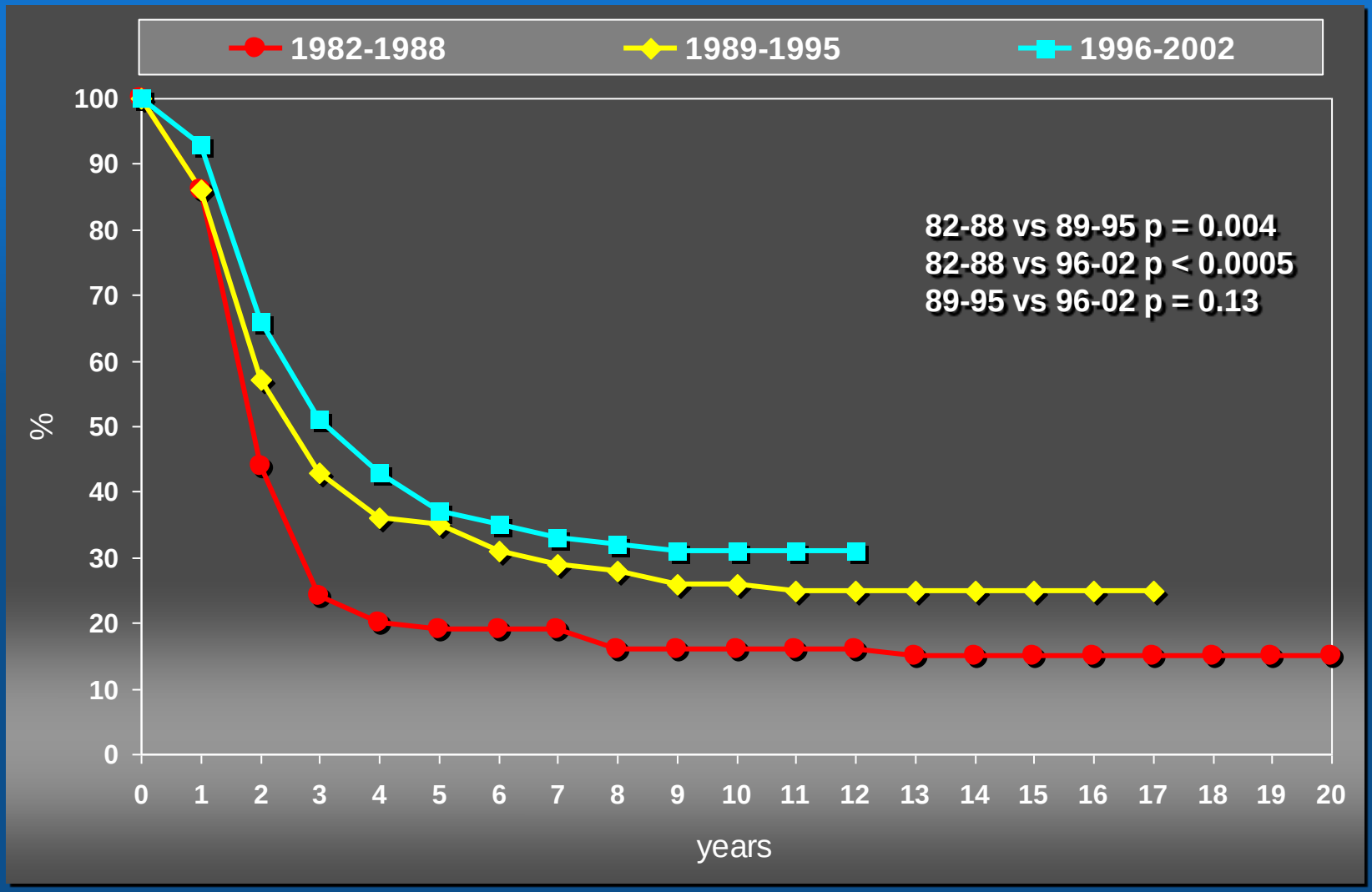
PAZIENTI NON CANDIDATI AI PROTOCOLLI: 426

Sopravvivenza a 5 anni: 30%
Sopravvivenza a 10 anni: 25%
Sopravvivenza a 15 anni: 24%

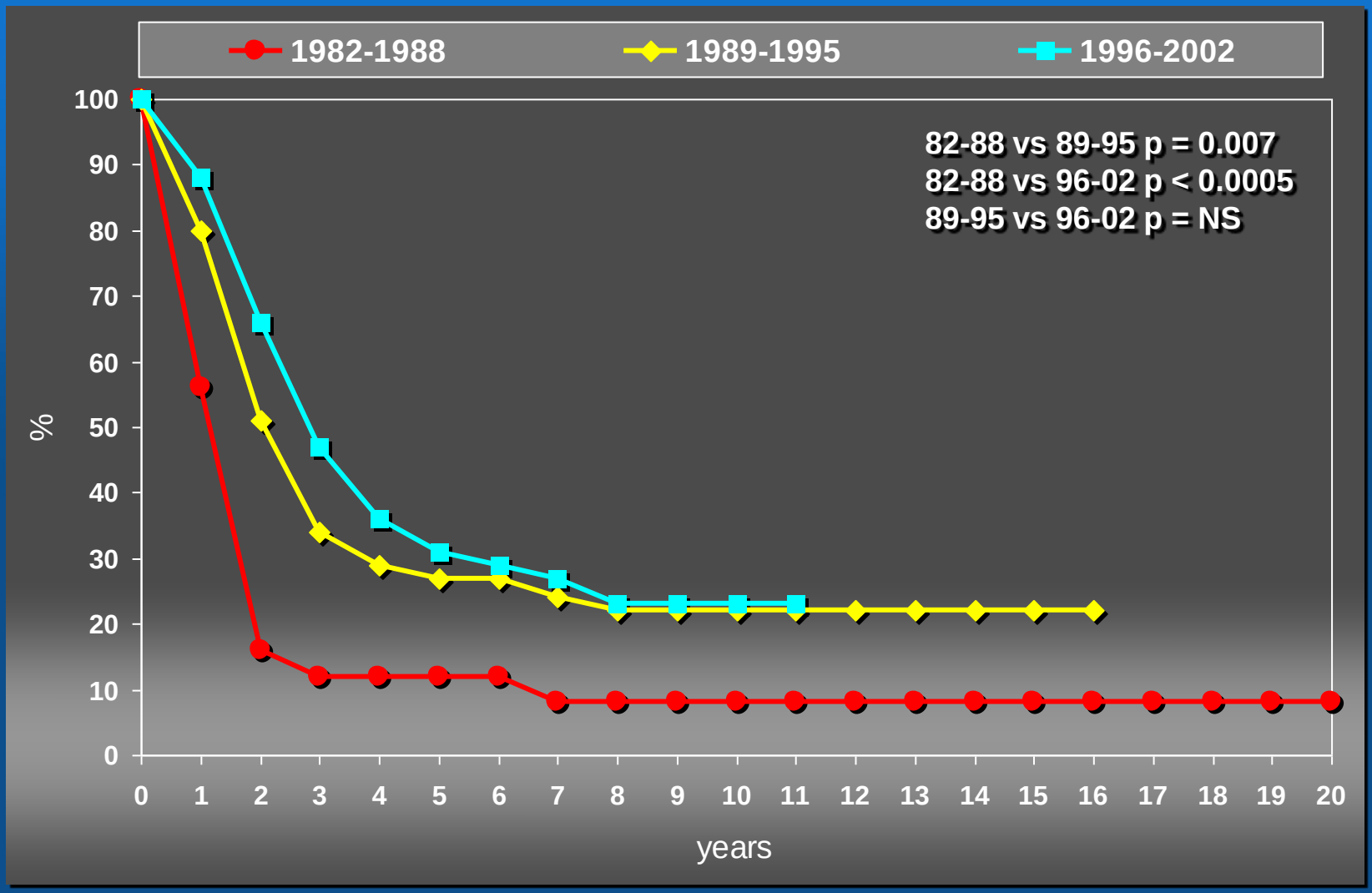
PAZIENTI CANDIDATI AI PROTOCOLLI – 1032 casi



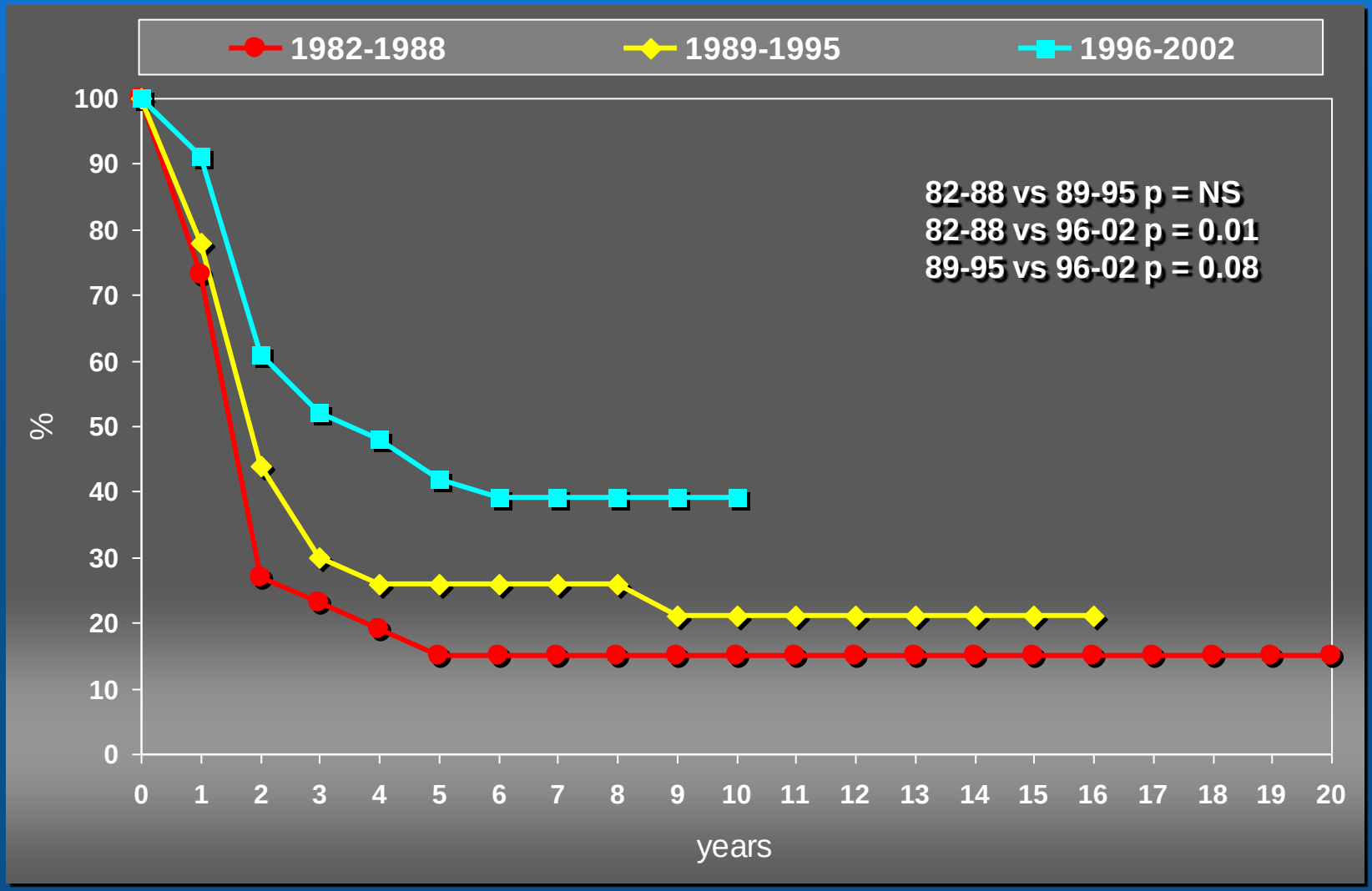
PAZIENTI NON CANDIDATI AI PROTOCOLLI – 426 casi



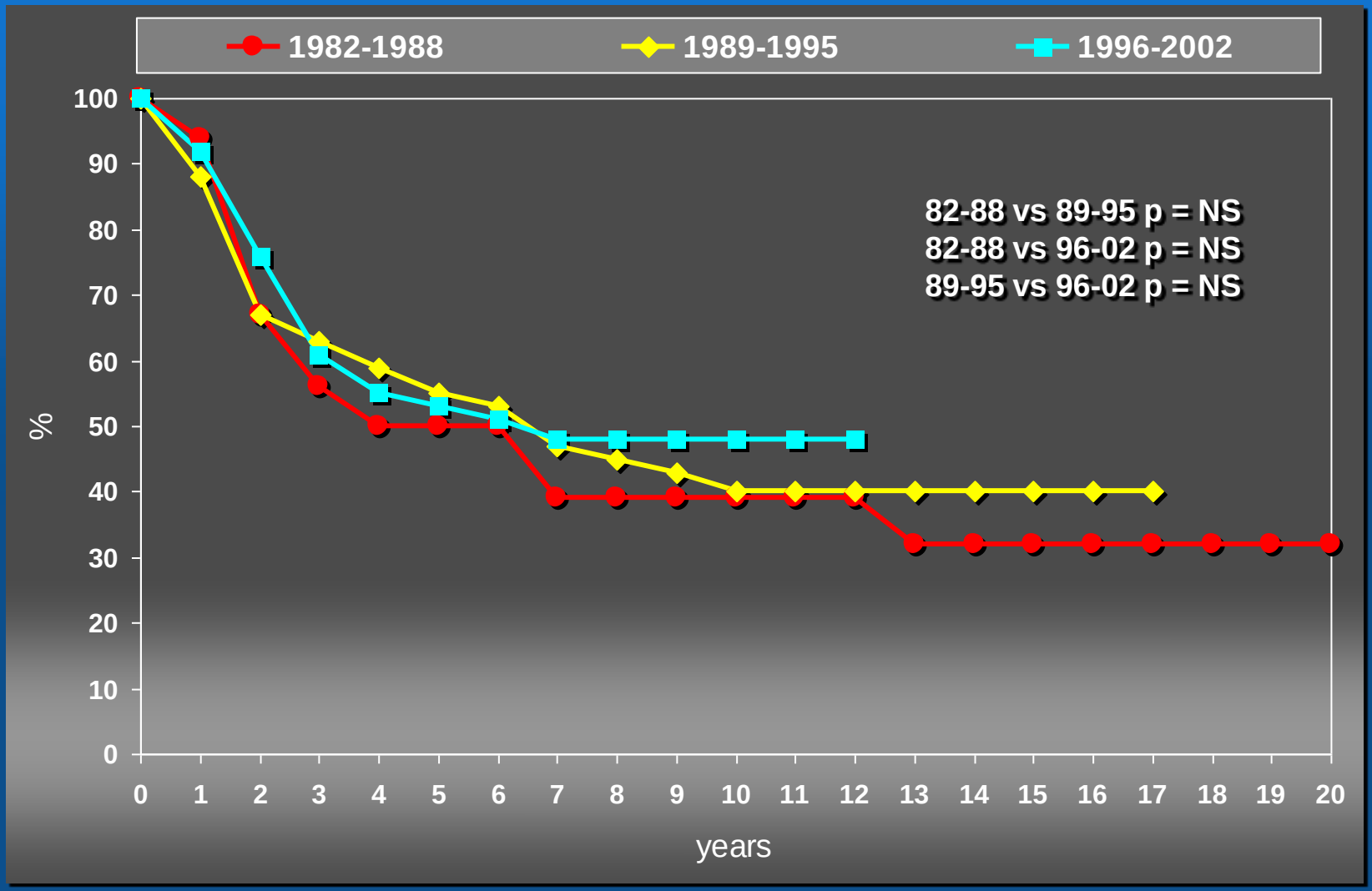
METASTATICI ALLA DIAGNOSI - SOPRAVVIVENZA



SOPRAVVIVENZA - SEDE ASSILE- LOCALIZZATI



SOPRAVVIVENZA - PAZIENTI OVER 40 - LOCALIZZATI



CONCLUSIONI

Le molte facce dell' osteosarcoma

- Nel passato ci siamo dedicati soprattutto ai pazienti con migliore prognosi
- Ora è tempo di riconsiderare le necessità di tutti gli altri pazienti, che sono circa la metà dell'intero gruppo

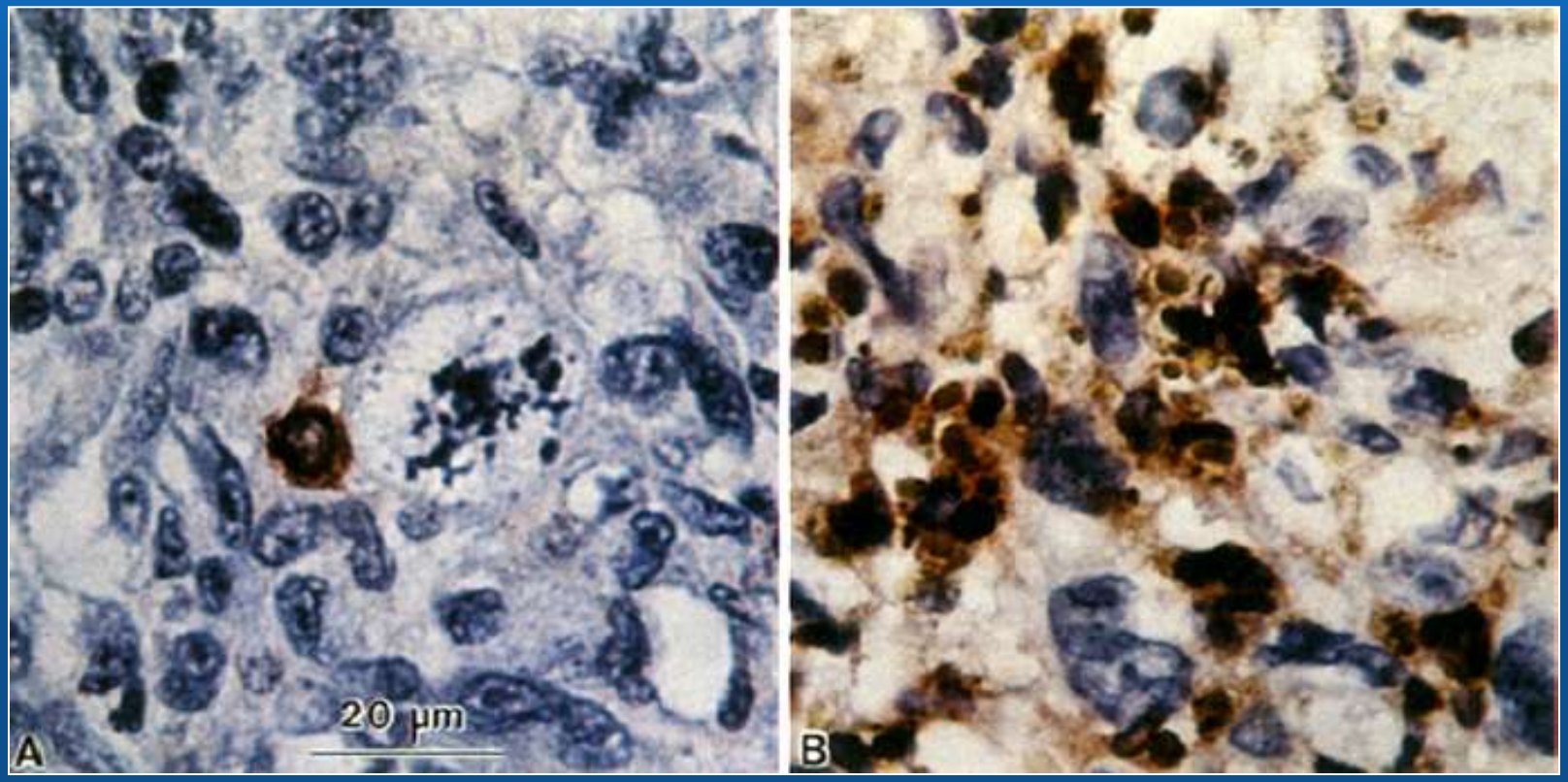
Genetica dell'osteosarcoma

Mutazioni e/o delezioni dei geni oncosopressori *P53* e *RB1* sono responsabili della tumorigenesi dell'Osteosarcoma, però…

…l'osteosarcoma è caratterizato dalla presenza ed insorgenza di anomalie cromosomiche estremamente complesse e non specifiche

MEPACT monotherapy induces infiltration of inflammatory macrophages into lung metastases

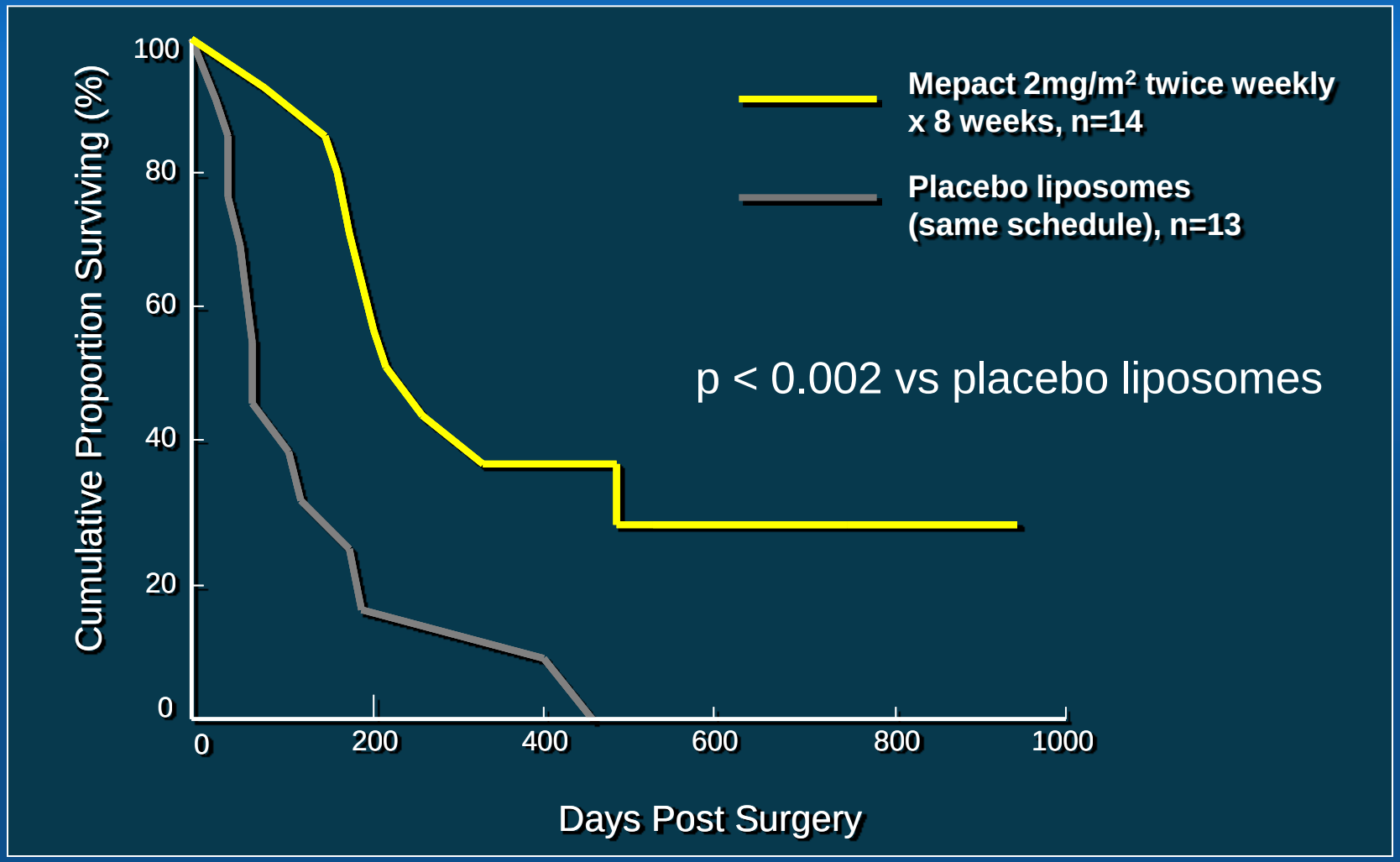
Pre-MEPACT **Post-MEPACT**



Kleinerman et al., Cancer Immunol. Immunother., 1992



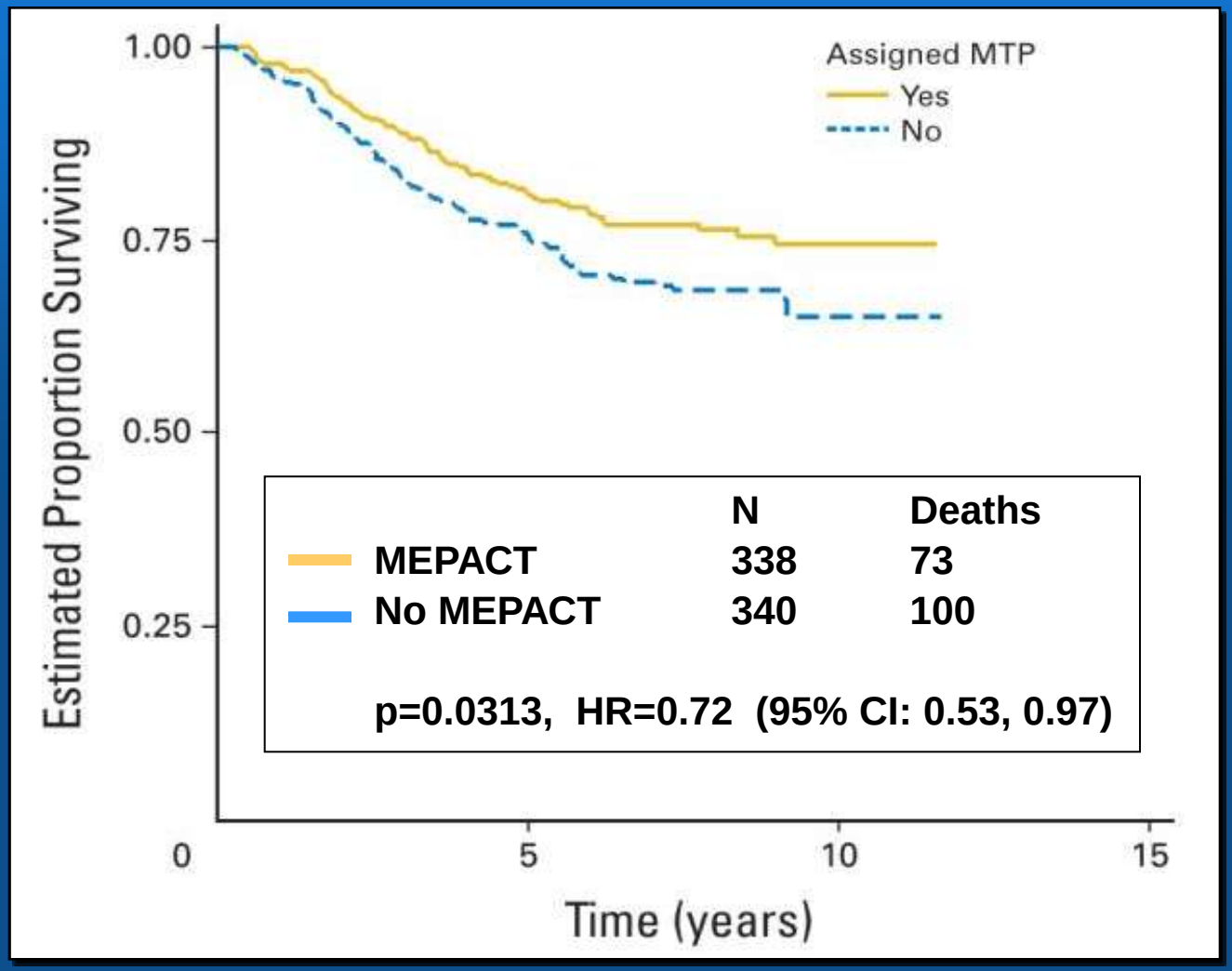
Improved Survival in Canine Osteosarcoma



Therapy for Osteosarcoma in Dogs With Intravenous Injection of Liposome-Encapsulated Muramyl Tripeptide

MacEwen EG et al. J Natl Cancer Inst. 1989;81:935-938.

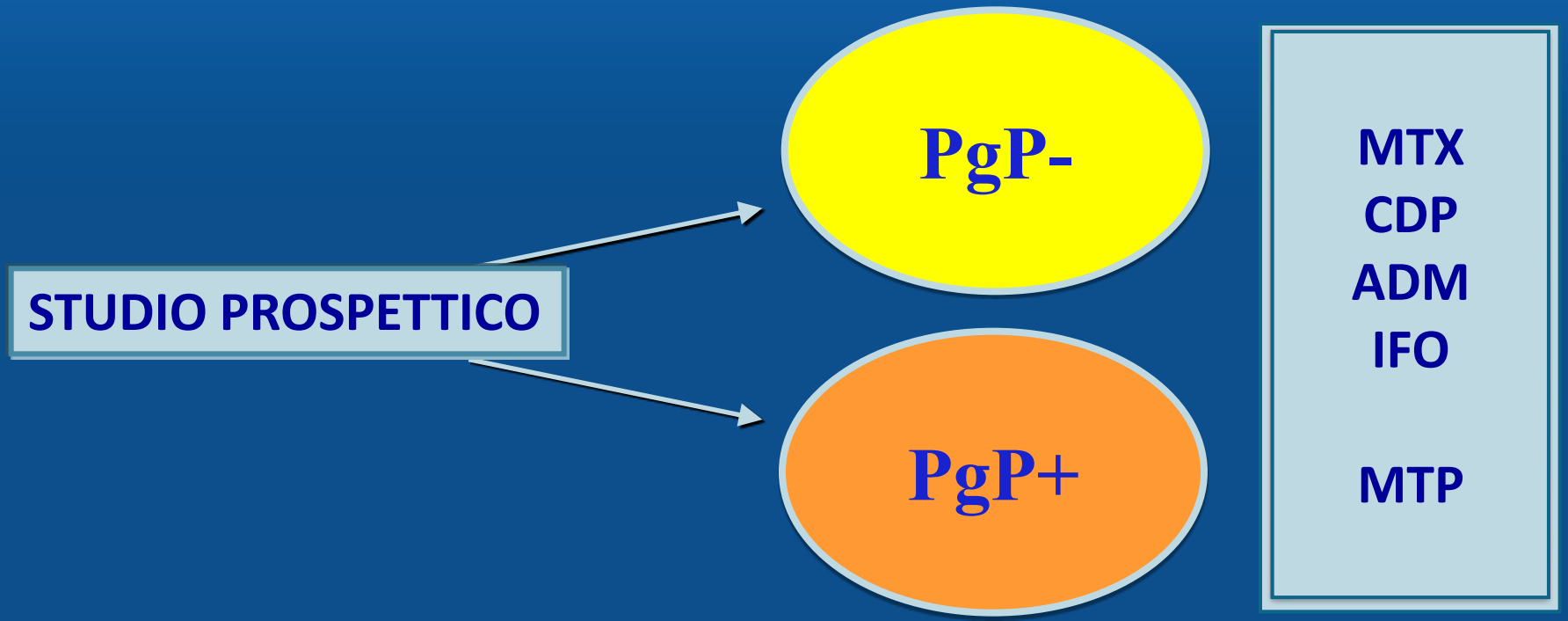
Overall Survival 2007 Dataset*
Reduction in Risk of Death ~ 30%



Meyers PA et al. J Clin Oncol. 2008;26:633-638

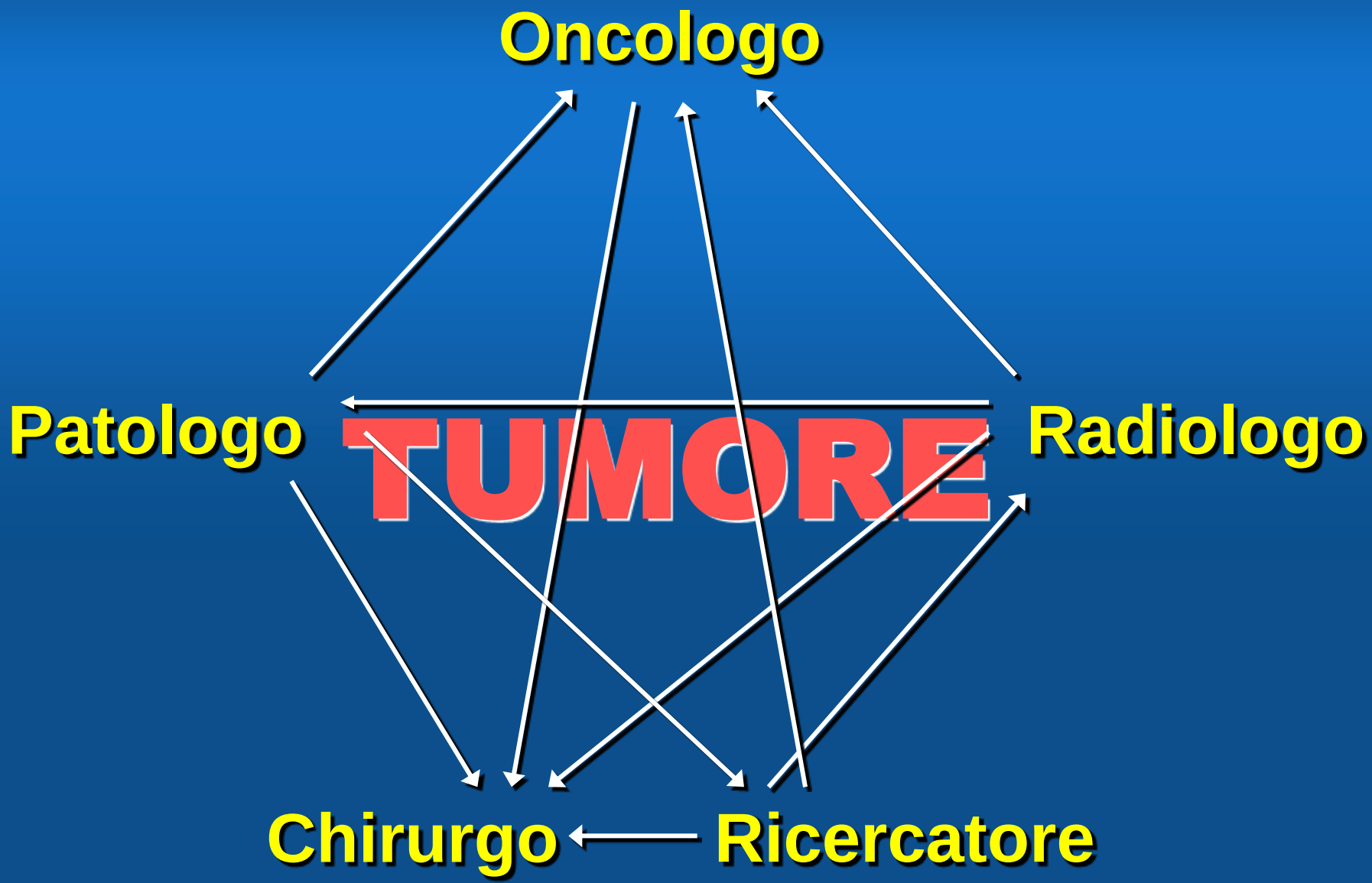
PROTOCOLLO ISG/OS-2

Osteosarcoma localizzato delle estremità
Stratificazione biologica basata sulla espressione di P-Glicoproteina



Conclusioni

Gli importanti risultati ottenuti nel trattamento dei sarcomi sono dovuti in gran parte alla centralizzazione dei pazienti in centri specializzati dove operano team multidisciplinari


Oncologo
Patologo
TUMORE
Radiologo
Chirurgo
Ricercatore

Italian Sarcoma Group



78 Centri

- **14 I.R.C.C.S.**
- **15 Università**
- **49 Ospedali**

303 Membri

Attivato nel 1997



uicc
global cancer control

IJC
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Osteosarcoma

- Età > 40: 38%
- Estremità: > 90% in età giovanile
- Sede assile: > 40% in età avanzata
- Stadio: No dati
- Sopravvivenza a 5 anni migliore in:
  - ✓ Giovani (53% vs 22%)
  - ✓ Estremità (48% vs 16%)

Osteosarcomi diagnosticati al Rizzoli negli anni 2001-2010

- **CASI TOTALI** **797**
  - ✓ **Basso grado** **80 (10%)**
- **ALTO GRADO** **717**
  - ✓ **Età > 40** **129 (18%)**
  - ✓ **Secondari** **45 (6%)**
  - ✓ **Loc. Assile** **119 (17%)**
  - ✓ **Metastatici** **119 (20%)***

**Su 609 casi*

PATIENTS

All diagnoses of high grade osteosarcoma,
independently from histological varieties, age, gender, and stage (localized or metastatic).

In the years 1982-2002 1656 cases were observed:

Excluded 191 (41 consultation, 129 low grade, 28 lost to follow-up)

Included 1458 cases

1032 with characteristics to be included in prospective clinical trials (classic histology, localized disease, age < 41, extremity site)

426 without these characteristcs

Minimum follow-up: 5 years

RESULTS

Median Follow-up 12 years (5-25)

ALL PATIENTS: 1458

Overall Survival:

51.8% (754 pts)

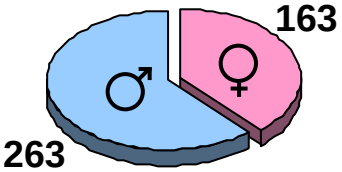
Continously disease free:

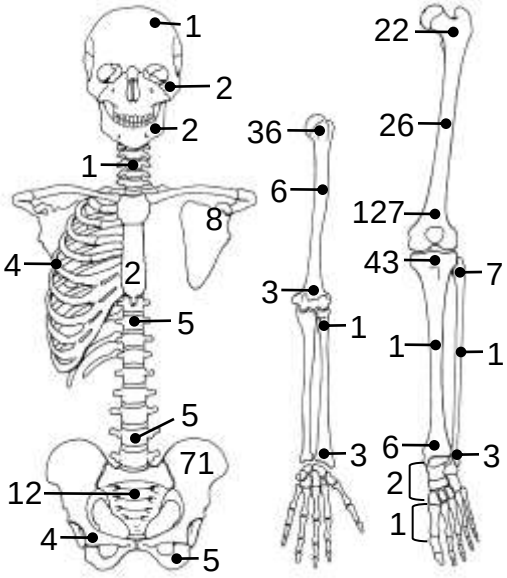
42.1% (613 pts)

Non candidates for protocols - 426 cases

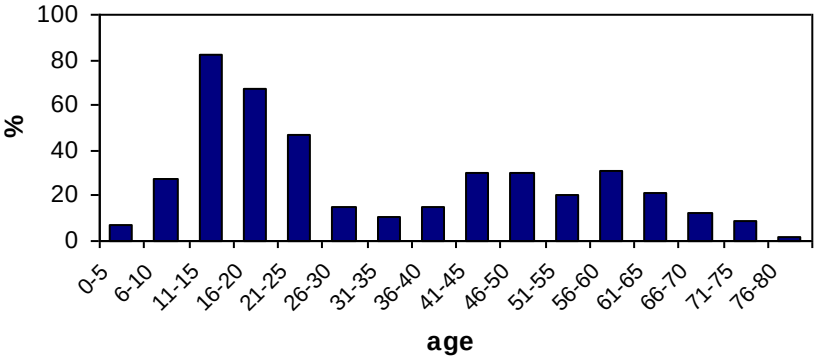
Osteosarcoma varieties:

✓ Classic Central	**285**
✓ Telangiectatic	**25**
✓ High Grade Surface	**20**
✓ Small Cell OS	**19**
✓ Maxillo-Facial	**4**
✓ Multicentric	**11**
✓ Secondary OS	**62**





+ 11 multicentric lesions

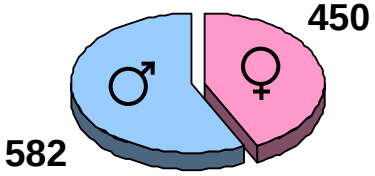


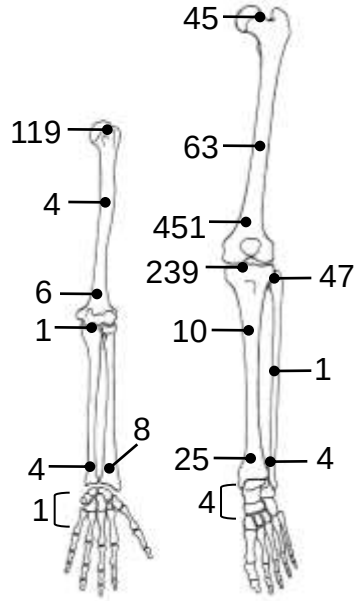
Median: **24 (2-78)**

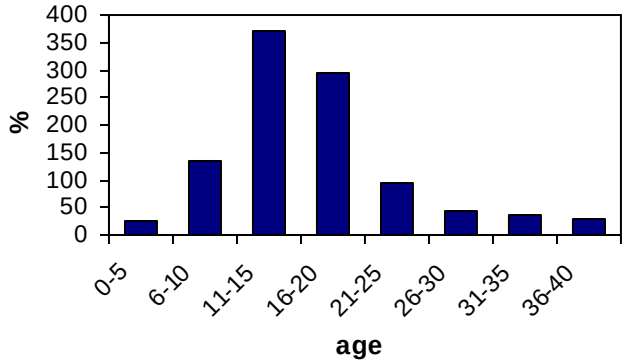
Candidate for protocols - 1032 cases

Osteosarcoma varieties:

✓ Classic Central	**924**
✓ Telangiectatic	**77**
✓ High Grade Surface	**31**





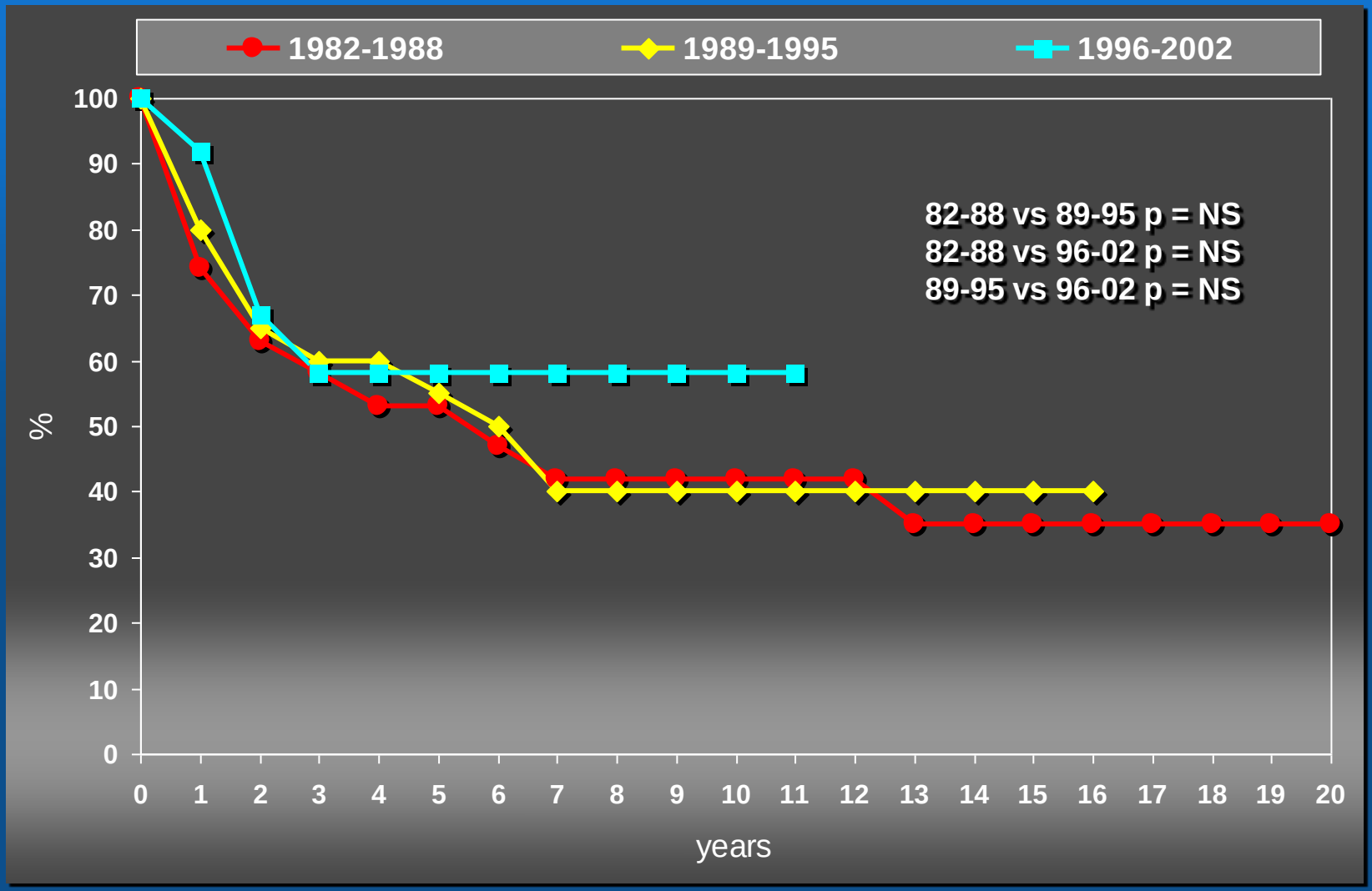


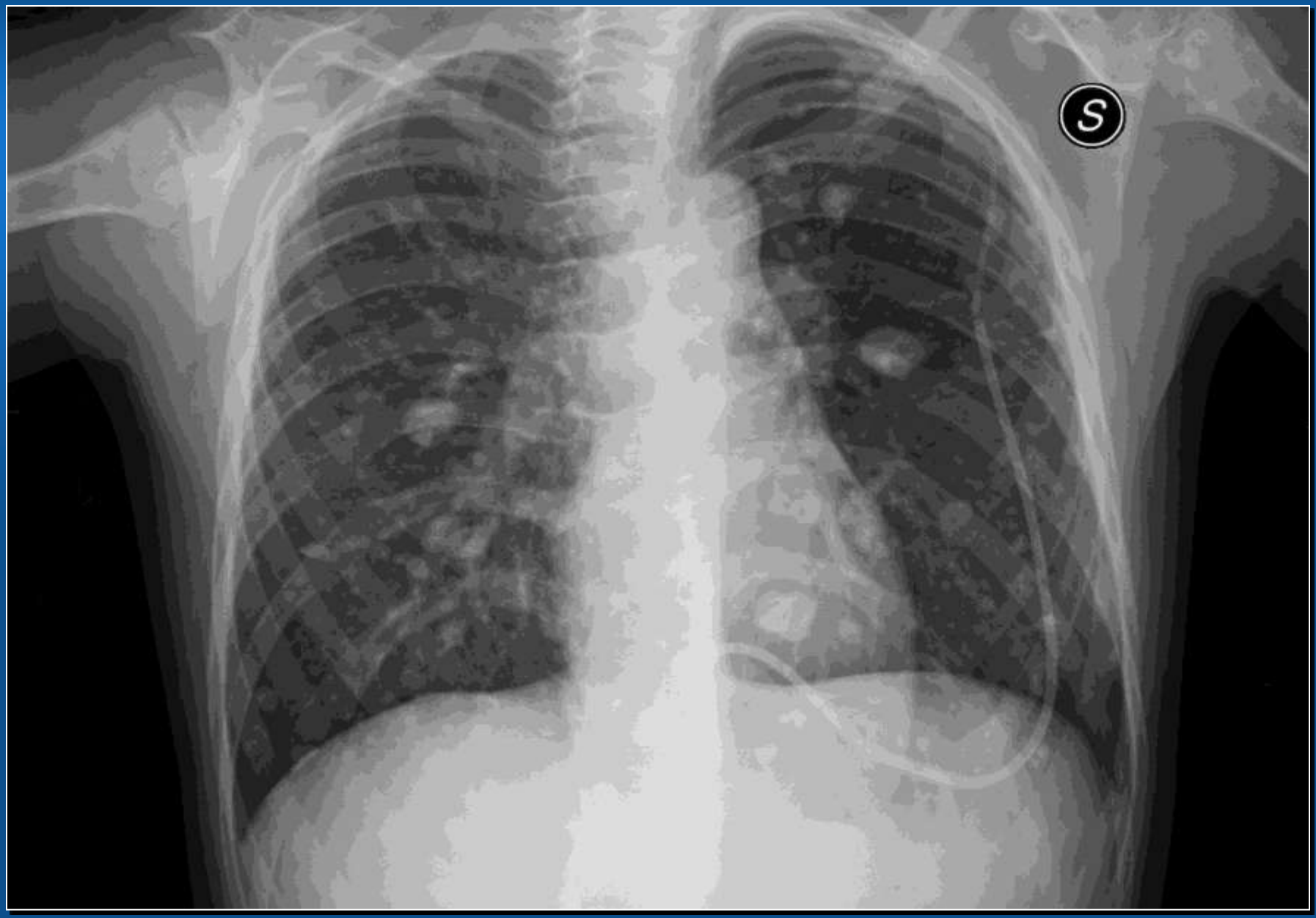
Median: **15 (2-40)**

ANALYSIS IN SUBGROUPS

- Metastatic patients at diagnosis
- Patients with axial site
- Different histologic varieties
- Patients with age > 40

SURVIVAL - VARIETIES - LOCALIZED




S

CONCLUSIONI

- Nonostante la mancanza di nuovi farmaci per l'osteosarcoma, la sopravvivenza è migliorata, particolarmente per i pazienti che avevano una prognosi peggiore.
- Dal momento che non sono stati usati nuovi farmaci, il miglioramento è dovuto sia a una più accurata strategia terapeutica che ad una chirurgia più aggressiva (sia per la malattia localizzata che sistemica).
- Ulteriori miglioramenti sono auspicabili per quei pazienti che ancora presentano una prognosi peggiore.
- Diverse strategie terapeutiche ed un trattamento aggressivo è pertanto auspicabile per questi pazienti a scarsa prognosi.