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GISG
German Interdisciplinary Sarcoma Group

Medizinische Fakultät Mannheim
der Universität Heidelberg

Universitätsklinikum Mannheim

State-of-the-Art

Bone sarcomas

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German Interdisciplinary Sarcoma Group (GISG)

Bone sarcomas - Background

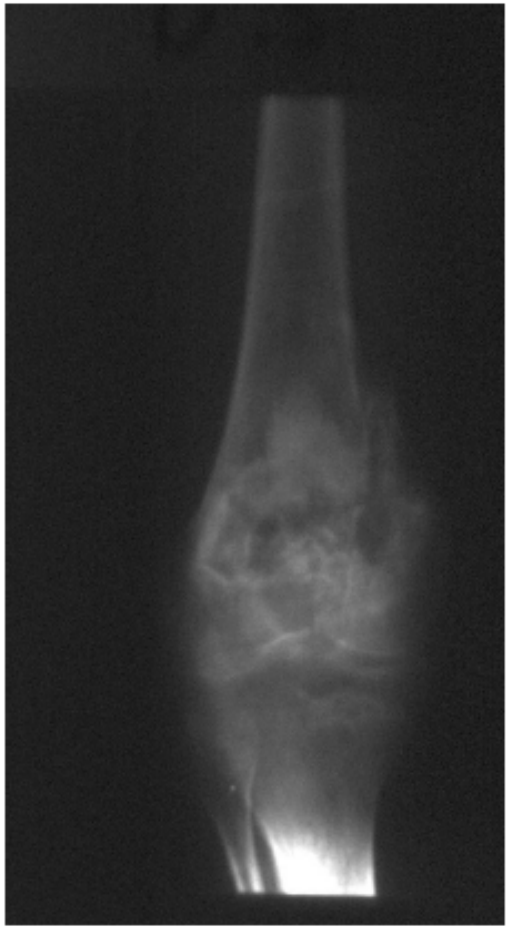
- Sarcomas are a heterogeneous group of rare tumours arising mainly from the embryonic mesoderm and can be localized anywhere in the body.
- They can be loosely grouped into two categories:

  - Bone sarcomas (20 %), mainly osteosarcomas and sarcomas of the Ewing family

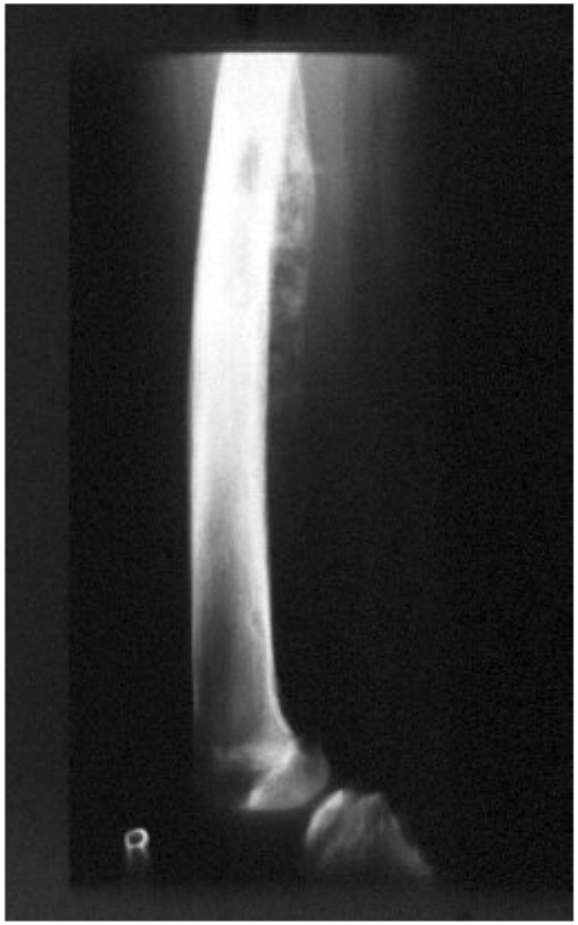
  - Soft tissue sarcomas (80 %)

Bone sarcomas - **Clinical presentation**

Bone sarcomas - **Radiological presentation**



Osteosarcoma



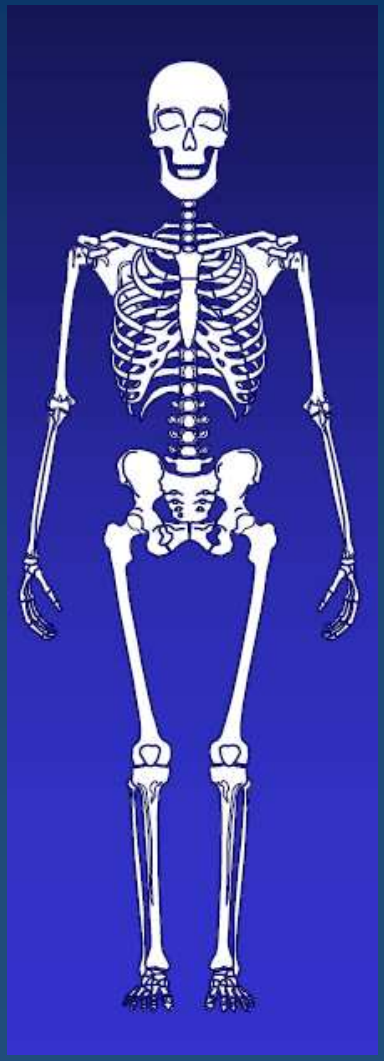
Ewing sarcoma

Bone sarcomas - Diagnosis

- In case of a clinical suspicion of a bone tumor **X-ray** could be initially performed.
- For the exact diagnosis and tumor spread **MRI** is the gold-standard.
- The radiological workup should be done before biopsy.
- **Staging** comprises a CT of the chest and a szintigraphy of the skeleton; for Ewing tumors a bone marrow aspiration is essential.
- For histological examination an incision **biopsy** is usually recommended in the light of the definitive surgical resection.
- An **interdisciplinary** treatment planning should be performed.

Osteosarcoma - **Localizations**

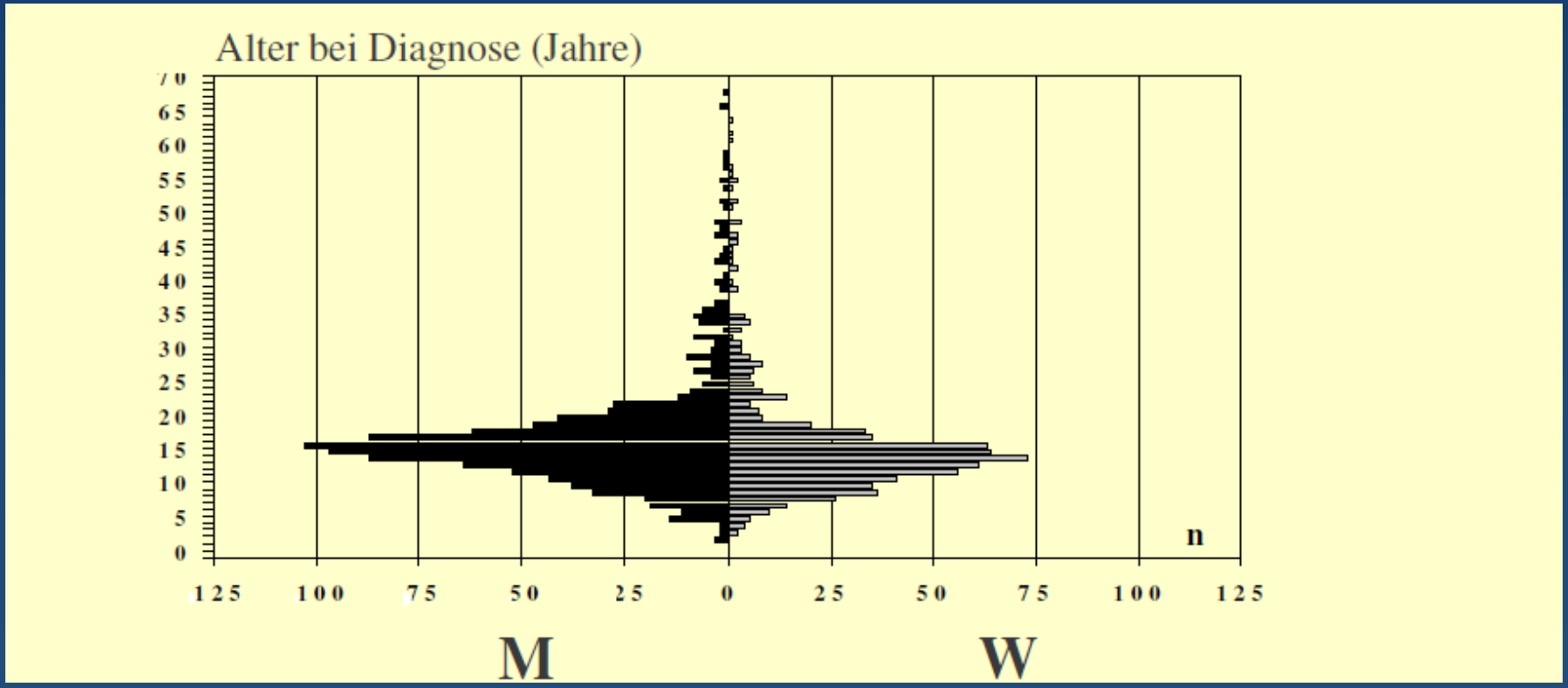
Clavicle	**< 1 %**
Scapula	**< 1 %**
Rib	**< 1 %**
Spinal column	**< 1 %**
Pelvis	**5 %**



Humerus	**10 %**
Ulna	**< 1 %**
Radius	**1 %**
Hand	**< 1 %**
Femur	**50 %**
Fibula	**6 %**
Tibia	**26 %**

Osteosarcoma - **Epidemiology**

- Median age 15 years [range: 2-68]
- Gender distribution



Osteosarcoma - **Histology**

- Spindle cells
- Morphological subtypes:

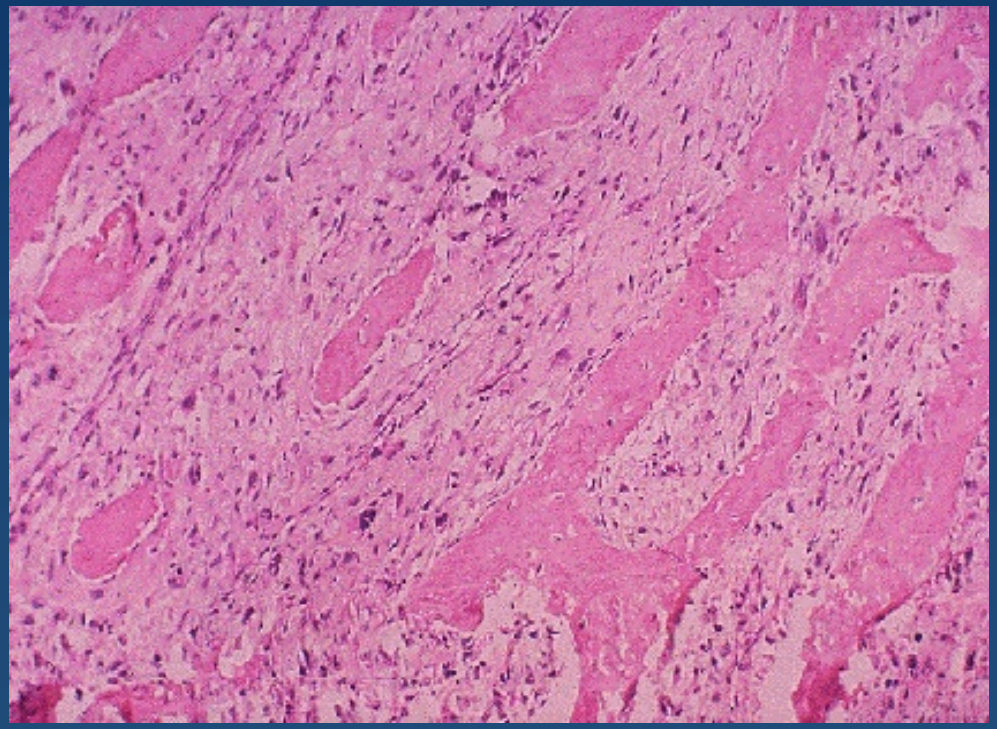
  - osteoblastic

  - chondroblastic

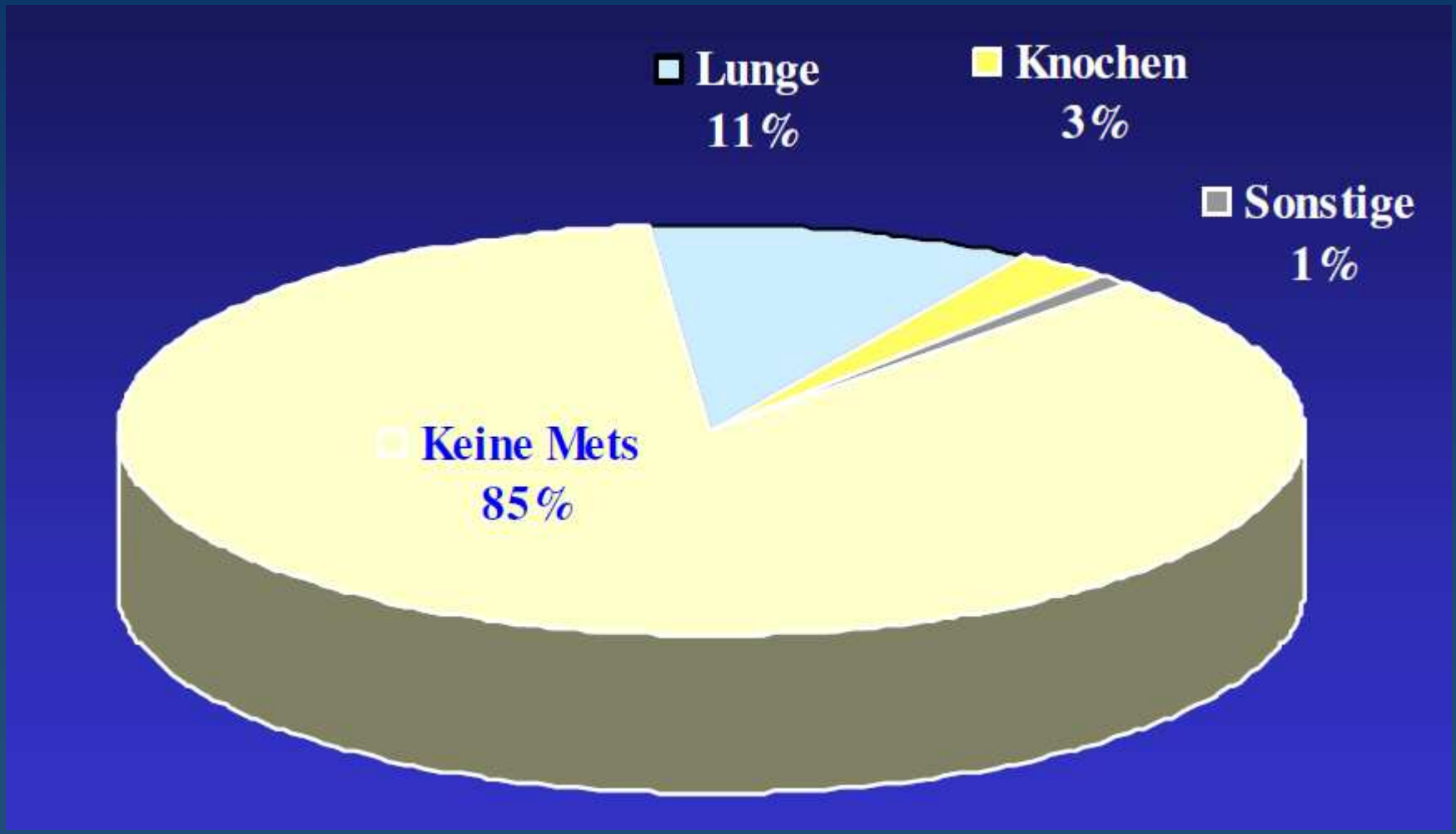
  - fibroblastic

  - teleangiectatic

  - …

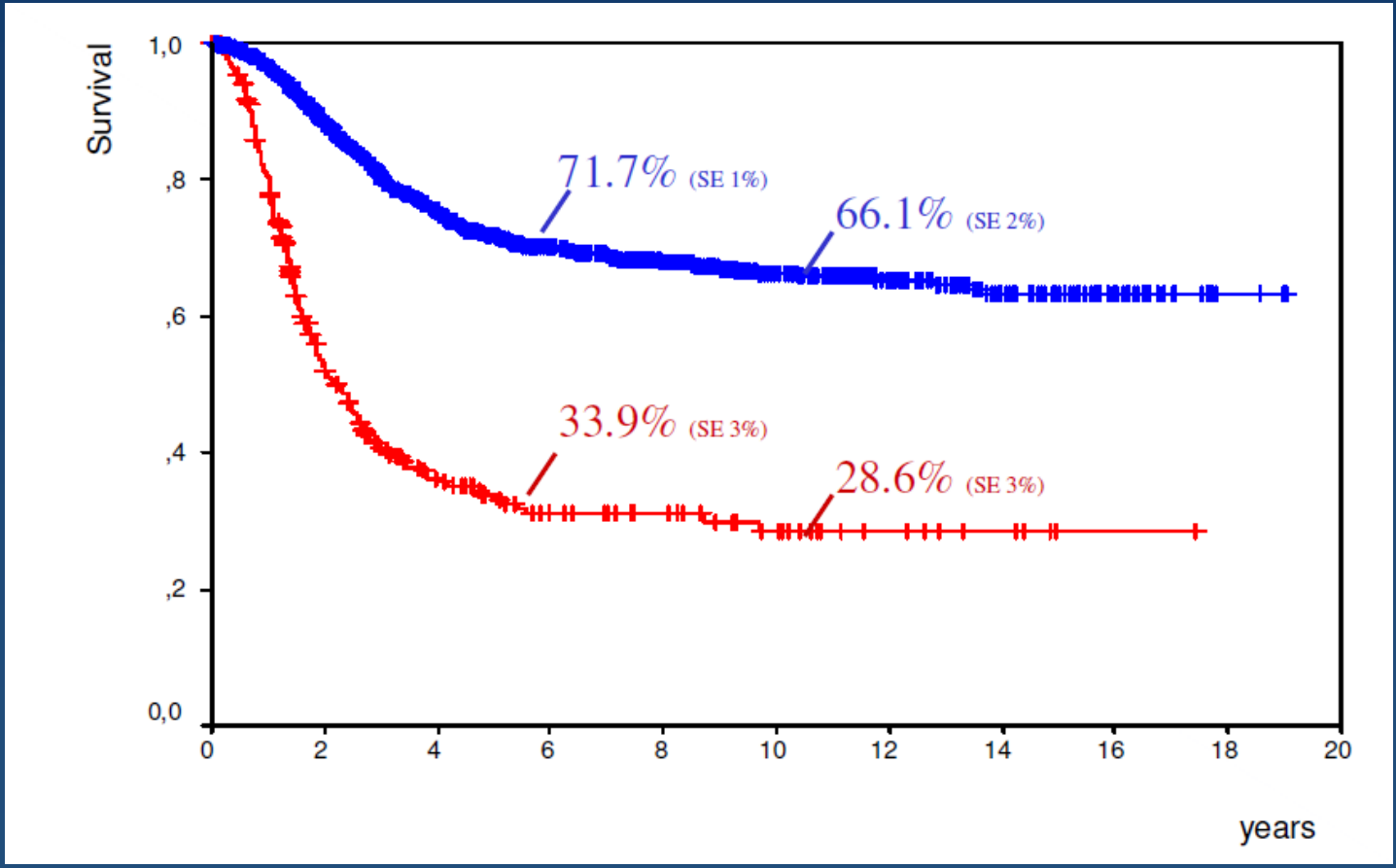


Osteosarcoma - **Primary metastases**



Osteosarcoma - **Survival**

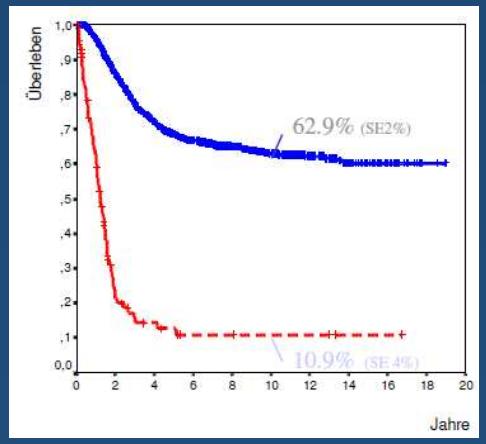
Localized extremity osteosarcomas (blue; n = 1406) vs. others (red; n = 296)



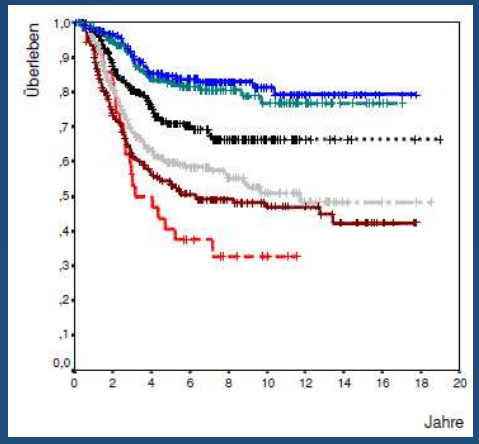
Osteosarcoma - **Prognostic factors**

- Primary metastases
- Tumor volume
- Tumor localization
- Complete resection of the primary tumor (a)
- Histological response according to Salzer-Kuntschik (grade I-VI; b)

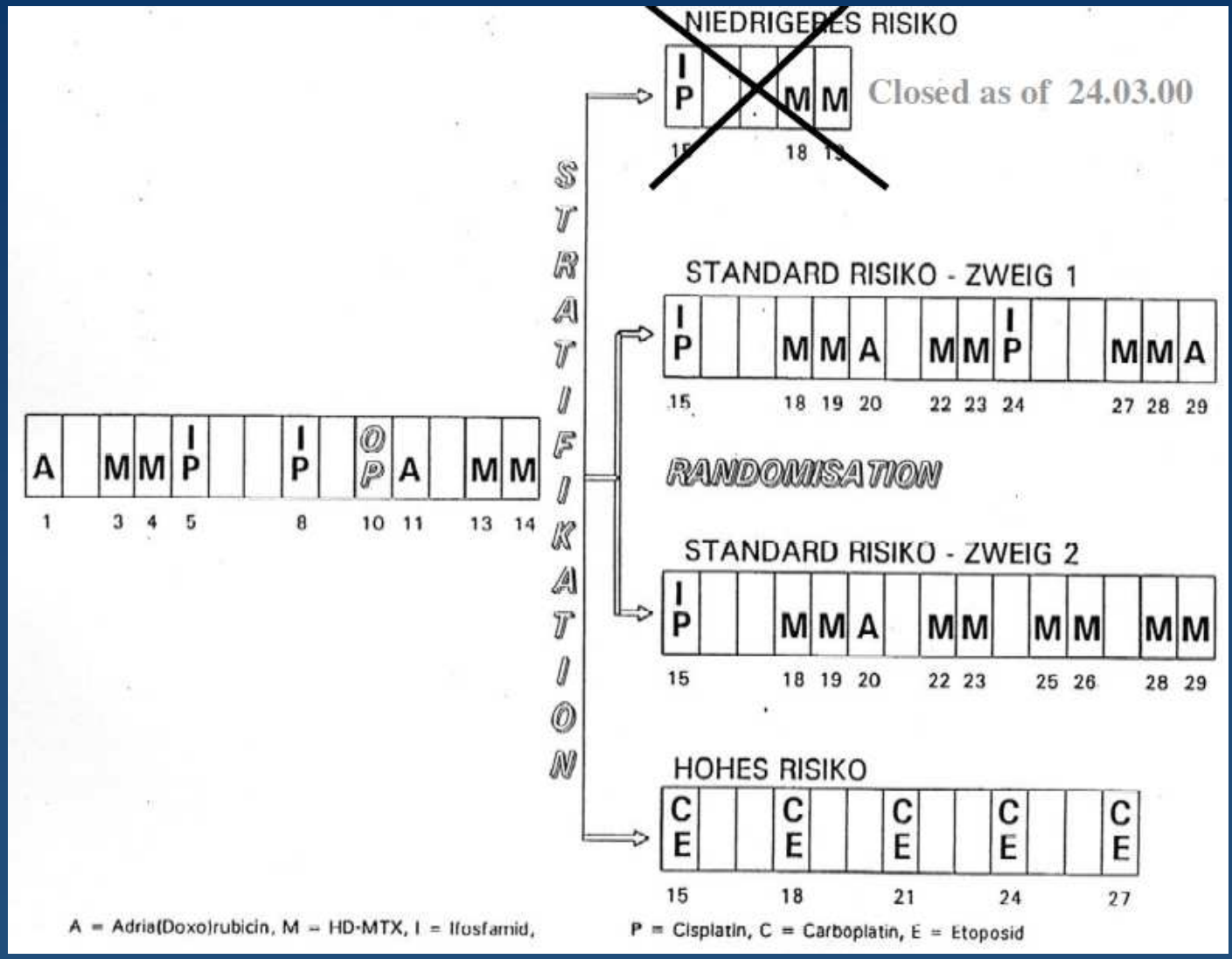
(a)



(b)



Osteosarcoma - **Multimodality treatment (COSS 96)**



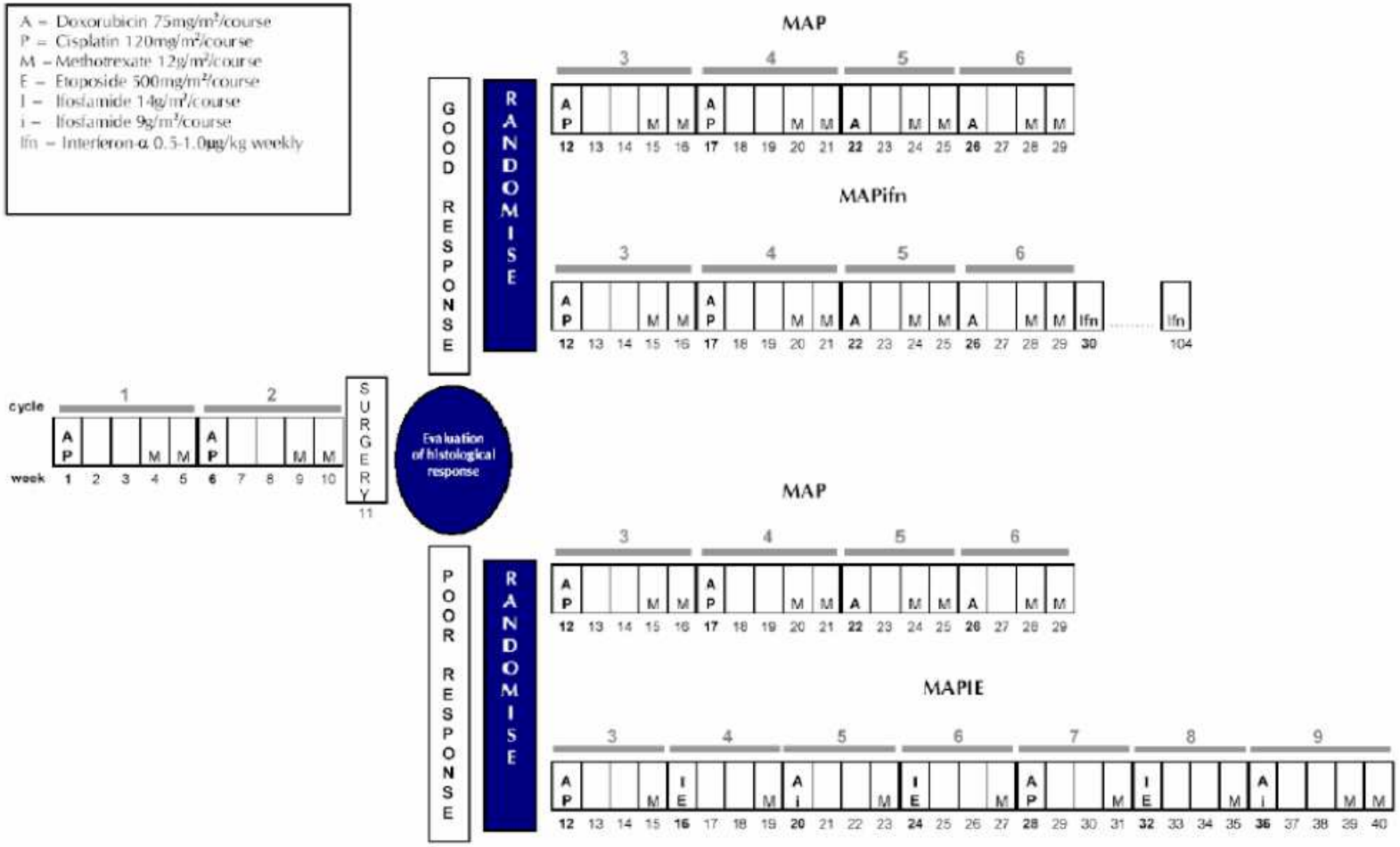
Osteosarcoma - **Multimodality treatment (EURAMOS-1)**

Age ≤ 40 years

Patients must fulfill the following criteria for registration into the trial:

1. Histological evidence of high grade osteosarcoma of the extremity or axial skeleton including those arising as second malignancies
2. Resectable disease (defined as disease that is amenable or may become amenable to complete and potentially curative resection. Referral to a recognized specialist center may be appropriate)
3. Age ≤ 40 years at date of diagnostic biopsy
4. Registration within 30 days of diagnostic biopsy

Osteosarcoma - **Multimodality treatment (EURAMOS-1)**



Note: Surgery for metastases should take place between weeks 11-20. See section 9.2.2.5

Osteosarcoma - **Multimodality treatment (EURO-B.O.S.S.)**

Age > 40 years

Cooperative Osteosarkomstudiengruppe

COSS

in Zusammenarbeit mit

Italian Sarcoma Group (ISG)
Scandinavian Sarcoma Group (SSG)

EURO-B.O.S.S

EUROpean Bone Over 40 Sarcoma Study

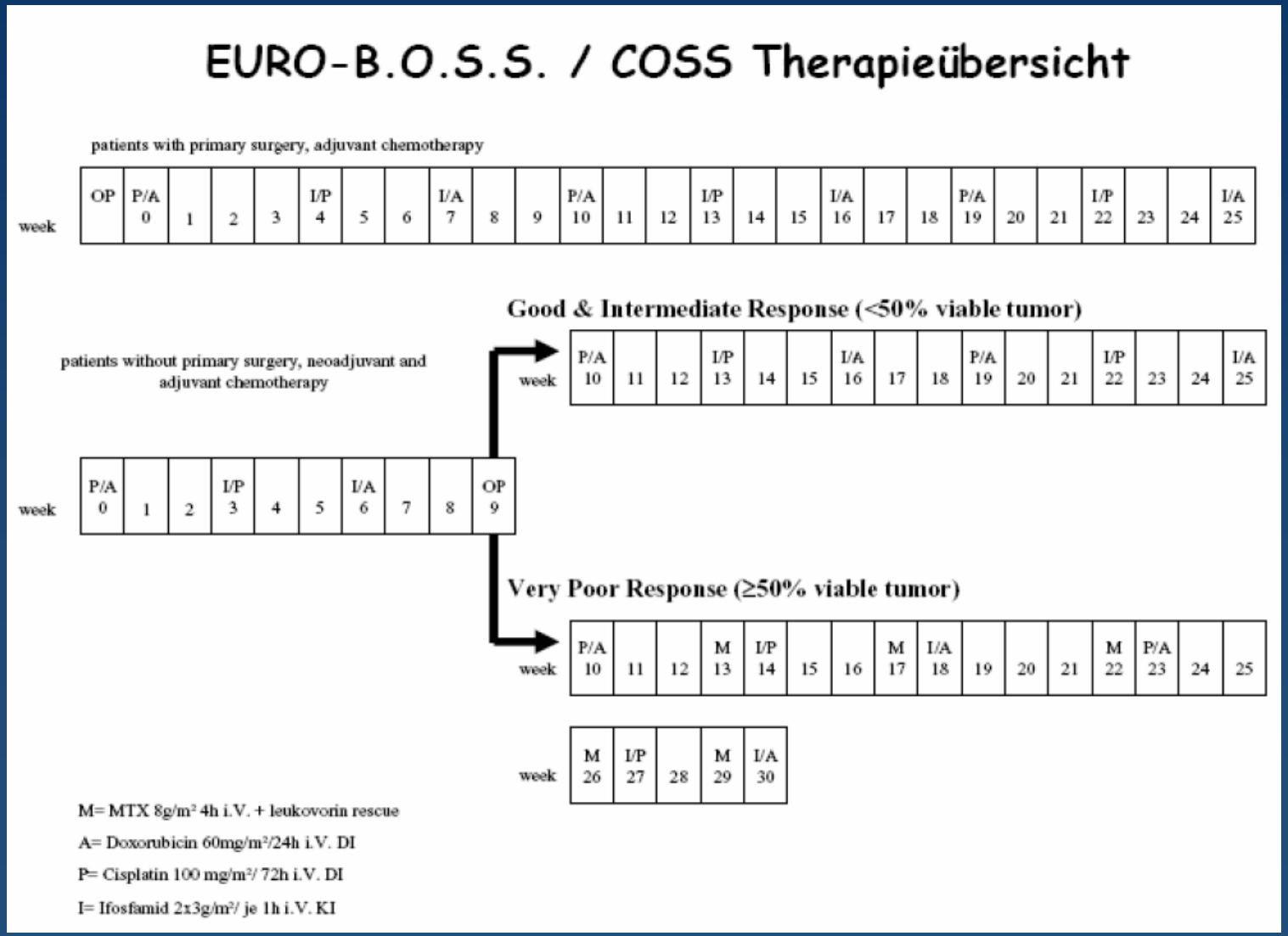
CRITERIA FOR ELIGIBILITY

1. Histologically proven diagnosis of high-grade sarcoma of bone of any site.

2. Histologic types: osteosarcoma (high-grade surface, central primary and secondary), fibrosarcoma, malignant fibrous histiocytoma, leiomyosarcoma, dedifferentiated chondrosarcoma, angiosarcoma.

3. Age: 41 - 65

Osteosarcoma - **Multimodality treatment (EURO-B.O.S.S.)**

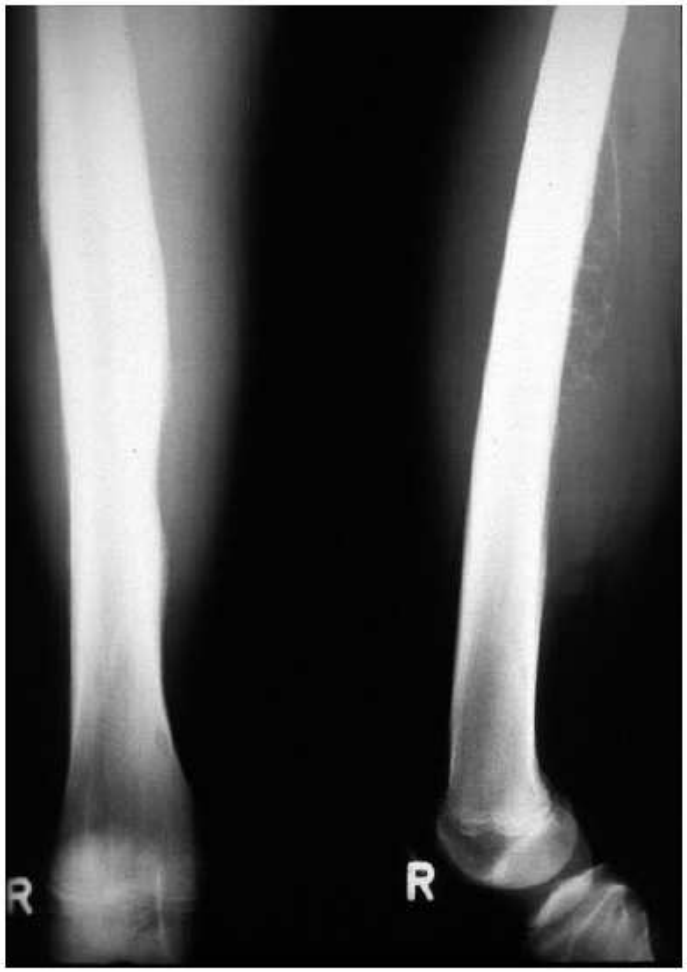


Osteosarcoma - **Summary**

- Multimodality treatment including surgery, radiotherapy and chemotherapy is essential.
- Poor histological response translates into a worse prognosis.
- Initial treatment intensity is important.
- Most relapses occur early in the course of the disease.
- Osteosarcoma relapses are difficult to treat and show a worse prognosis.
- Possible chemotherapeutic treatments for relapse include carboplatin, etoposide or high-dose ifosfamide.

Ewing sarcoma - **X-ray presentation**

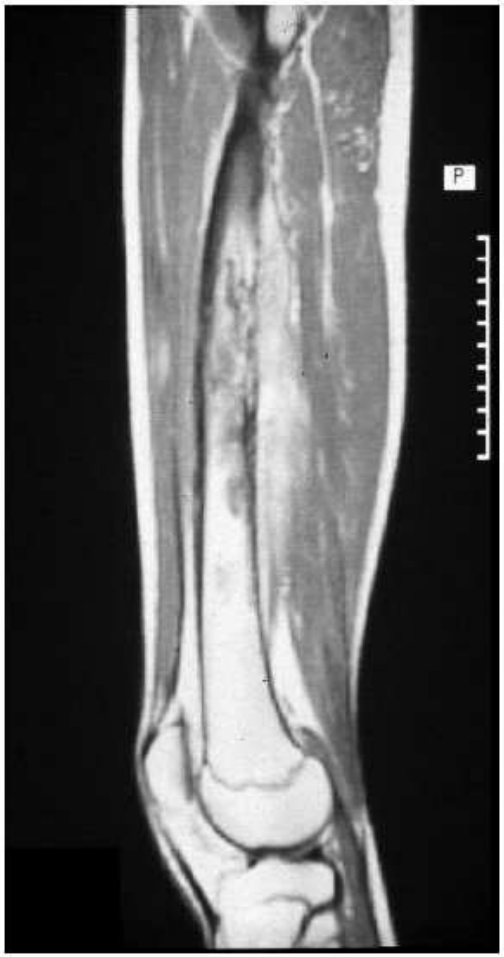
Diaphyseal tumour



Periosteal lamellation (circular)

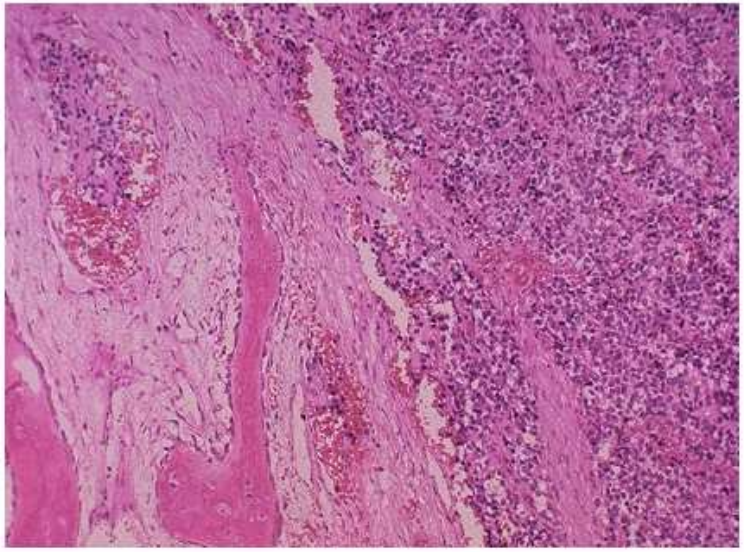
Massive swelling of soft tissue

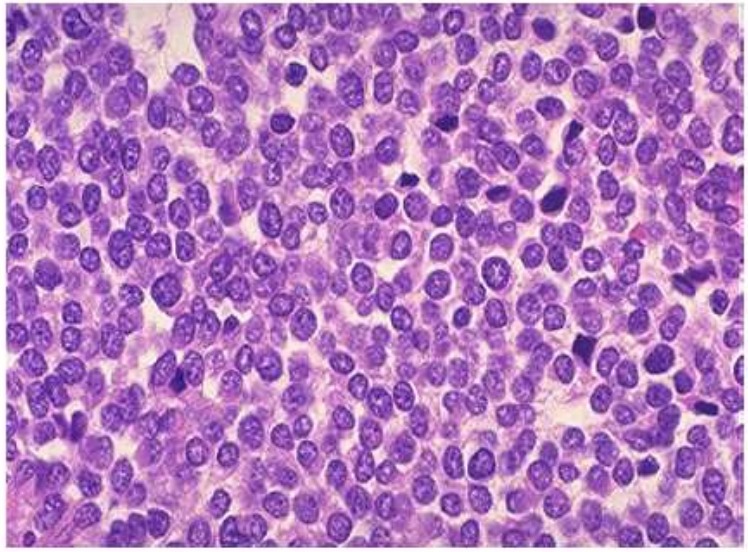
Ewing sarcoma - **MRI presentation**



- Intraossous extension
- Soft tissue extension
- Topography
- Skip lesions?

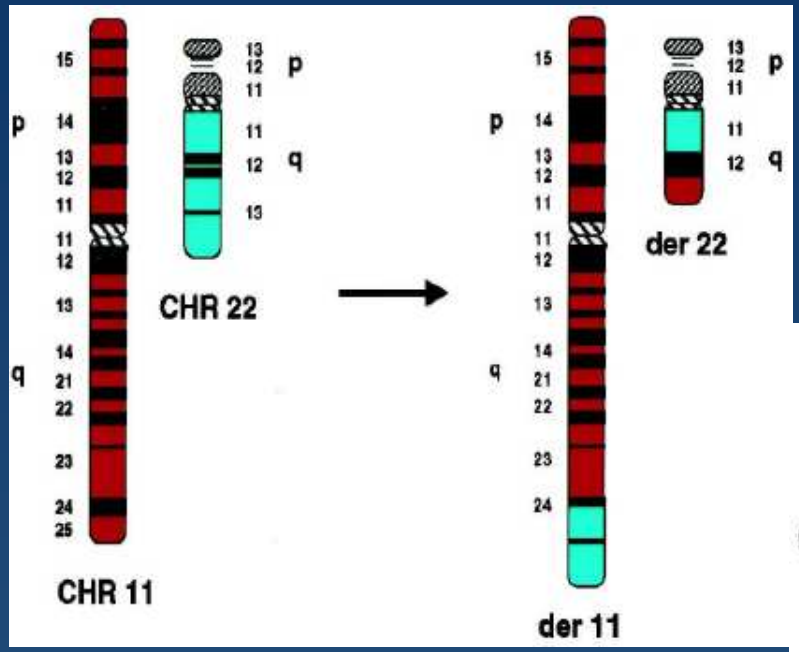
Ewing sarcoma - **Histology**



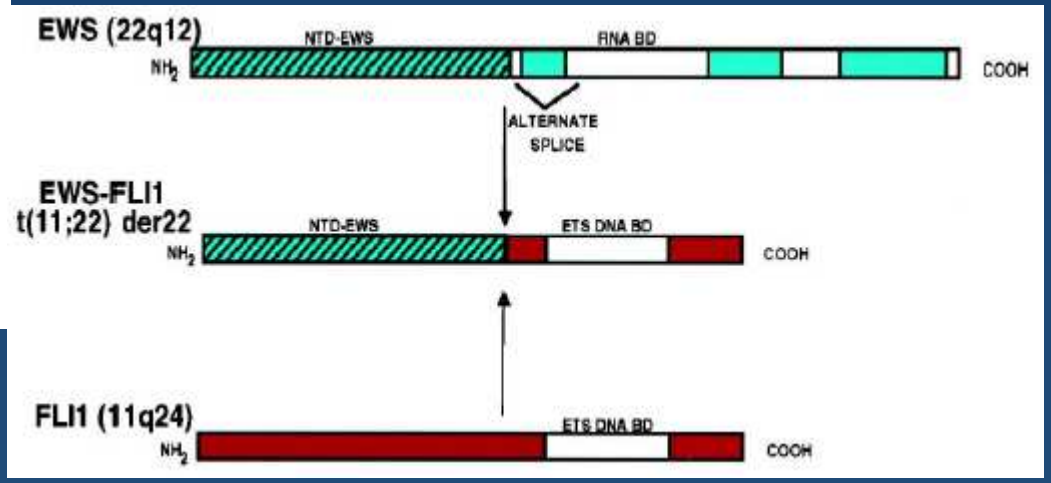


- malignant cell population
- infiltrating growth
- PAS positive (glycogen)
- CD99/Mic2 positive
- -/+ neuronal differentiation (ES -> atyp. ES -> PNET)
- small blue round cell
- some mitoses

Ewing sarcoma - **EWS-FLI1: t(11;22)(q24;q12)**

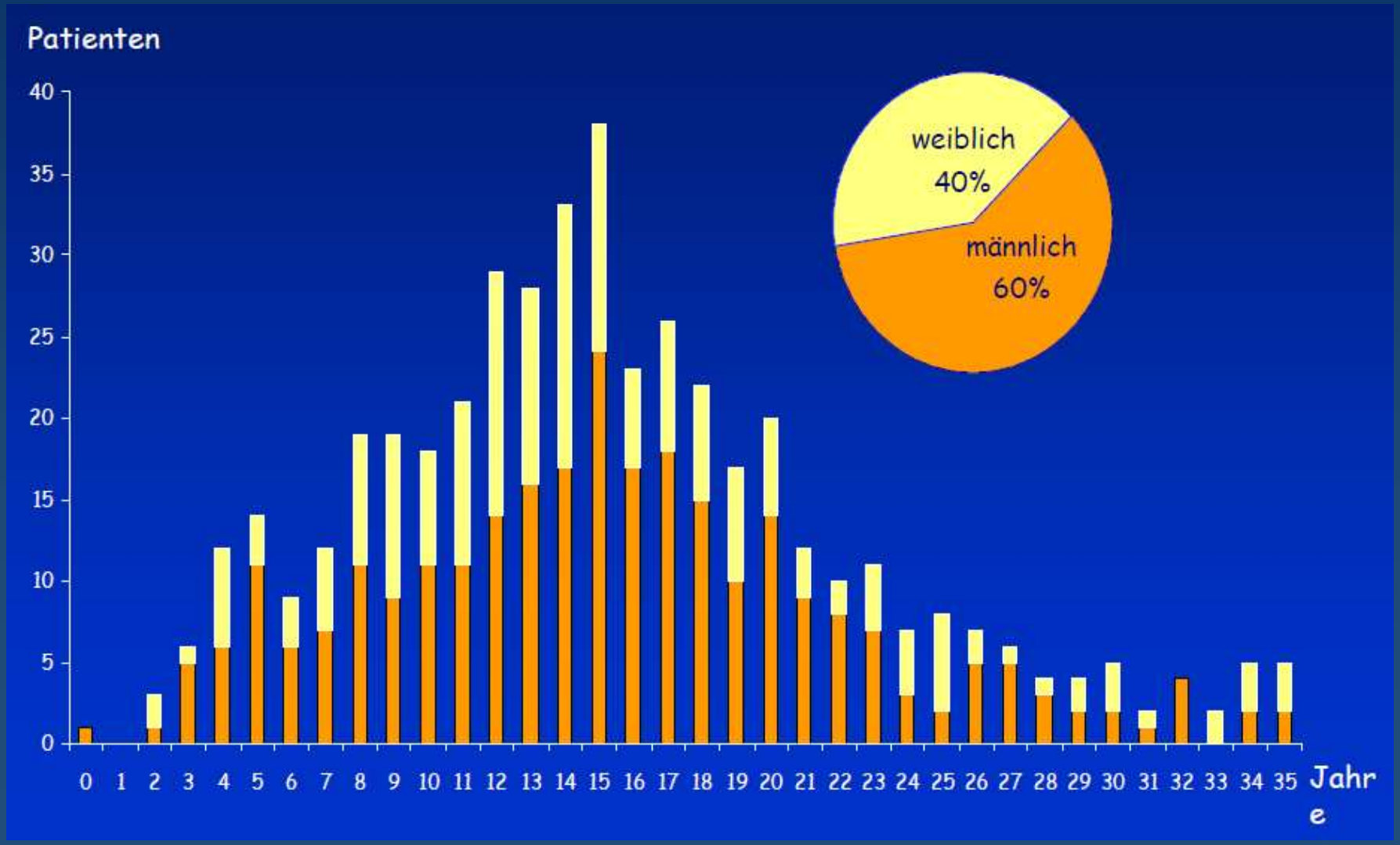


Molecular biology of the Ewing‘s sarcoma / primitive neuroectodermal tumor family



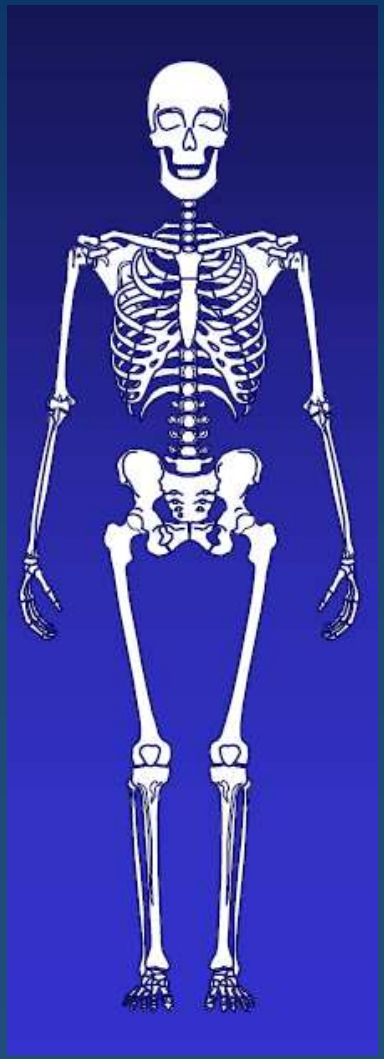
De Alava et al. J Clin Oncol 2000; 18: 204-213

Ewing sarcoma - **Epidemiology**



Ewing sarcoma - **Localizations**

Head	**3 %**
Clavicle	**1 %**
Scapula	**4 %**
Rib	**9 %**
Sternum	**< 1 %**
Spinal column	**6 %**
Pelvis	**23 %**



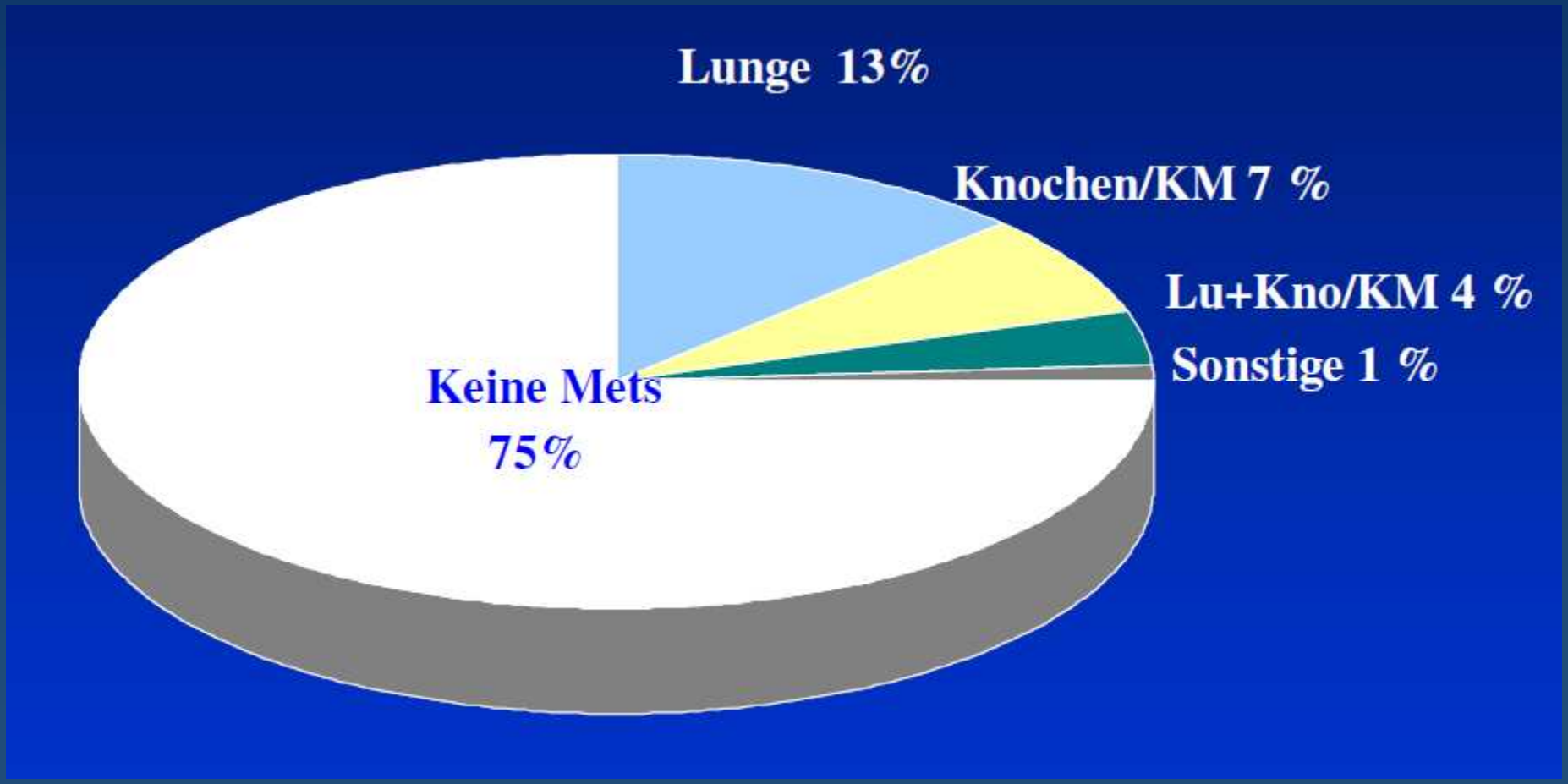
Soft tissue	**< 1 %**
Humerus	**5 %**
Ulna	**1 %**
Radius	**1 %**
Hand	**1 %**
Femur	**22 %**
Fibula	**10 %**
Tibia	**10 %**
Foot	**3 %**

Ewing sarcoma - Diagnosis

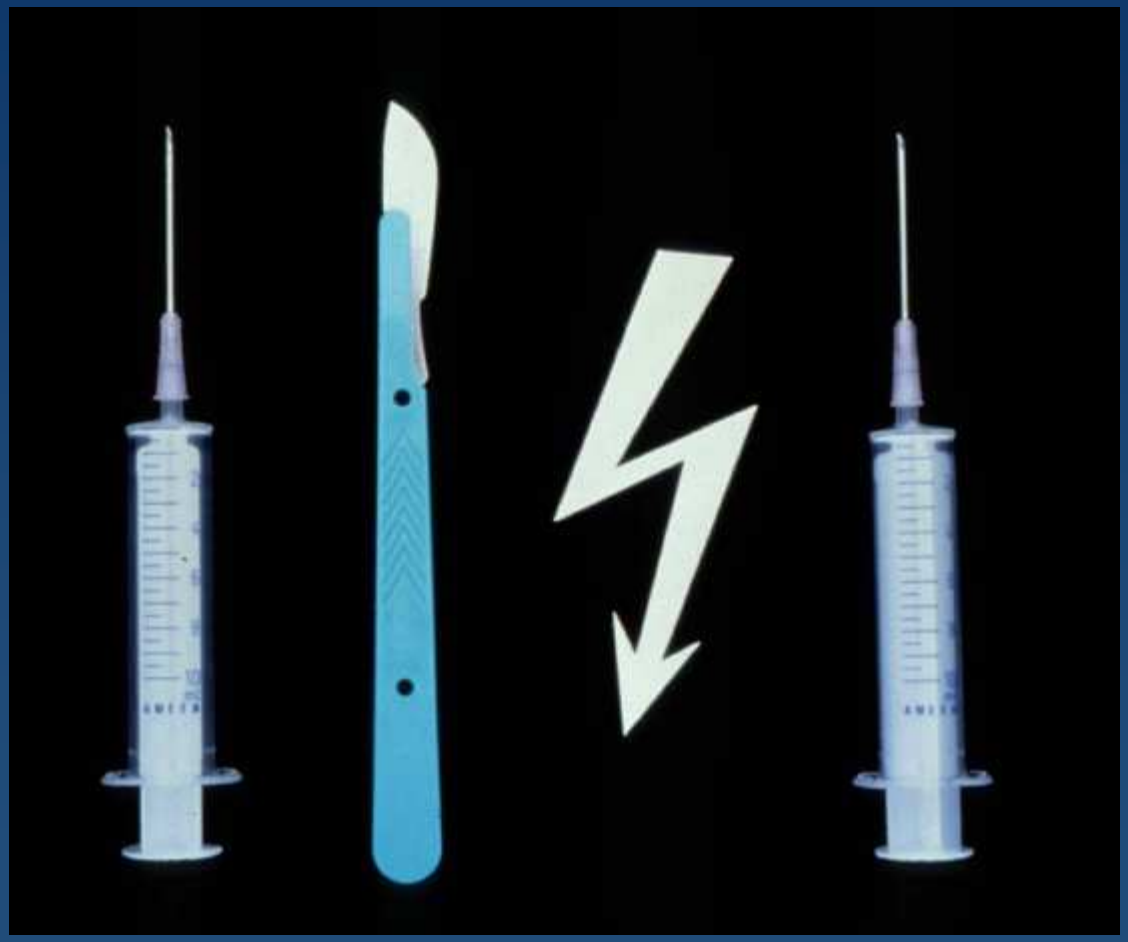
Staging procedure for detection of possible metastases comprises:

- Whole body 99mTc szintigraphy of the skeleton
- CT of the chest
- Bone marrow aspiration is essential to exclude an infiltration

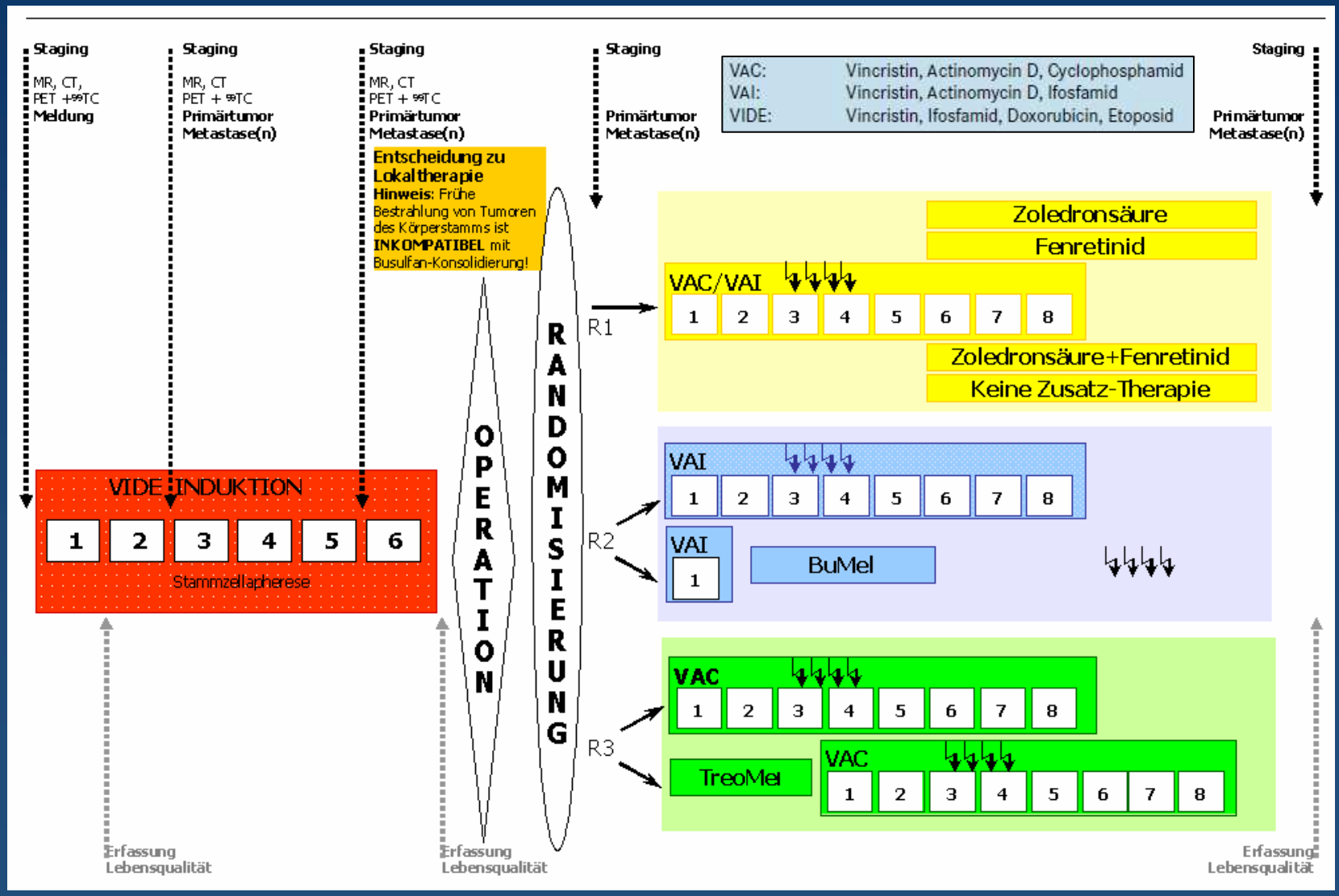
Ewing sarcoma - **Primary metastases**



Ewing sarcoma - **Multimodality treatment**



Ewing sarcoma - **Multimodality treatment (EWING-2008)**



Ewing sarcoma - **Summary**

- Multimodality treatment including surgery, radiotherapy and chemotherapy is essential.
- Poor histological response translates into a worse prognosis.
- Initial treatment intensity is important.
- Most relapses occur early in the course of the disease.
- Ewing sarcoma relapses show a worse prognosis.
- Possible chemotherapeutic treatments for relapse include topoisomerase inhibitors (etoposide, irinotecan, topotecan) and alkylating agents (ifosfamide, cyclophosphamide, temozolomide).

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Questions?