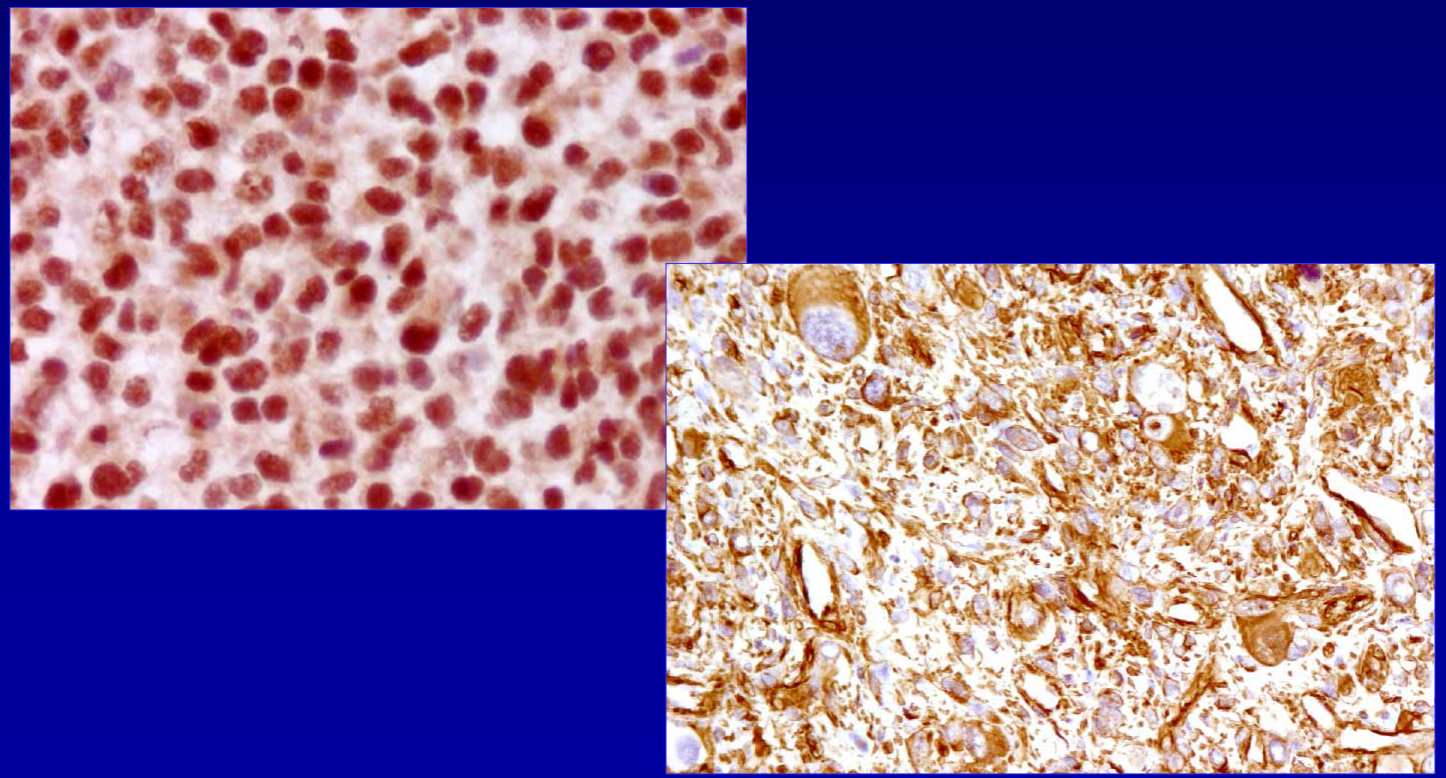
Immunohistochemistry of soft tissue tumors



Immunohistochemistry

- **Major advances :**
  - **→ antigen retrieval techniques (HIER)**
  - **→ sensitive detection systems**
  - **→ numerous antibodies of good quality**
- **Standardization :**
  - **→ automated immunostainers**
  - **→ quality assurance programs**
- **Impressive amount of new information :**
  - **→ 12 000 papers/year**
  - **→ internet (Pubmed, Immunoquery,…)**

Immunohistochemistry

- Future of IHC is promising
- Tissue microarray
- cDNA microarray

Immunohistochemistry of soft tissue tumors

- STT: several lines of differentiation
- Numerous pseudosarcomatous benign lesions
- Non-mesenchymal malignant tumors

Soft tissue tumors
Immunohistochemistry
Conditions of use

- Complementary to H and E
- Quality of technique
- Panel of markers
- Quality of interpretation

Basic panel of antibodies for soft tissue tumors

- Cytokeratin
- EMA

} Sarcomatoid carcinoma
Synovial sarcoma,...

- S100 protein

Nervous and melanocytic T

- Desmin
- Smooth muscle actin

} Muscle tumors
Myofibroblastic lesions

- CD34

Numerous tumors

Immunohistochemistry of soft tissue tumors
Basic panel

- AE1/AE3
- EMA
- S100 protein
- SMA
- Desmin
- CD34
- CD99
- CD31
- HMB45/Melan A
- CD20/CD3/CD30
- Chromogranin A

Immunohistochemistry of soft tissue tumors
New antibodies

- Myogenin
- H-caldesmon
- CD117 (c-kit)
- HHV8
- MDM2/CDK4
- CD163

Immunohistochemistry of soft tissue tumors
Unuseful antibodies

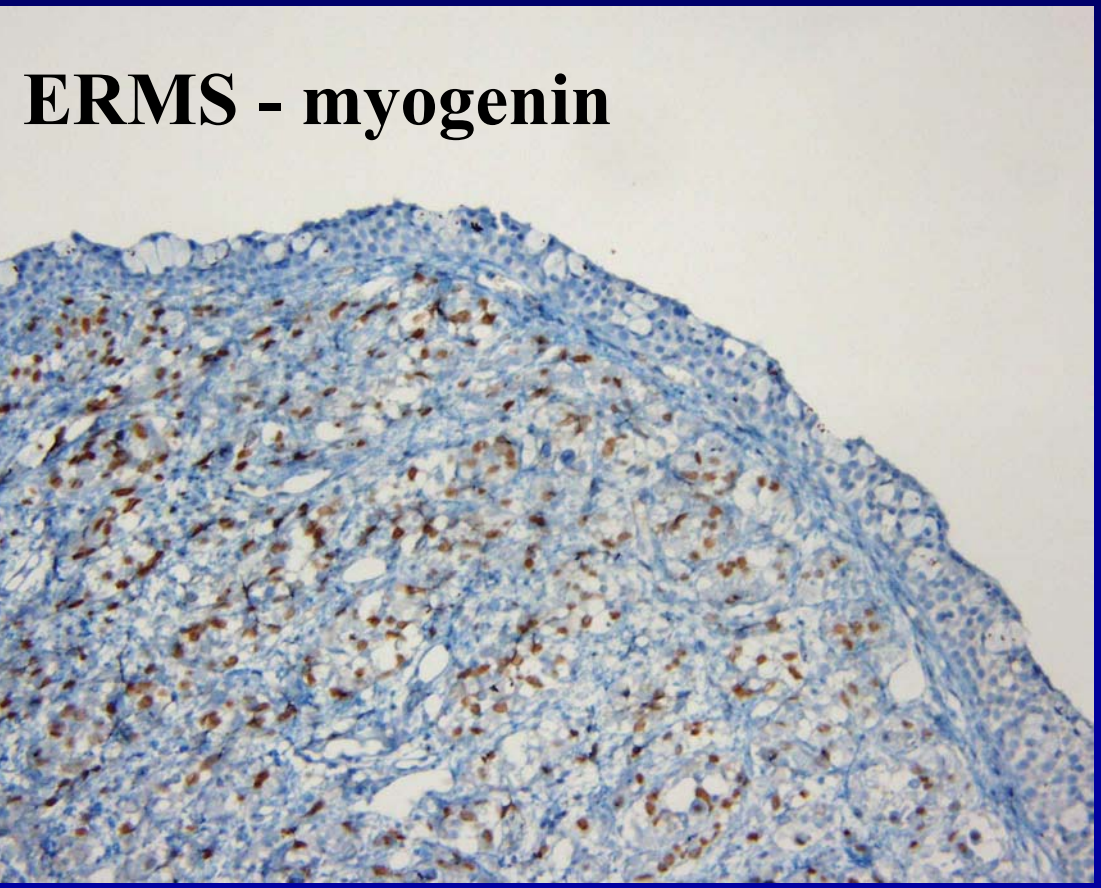
- Vimentin
- BCL2
- Antichymotrypsin
- Myoglobin
- NSE

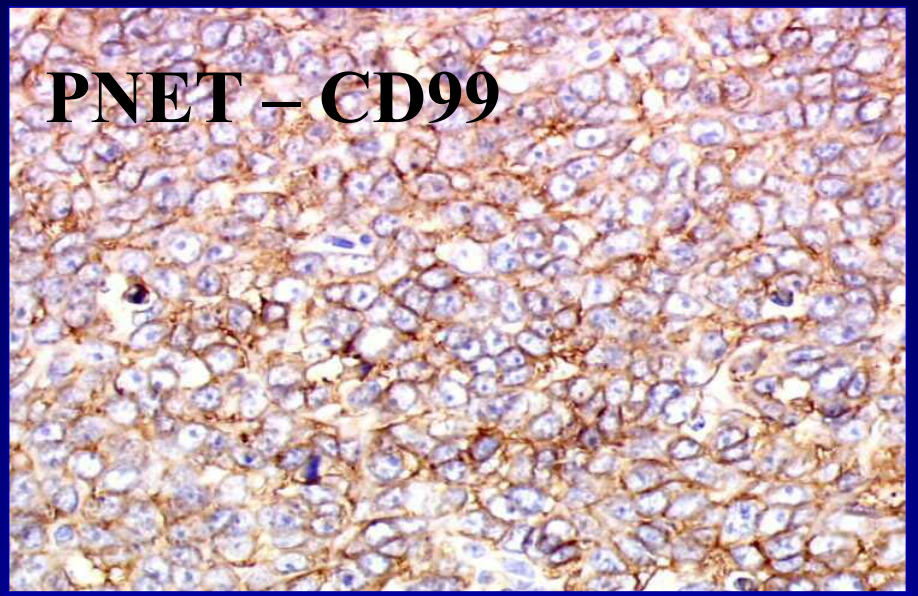
Soft tissue tumors
Immunohistochemistry
Interpretation

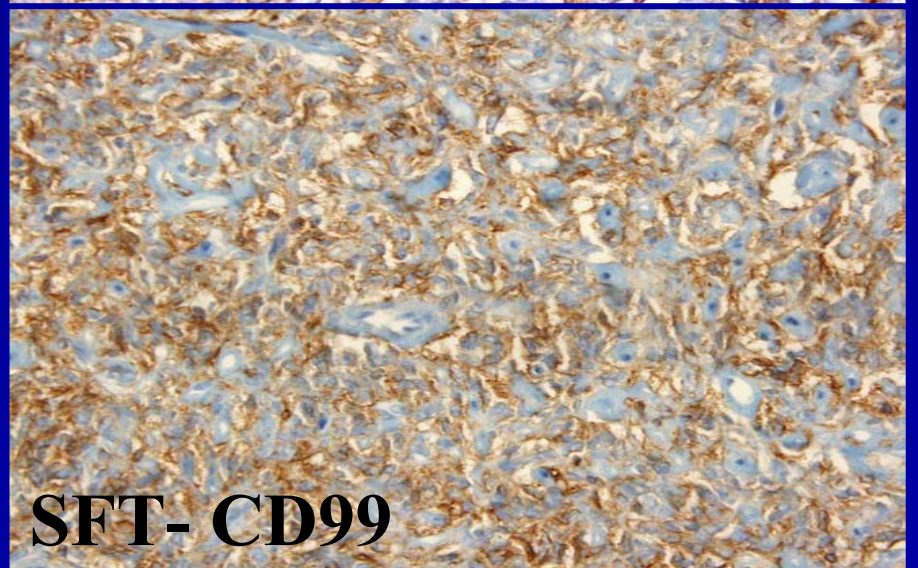
- Quality of technique
- Type of positivity
- Expected positivities
- Unexpected positivities

Soft tissue tumors
Immunohistochemistry

Type of positivity







Poorly specific markers

- CD34
- CD99
- EMA
- S100 protein
- SMA

Soft tissue tumors which are CD34 positive

- Vascular tumors
- DFSP
- Solitary fibrous tumor
- GIST
- Spindle cell/pleomorphic lipomas
- Some nervous tumors
- Epithelioid sarcoma

Soft tissue tumors which are CD99 positive

- PNET
- Synovial sarcoma
- Solitary fibrous tumor
- Mesenchymal chondrosarcoma
- Neuroendocrine carcinoma
- Lymphoblastic lymphoma
- Alveolar rhabdomyosarcoma

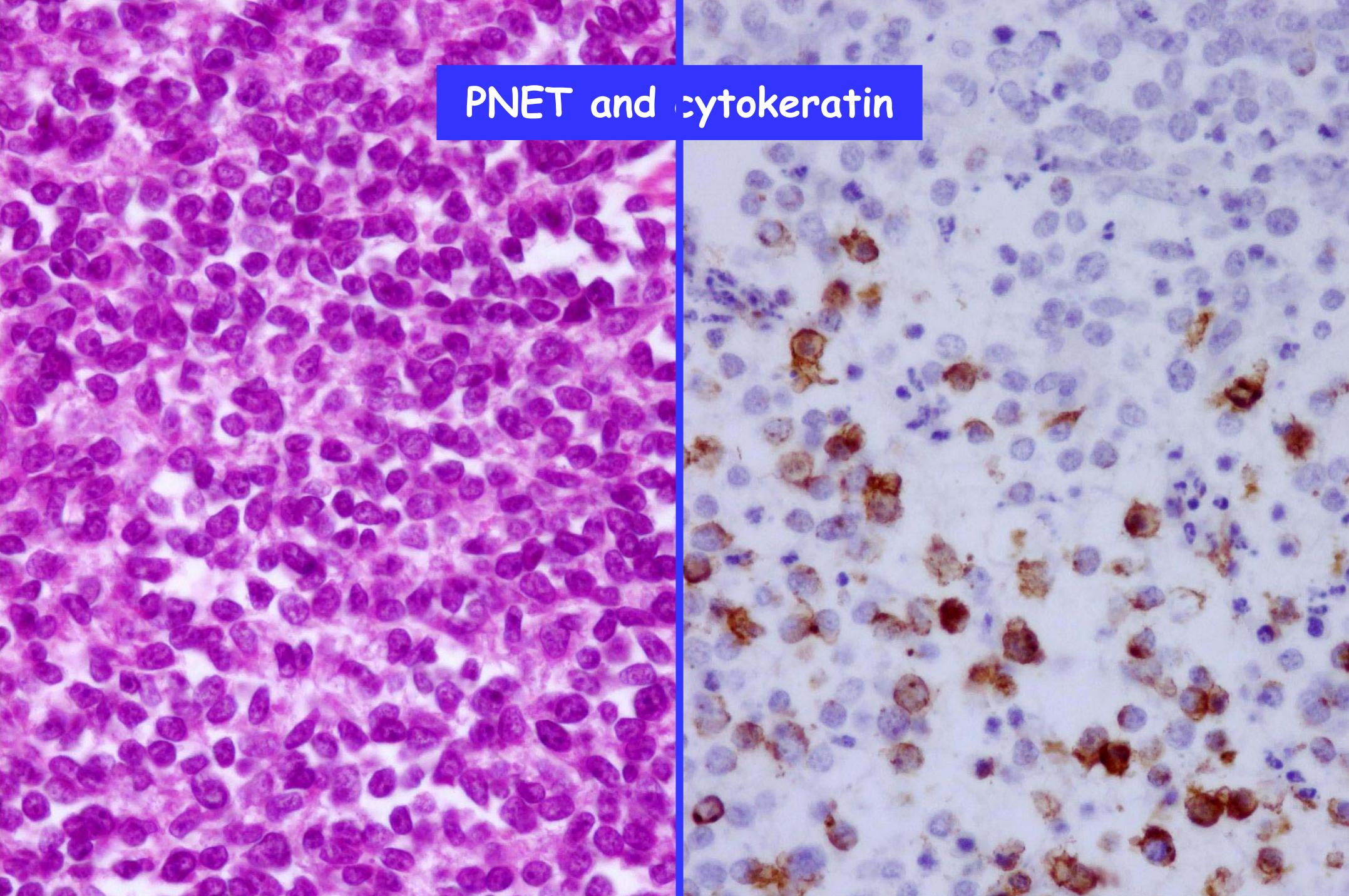
Markers with unexpected positivities

- Cytokeratin
- Desmin
- CD31
- CD117
- Fli-1….

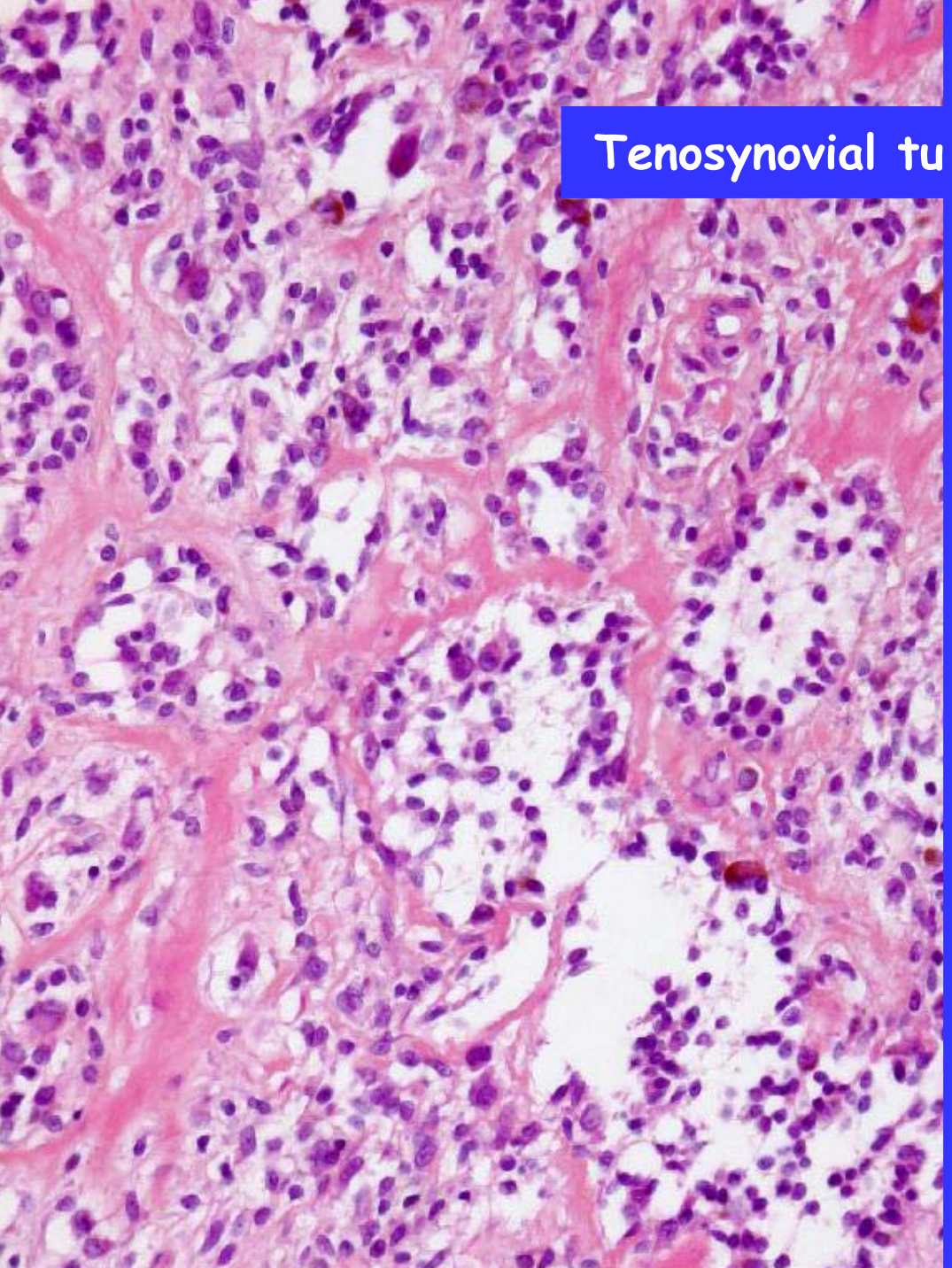
Unexpected positivity for cytokeratin

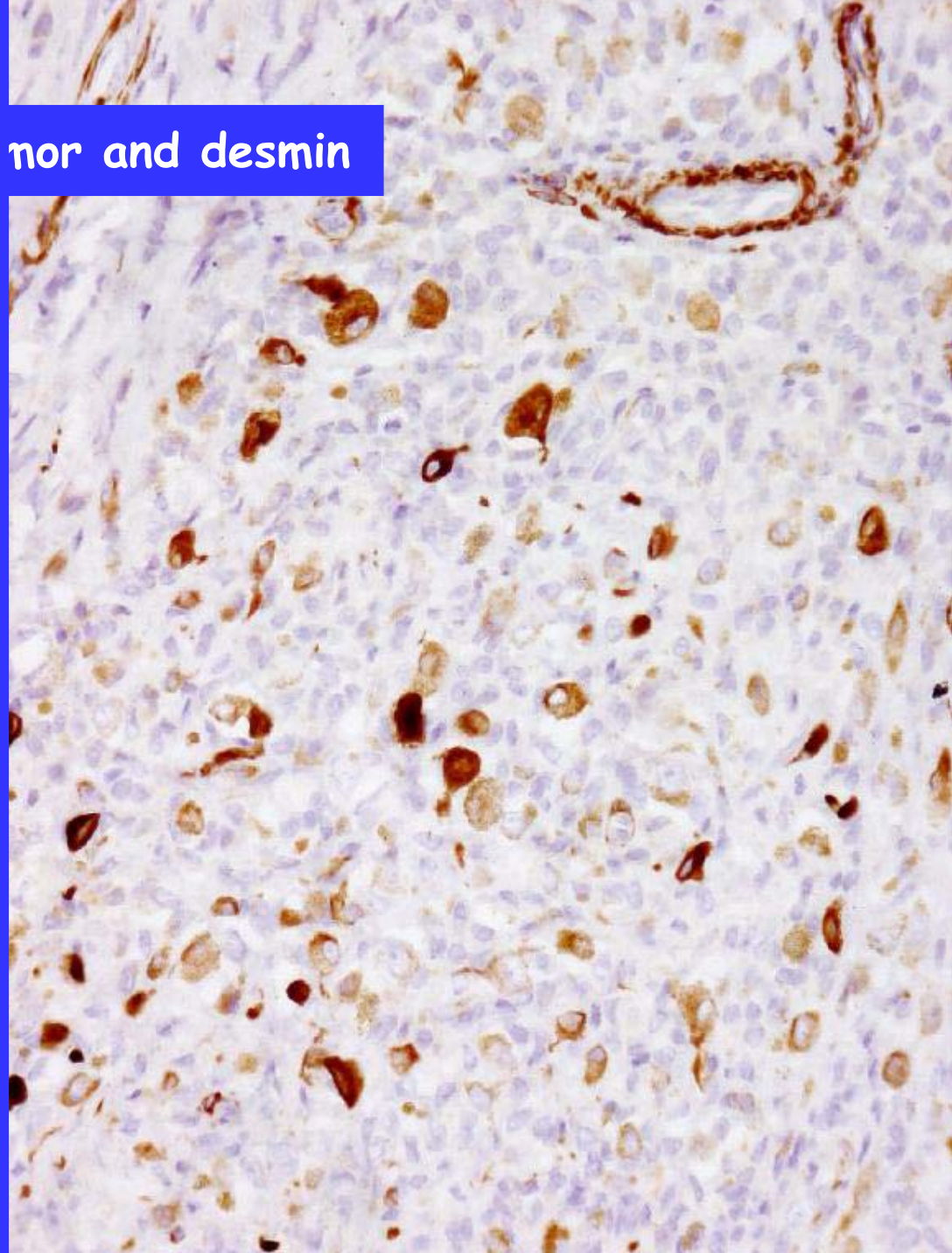
- Leiomyosarcoma
- Rhabdomyosarcoma
- PNET
- Epithelioid vascular tumors
- Melanoma

PNET and cytokeratin

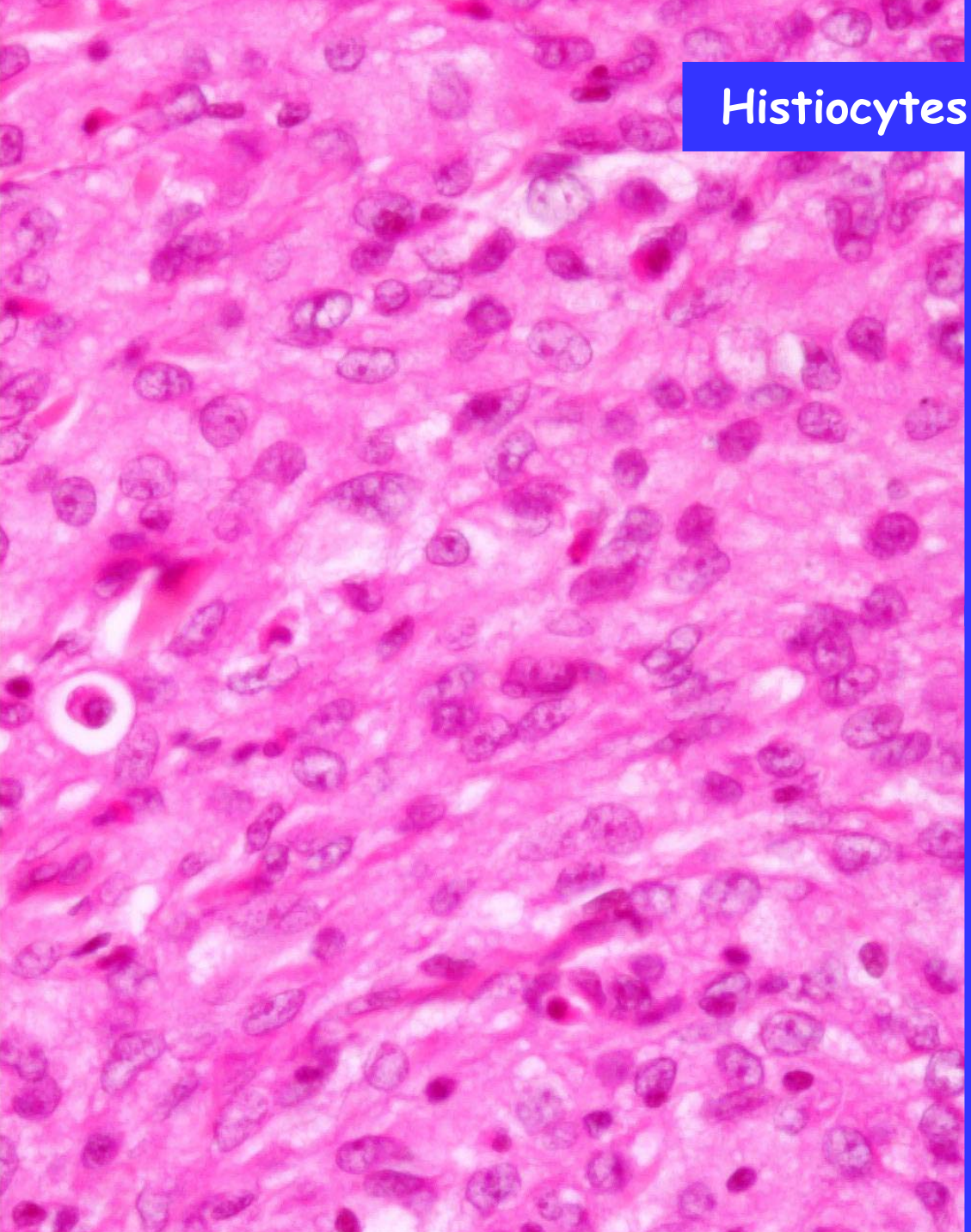


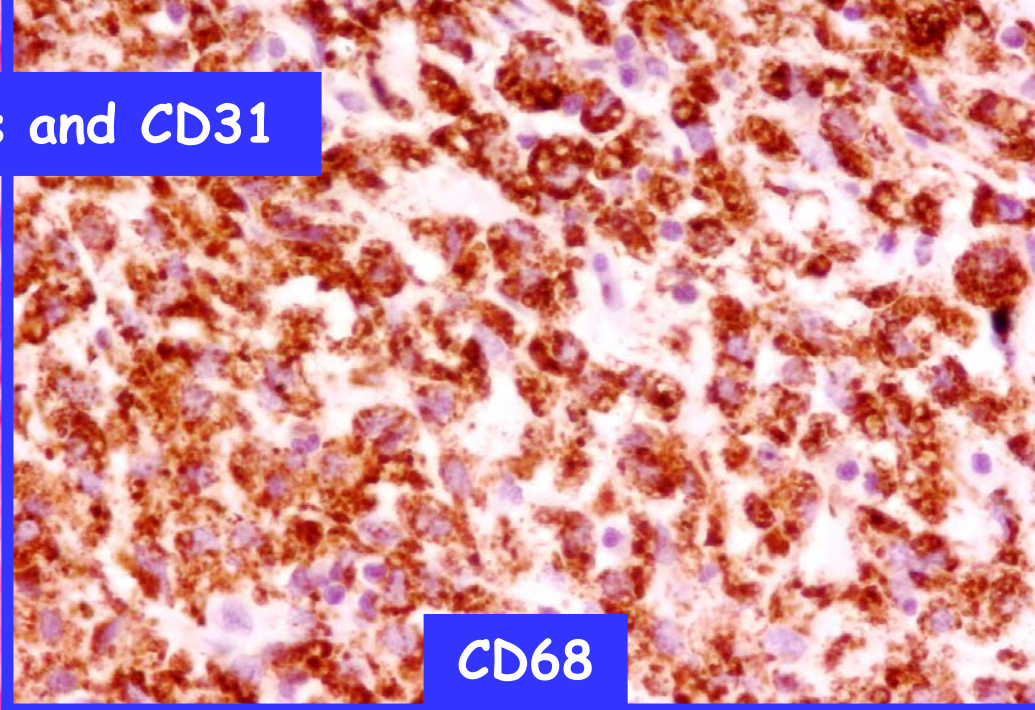
Tenosynovial tumor and desmin



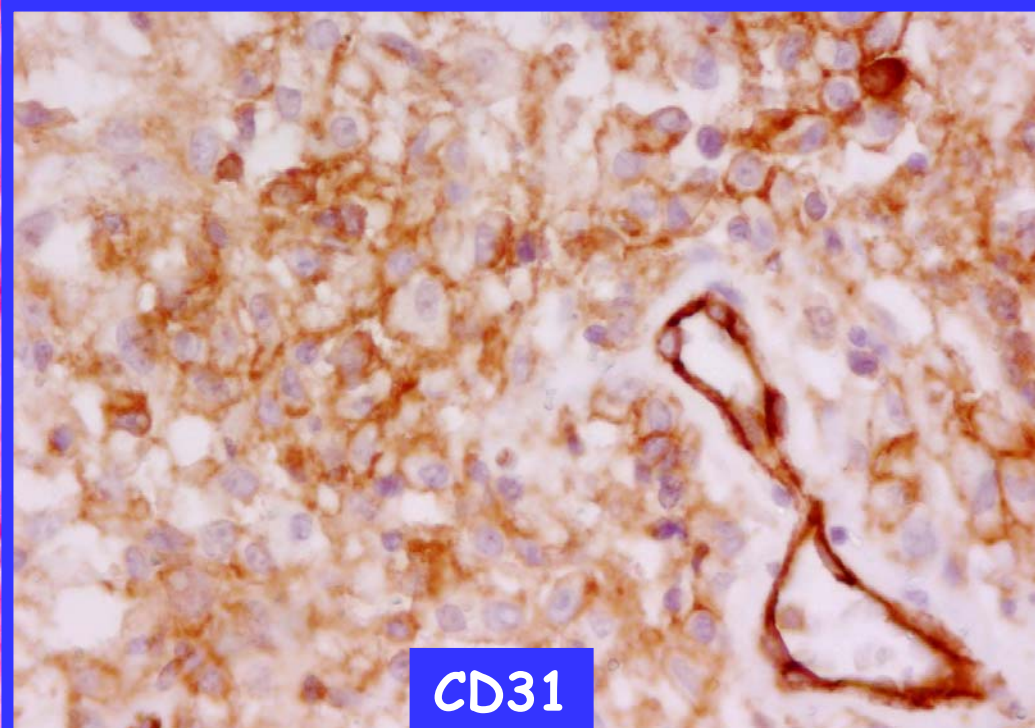


Histiocytes and CD31





CD68



CD31

Soft tissue tumors
Immunohistochemistry
Practical interests

- **Identification of a benign lesion**
- **Nature of an undifferentiated malignant tumor**
- **Classification of a sarcoma**

Soft tissue tumors
Immunohistochemistry
Benign vs malignant

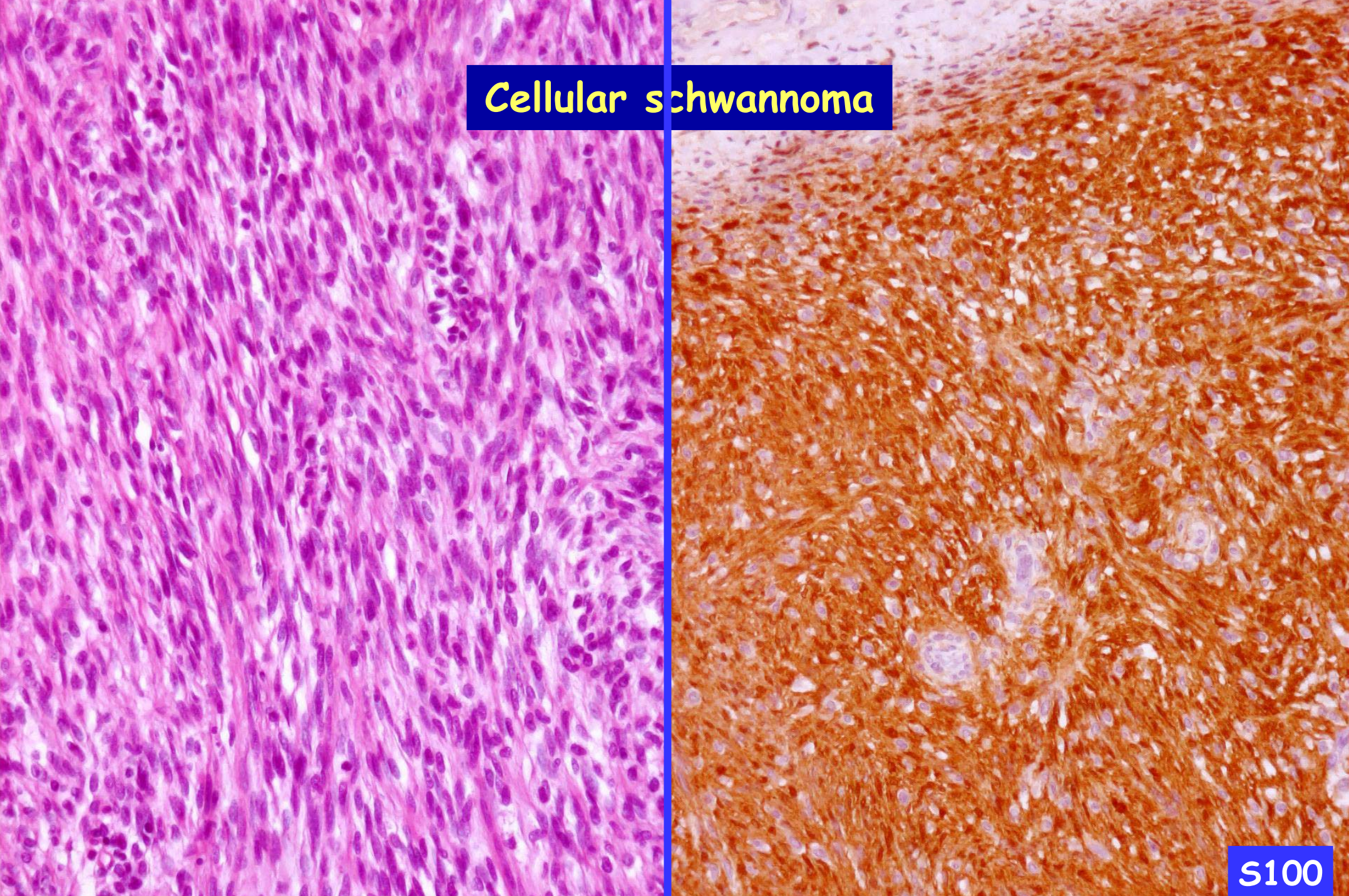
- **Major and frequent problem**
- **Solution : - clinical context**
  - H and E
- **Usefulness of IHC**

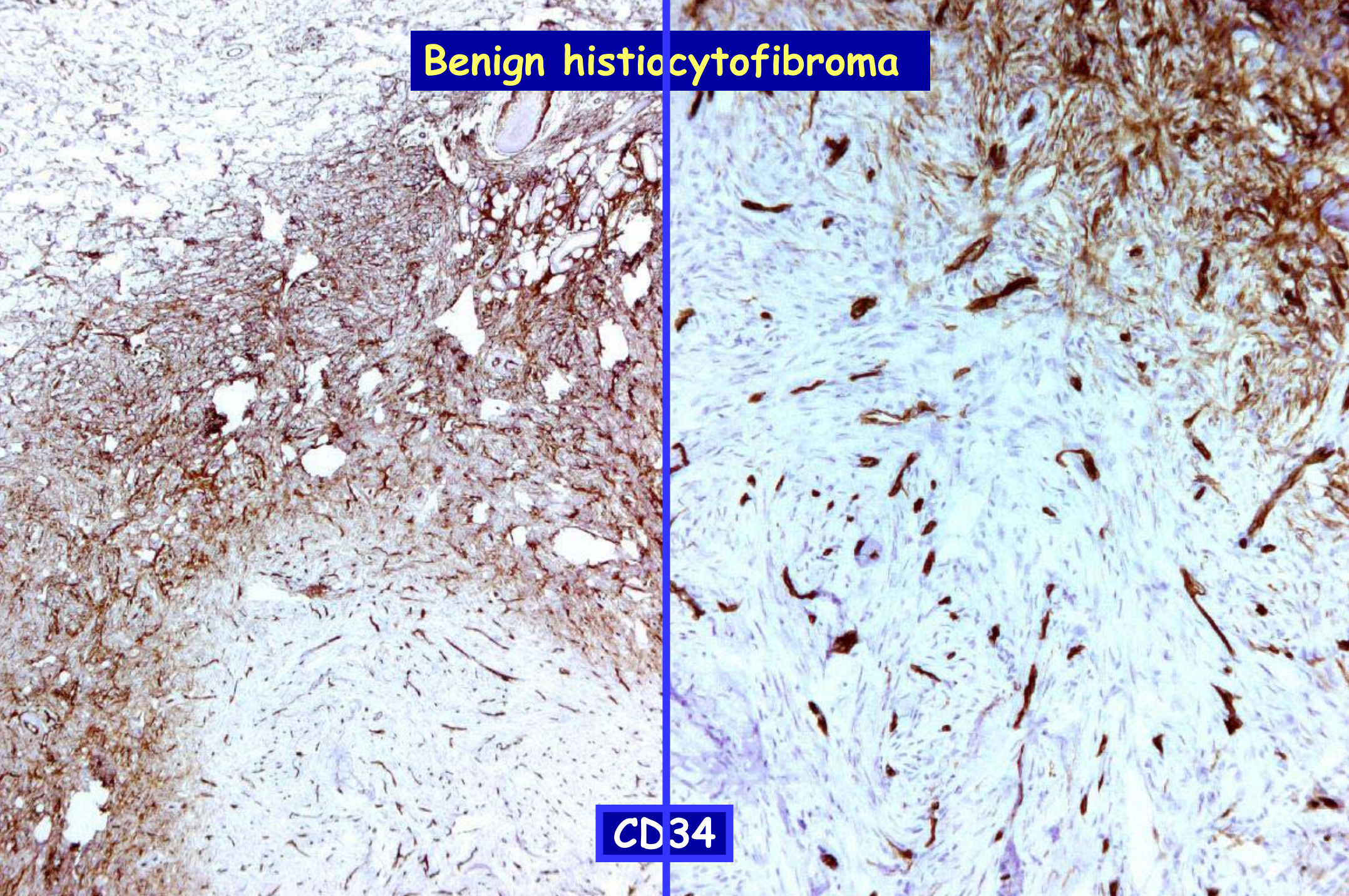
Soft tissue tumors
Immunohistochemistry
Rare/atypical benign lesions

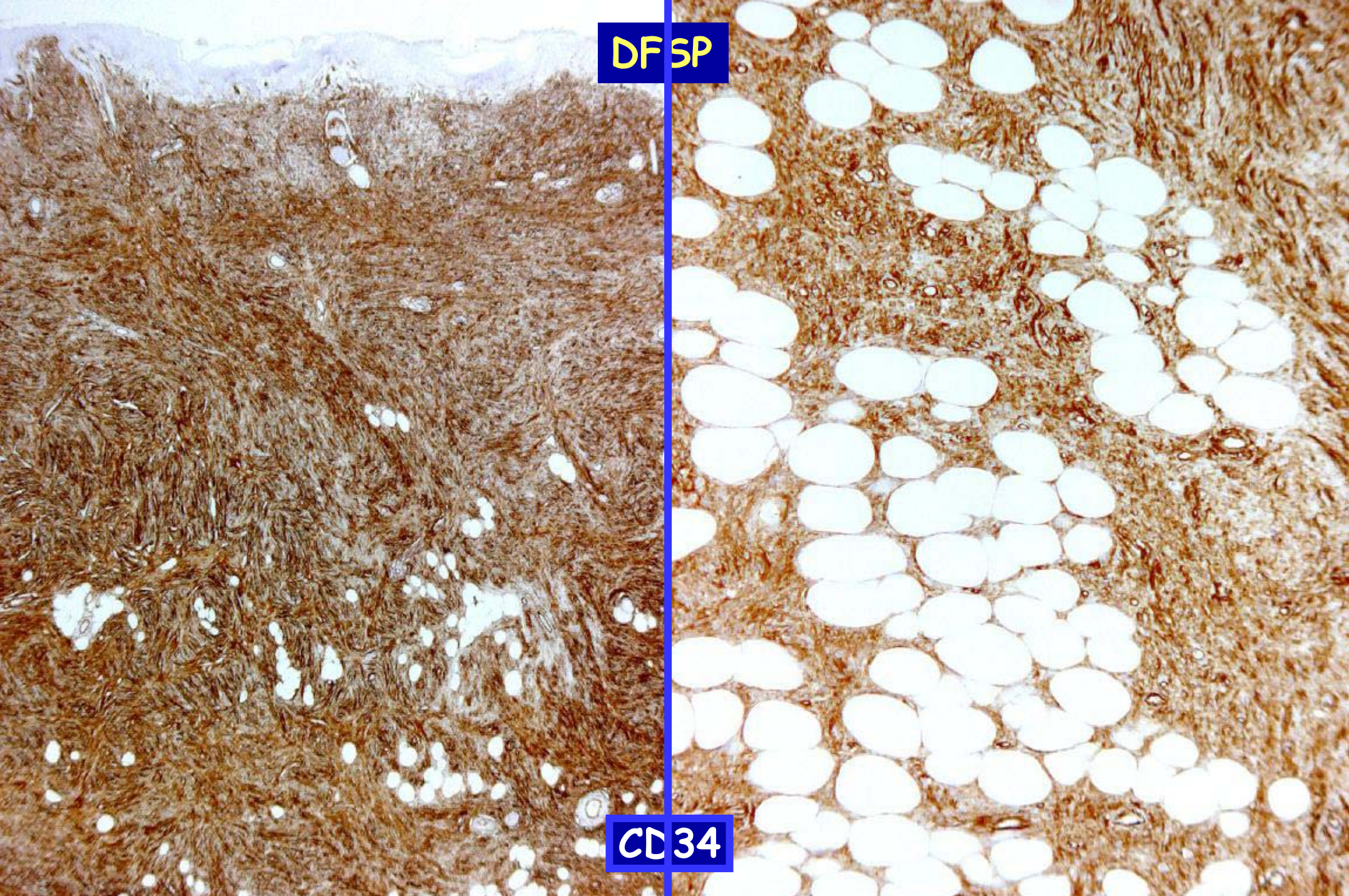
- **Nerve sheath tumors**
- **Histiocytic lesions**
- **Rare tumors : (paraganglioma, glomus T, SFT, angiomyolipoma, myoepithelioma)**
- **Myofibroblastic lesions**

Atypical/rare benign nerve sheath tumors - *S100 protein*

- Ancient schwannoma
- Cellular shwannoma
- Myxoid neurofibroma
- Neurofibroma with nuclear atypia
- Diffuse neurofibroma
- Granular cell tumor

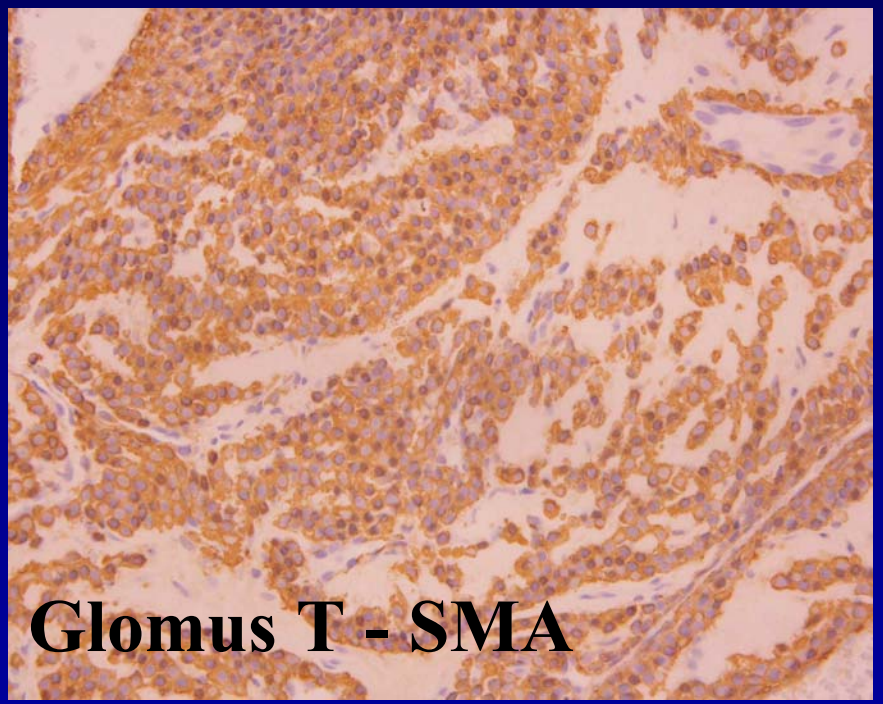

Cellular schwannoma
S100


Benign histiocytofibroma
CD34


DFSP
CD34

Rare benign tumors

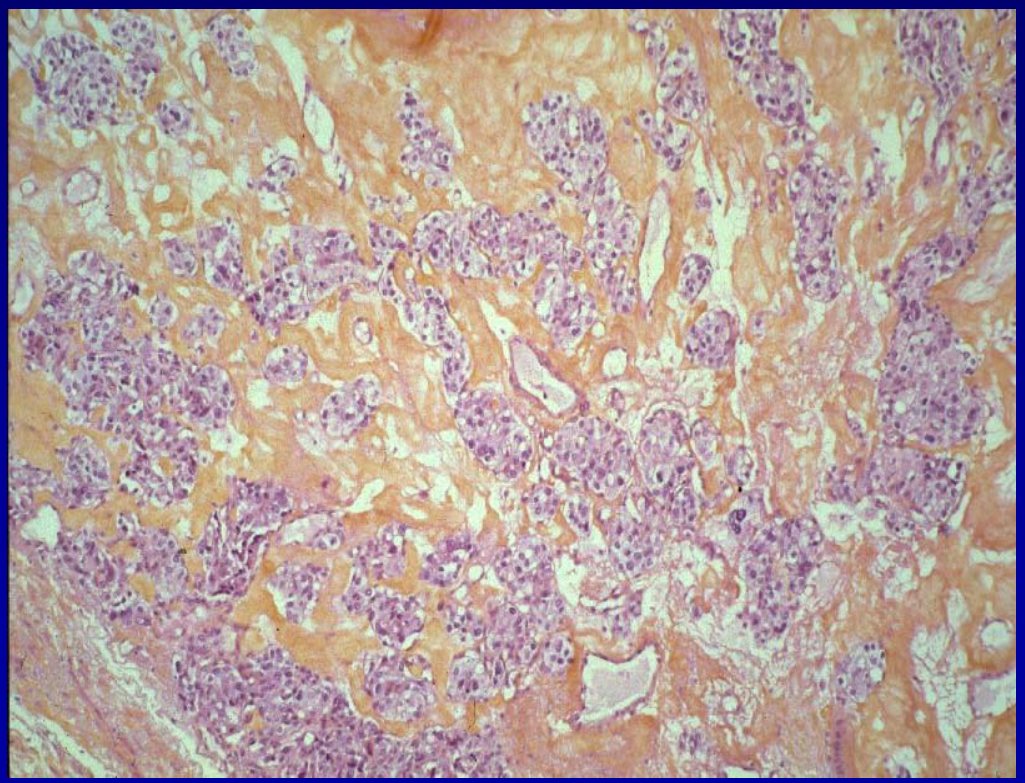
- **Paraganglioma :**
  - chromogranin A, S100+
- **Glomus T :**
  - SMA, caldesmon +
- **SFT :**
  - CD 34 +
- **Myoepithelioma :**
  - AE1/AE3, PS100+
- **Perineurioma :**
  - EMA+

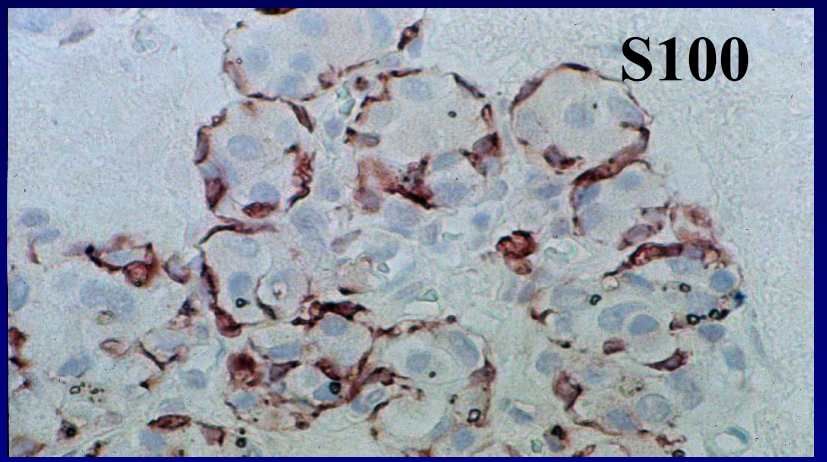


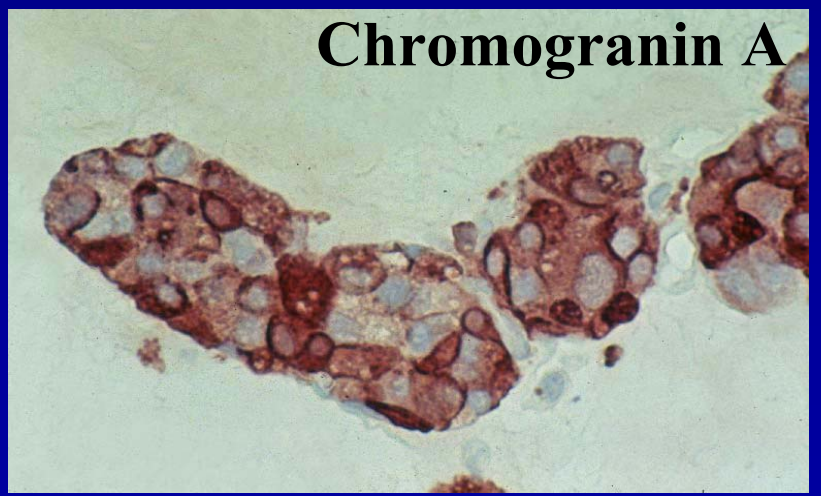
Glomus T - SMA

Rare benign tumors

- **Paraganglioma : S100 and Chromogranin A +**







Soft tissue tumors
Immunohistochemistry
Practical interests

- Identification of a benign lesion
- Nature of an undifferentiated malignant tumor
- Classification of a sarcoma

Non-mesenchymal malignant tumors

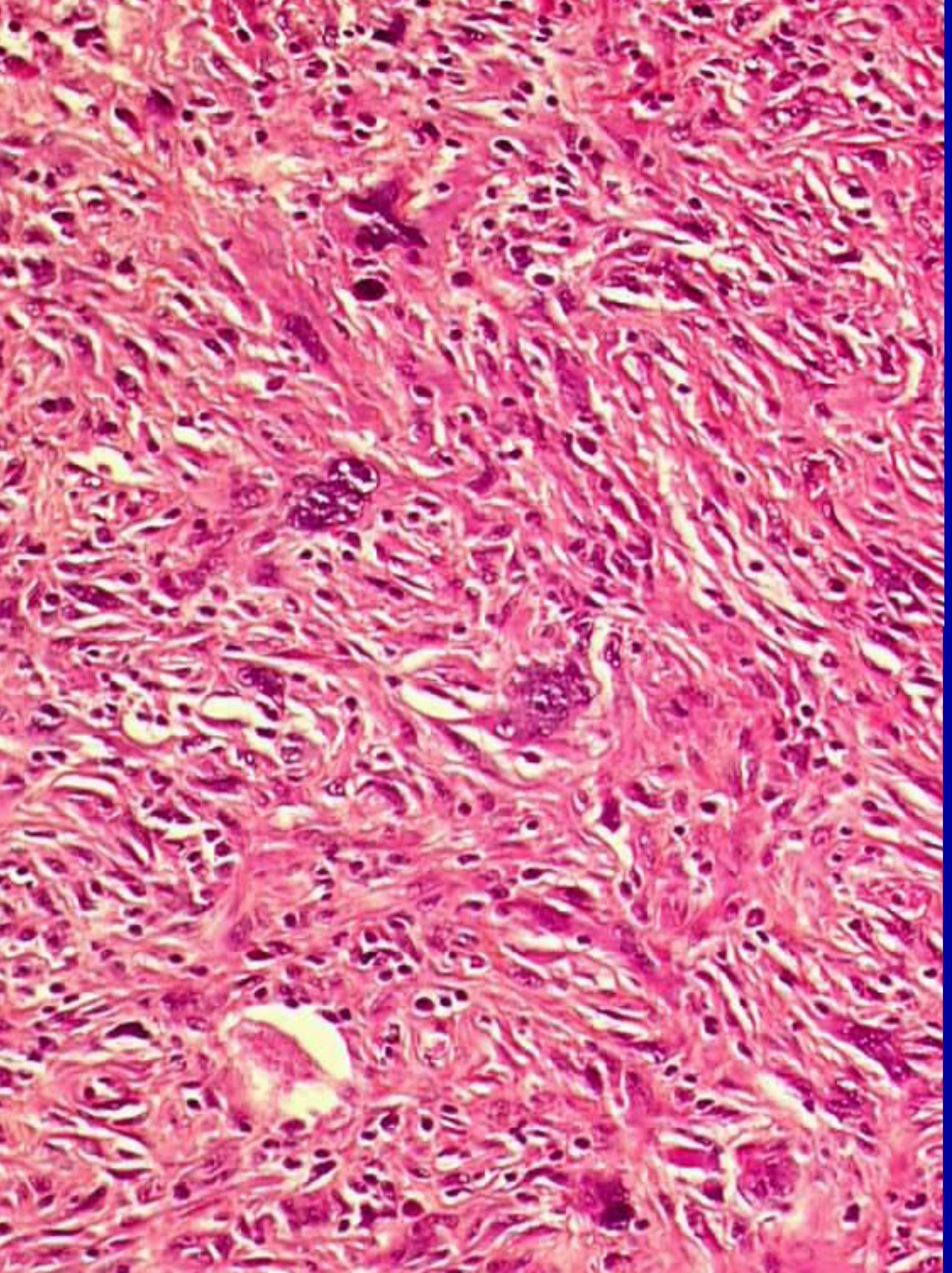
- Carcinoma
- Melanoma
- Lymphomas

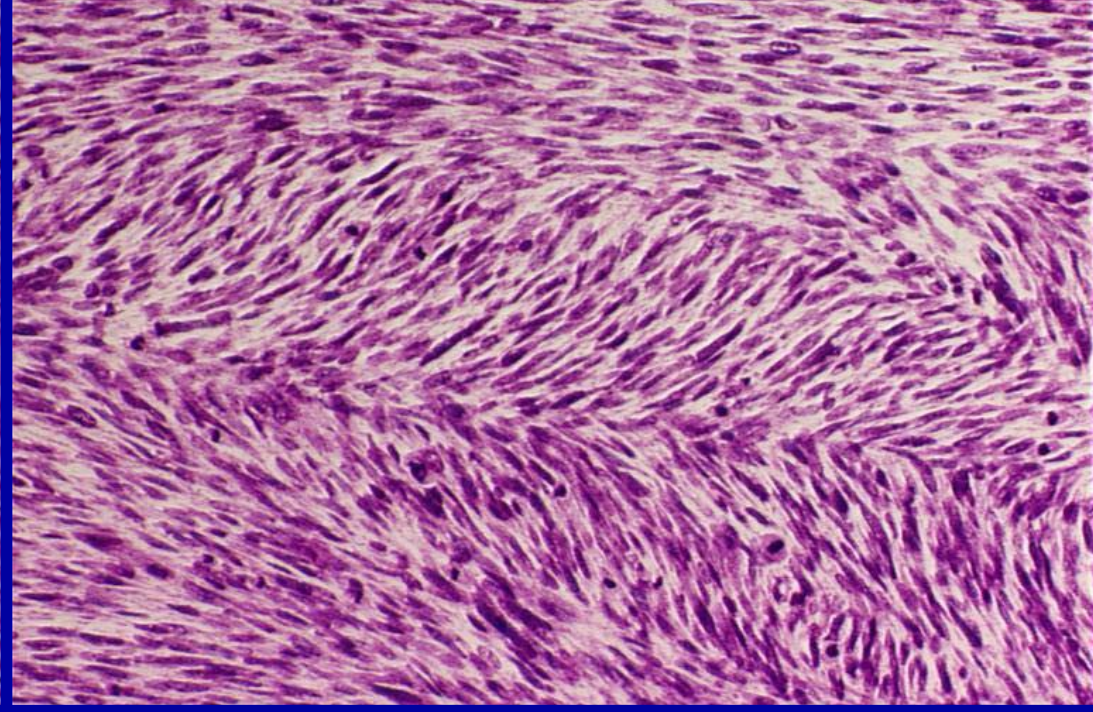
Be careful if :

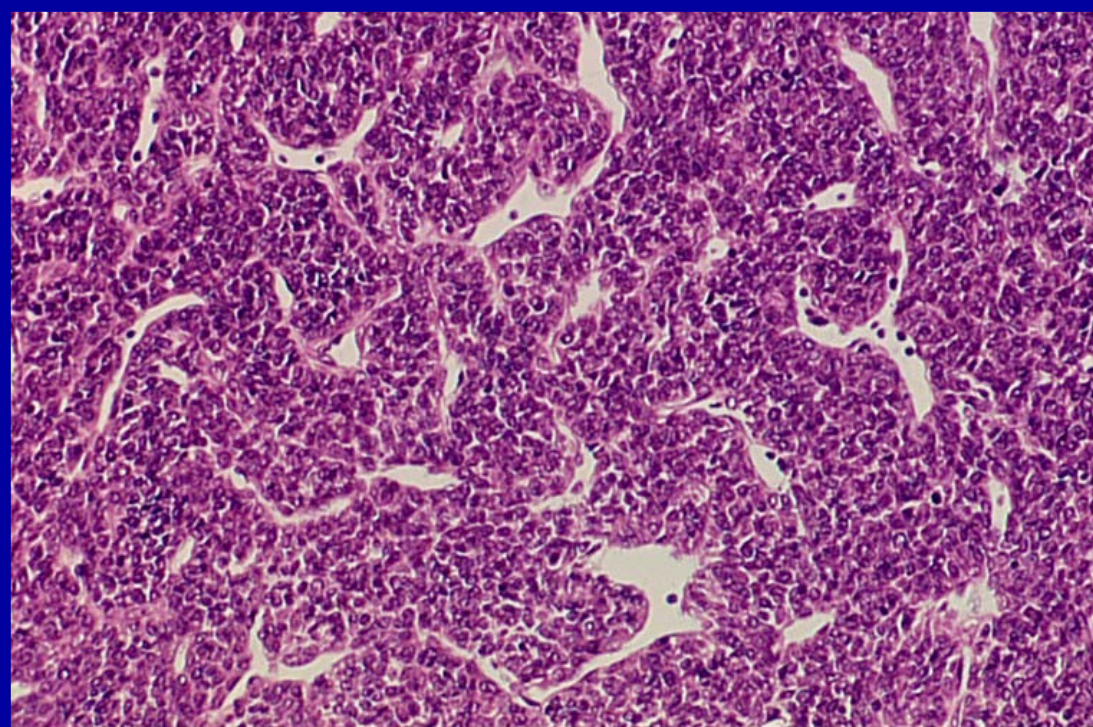
- Previous history of cancer
- Some localisations
- Non-specific pattern

Non-mesenchymal malignant tumors
Localisations at risk

- Skin and mucosae
- Lymph node areas
- In the vicinity of some viscera (lung, kidney, thyroid, breast…)

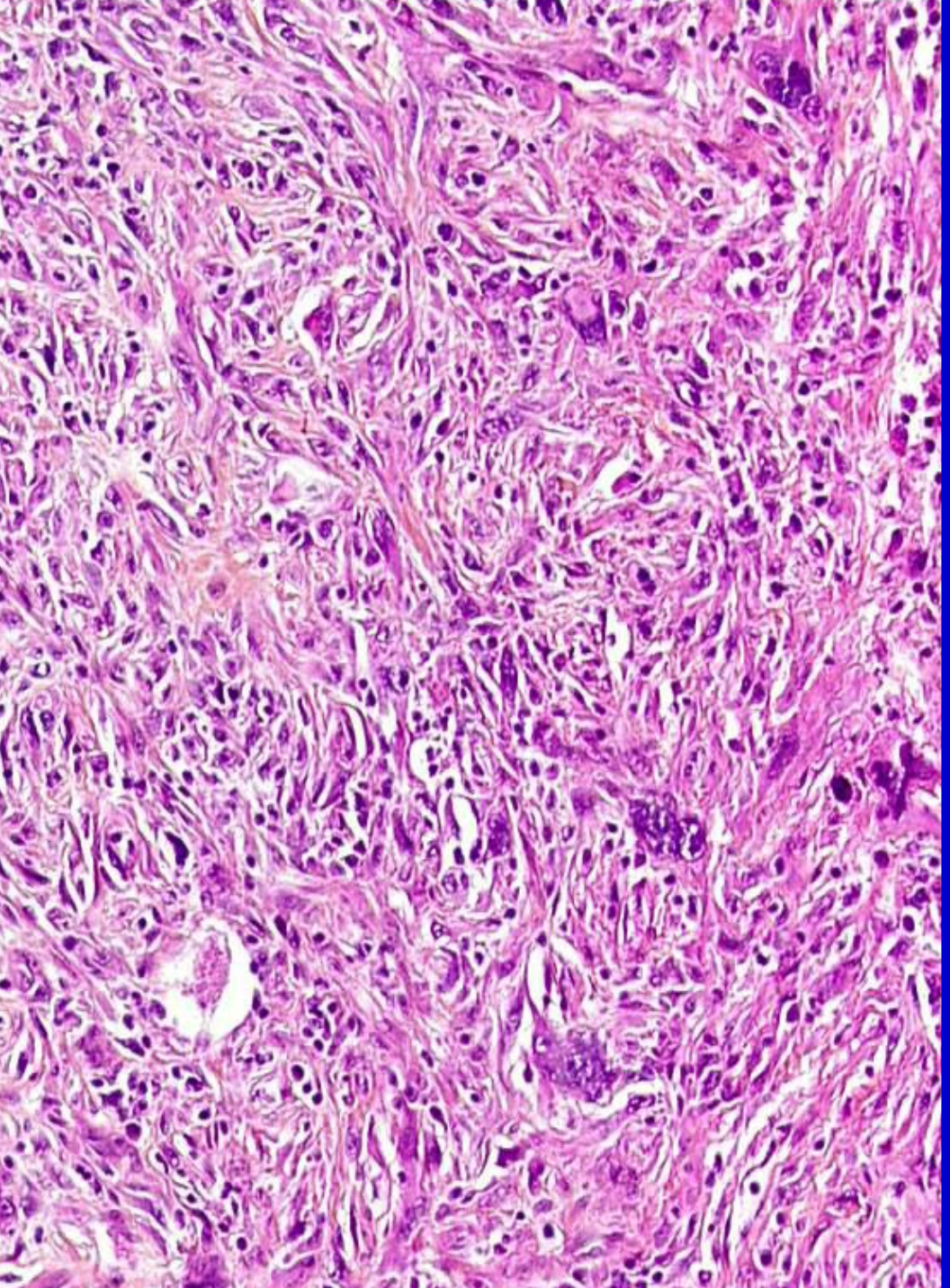


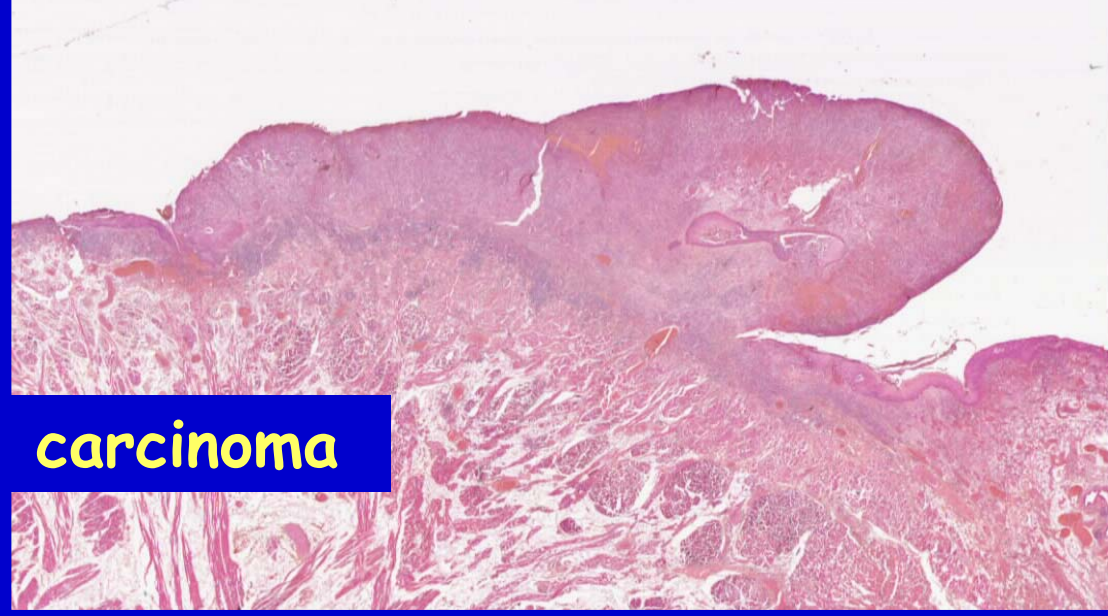


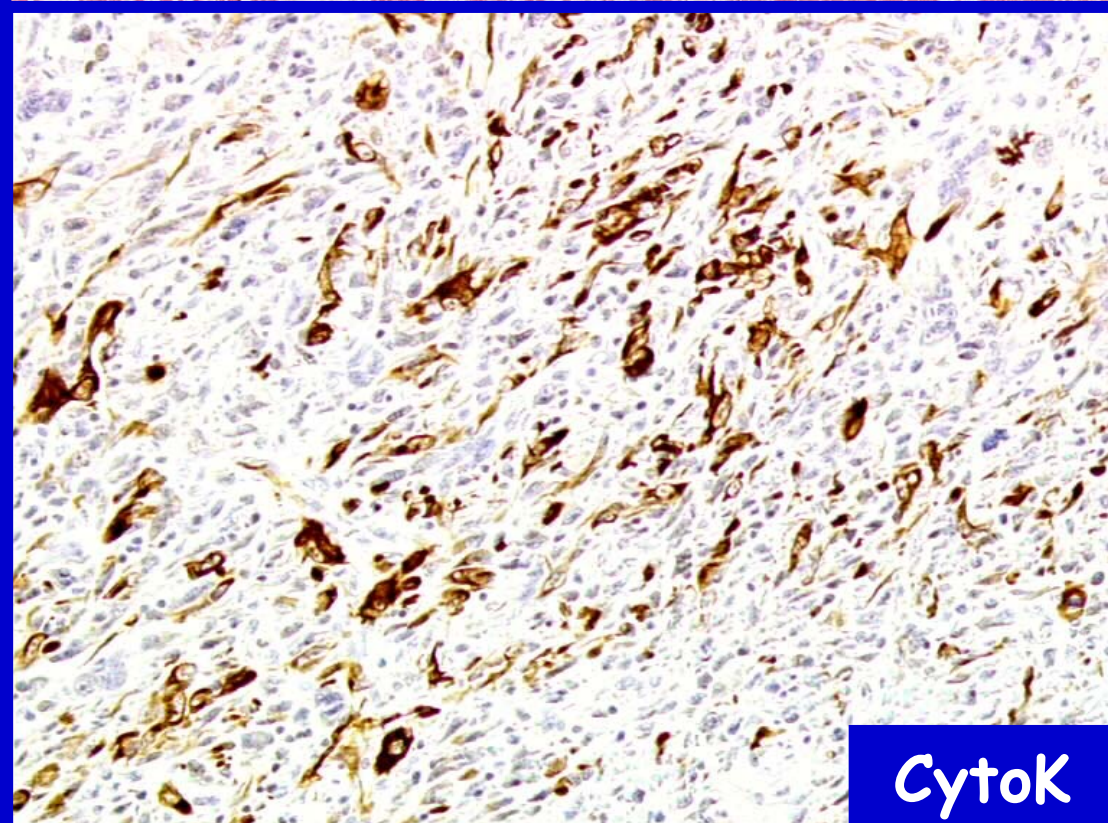


Non-mesenchymal malignant tumors
Solutions

- If previous history: compare both tumors
- Correct sampling
- IHC : AE1/AE3, S100, CD20,….




carcinoma


CytoK

Soft tissue tumors
Immunohistochemistry
Practical interests

- Identification of a benign lesion
- Nature of an undifferentiated malignant tumor
- Classification of a sarcoma

Classification of a sarcoma
Immunohistochemistry usefulness

- **Sarcomas with specific IHC**
- **Sarcomas with useful markers**
- **Sarcomas with no specific markers**

Sarcomas with specific IHC

- Rhabdomyosarcoma
- Vascular sarcomas
- GIST
- Dedifferentiated liposarcoma
- Epithelioid sarcoma
- Clear cell sarcoma
- Intra-abdominal desmoplastic tumor

Myogenic transcription factors

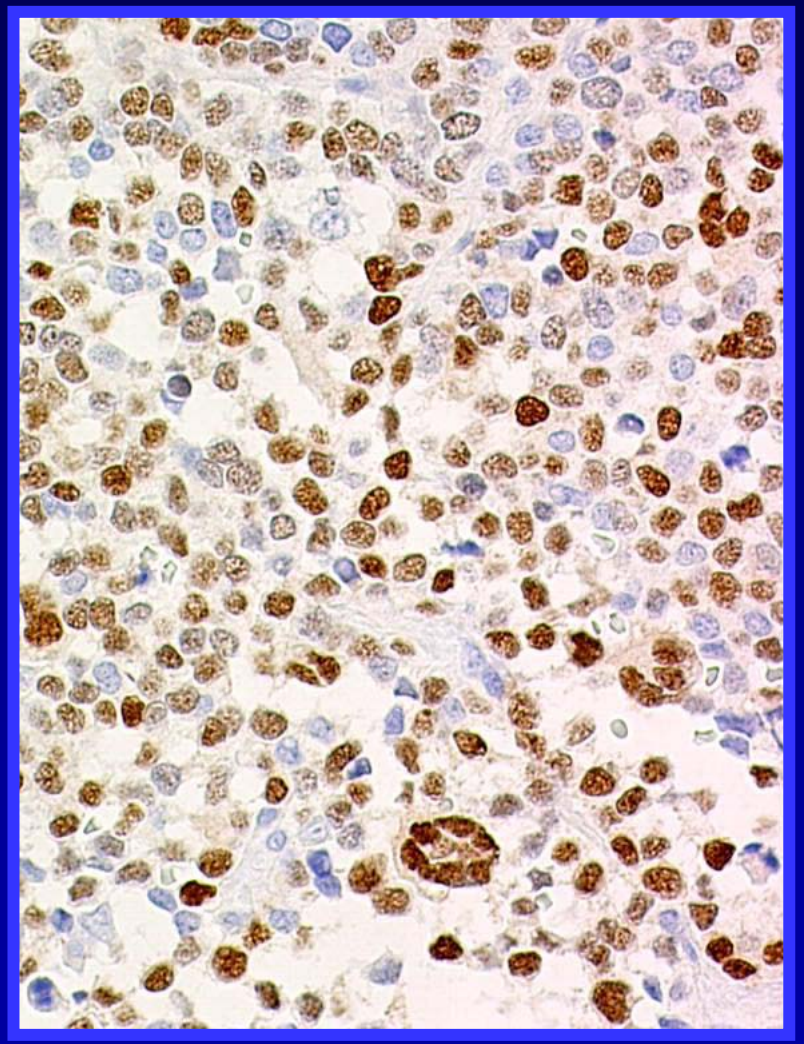
Myogenin and MyoD1

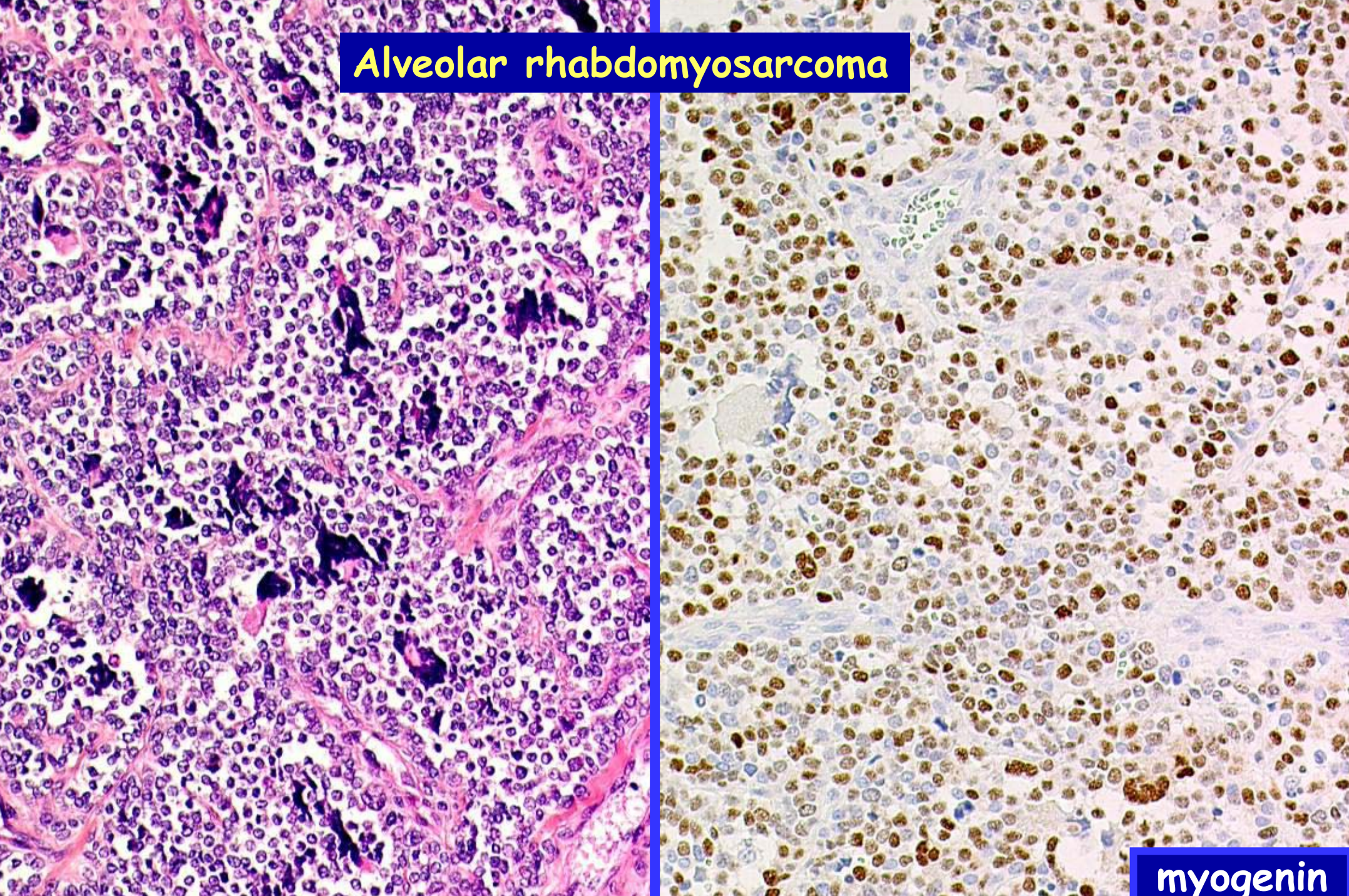
Immature skeletal muscle

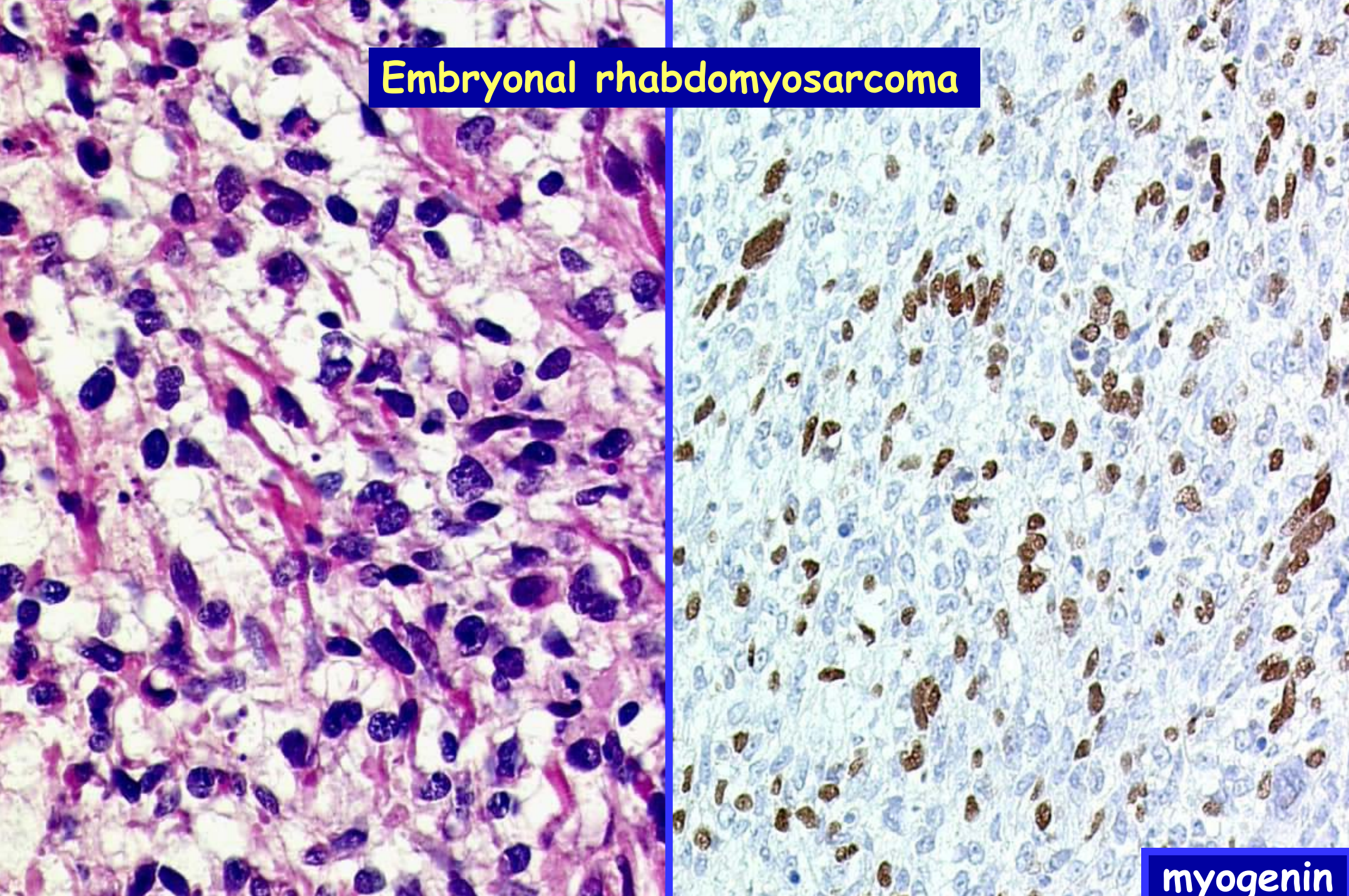
Specific marker :

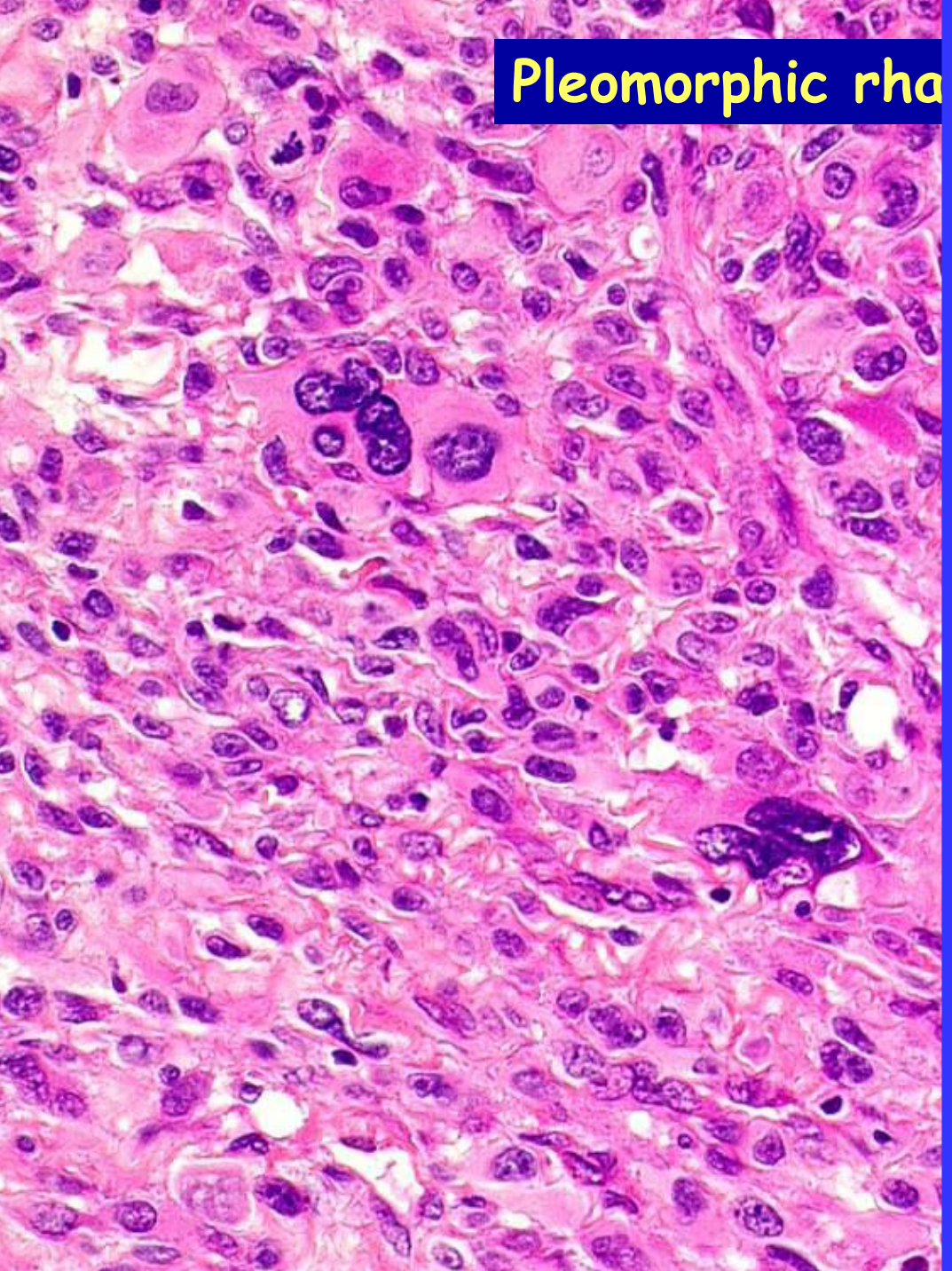
- myogenin > myoD1
- nuclear positivity
- regenerative muscle

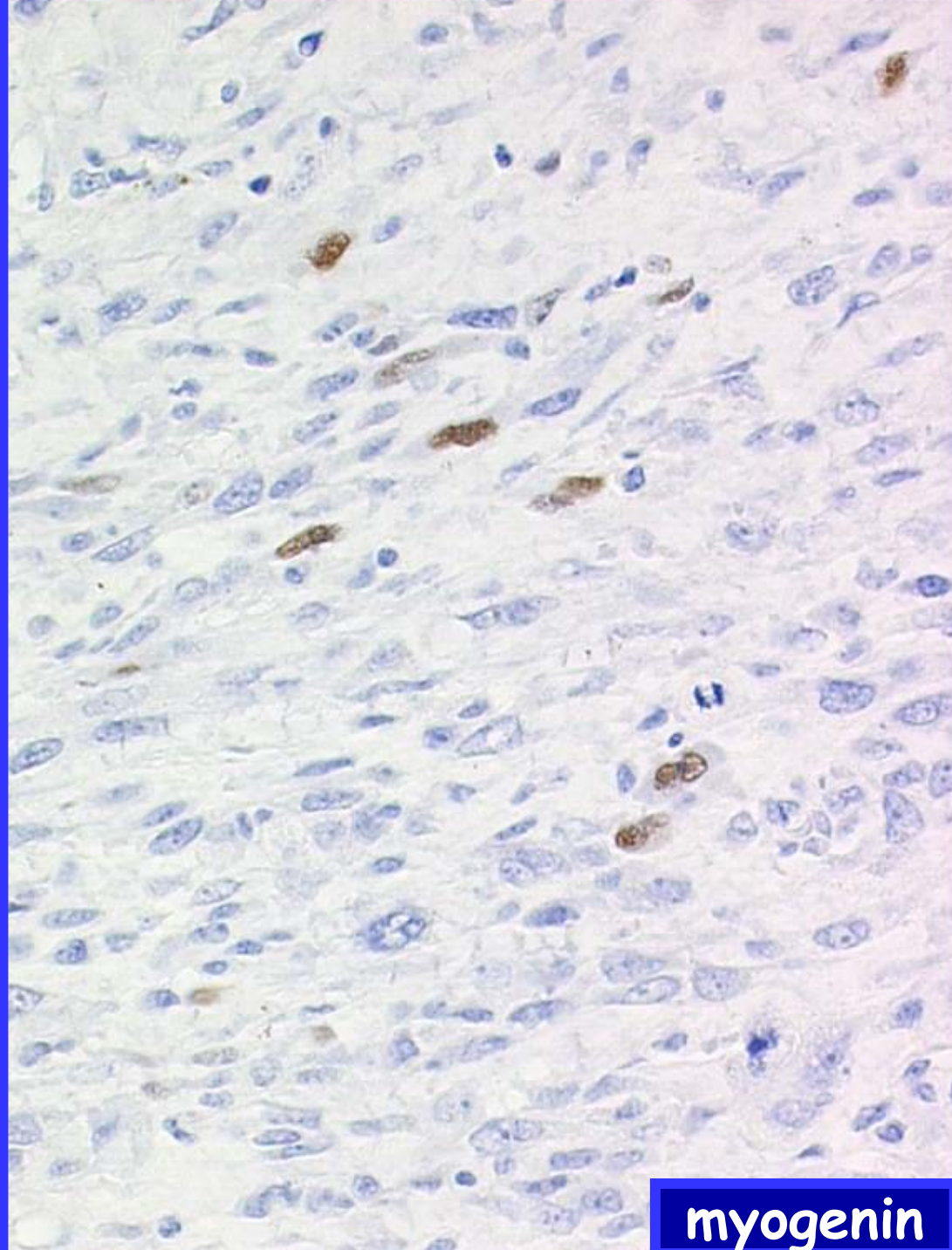
Sensitivity and histologic types




Alveolar rhabdomyosarcoma
myogenin


Embryonal rhabdomyosarcoma
myogenin


Pleomorphic rha


myogenin

Vascular sarcomas

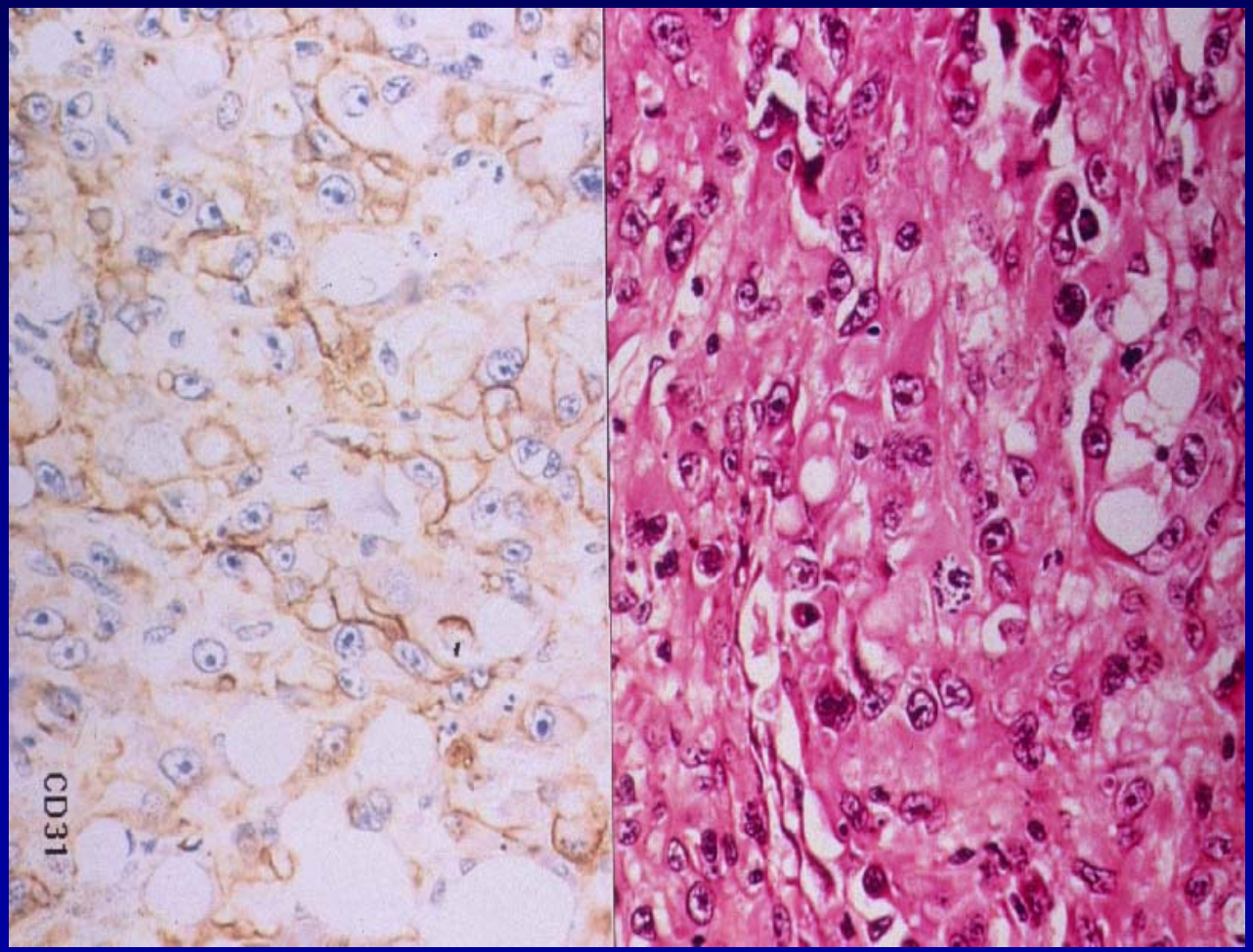
- Spindle cell angiosarcoma
- Epithelioid angiosarcoma
- Kaposi sarcoma
- Epithelioid hemangioendothelioma

Vascular sarcomas
Useful markers

- **CD 31 +**
- **CD 34 +**
- **Factor 8 +**
- **FLI1 +**
- **HHV8 +/-**
- **cytokeratin +/-**
- **EMA +/-**
- **C-Kit +/-**

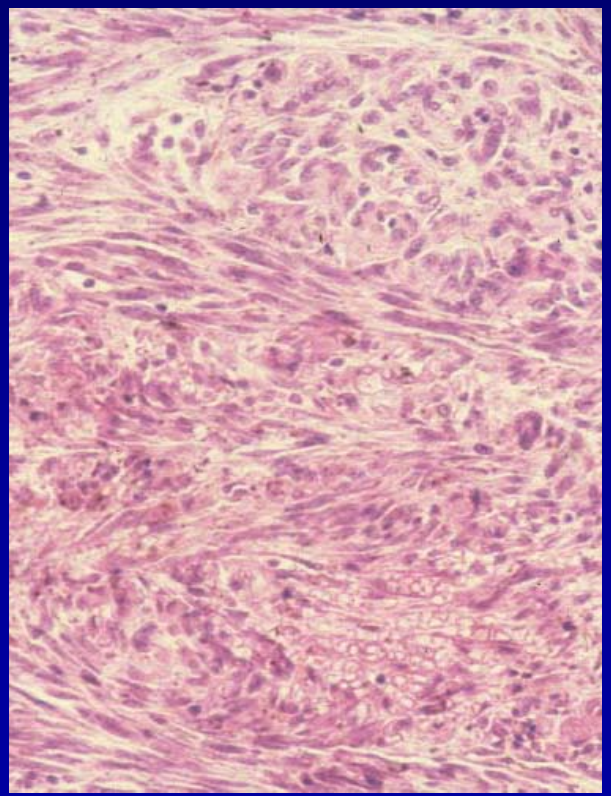
Vascular sarcomas
Useful markers

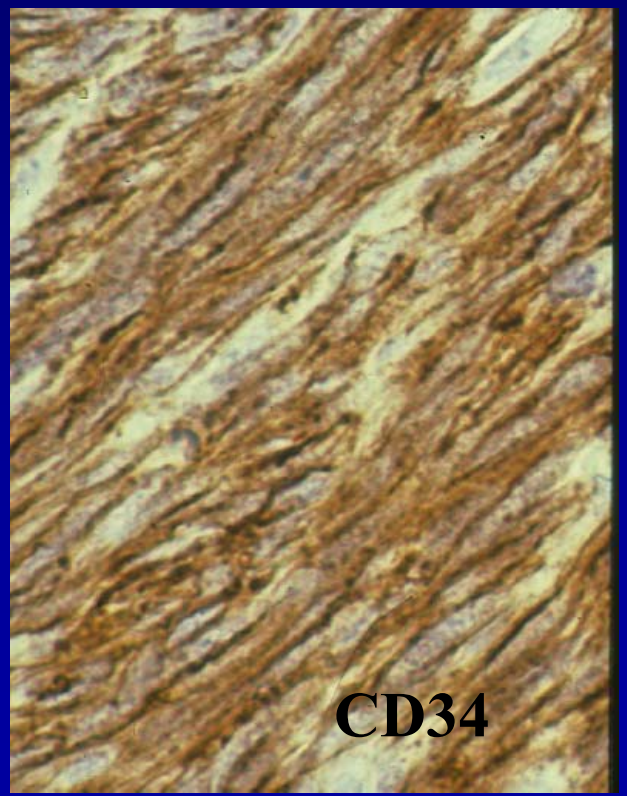
- **Epithelioid angiosarcoma: CD31,CD34 +**

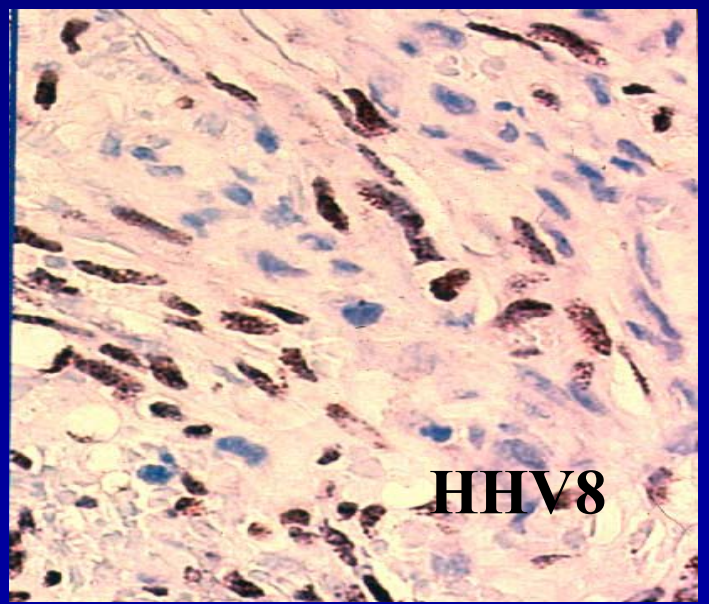


Vascular sarcomas
Useful markers

- **Kaposi sarcoma: CD34, CD31 and HHV8+**

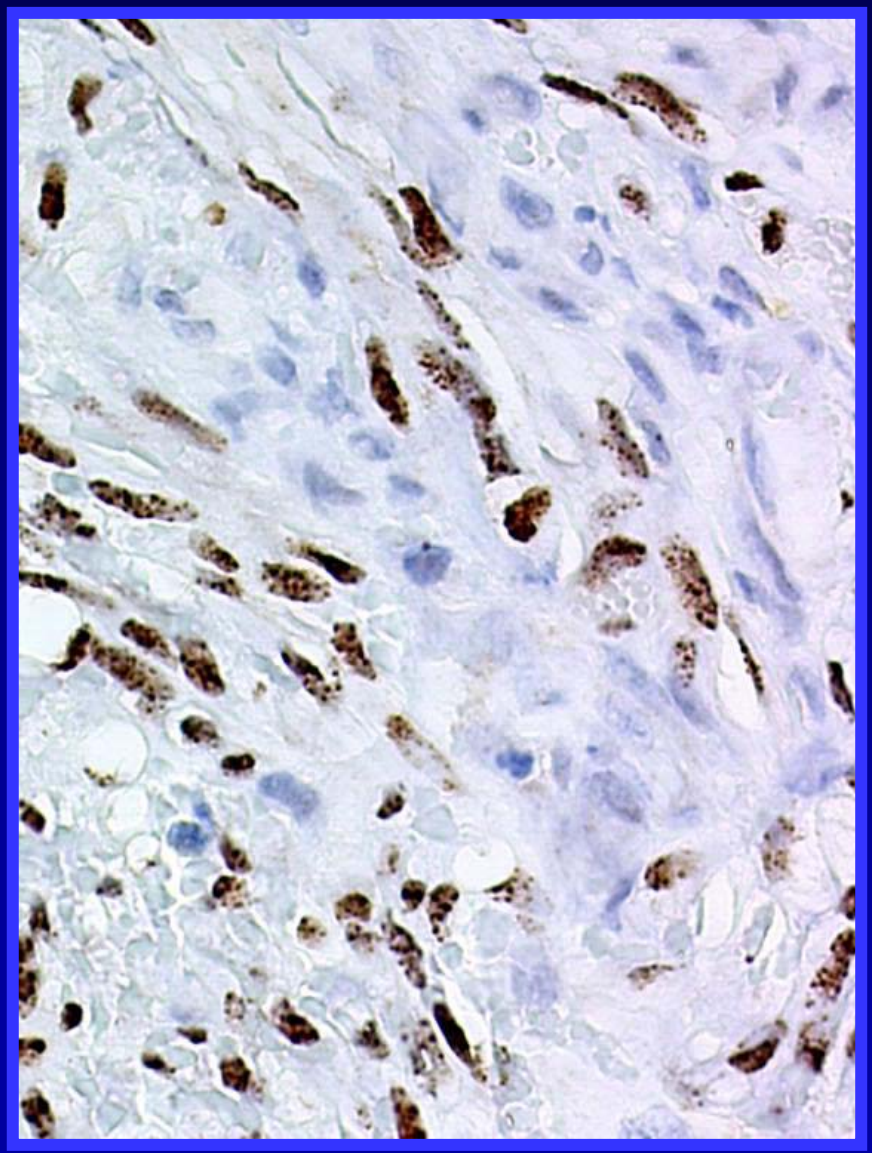


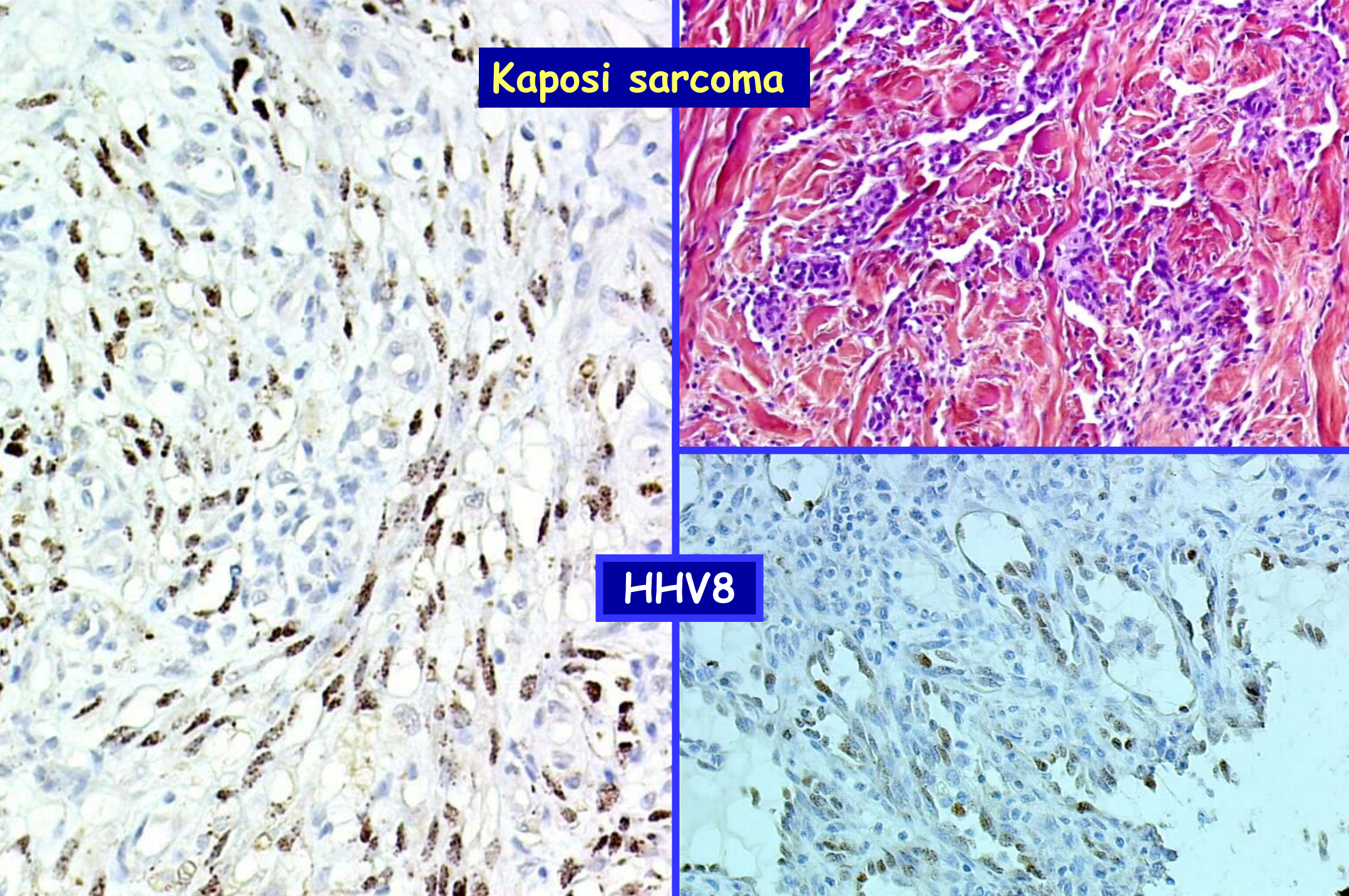




Human Herpes Virus 8 (HHV8)

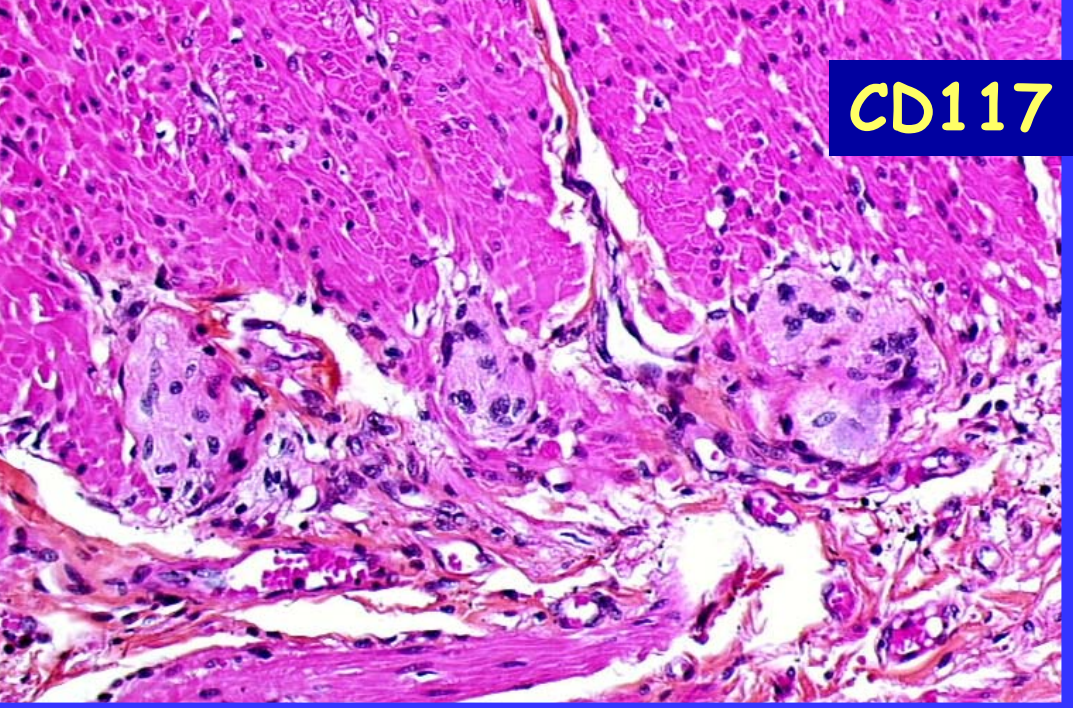
- Kaposi sarcoma
- Effusion lymphoma
- Castleman disease
- Nuclear positivity



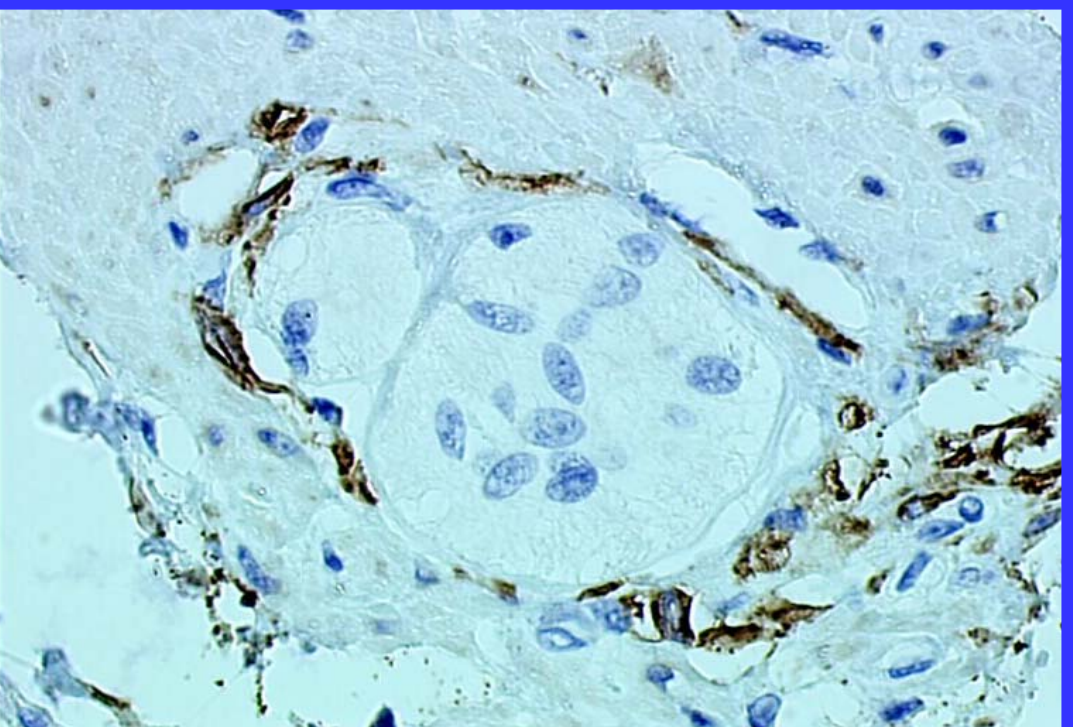

Kaposi sarcoma
HHV8

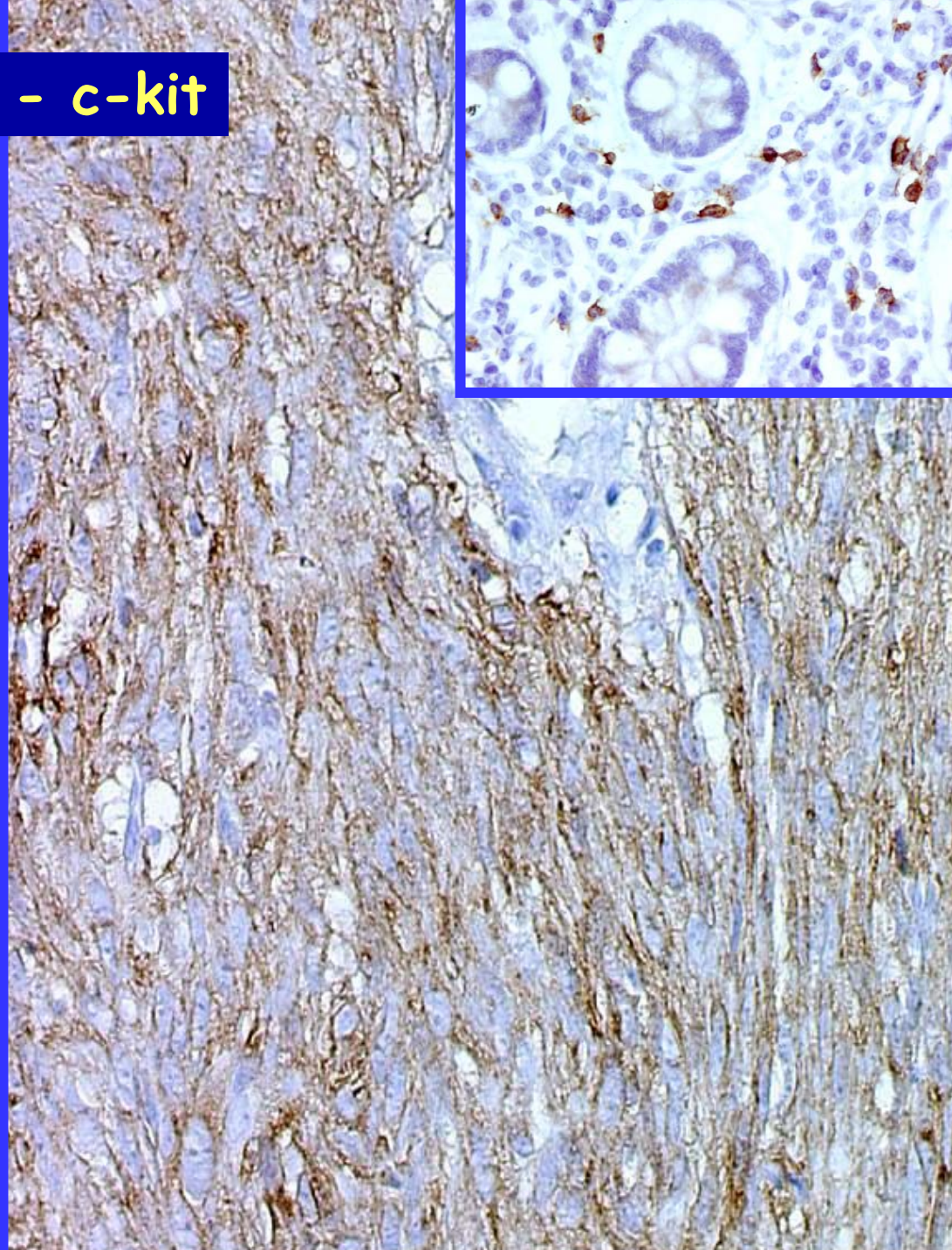
CD117 (c-kit)

- C-kit ➡ tyrosine kinase receptor
  (mast cells, melanocytes, germ cells,
  interstitial cells of Cajal)
- GIST : mutation of c-kit ➡ permanent TK activity
- CD117 positive in 95 % of GIST
- CD117 positivity is required for imatinib treatment



CD117 - c-kit





CD117 positivity

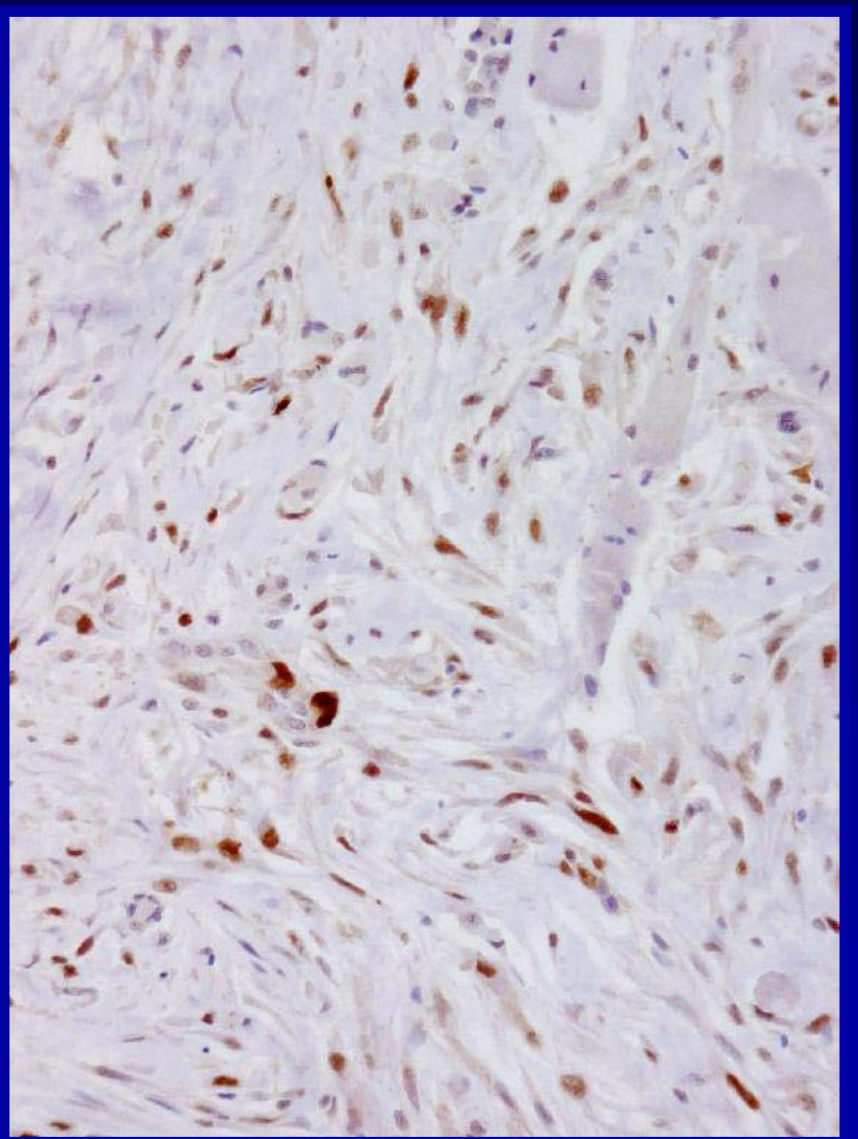
- GIST
- Mast cell disease
- Seminoma
- Melanoma
- CML
- Angiosarcoma
- PNET
- Chondrosarcoma
- Synovial sarcoma
- Carcinomas

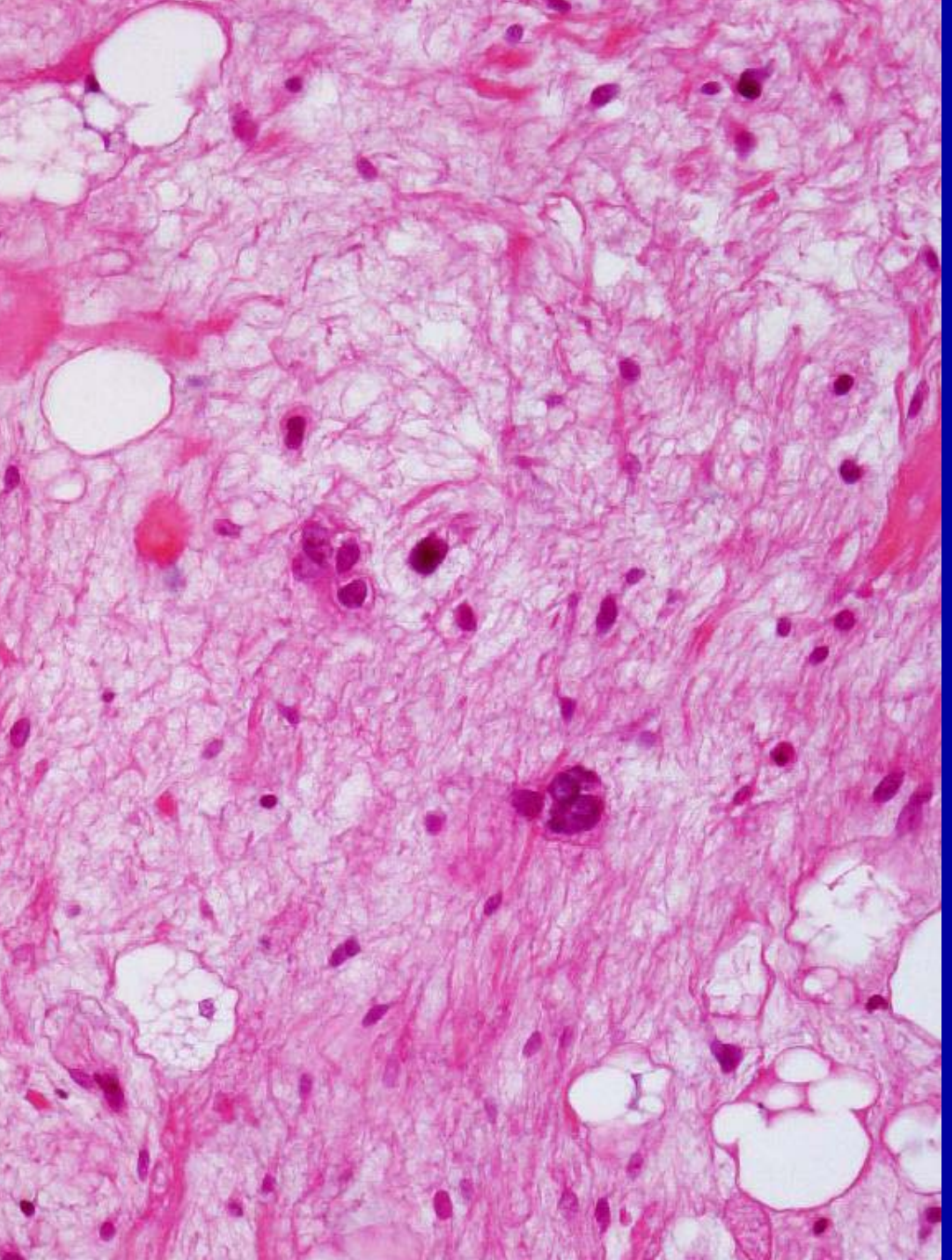
Immunohistochemistry of GIST

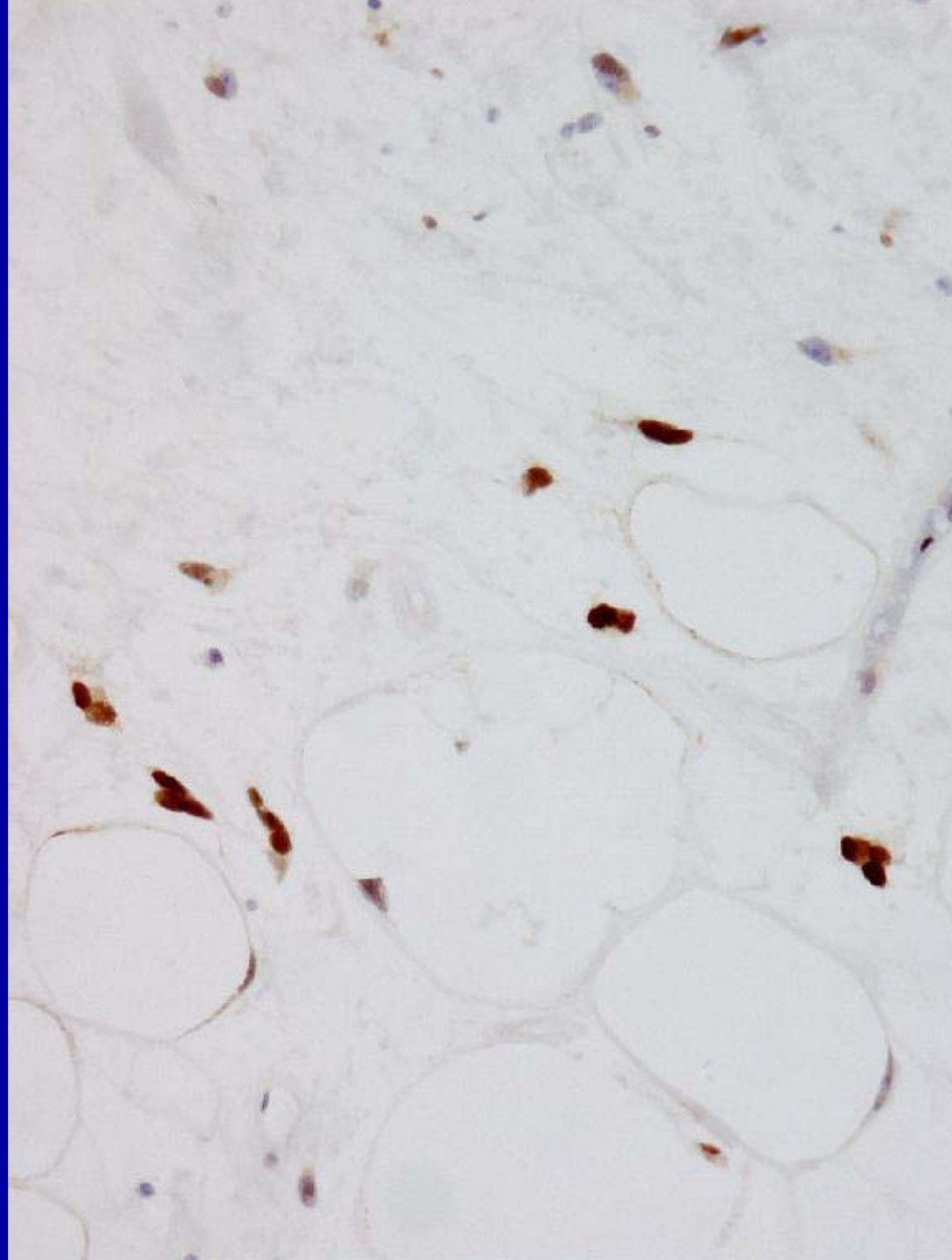
- CD117 95%
- CD34 60-70%
- H-caldesmon 80%
- SMA 15-60%
- S100 protein 5-10%

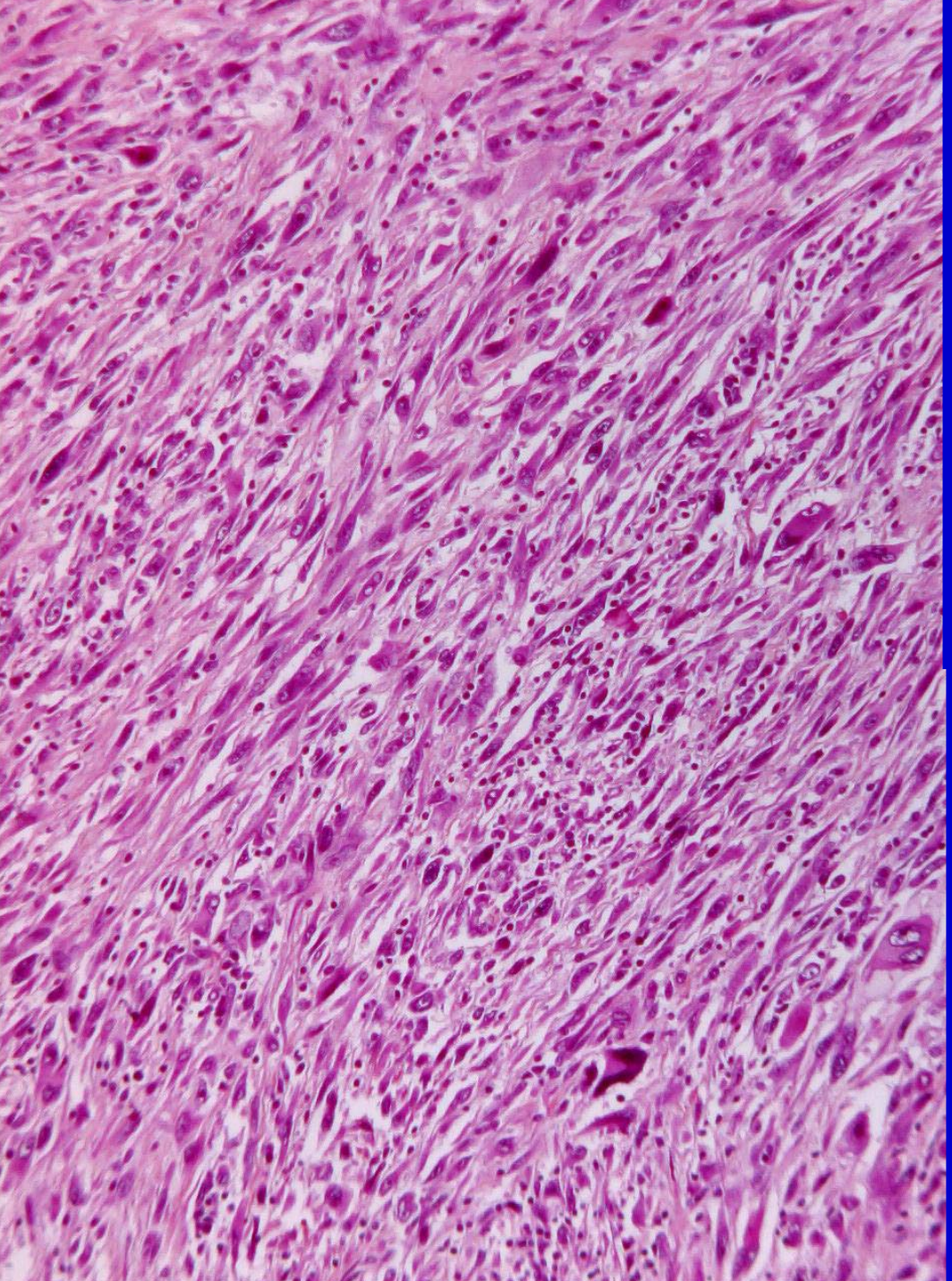
MDM2/CDK4

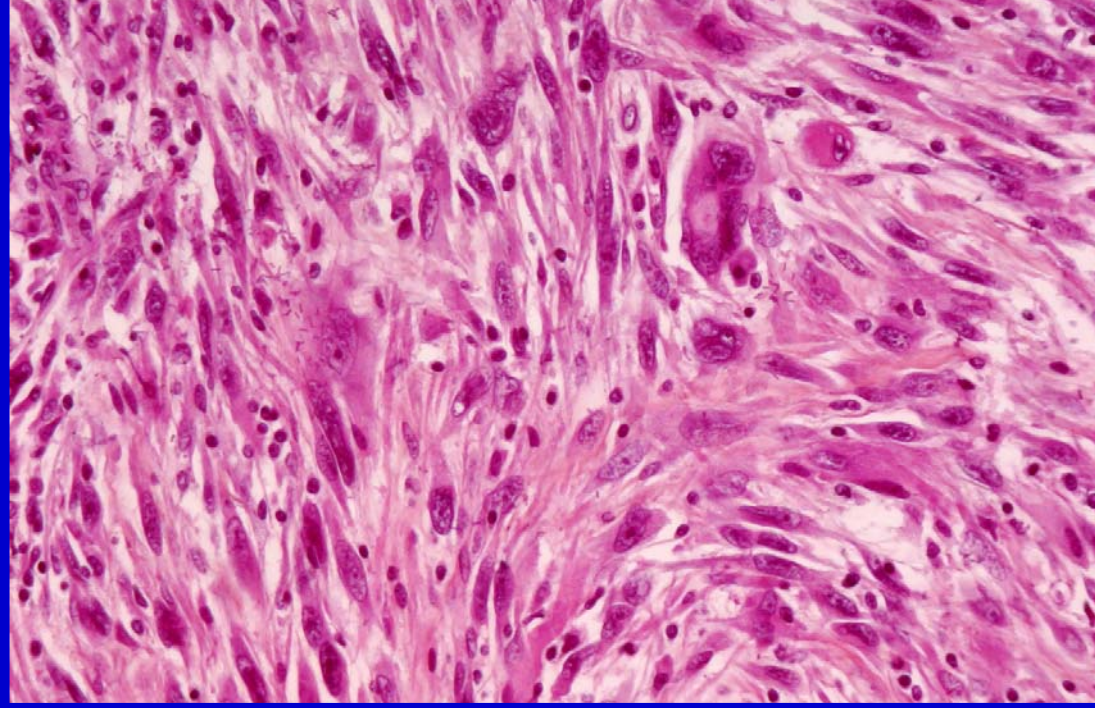
- MDM2: Inhibitor of P53 protein
- MDM2/CDK4 amplification in well diff/dediff liposarcomas
- IHC with IF2 antibody for MDM2
- Diagnosis of dediff. liposarcoma

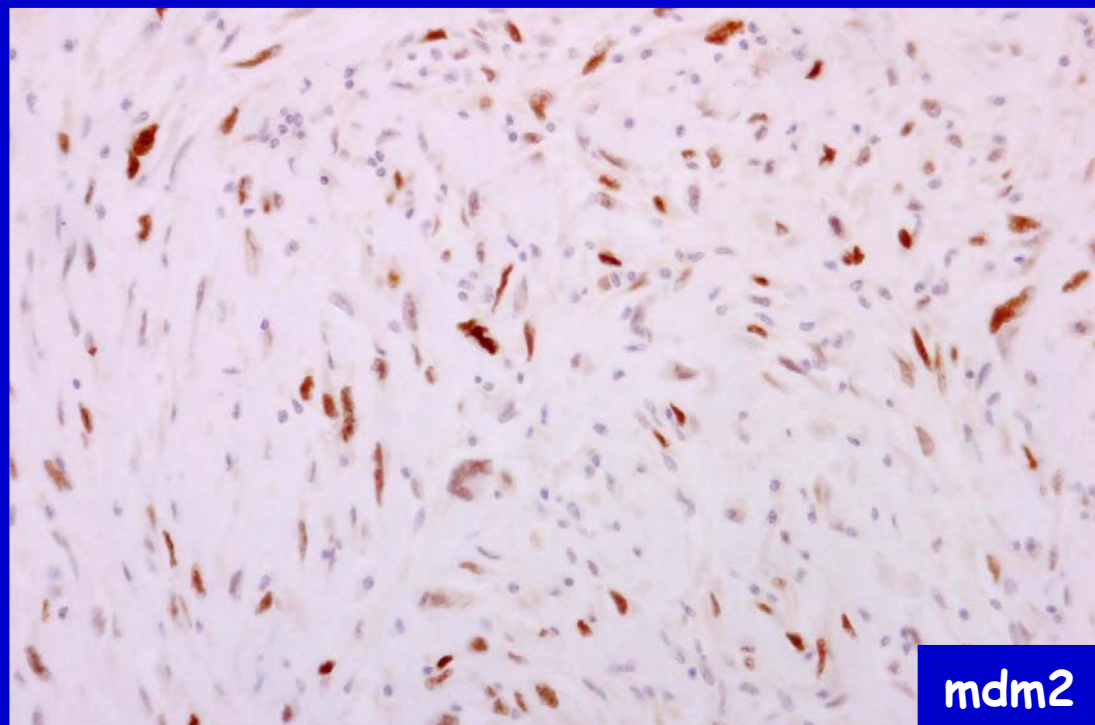


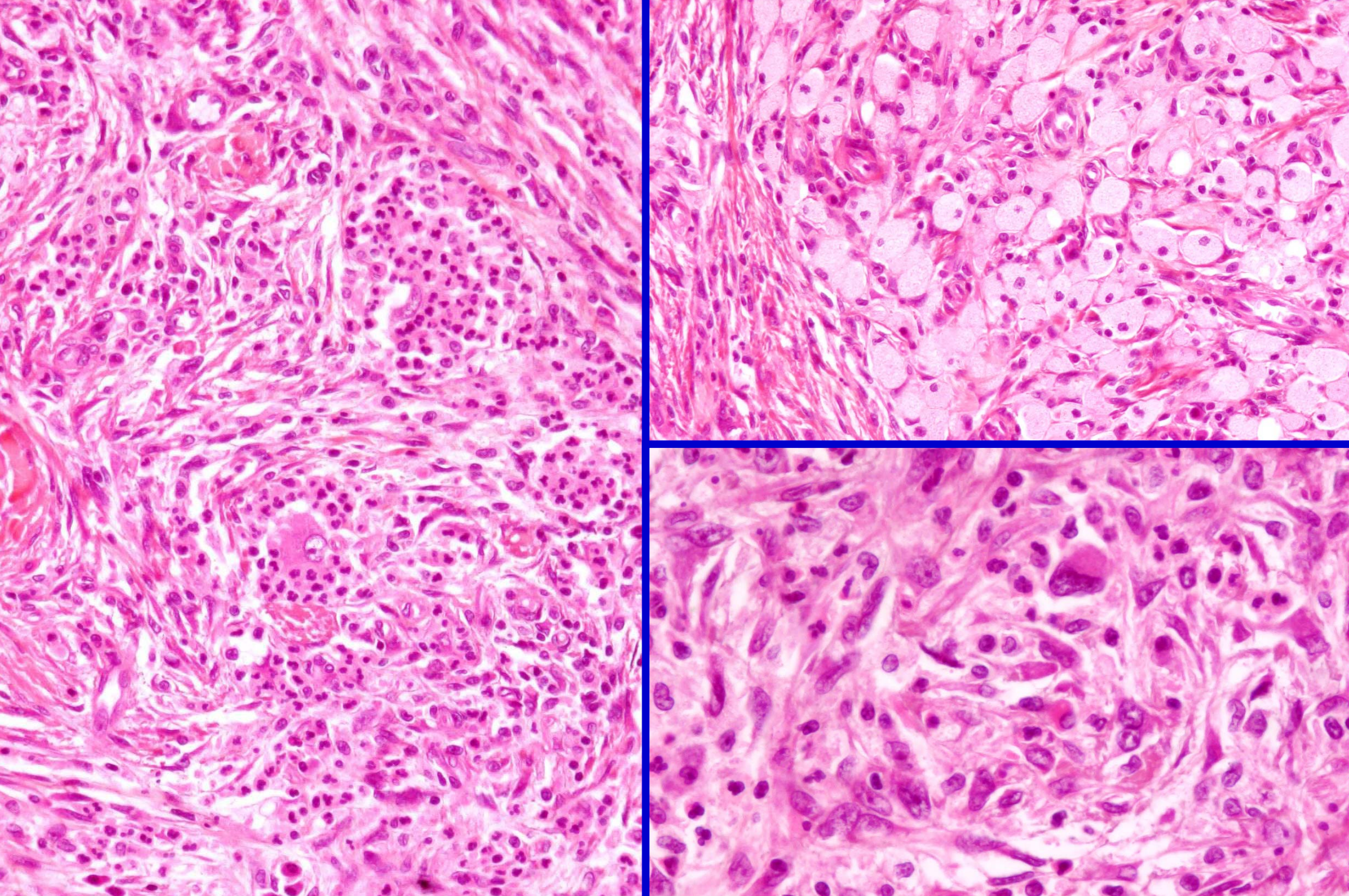


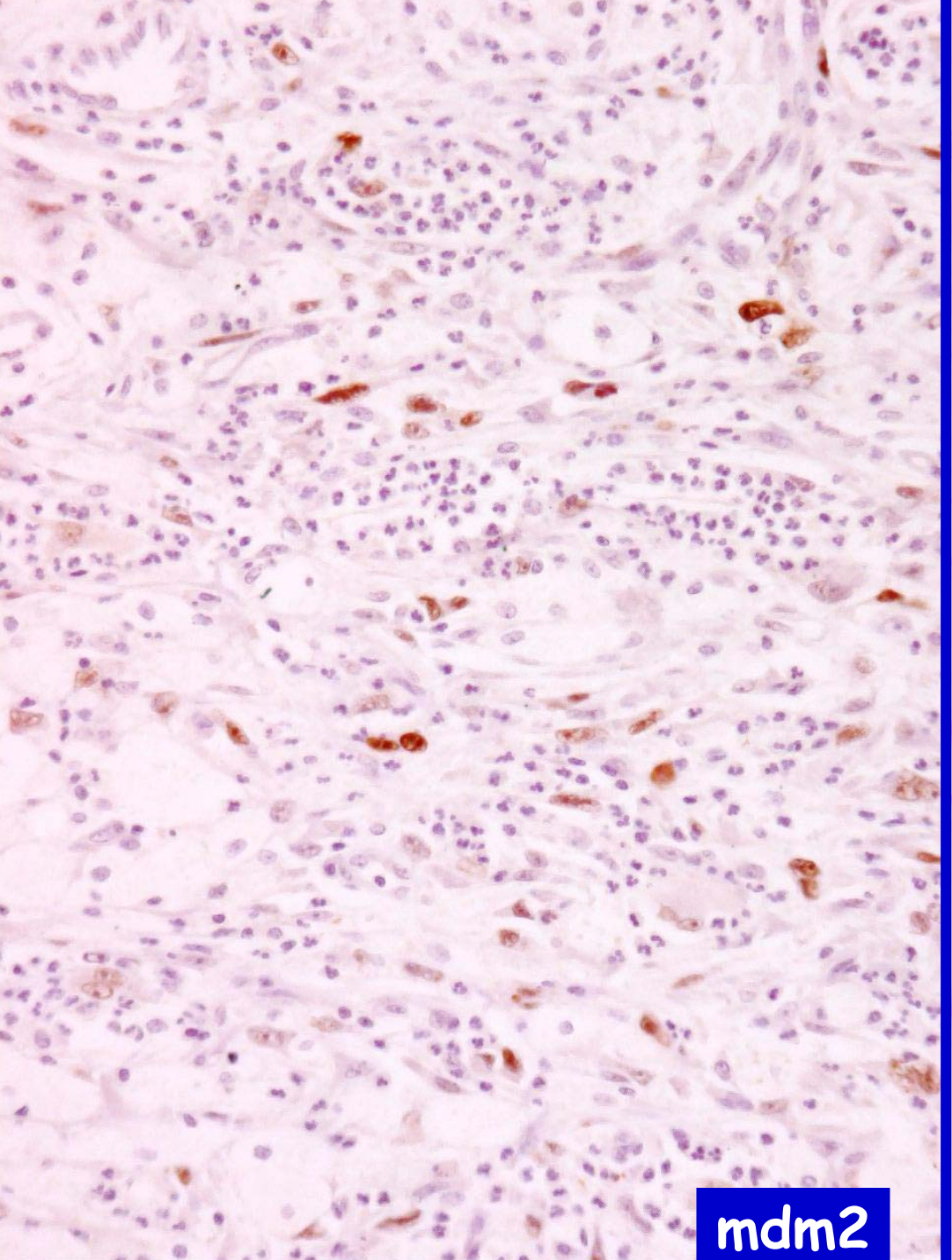




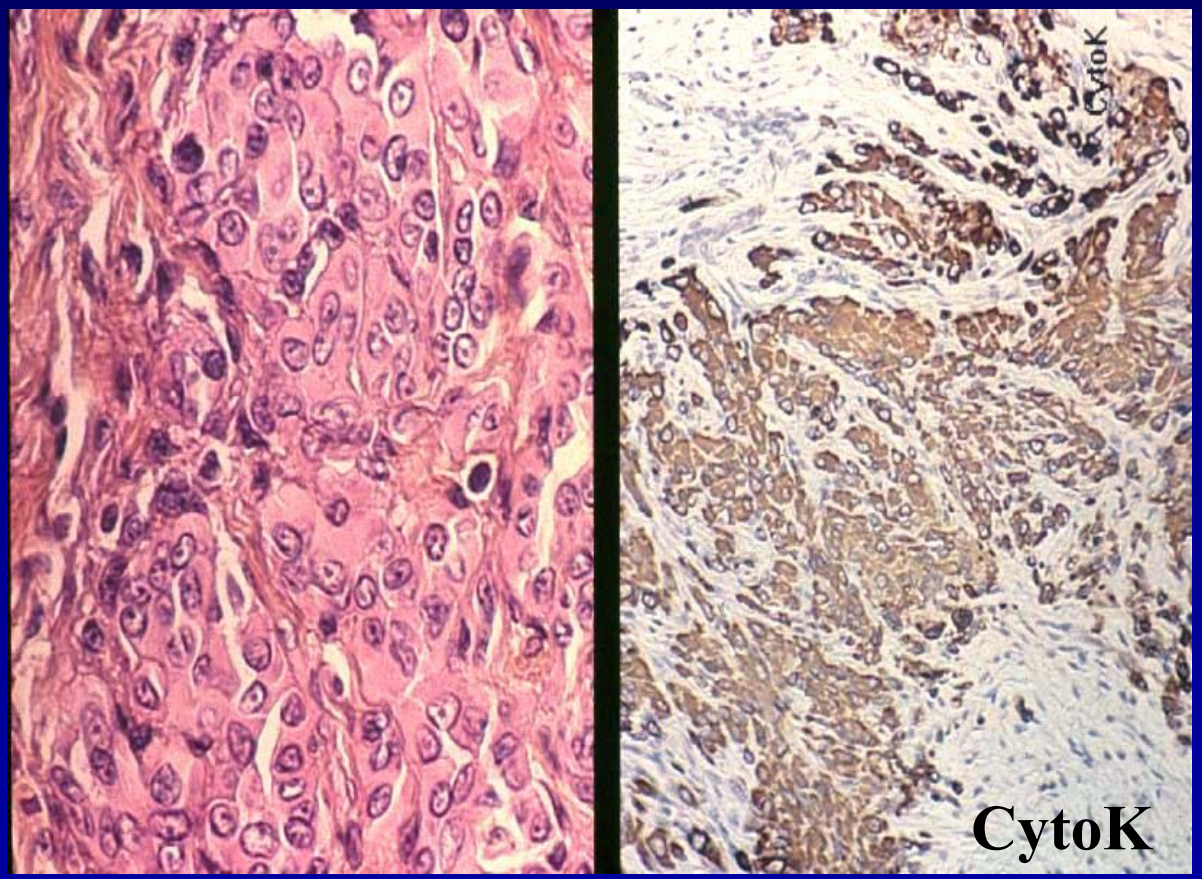



mdm2




mdm2

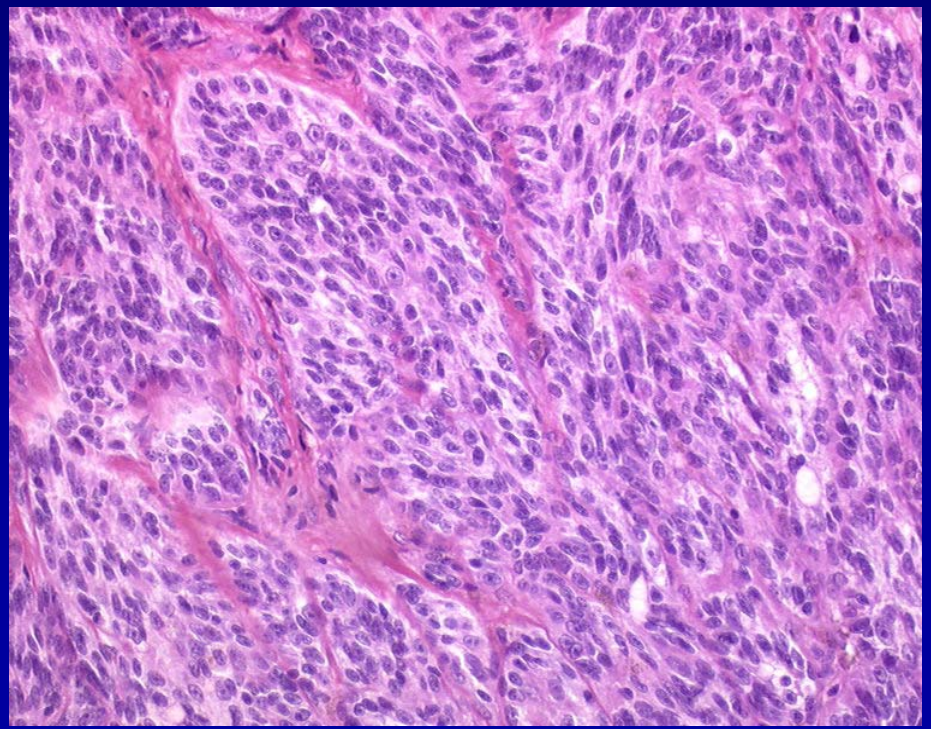
Epithelioid sarcoma

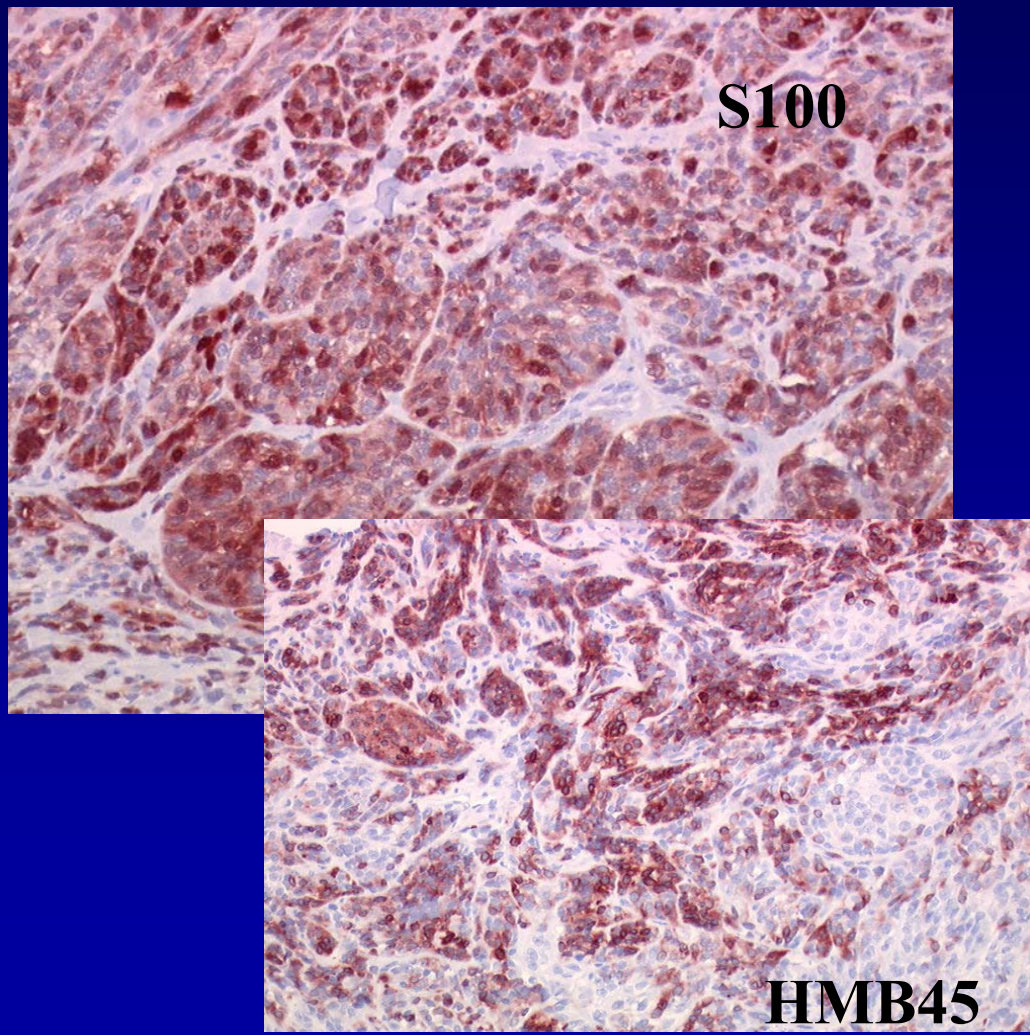


- **Useful markers : , CytoK, EMA, CD34+ and CD31-**

Clear cell sarcoma/Soft tissue melanoma

- Useful markers: S100, HMB45, MELAN A, MART1 +





Classification of a sarcoma
Immunohistochemistry usefulness

- **Sarcomas with specific IHC**
- **Sarcomas with useful markers**
- **Sarcomas with no specific markers**

Sarcomas with useful markers

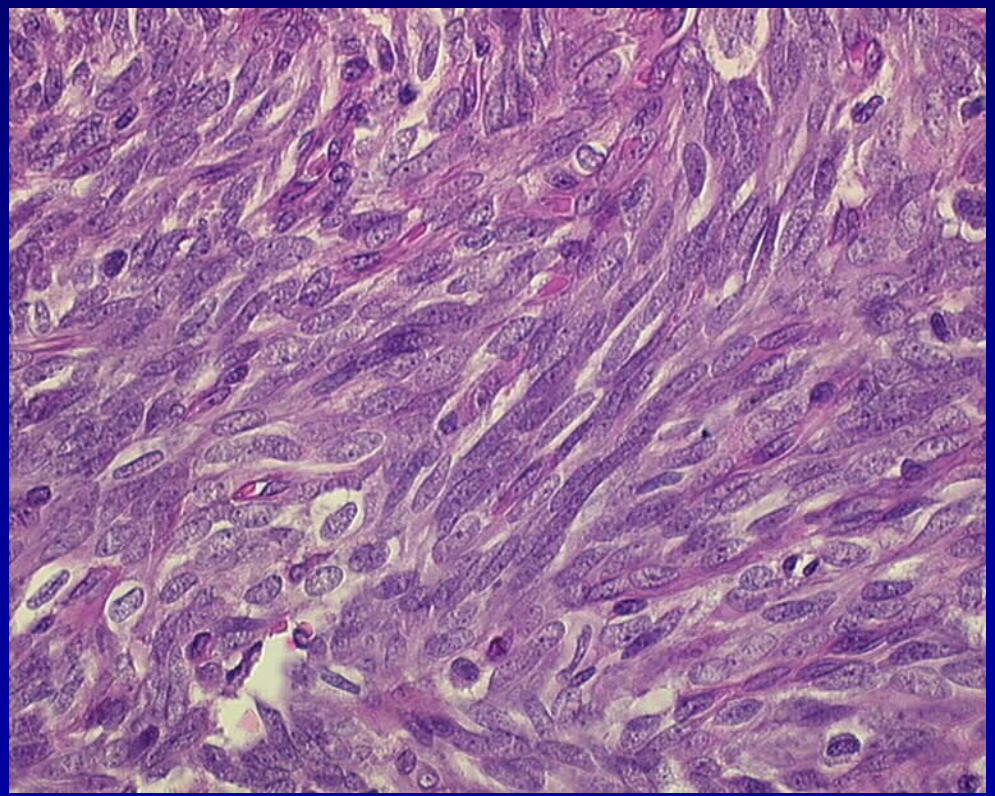
- Synovial sarcoma
- Leiomyosarcoma
- PNET
- DFSP
- MPNST
- Extra-skeletal myxoid chondrosarcoma

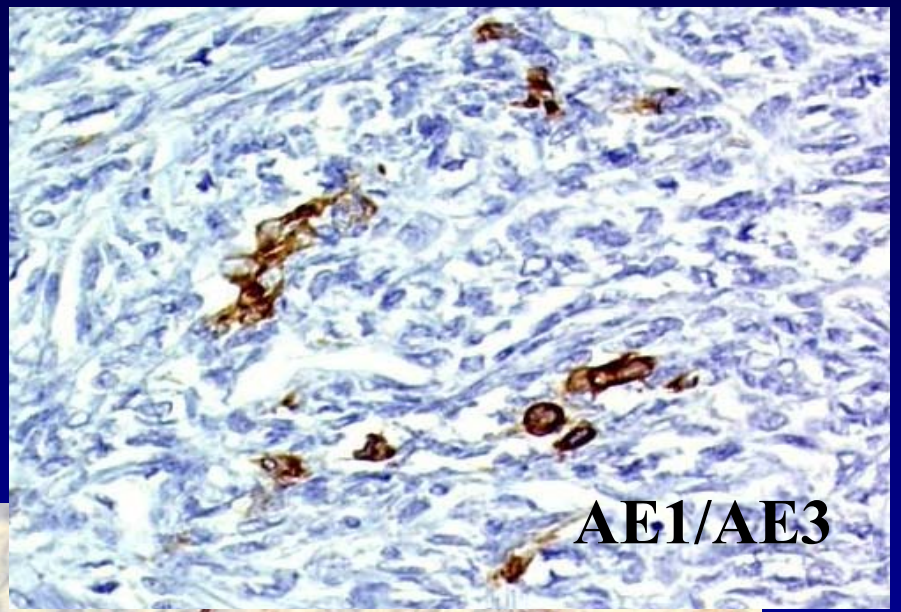
Synovial sarcoma
Useful markers

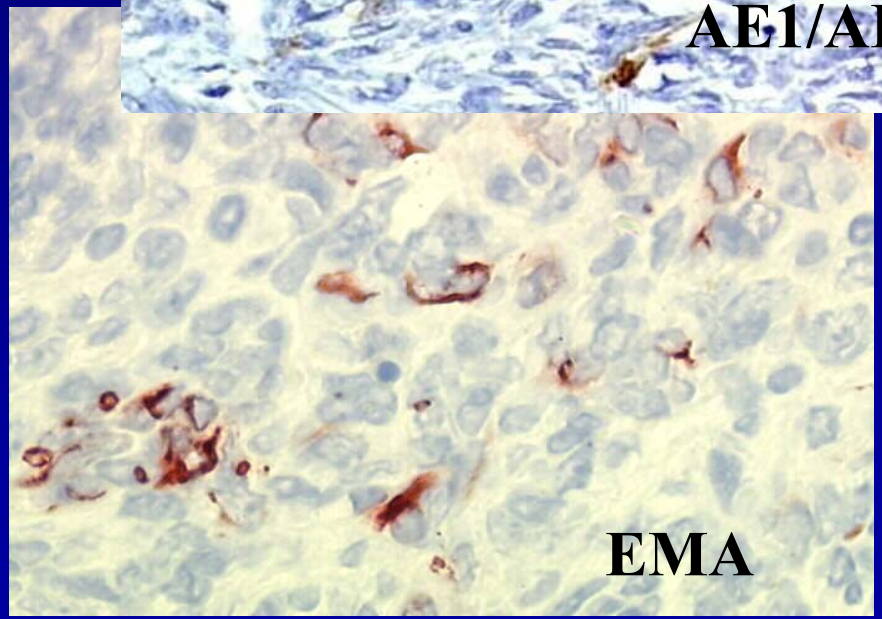
- AE1/AE3 + (65%)
- EMA + (95%)
- CD34 - (+ 5%)
- S100 + (30%)
- CD99 + (>50%)

Spindle cell synovial sarcoma

– Useful markers:
EMA,
AE1-AE3, CD34





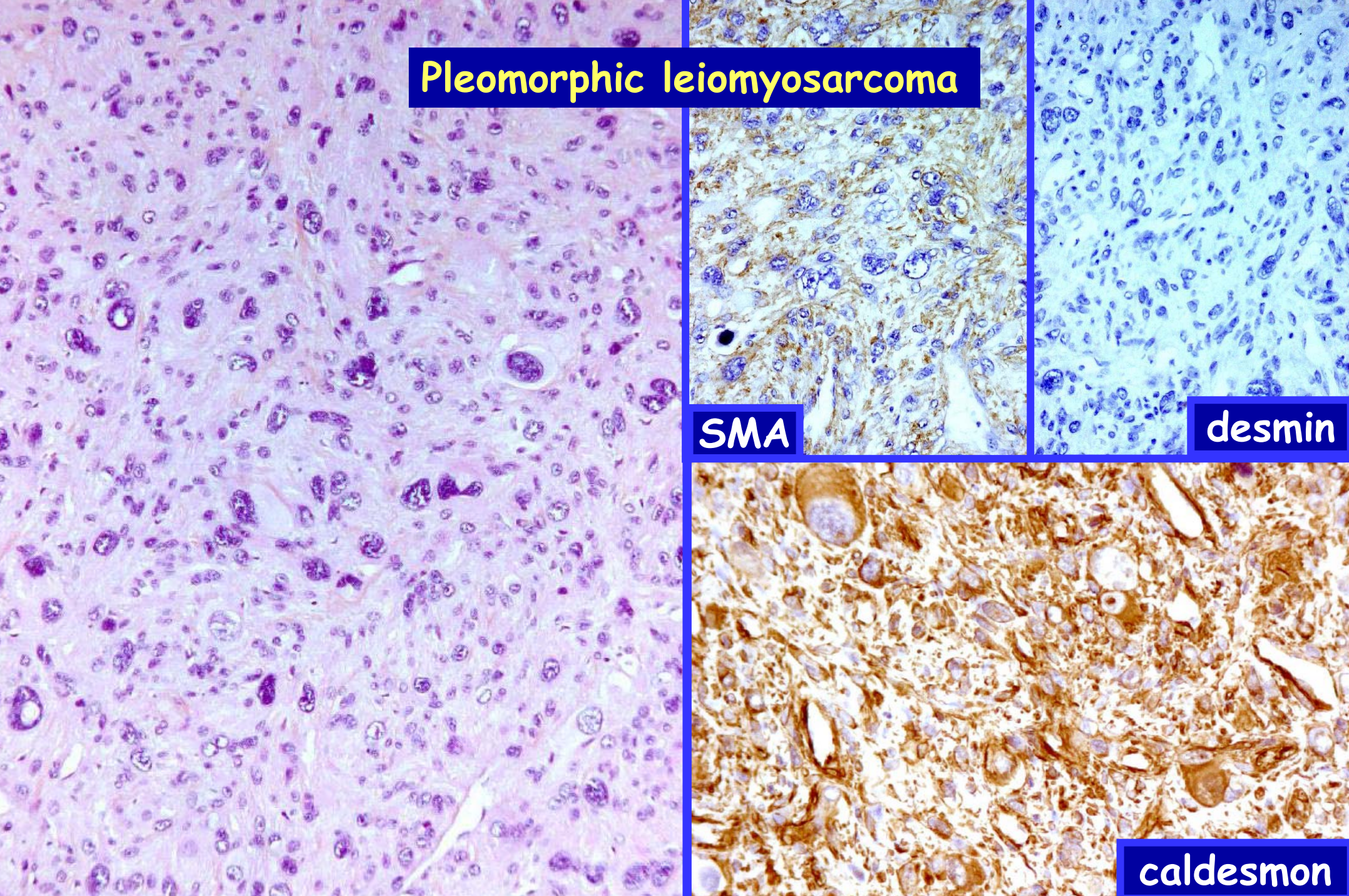


Leiomyosarcoma
Useful markers

- H-caldesmon (40-70%)
- SMA (70%)
- Desmin (50%)

H-caldesmon

- Regulator of smooth muscle contraction
- Positivity in: - smooth muscle tumors
  - glomus tumor
  - GIST
  - angiomyolipomas
- Negative in: - myofibroblastic proliferations
  - skeletal muscle tumors


Pleomorphic leiomyosarcoma
SMA
desmin
caldesmon

Muscular markers

- Desmin : smooth muscle and skeletal muscle
- Smooth muscle actin : smooth muscle and myofibroblasts
- Myogenin : immature skeletal muscle
- H-caldesmon : smooth muscle

Sarcomas with useful markers

- Synovial sarcoma
- Leiomyosarcoma
- PNET
- DFSP
- MPNST
- Extra-skeletal myxoid chondrosarcoma

Tumors with no specific marker

- Fibrosarcoma
- Myxofibrosarcoma
- Low-grade fibromyxoid tumor
- Osteosarcoma
- Myxoid/round cell liposarcoma
- Pleomorphic liposarcoma
- Pleomorphic MFH

Immunohistochemistry of soft tissue tumors Conclusions

- Major tool for soft tissue tumors
- Quality of technique
- Panel of markers depending on H and E
- Global interpretation