

The challenge to best assess a patient presenting with a retroperitoneal mass

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Disclosure slide

- I have no conflict of interest

Challenges in Retroperitoneal Masses

- RP = common site for several unrelated histologies
- Sarcomas
 - Dedifferentiated liposarcoma
 - Leiomyosarcoma
 - Solitary Fibrous Tumor
 - PEComa
- Lymphoma
- Carcinoma

Challenges in Retroperitoneal Masses

- Use of core biopsy makes diagnoses challenging
- Small amount of tissue
- Necrosis
- Key diagnostic features overlooked

Diagnostic Errors in Pathology of Sarcomas

- Clinical trials
 - 7-10%
- Second opinion
 - 15-35%
- Rare Cancer Networks
 - 5-40%

Source of Errors in Pathology of Sarcomas/Rare Cancers

- Diagnosis intrinsically difficult
 - Common criteria of malignancy not always applicable
 - Several mimics
 - Benign lesions mimicking malignancies and vice versa
 - Complex integration of morphology, immunophenotype and genotype
 - Failure of ancillary techniques

Relevance of Correct Classification

- Rationale of clinical decision making
- Prognosis
- Prediction of response
- Conventional morphology = powerful tool
- Integration with immunohistochemistry is a diagnostic standard
- Molecular genetics increasingly helpful in selected situations

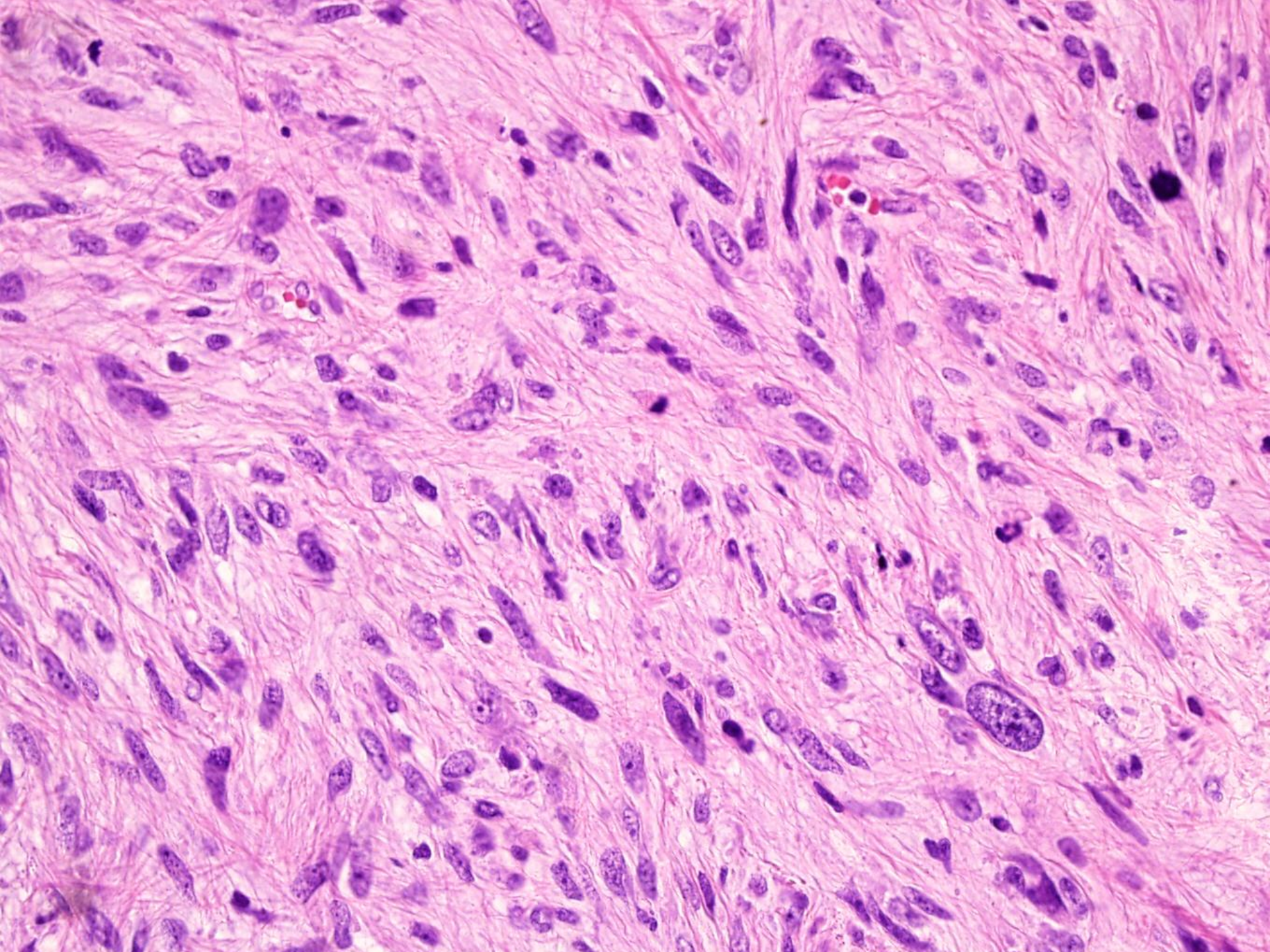
Case History

- 56 year old male
- Large retroperitoneal mass



Differential Diagnosis

- Sarcoma
- Lymphoma
- ...



Differential Diagnosis

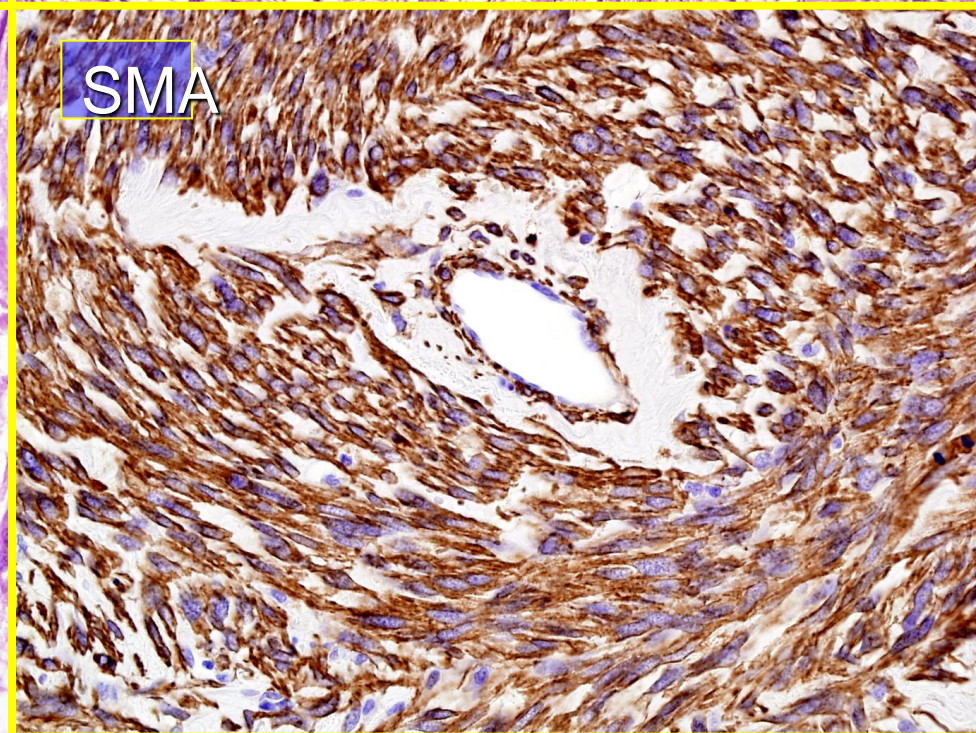
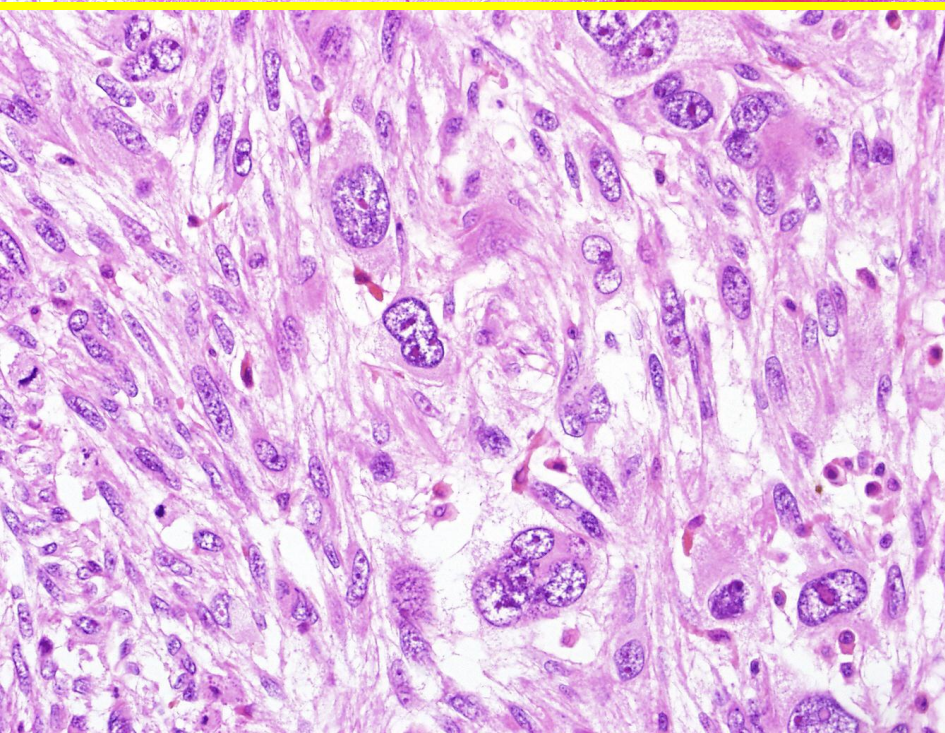
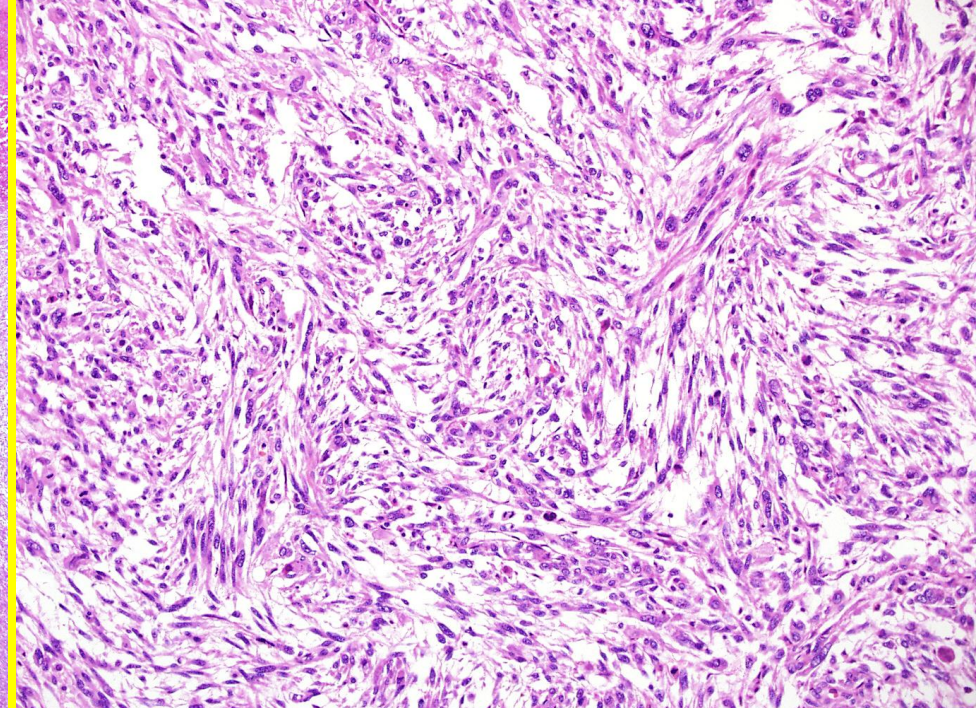
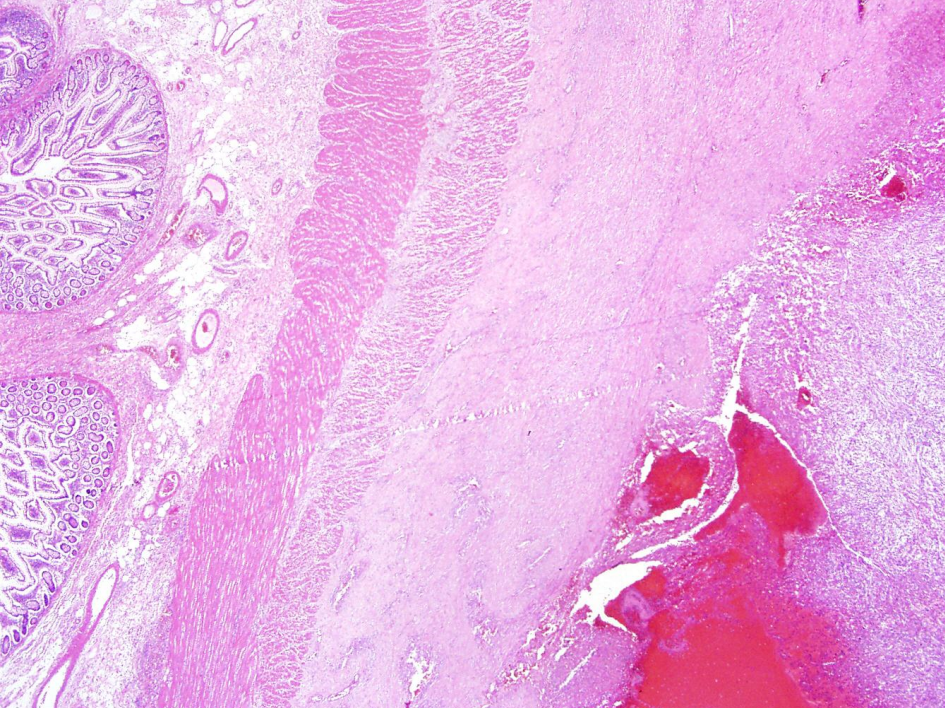
- Pleomorphic neoplasm
- Most likely sarcoma
- Which Sarcoma?
- Does it matter?

Differential Diagnosis

- Dedifferentiated liposarcoma
- Leiomyosarcoma
- Malignant PEComa
- Malignant SFT

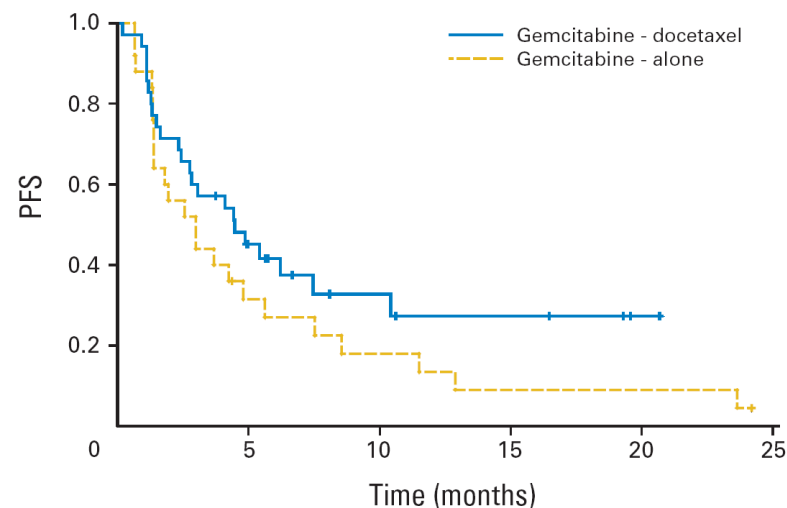
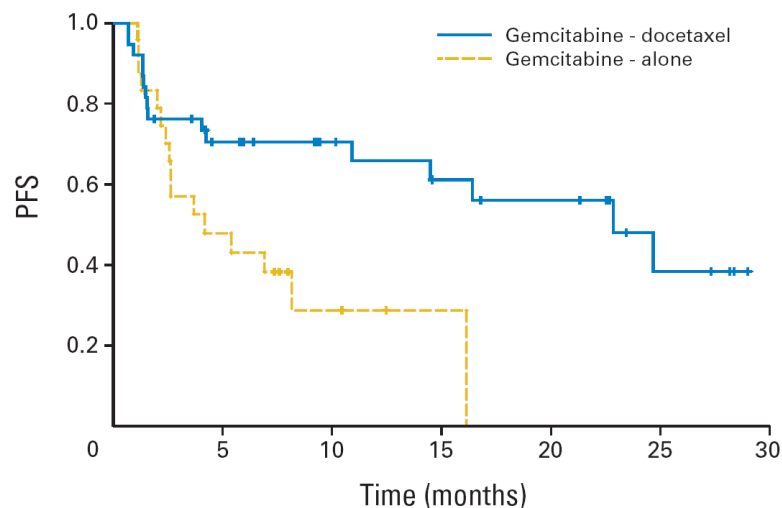
Leiomyosarcoma

- Intra-abdominal LMS
 - retroperitoneum, mesentery, omentum, large veins
 - 5th-7th decade
 - 5-year survival = 25% (mets to lungs & liver)
- Subcutaneous and deep soft tissue LMS
 - thigh
 - 5-year survival = 65% (50% mets)
- Cutaneous LMS (atypical smooth muscle tumors)
 - limbs/head & neck
 - Young adults, M > F
 - no mets



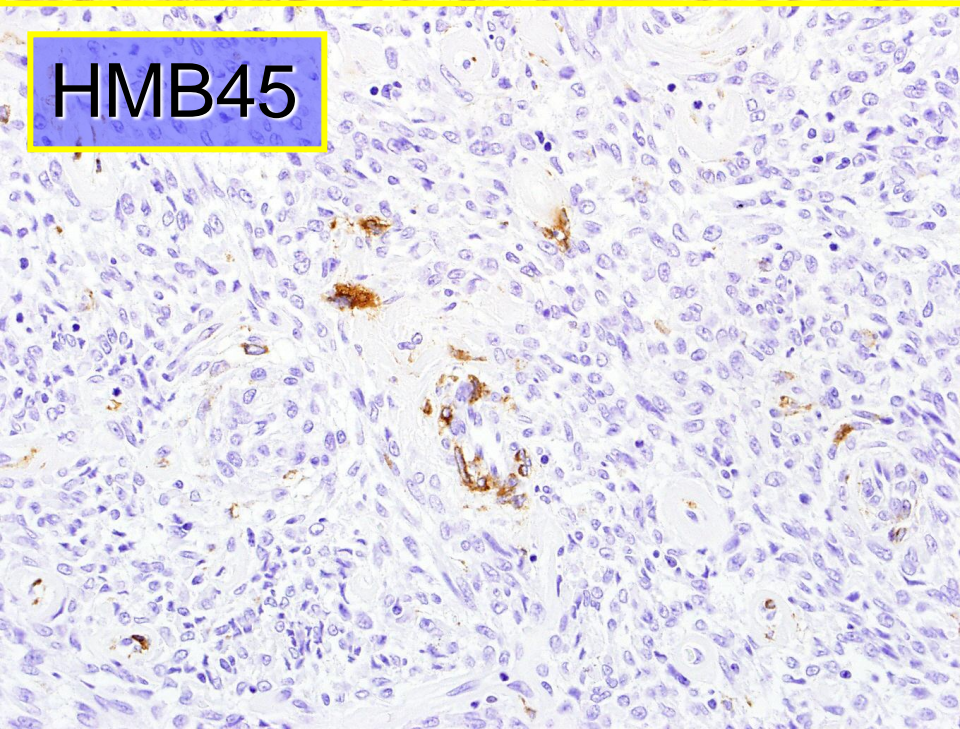
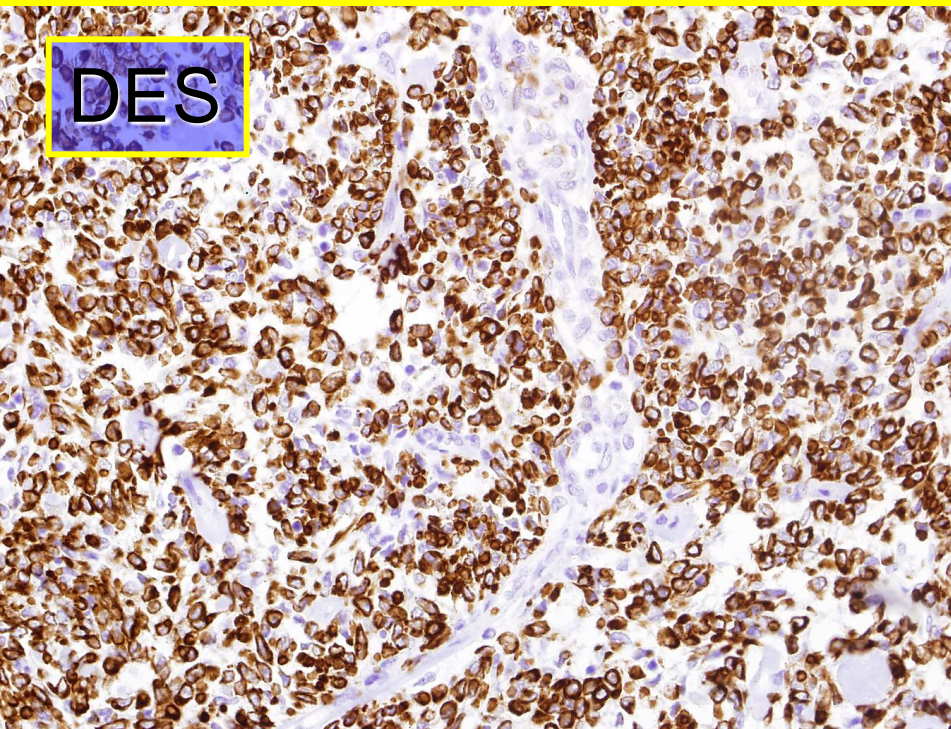
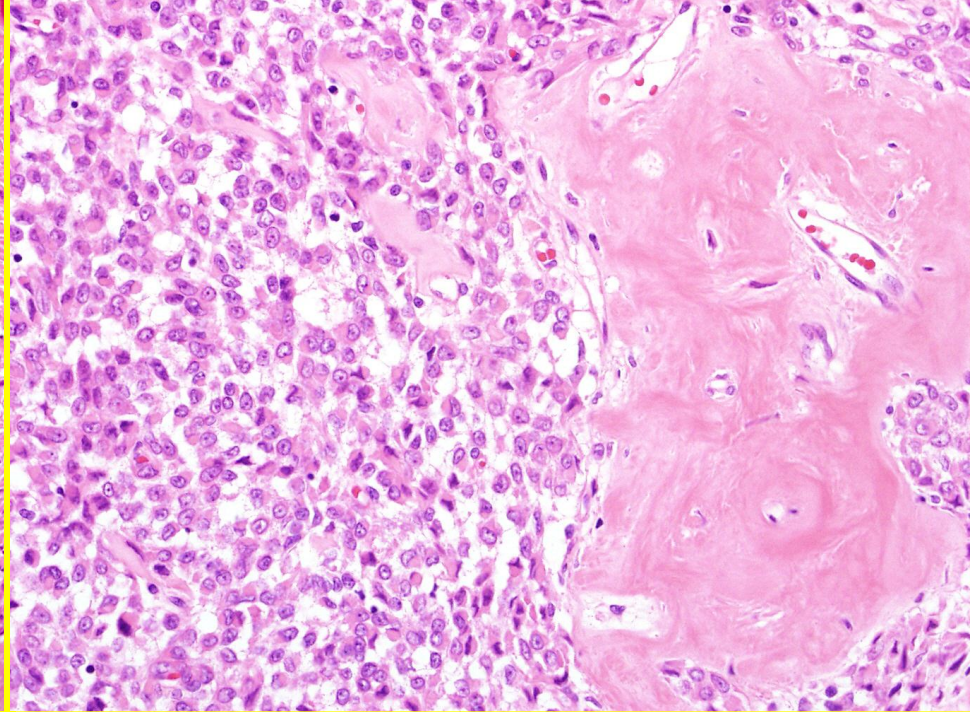
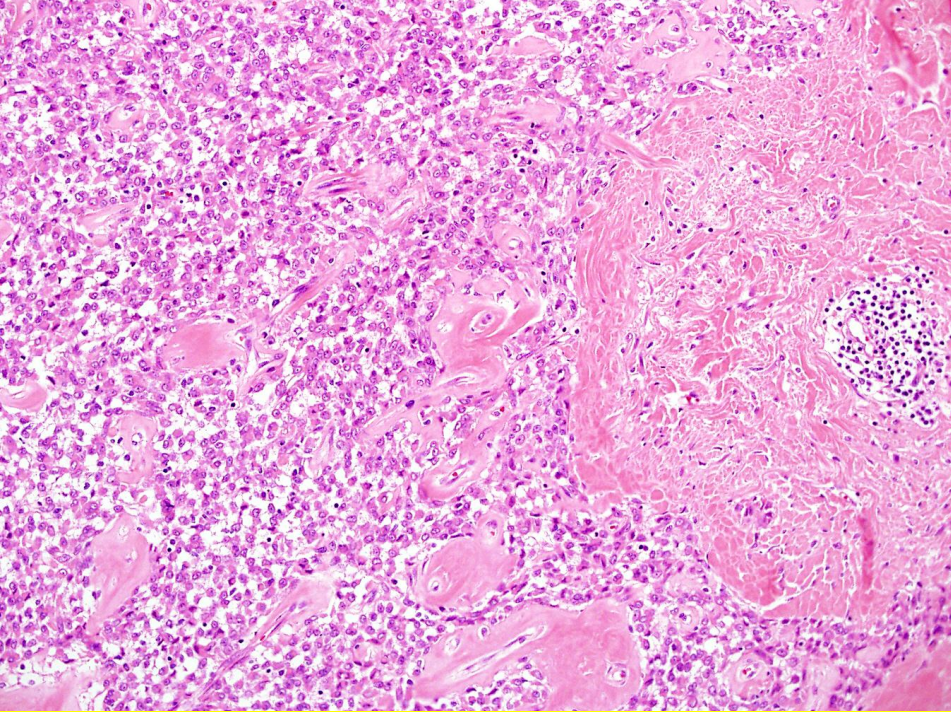
Randomized Phase II Study of Gemcitabine and Docetaxel Compared With Gemcitabine Alone in Patients With Metastatic Soft Tissue Sarcomas: Results of Sarcoma Alliance for Research Through Collaboration Study 002

Robert G. Maki, J. Kyle Wathen, Shreyaskumar R. Patel, Dennis A. Priebe, Scott H. Okuno, Brian Samuels, Michael Fanucchi, David C. Harmon, Scott M. Schuetz, Denise Reinke, Peter F. Thall, Robert S. Benjamin, Laurence H. Baker, and Martee L. Hensley



PEComa

- Myogenic/melanocytic phenotype
- Female predominance
- Wide anatomic distribution
- Retroperitoneum followed by the viscera and the limbs
- Epithelioid and spindle cell proliferation organized in a Perivascular growth pattern
- Variable association with TS
- Criteria of malignancy not fully validated

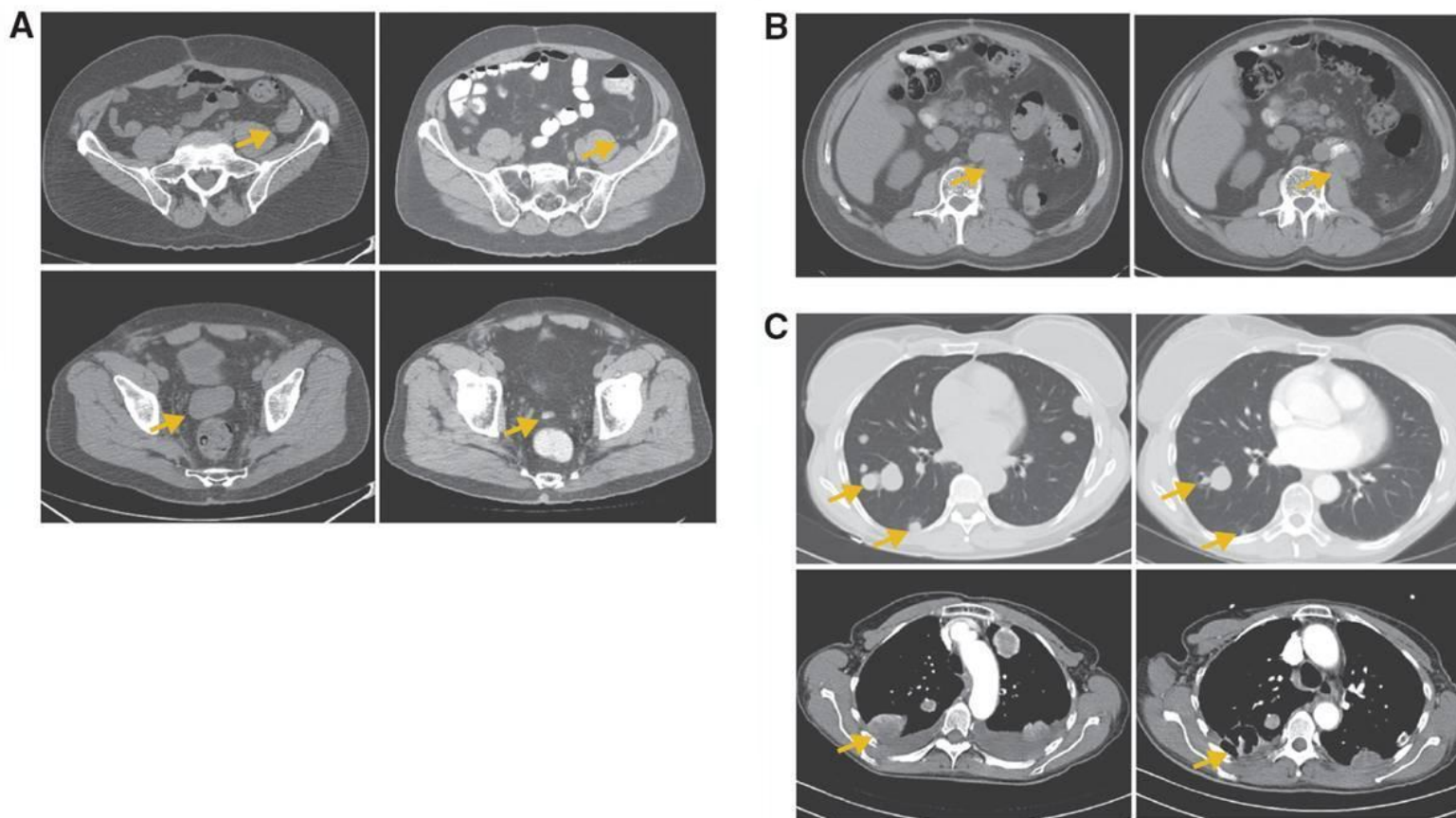


DES

HMB45

Clinical Activity of mTOR Inhibition With Sirolimus in Malignant Perivascular Epithelioid Cell Tumors: Targeting the Pathogenic Activation of mTORC1 in Tumors

Andrew J. Wagner, Izabela Malinowska-Kolodziej, Jeffrey A. Morgan, Wei Qin, Christopher D.M. Fletcher, Natalie Vena, Azra H. Ligon, Cristina R. Antonescu, Nikhil H. Ramaiya, George D. Demetri, David J. Kwiatkowski, and Robert G. Maki

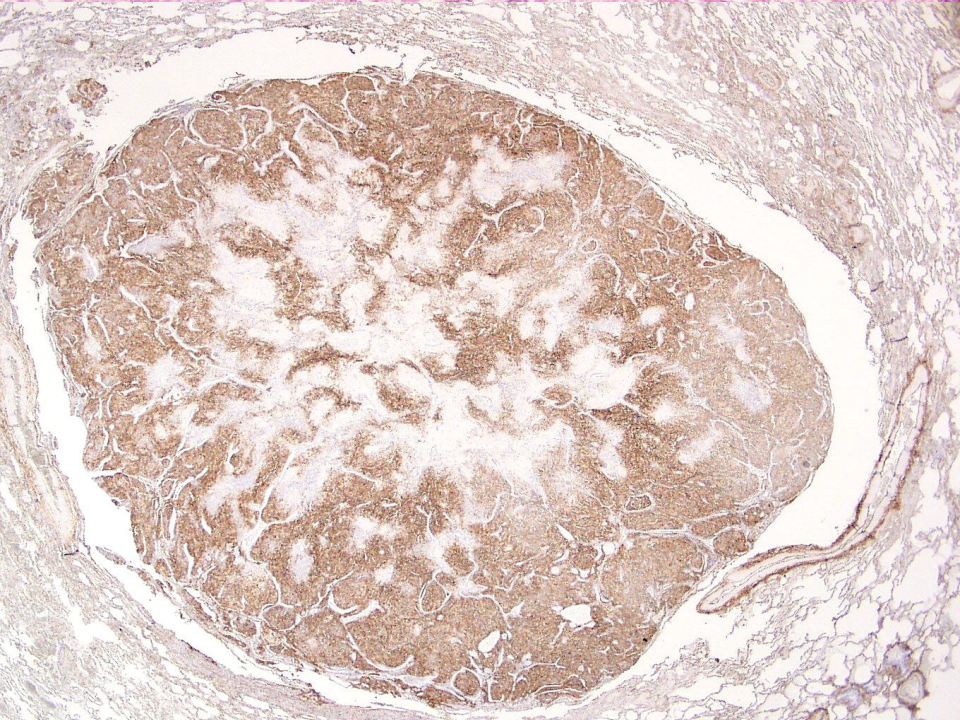
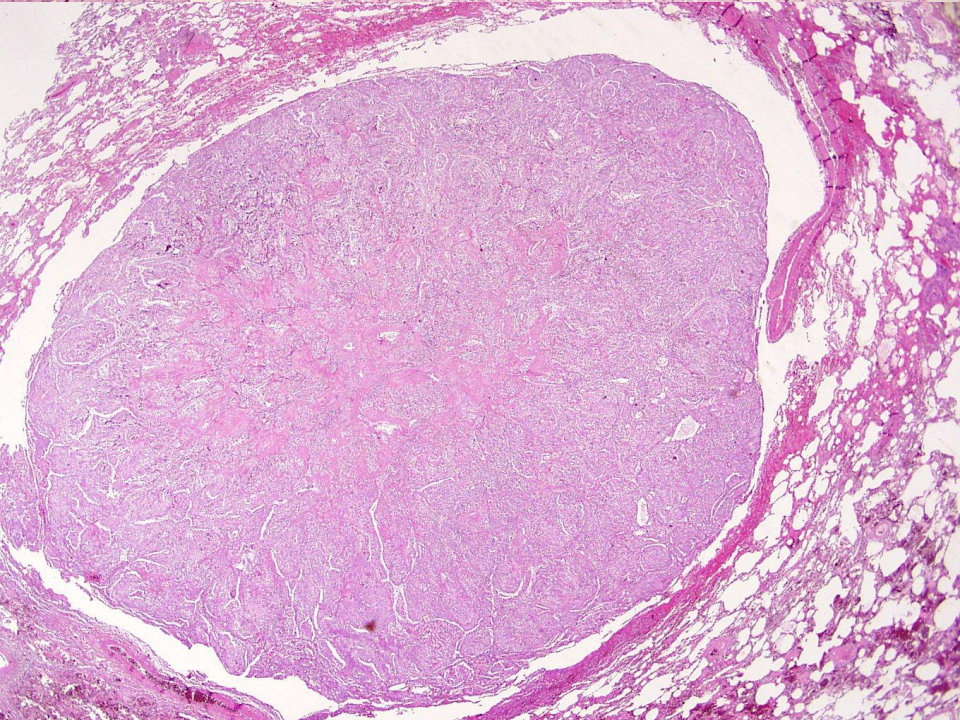
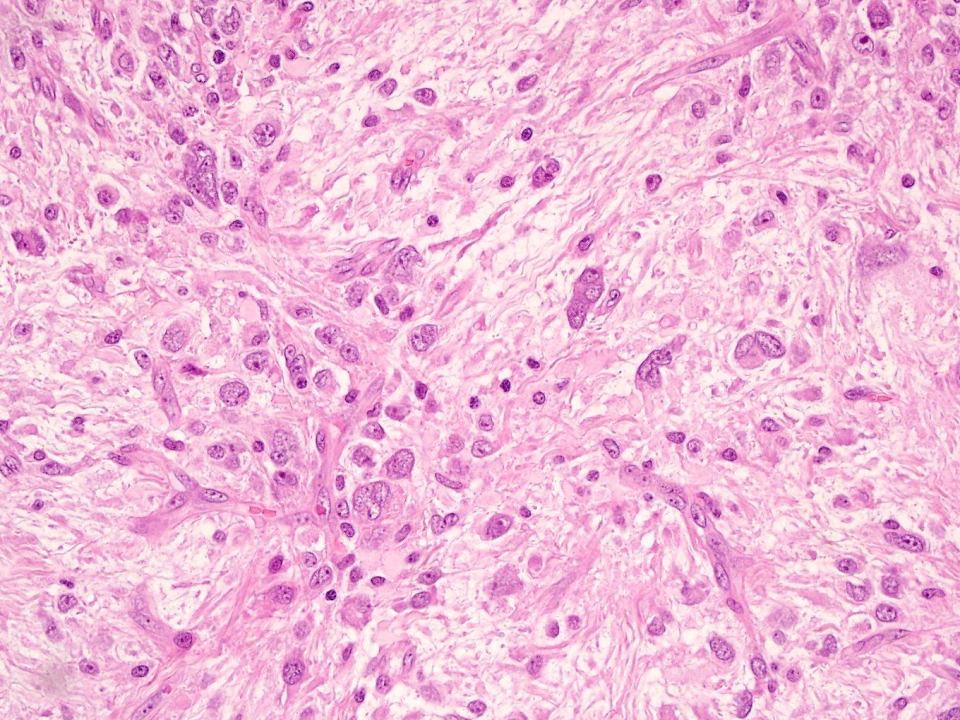
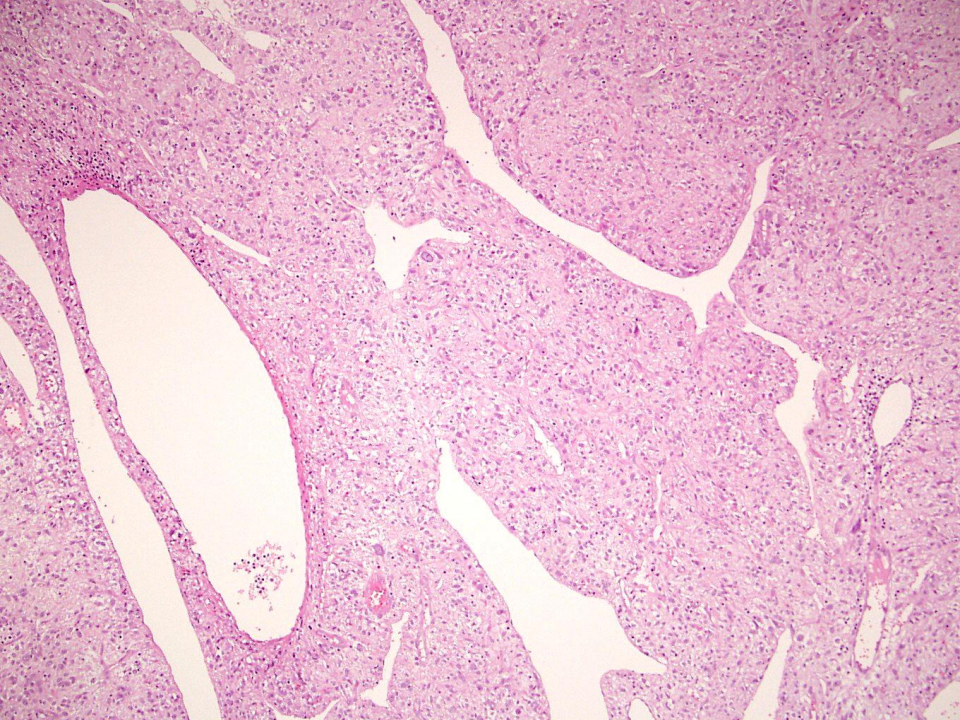


Solitary Fibrous Tumor

- Ubiquitous lesion
 - pleura, peritoneal surface, mediastinum, retroperitoneum, upper respiratory tract, orbit and urogenital tract
- Superficial soft tissue (40%)
- Deep soft tissue of extremities
- Broad age range (20-70) / M = F
- Systemic signs
 - hypoglycemia and digital hyppocratism
 - insulin-like growth factor

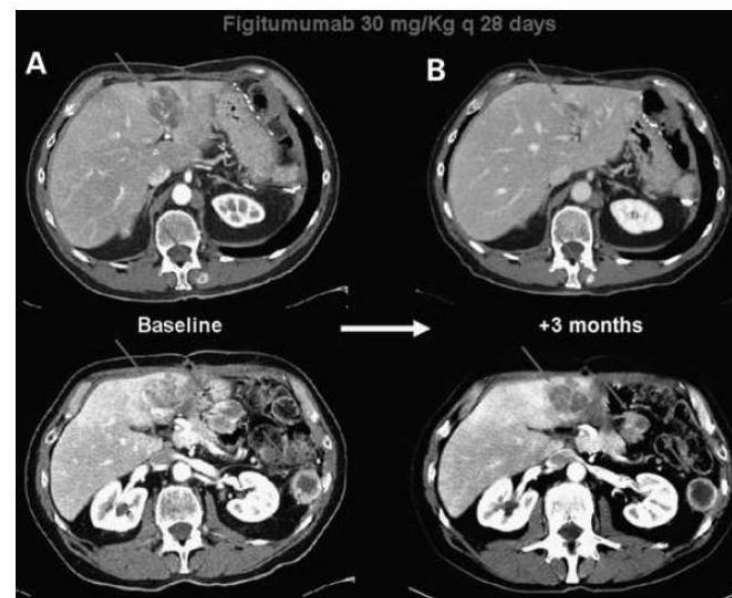
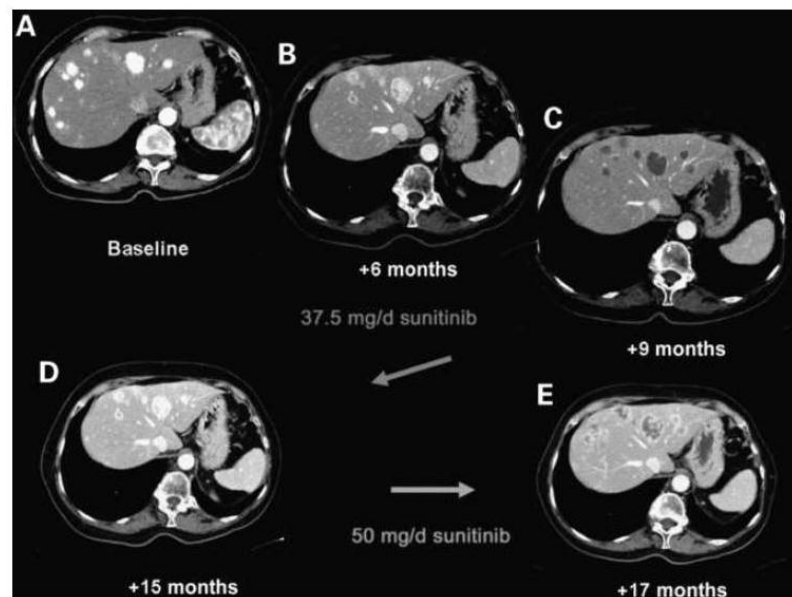
Solitary Fibrous Tumor

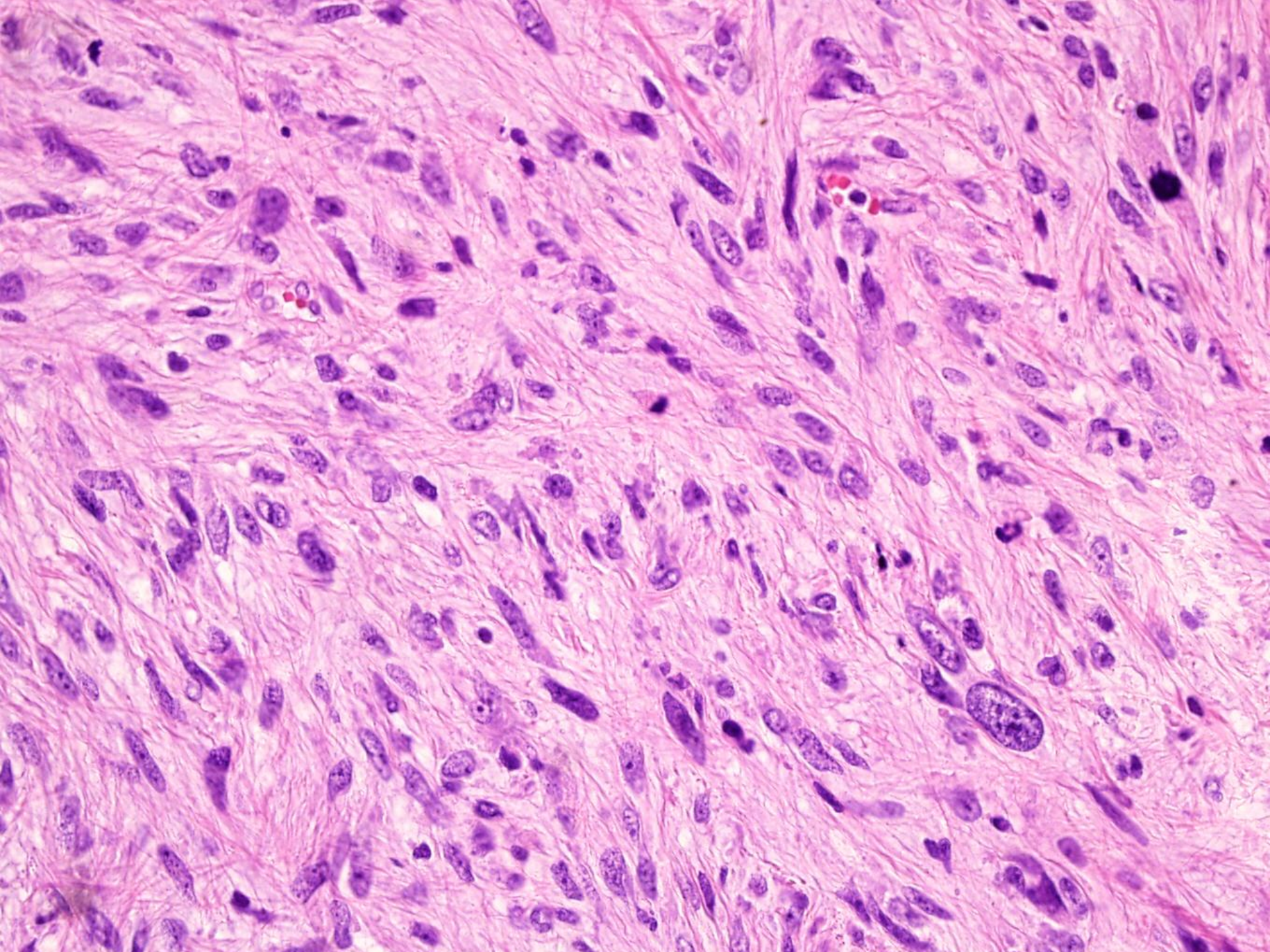
- Unpredictable behavior
- 10-15% behave aggressively
- No strict correlation between morphology and behavior
- Prognostic parameters
- Cytologic atypia
- tumor necrosis
- > 4 mitoses/10HPF



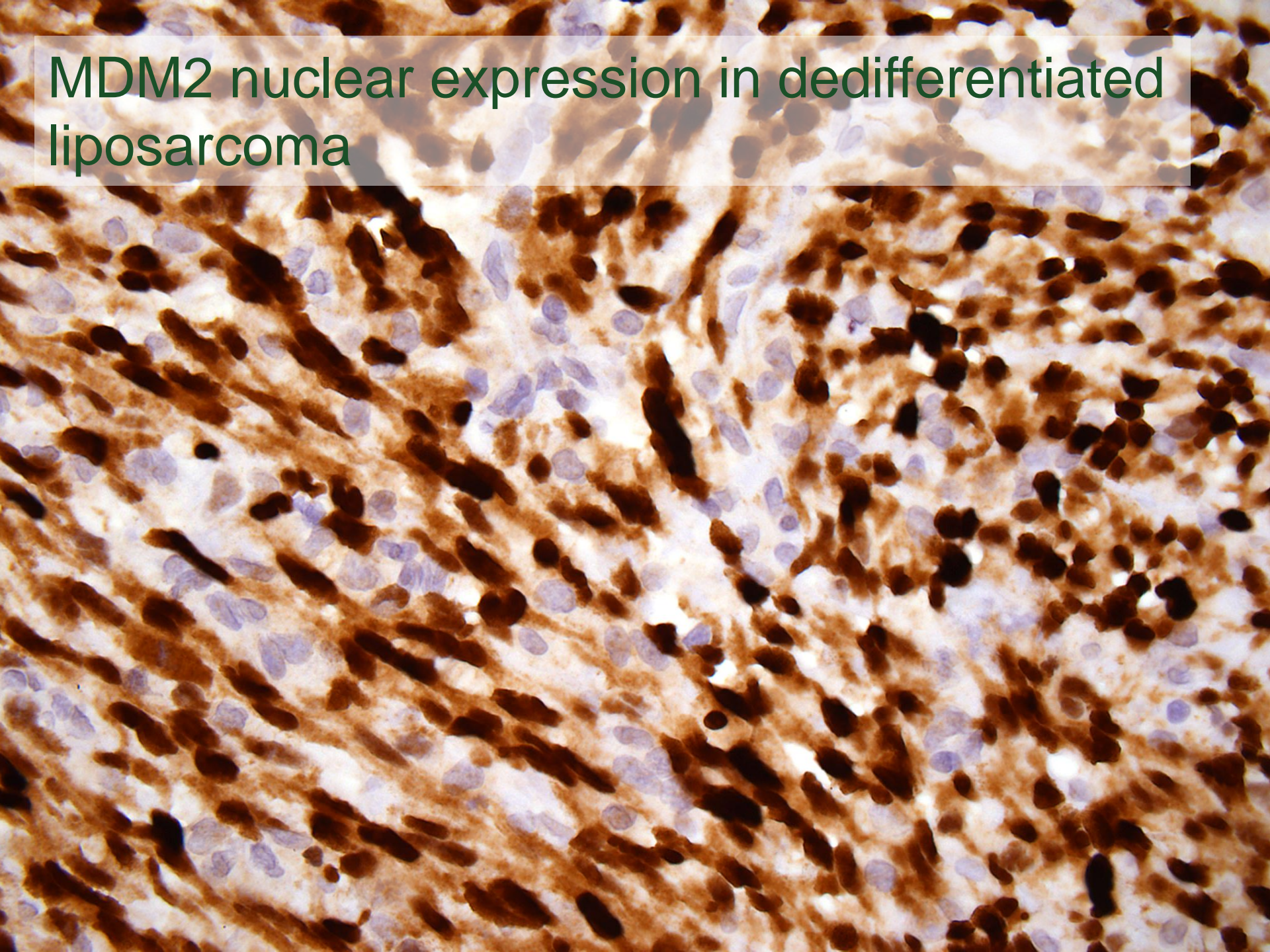
Sunitinib Malate and Figitumumab in Solitary Fibrous Tumor: Patterns and Molecular Bases of Tumor Response

Silvia Stacchiotti¹, Tiziana Negri², Elena Palassini¹, Elena Conca², Alessandro Gronchi³, Carlo Morosi⁴, Antonella Messina⁴, Ugo Pastorino³, Marco A. Pierotti⁵, Paolo G. Casali¹, and Silvana Pilotti²

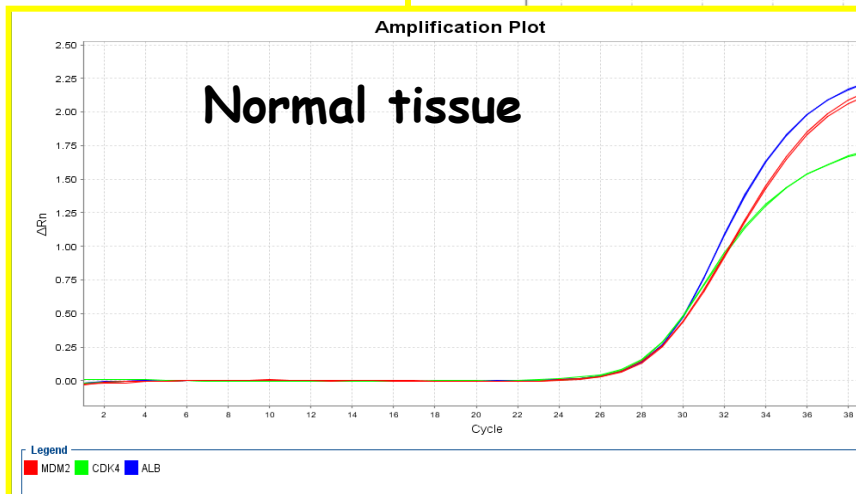
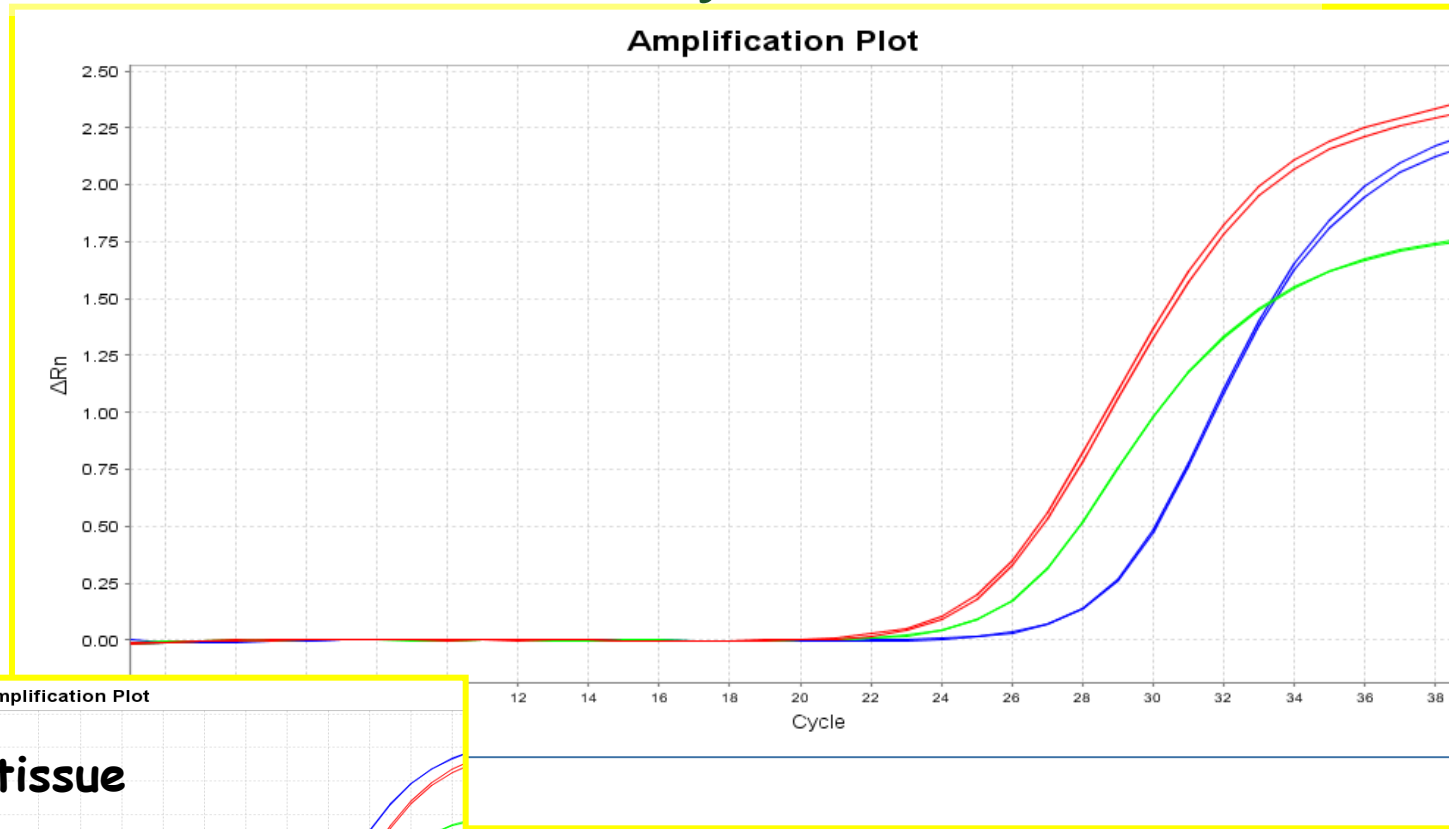




MDM2 nuclear expression in dedifferentiated liposarcoma

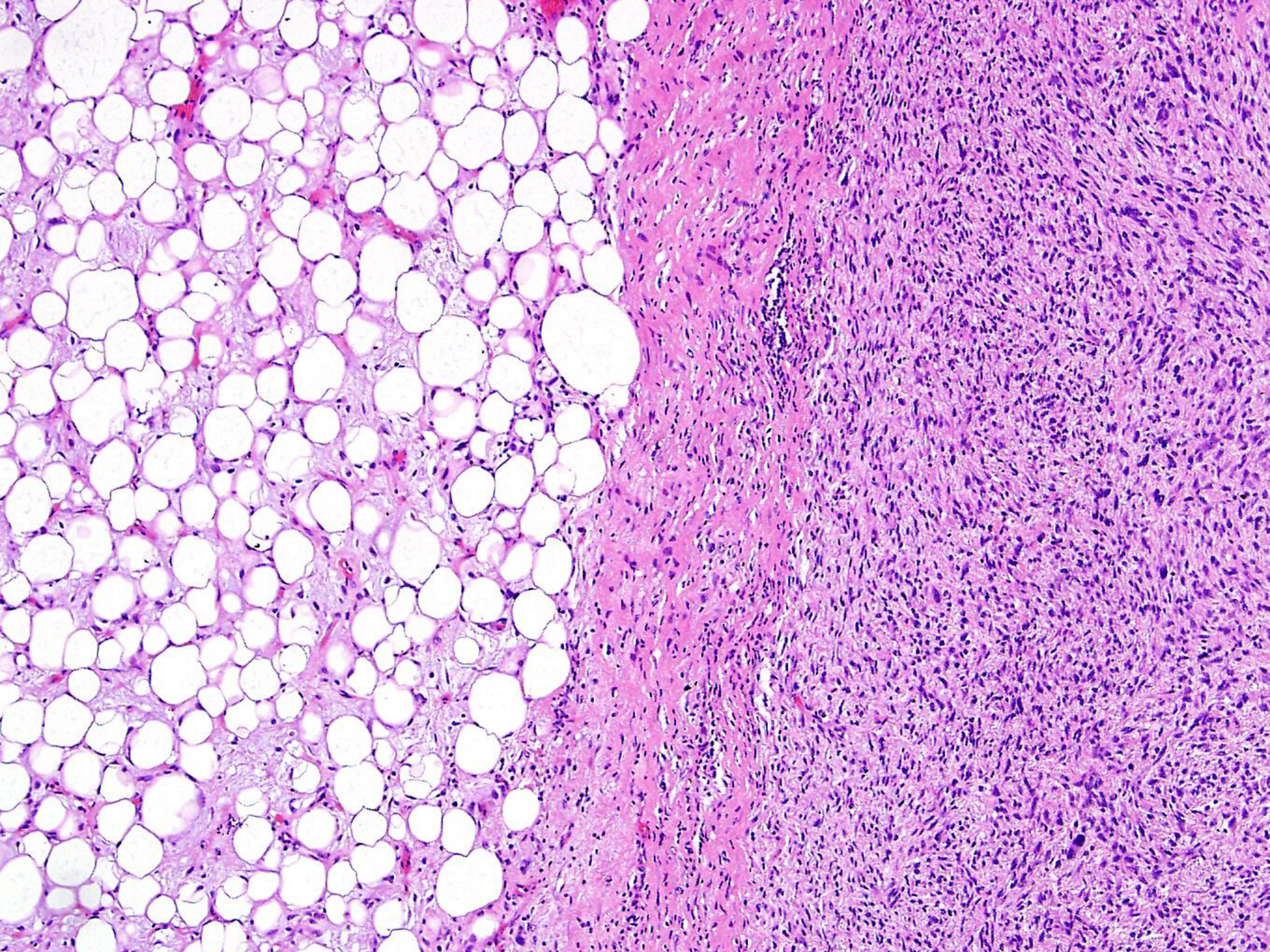


MDM2 amplification in dedifferentiated Liposarcoma assessed by real-time PCR



Dedifferentiated liposarcoma

- Retroperitoneum of adults
- De novo (90%)
- Abrupt transition from WD liposarcoma to high grade non lipogenic sarcoma
- Rarely two components co-mingled
- Rarely non lipogenic component is low grade
- Rarely dedifferentiated component lipogenic
- MDM2/CDK4 overexpression/amplification



Dedifferentiated liposarcoma

- Recurrence rate (41-50%)
- Mets =17%
- Overall mortality (28%)
- Multivisceral surgical resection may improve outcome

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Aggressive Surgical Policies in a Retrospectively Reviewed Single-Institution Case Series of Retroperitoneal Soft Tissue Sarcoma Patients

Alessandro Gronchi, Salvatore Lo Vullo, Marco Fiore, Chiara Mussi, Silvia Stacchiotti, Paola Collini, Laura Lozza, Elisabetta Pennacchioli, Luigi Mariani, and Paolo Giovanni Casali

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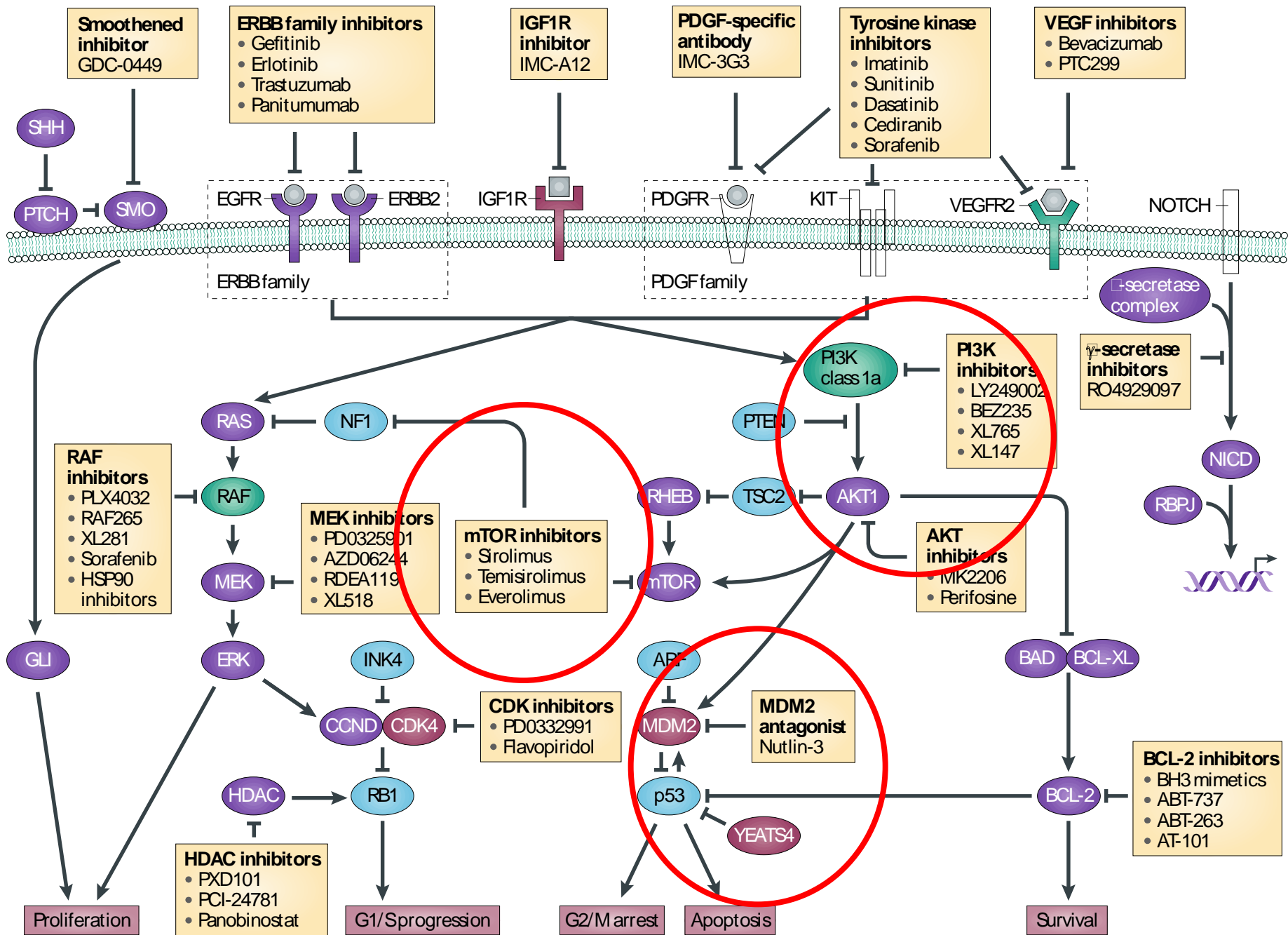
ORIGINAL REPORT

Primary Retroperitoneal Sarcomas: A Multivariate Analysis of Surgical Factors Associated With Local Control

Sylvie Bonvalot, Michel Rivoire, Marine Castaing, Eberhard Stoeckle, Axel Le Cesne, Jean Yves Blay, and Agnès Laplanche

MDM2 and WD/ Dedifferentiated LPS

- Existence of a molecular mechanism
 - Overexpression and amplification of MDM2(and CDK4/HMGA2)
- Diagnostic application
- Possibility to target that molecular mechanism
 - Nutlin A3 targets MDM2 \Rightarrow apoptosis and growth arrest
 - CDK4 inhibitors
- Clinical trial



Take-home messages

- Retroperitoneal masses are a challenge
- Differential diagnosis is broad
- Combination of morphology and genetics is extremely helpful
- Accurate diagnosis sets the ground for optimal management

