

# SARC004

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## Neoadjuvant Imatinib in DFSP

May 2009 Update  
Scott Schuetze, MD

# Pre-operative Imatinib in DFSP

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## ■ Objectives

- Determine effects of imatinib on phosphorylation of PDGFRB in DFSP
- Correlate inhibition of PDGFRB with:
  - Plasma levels of imatinib
  - Inhibition of downstream kinases
  - Inhibition of tumor proliferation
  - Induction of apoptosis
- Bank patient matched tissue for future study

# Treatment Plan

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- Pre-imatinib fresh tumor for molecular studies
- Imatinib 400 mg bid for 10 to 14 days prior to planned surgical resection
- Blood draw for imatinib plasma level within 24 hrs of surgery
- Collect tumor for study at surgery
- 13 evaluable patients (viable matched tumor tissue/subject taking imatinib)

# Study Specimens

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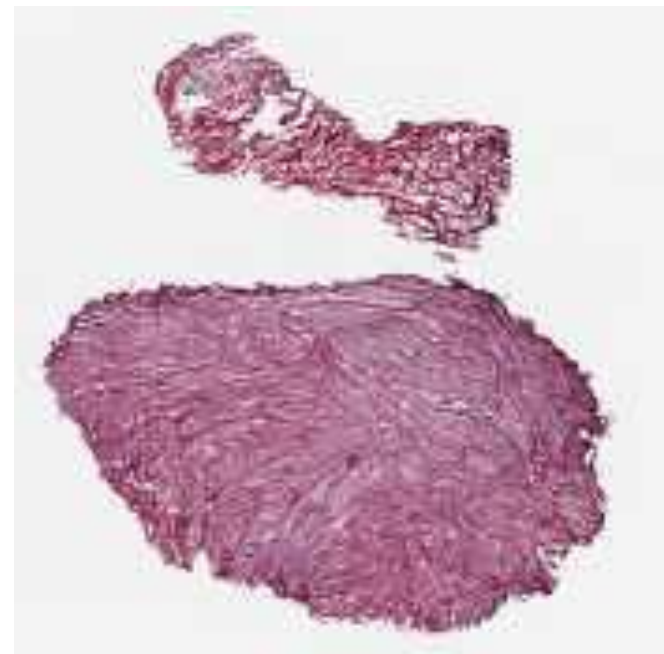
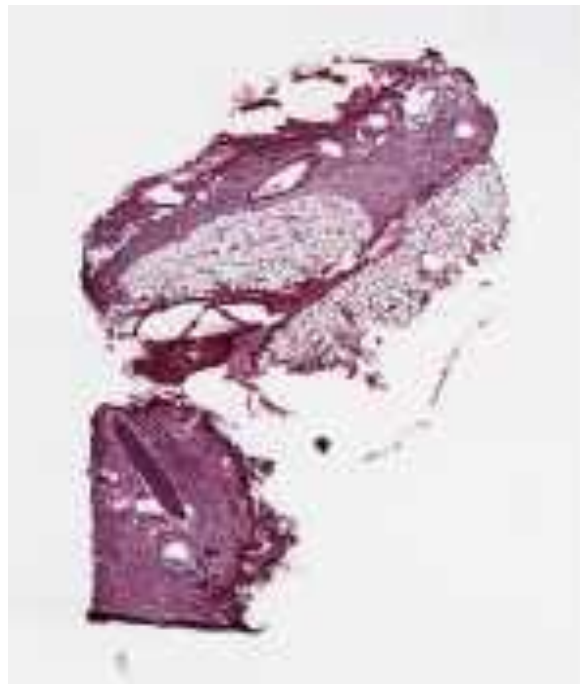
- 13 matched pairs pre and post imatinib treatment
- 13 pre-surgery plasma imatinib levels (range 1068 – 4767 ng/ml, mean 3182 ng/ml)

# DFSP Samples – MDA 7 & 5

Pre

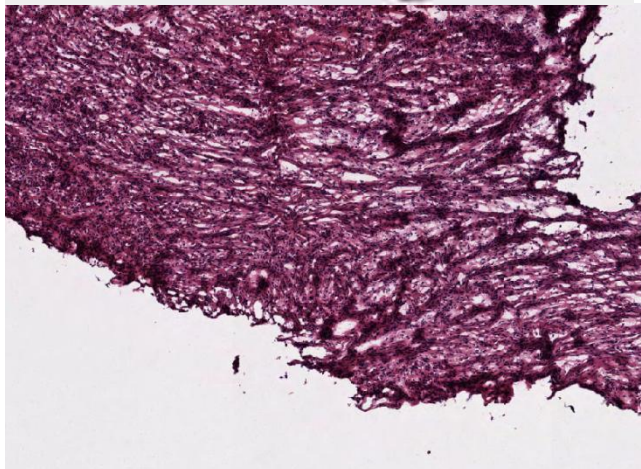
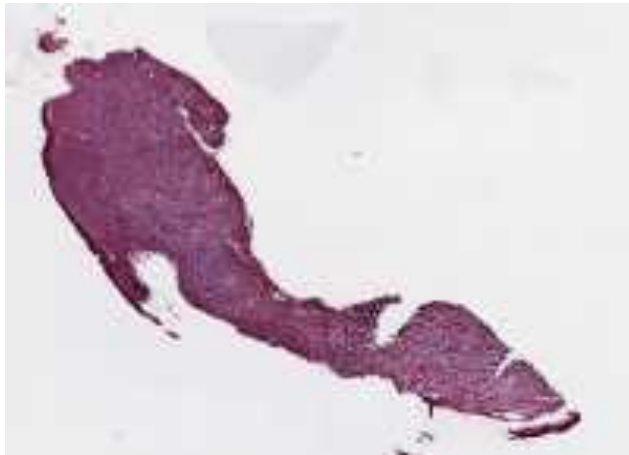


Post

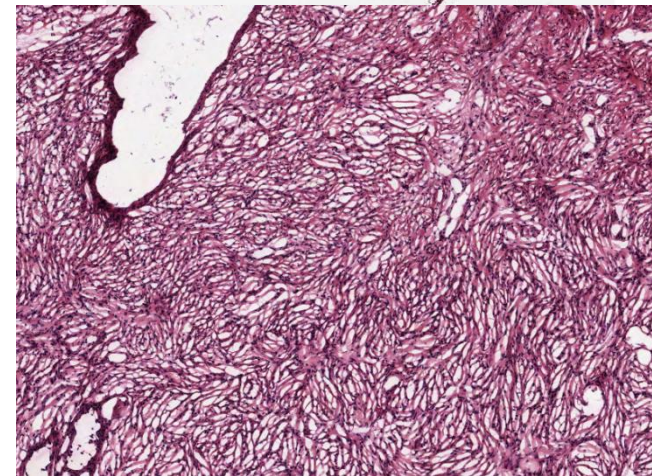
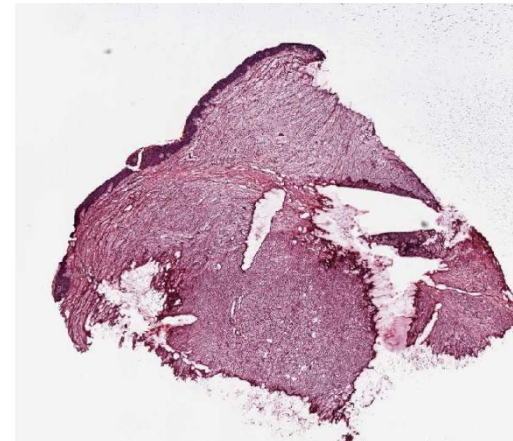


# DFSP Sample – UM03

Pre



Post



# DFSP: Proposed Analysis

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- Morphology
- Verify presence of t(17;22).
- Evaluate change in proliferation
- Evaluate change in apoptosis
- Evaluate change in kinase phosphorylation

# DFSP – Histologic Description

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- Description of morphology and necrosis on H&E sections

# DFSP Translocation Studies

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- Describe COL1A1-PDGFB rearrangement in DFSP samples – requires 3 thick slices from FFPE tissue (resection specimen or clinical biopsy) DNA extraction for PCR
- Detect rearrangement using FISH – requires unstained slide from FFPE tissue
- Does not require use of research specimen if sample is limited

# DFSP – Proliferation / Apoptosis

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- Determine % Ki-67 + cells in pre vs post treatment specimens using slides from FFPE or frozen specimen – proliferation
- Determine relative change in apoptosis rate in pre vs post treatment specimens using slide from FFPE or frozen specimen for TUNEL assay and cleaved caspase stain – apoptosis

# DFSP – Kinase Pathway

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- Compare phosphorylated to total kinase ratios in pre and post treatment samples
- Protein extraction from research specimens
- Use antibody array against broad panel of kinases – require approx 100 ng protein
  - PDGFRB – Akt – mTOR – S6kinase
- Test assay/methods on non-research frozen DFSP samples in UM sarcoma bank