#9001

Antivascular and Apoptotic Effects of Imatinib in GIST

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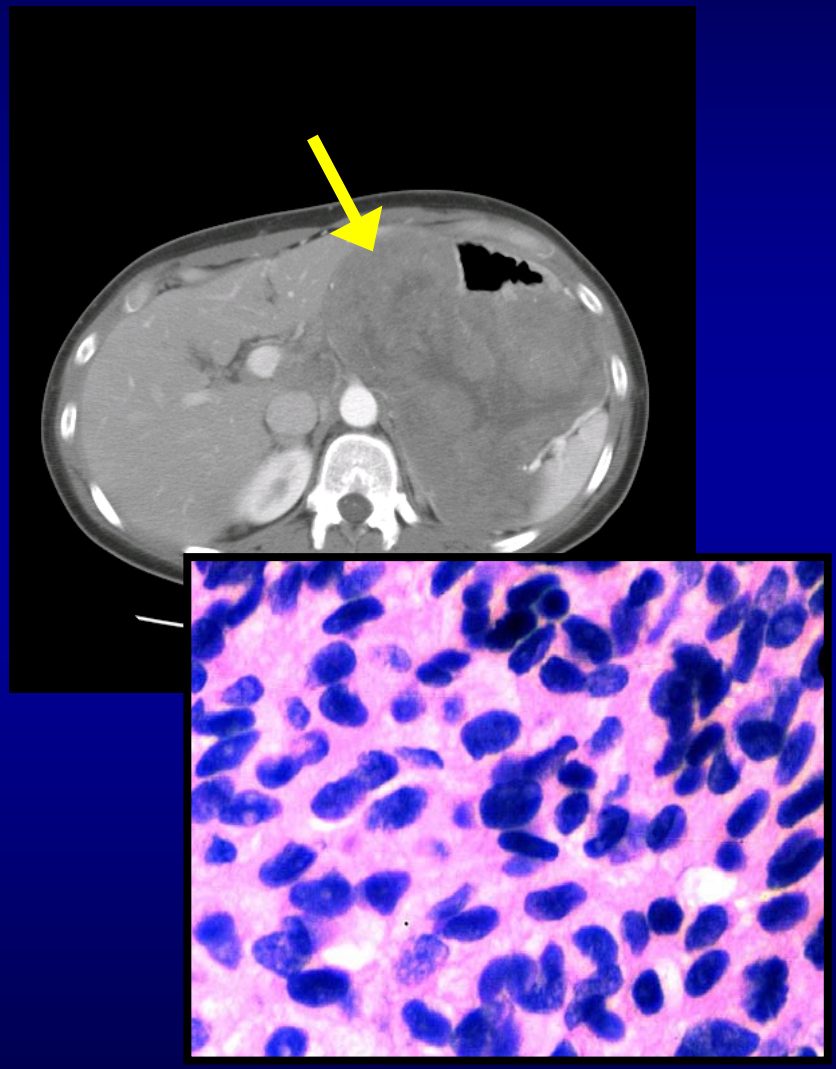
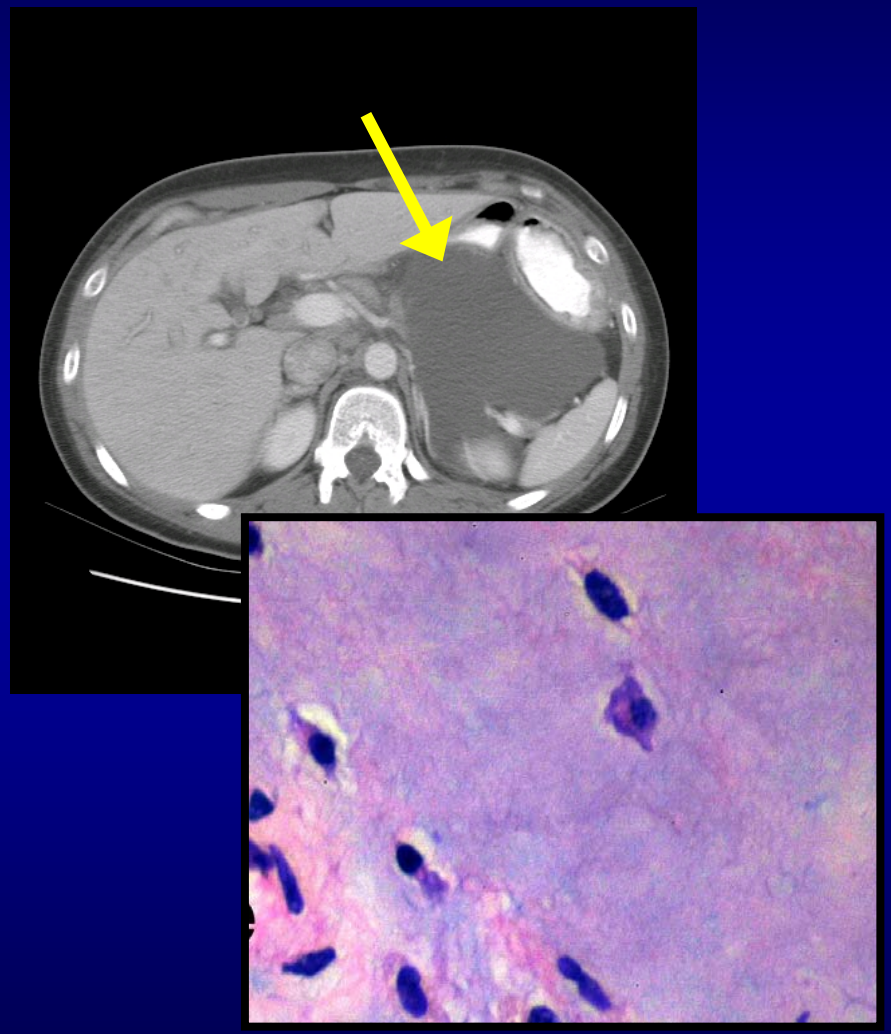
Background (cont)



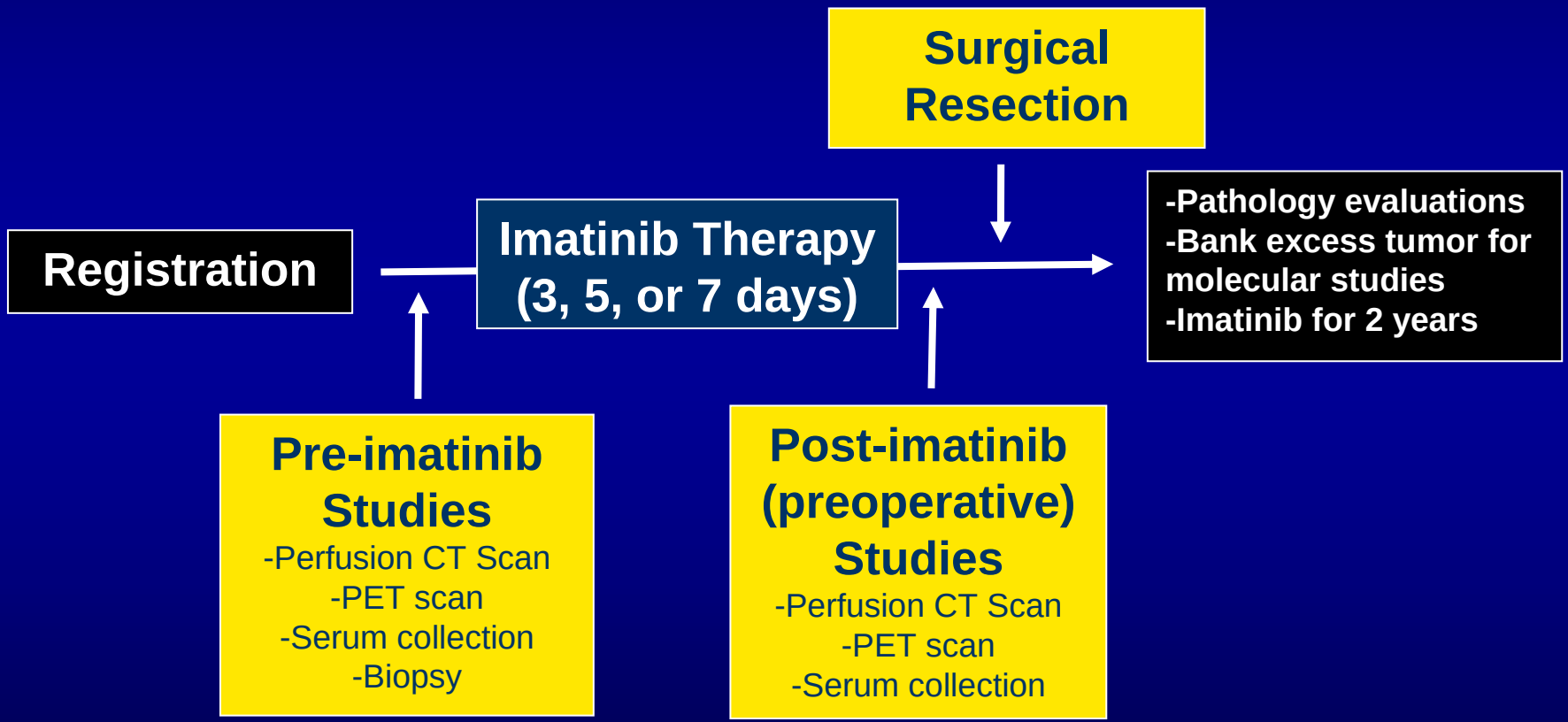


Hypotheses

- Effects of imatinib begin during the first week of therapy
- Imatinib therapy perturbs vascular physiology in GIST
- Imatinib induces apoptosis of GIST cells

MDACC ID03-0023

Preoperative plus postoperative imatinib for patients with Kit(+) GIST



Patient Characteristics

n=13

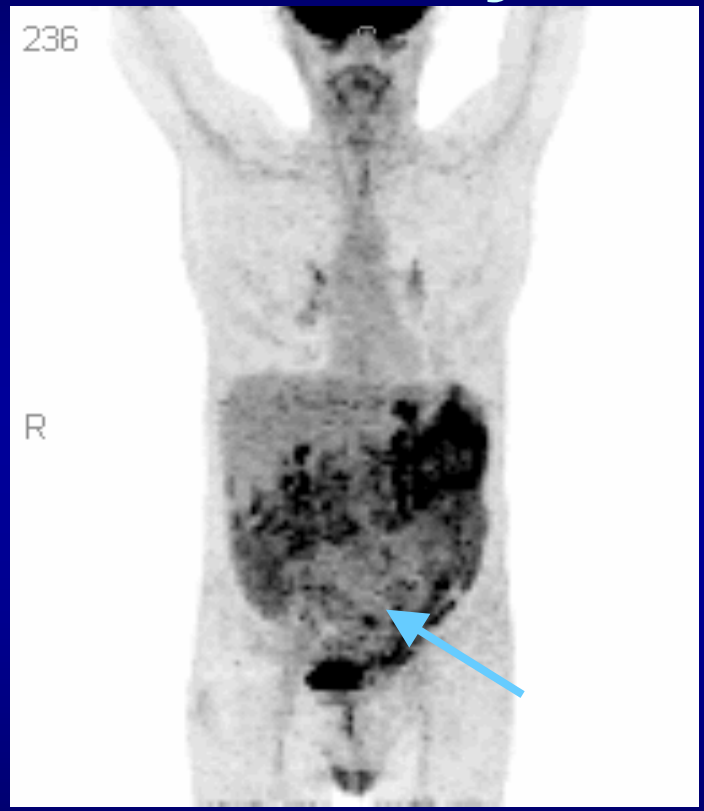
Characteristic	Value
Age (median)	52 (range 38-67)
Gender (M/F)	7/6
Primary Site of Tumor	
- Stomach	6
- Small Intestine	5
- Colon	2

Preoperative Imatinib Toxicity

Grade 3/4

Toxicity	Number of Patients (*n=13*)
Nausea/emesis	2
Abdominal pain	1
GI Hemorrhage	1
Hypovolemia	1
None	11

PET Response at Day 5



Pre-imatinib

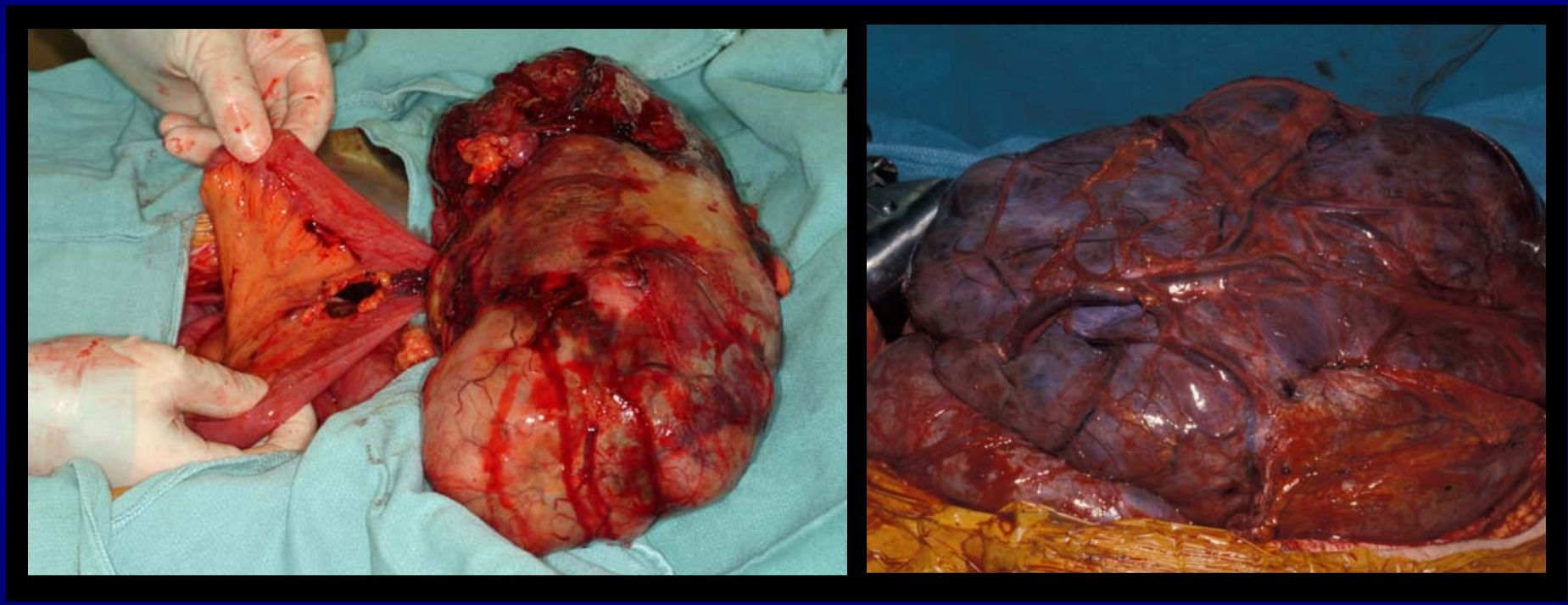
Post-imatinib (Day 5)

PET Response Data
n=12

	3 Days	5 Days	7 Days	Total
Responders	3	2	3	8
Non-responder	1	2	1	4

Courtesy Homer Macapinlac, M. D.

Surgical Findings



Preoperative Imatinib (3 days)

No Preoperative Imatinib

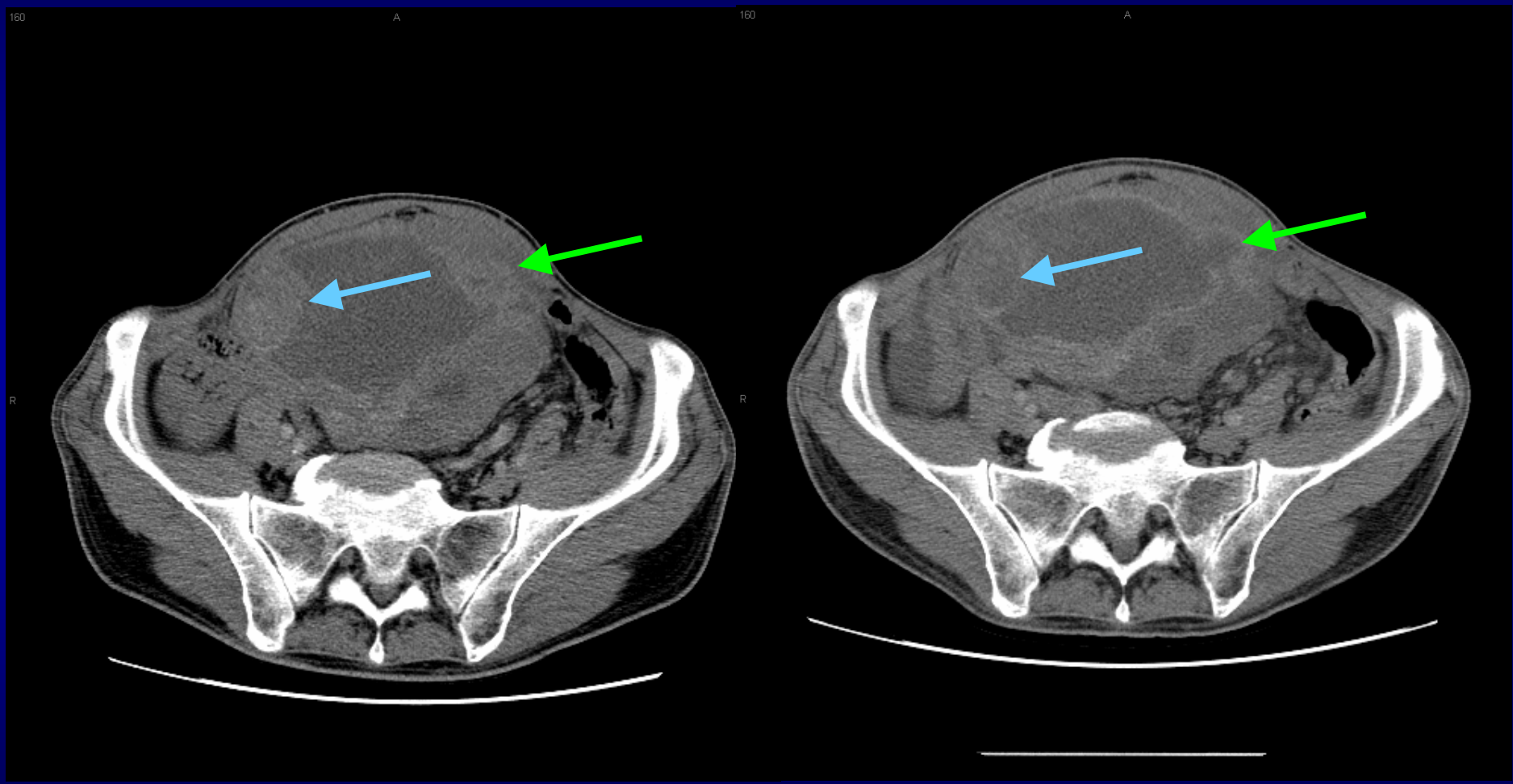
Courtesy Kelly Hunt, M. D.

Perfusion Computed Tomography (CT)

- Allows quantitative measurement of tumor vascular physiology
- Non-invasive, rapid
- Validated in oncology
  - Detection of metastases
  - Indicator of malignancy
  - Assessment of response to therapy

Effect of Imatinib on Perfusion CT

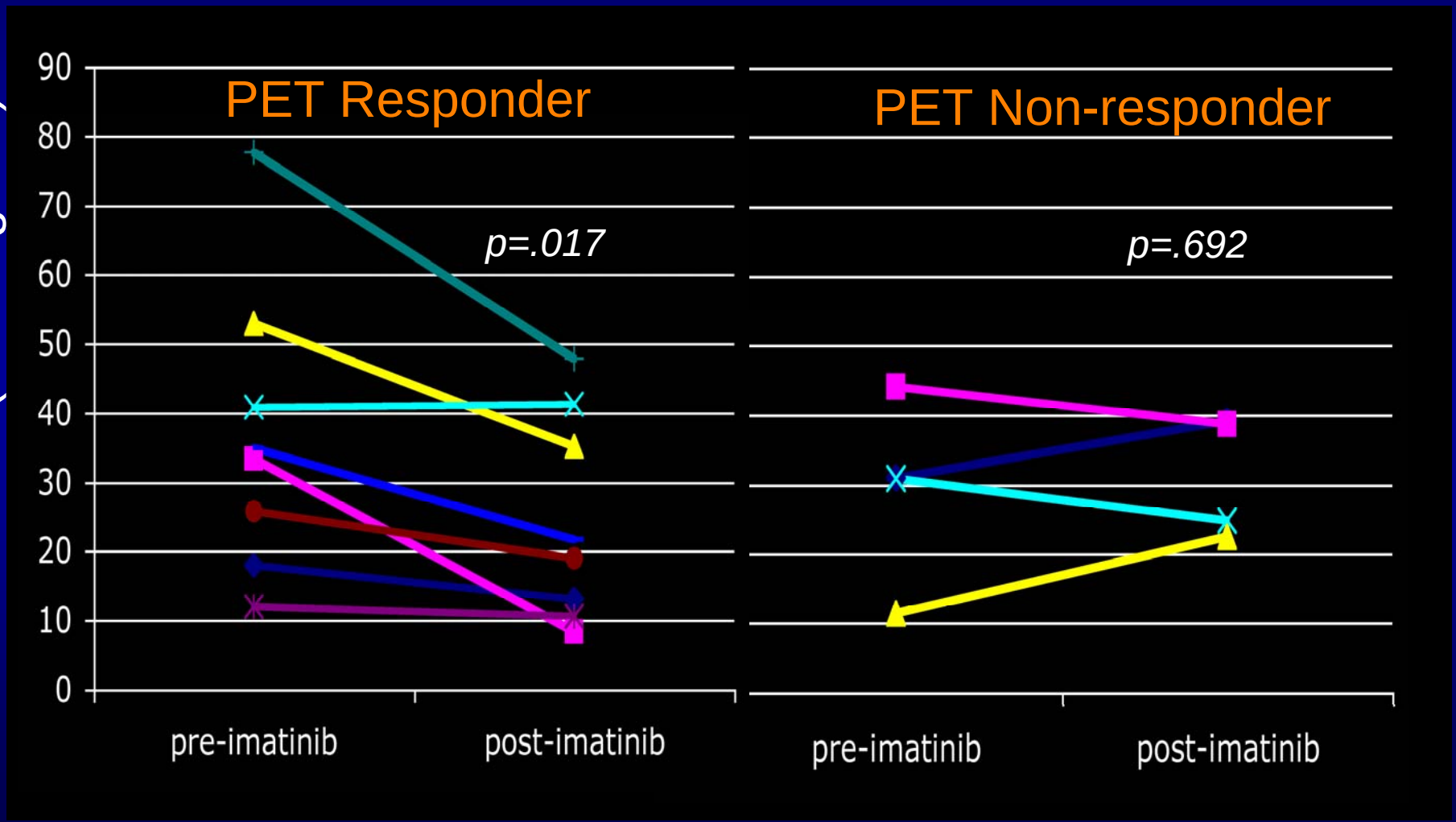
5 days of therapy



Pre-imatinib

Post-imatinib (Day 5)

Effect of Imatinib on Perfusion CT

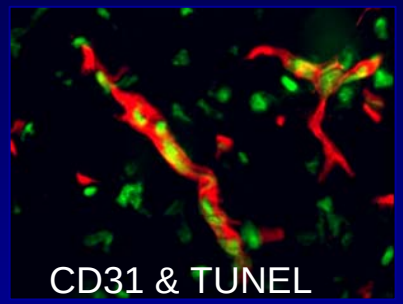


Effect of Imatinib on Vascular Physiology by Perfusion CT

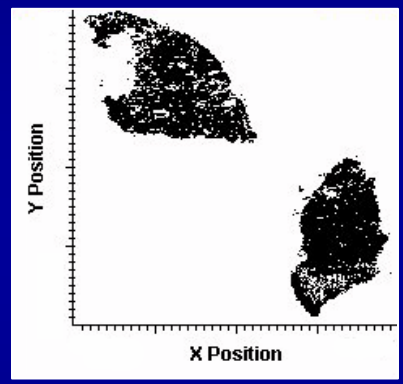
Perfusion Parameter	Pre-Imatinib	Post-Imatinib	*P* Value
BF (mL/100g/min)	36.84	24.55	0.017
BV (mL)	3.90	2.84	0.005
MTT (s)	9.47	9.96	0.26

Laser Scanning Cytometry (LSC)

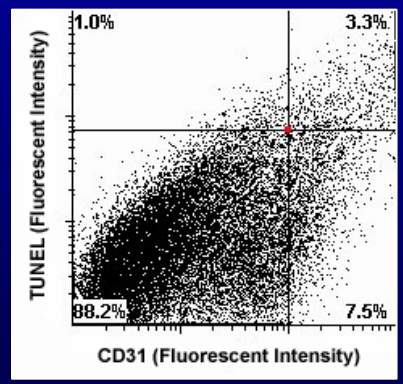
Immunofluorescent
Staining
of Target Antigen



Scan Specimen using the LSC
to Generate a Tissue Map



Quantitate Cell Number
Based on Gating Labelled cells
Reported as a % of Total Cells Counted



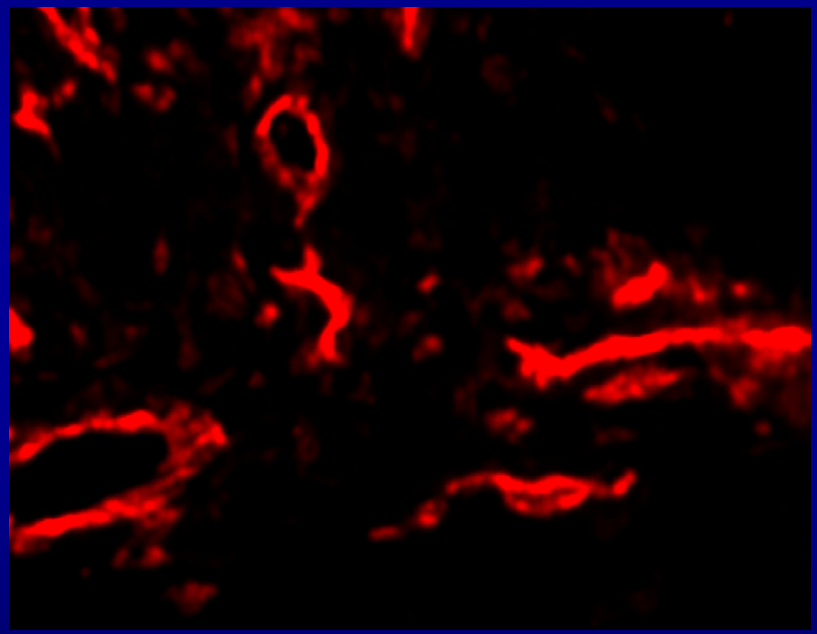
Scattergram

Courtesy Darren Davis, Ph. D.

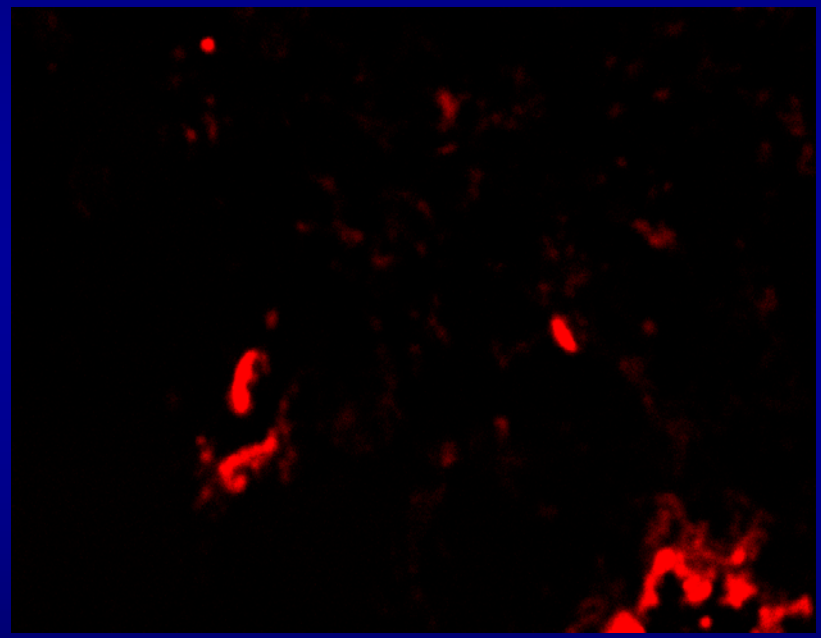
Effect of Imatinb on MVD

3 days of therapy

Pre-Imatinib

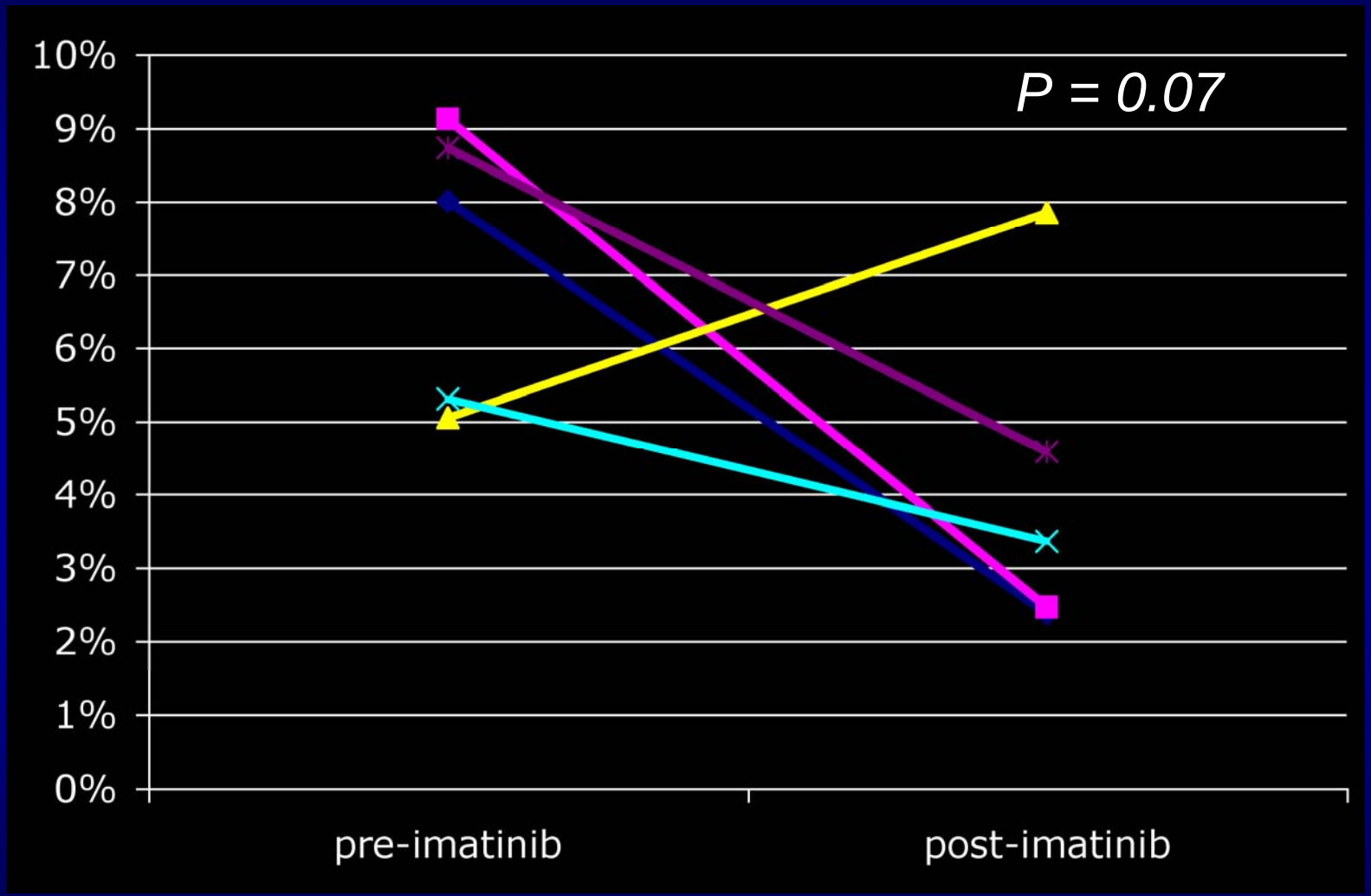


Post-Imatinib



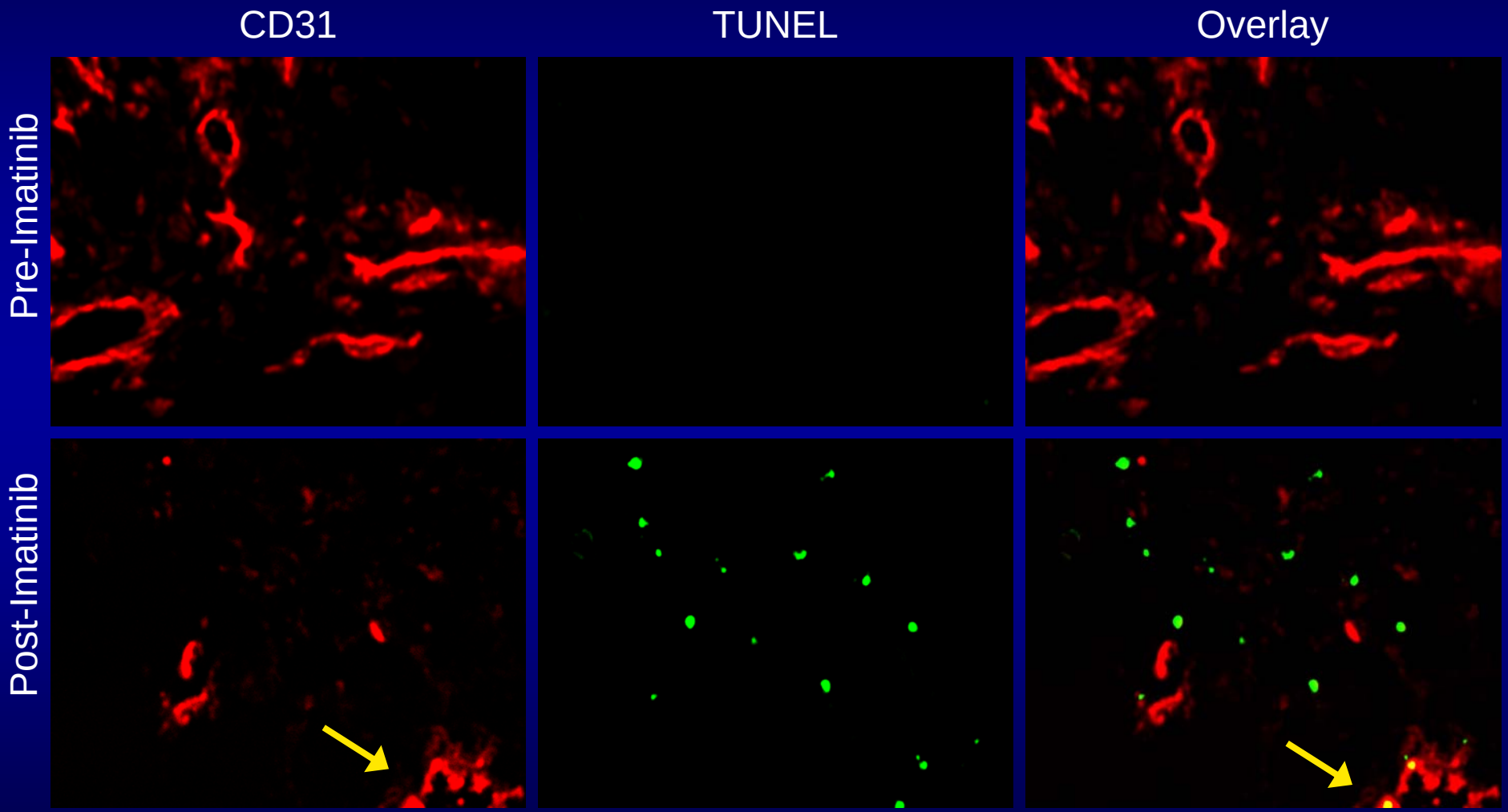
CD-31 immunofluourescent staining of GIST vessels

Effects of Imatinib on MVD



Endothelial Cell Apoptosis

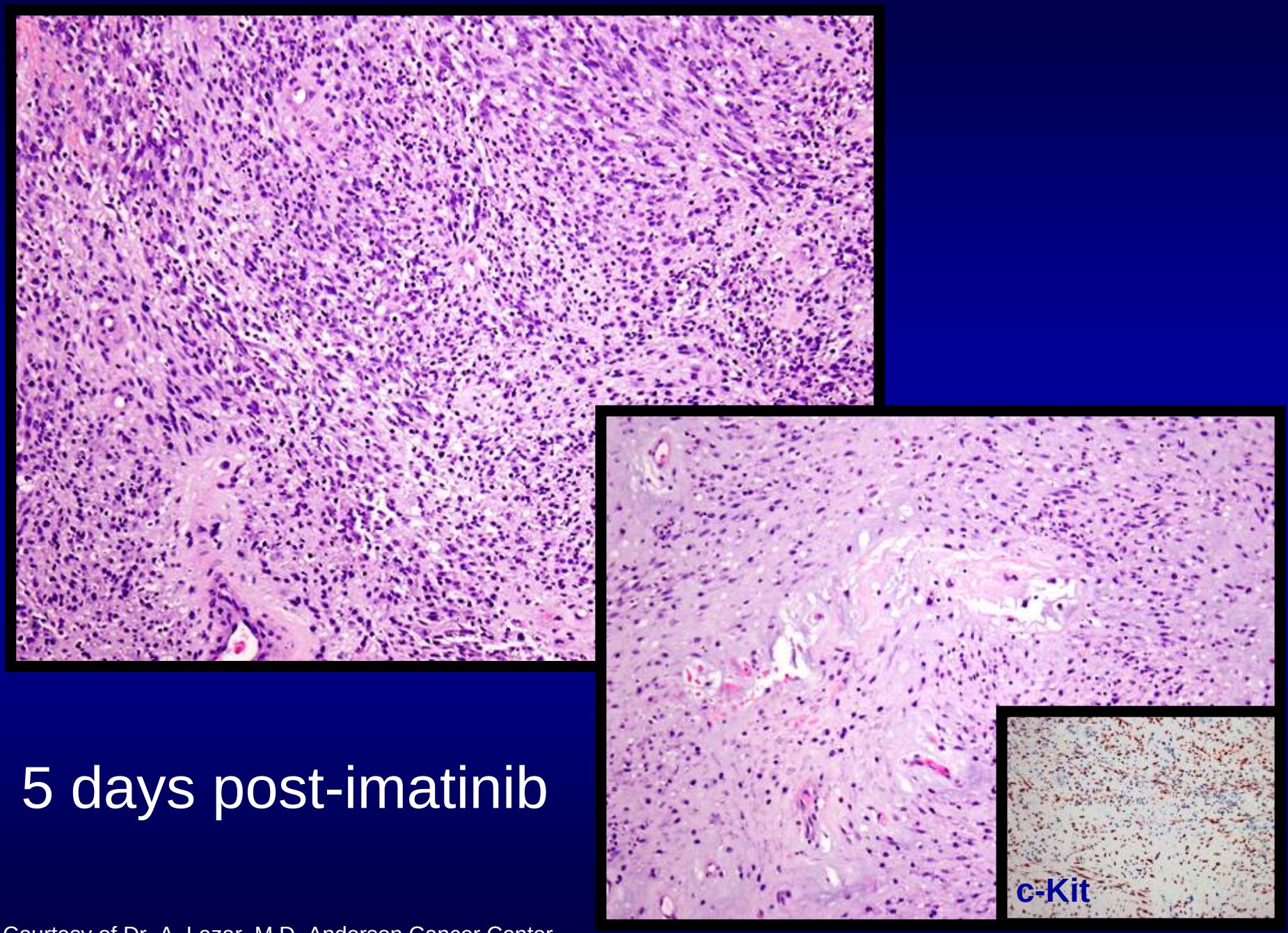
3 days post-imatinib



Vascular Effects of Imatinib

- GISTs with response by PET show a significant decrease in BF and BV after imatinib therapy
- There is a trend toward a decrease in MVD after imatinib
- Endothelial cell apoptosis was observed

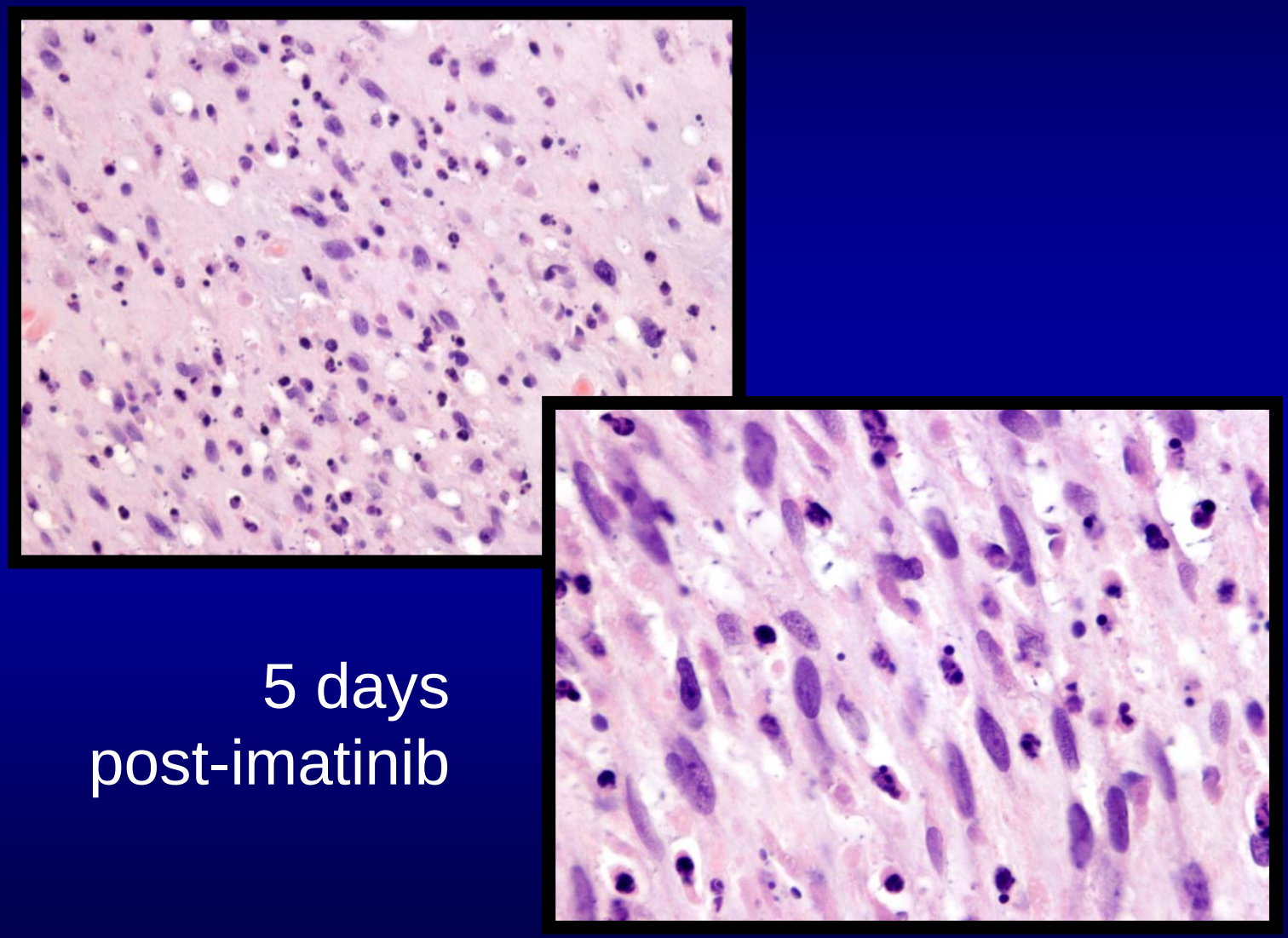
Apoptotic Effects of Imatinib in GIST



5 days post-imatinib

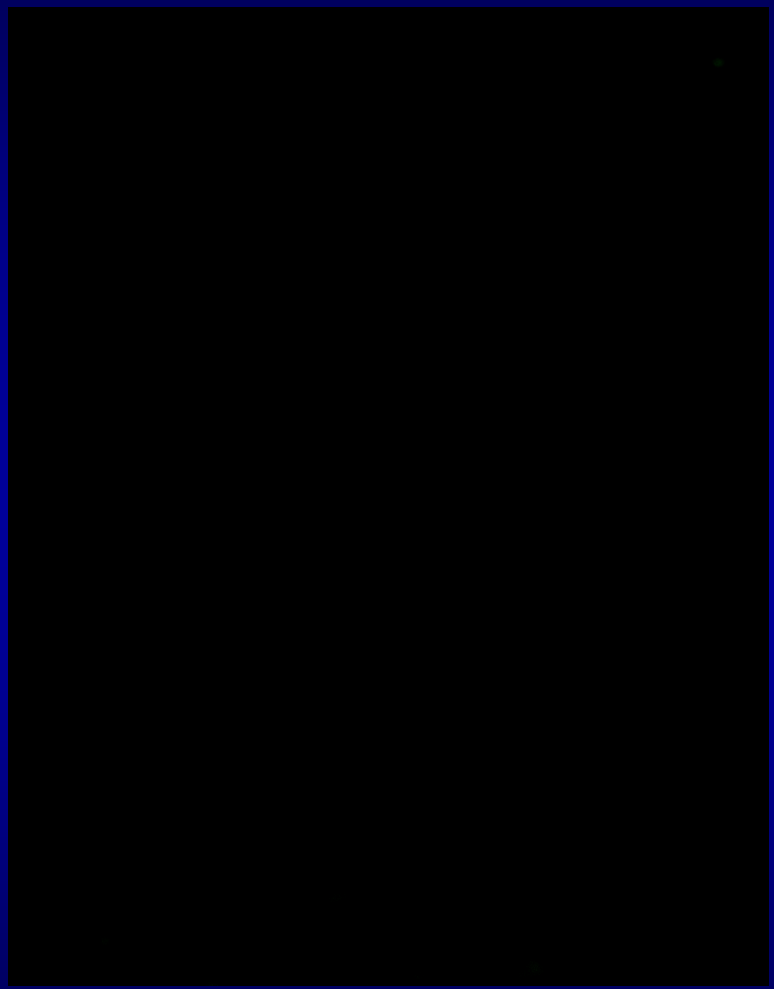
Courtesy of Dr. A. Lazar, M.D. Anderson Cancer Center

Apoptosis After Imatinib

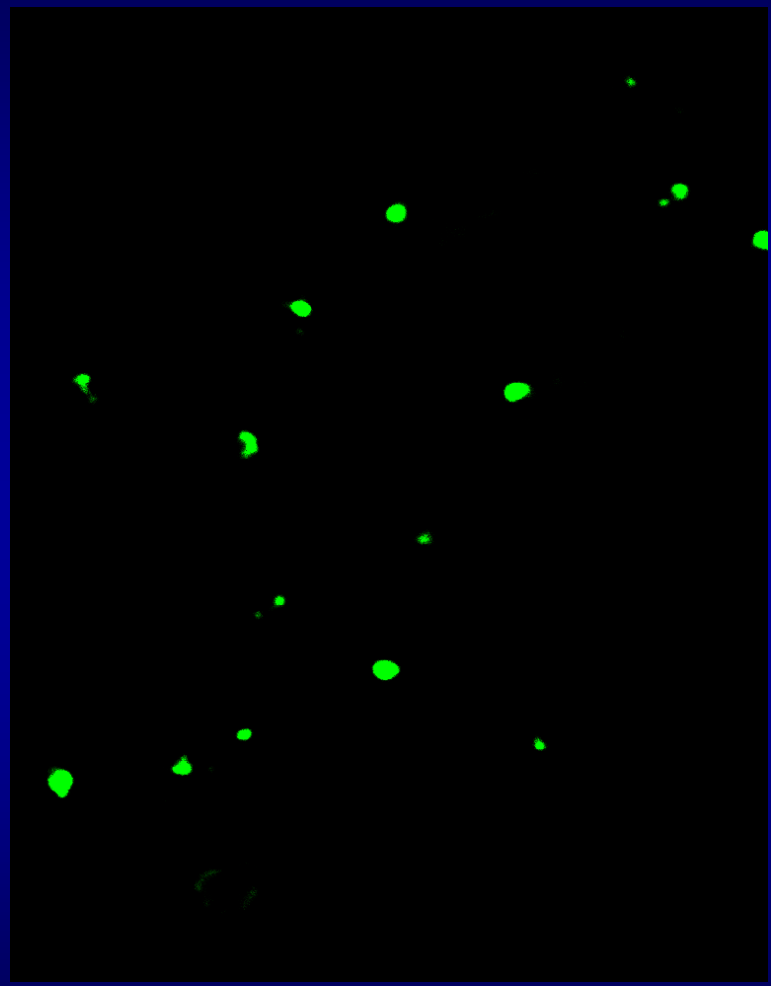


5 days
post-imatinib

Effect of Imatinib on Apoptosis



Pre-Imatinib



Post-Imatinib

Immunofluourescent TUNEL Assay

Effect of Imatinib on Apoptosis

- Apoptosis was observed in GIST tissue after imatinib therapy by light microscopy and immunofluourescent LSC
- This effect is observe after less than 1 week of therapy

Conclusions

- Perfusion CT of GIST enables assessment of changes in vascular physiology early in imatinib therapy
- Immunofluourescent LSC allows detection of GIST cell and endothelial cell apoptosis after less than 1 week of therapy imatinib

Thanks

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