GIST SUMMIT 2025

GIST DAY OF LEARNING TEXAS

The Pathology of GIST

Alexander J Lazar MD/PhD

Professor

Departments of Pathology, Genomic Medicine, Dermatology, & Translational Molecular Pathology

UT MD Anderson Cancer Center

Saturday 1 March 2025

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

MD Anderson
Moon Shots Program

Disclosure information

Saturday 1 March 20225

Overview of Soft Tissue: WHO, Grading, Staging

Alexander Lazar MD/PhD

I have the following financial relationships:

AbbVie, Adaptimmune, AJCC, Astra-Zeneca, Bain Capital, Bayer, Bio-AI Health, BMS, CAP, Caris, Deciphera, Elsevier, Foghorn Therapeutics, Gothams, GSK, Illumina, Invitae / Archer DX, Iterion Therapeutics, Merck, Modella AI, Novartis, Nucleai, OncoKB (MSKCC), Paige, Pfizer, Regeneron, Roche / Genentech, SpringerNature, SpringWorks, Tempus, ThermoFisher, USCAP

(mostly clinical trials, research support, sci ad boards, consulting)

These relationships are **NOT** considered relevant to the content of this lecture.

Stages Repertory Theatre

OYL THEATER COMPANY

BALLS

by Kevin Armento and Bryony Lavery

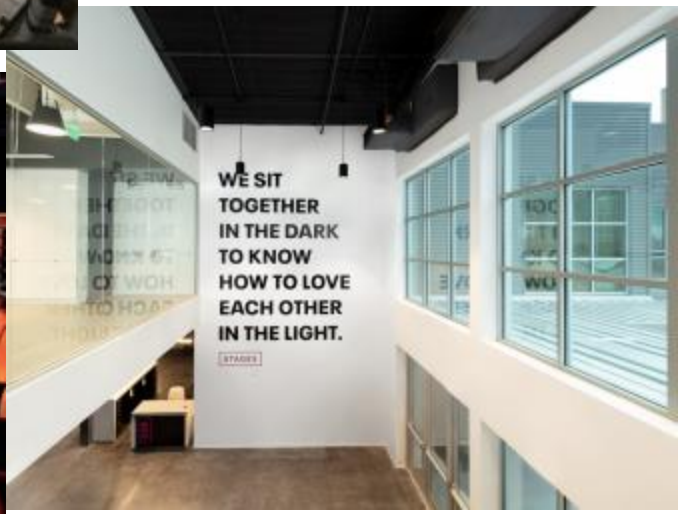
Tickets start at $25
713.527.0123
stagestheatre.com

Outstanding Sound Design in a Play

- Brendan Aanes, *Balls*, One Year Lease Theater Company/Stages Repertory Theatre/59E59
- Gareth Fry, *Harry Potter and the Cursed Child*
- Tom Gibbons, *1984*
- Tom Gibbons, *People, Places & Things*, National Theatre/St. Ann's Warehouse/Bryan Singer Productions/Headlong
- Stefan Gregory, *Terrus*, Young Vic/Park Avenue Armory
- Palmer Heffernan, *Today is My Birthday*, Page 73 Productions

STAGES


STAGES
AT THE
GORDY


WE SIT
TOGETHER
IN THE DARK
TO KNOW
HOW TO LOVE
EACH OTHER
IN THE LIGHT.

OYL
THEATER
COMPANY

STAGES


PLUMSHUGA: THE RISE OF LAUREN ANDERSO


The New York Times

CAST

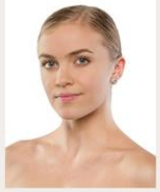
DEQUINA MOORE
Lauren

KELLEN HORNBUCKLE
Dancer Lauren

ERIC BEST
Carlos

MYA BRYANT
Lauren's Mother

RAFAELA HENRIQUE
Firebird, (Sugar Plum Fairy)



BRIDGET KUHNS
Sugar Plum Fairy

DANAE MCGLOTHEN
Young Lauren

LAYLA PORTER
Firebird, Cleopatra, (Dancer Lauren)

JESSICA COLLADO
Sugar Plum Fairy

DWAYNE COOK
Lauren's Father

CAMERON EDWARDS
Love

KHARMA GRIMES
Addiction

ELLIOTT ROGERS

KALEN WRIGHT
Young Lauren

EMRY AMOKY
(Carlos)

MAGNOLY BATISTA

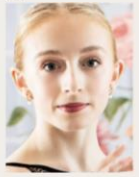
LAUREN BURKE
Ensemble

ELI GO
(Dominic)

REMIE GOINS
Student

HART ISAACOFF
(Dominic)

MACY RICHTER
Student, (Firebird)

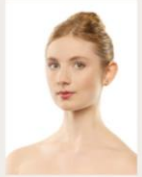


BRETT RULE
Student

RAFAEL TILLERY
Ensemble

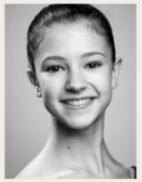
MCKENNA ARMWOOD

ISABELLA KESSLER
Student



ZOE LUCICH
(Firebird, Sugar Plum Fairy)

JUSTINE MARCOV
Student



OLIVIA MCBAIN
Student, (Firebird)

AMELIA MCGRAVEY

ALYSSA PRATT

NATALIA SCHEINSON

RENEE SHUBOV

ALLISON WHITLEY


ALLEY
THEATRE
SEARED
SEARED
Elizabeth Bunch
Emily
Chris Hutchison
Mike
Christopher Salazar
Harry
BY
THERESA REBECK
DIRECTED BY
BRANDON WEINBRENNER
FEBRUARY 7 - MARCH 2
ROUNDING OUT THE CAST IS
as Rodney

GIST Pathology: Lecture Overview

1. **How do you do pathology?**
2. **What information is in my pathology report?**
3. **Why is that information there?**
4. **Is this information is useful?**

What happens to my tumor in pathology?

Tumor sample is received from the OR and logged into computer.

Tumor is examined by a pathologist.

Tumor is sampled and placed in plastic cassettes for further processing.

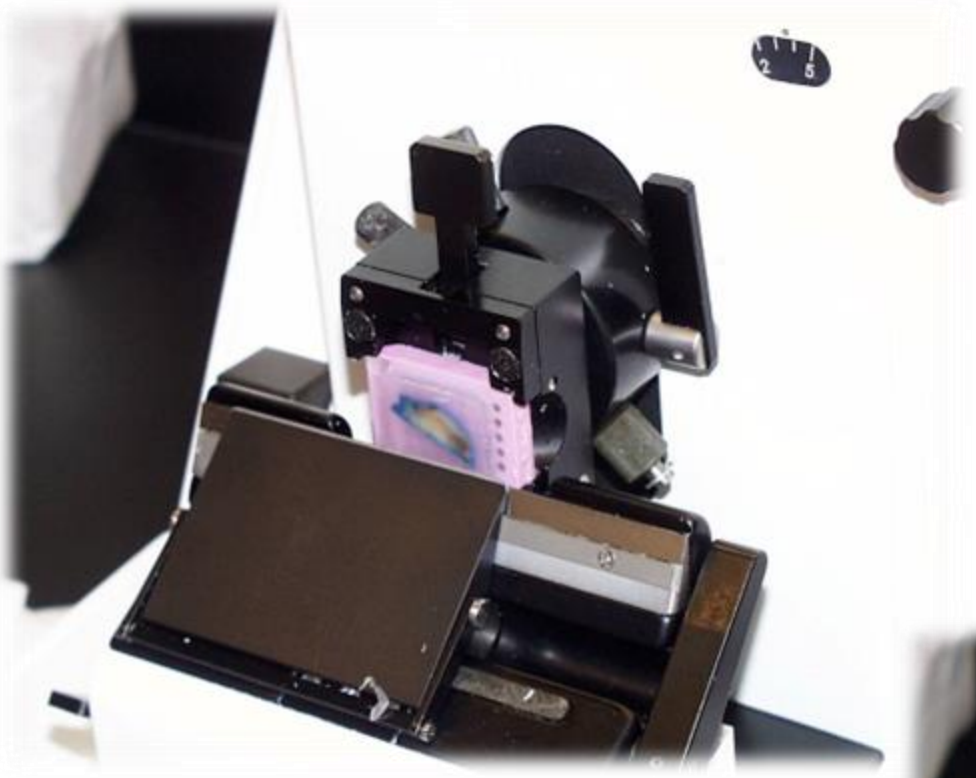
Tumor is also given to cytogenetics, tumor bank, molecular diagnosis and electron microscopy when appropriate.

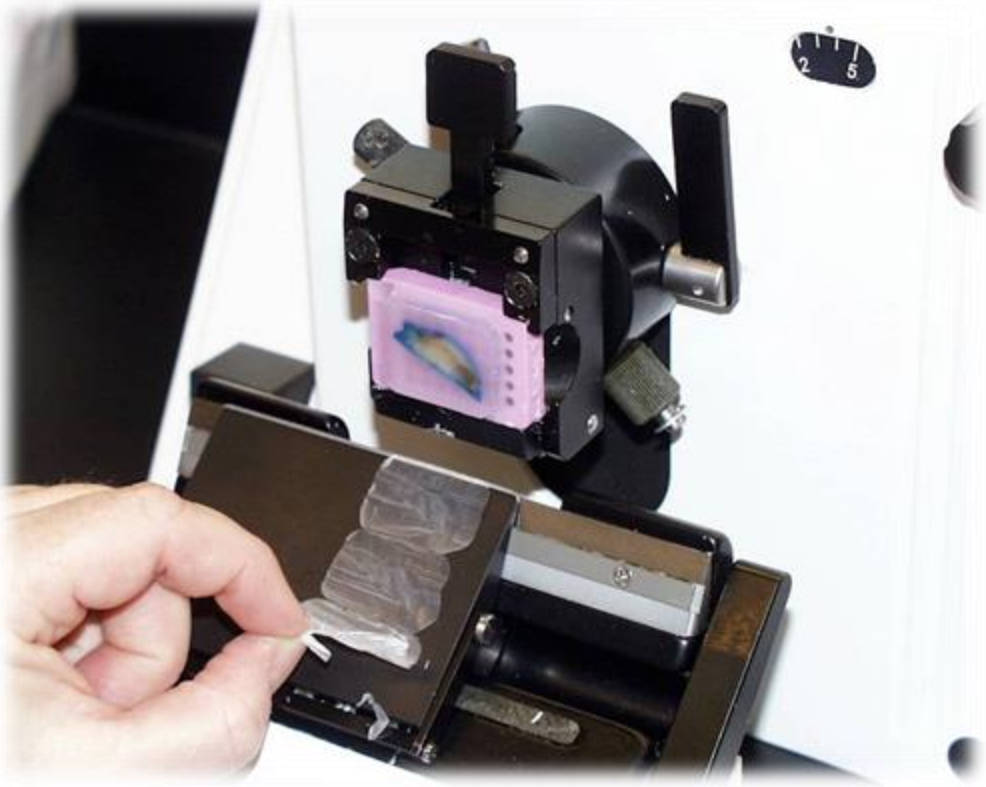
The tissue blocks are fixed in formalin and then loaded on a tissue processor overnight.

Tissue processing is done overnight and utilizes graded treatments of formalin, ethanol, xylene and paraffin.

Blocks are retrieved from the tissue processor.

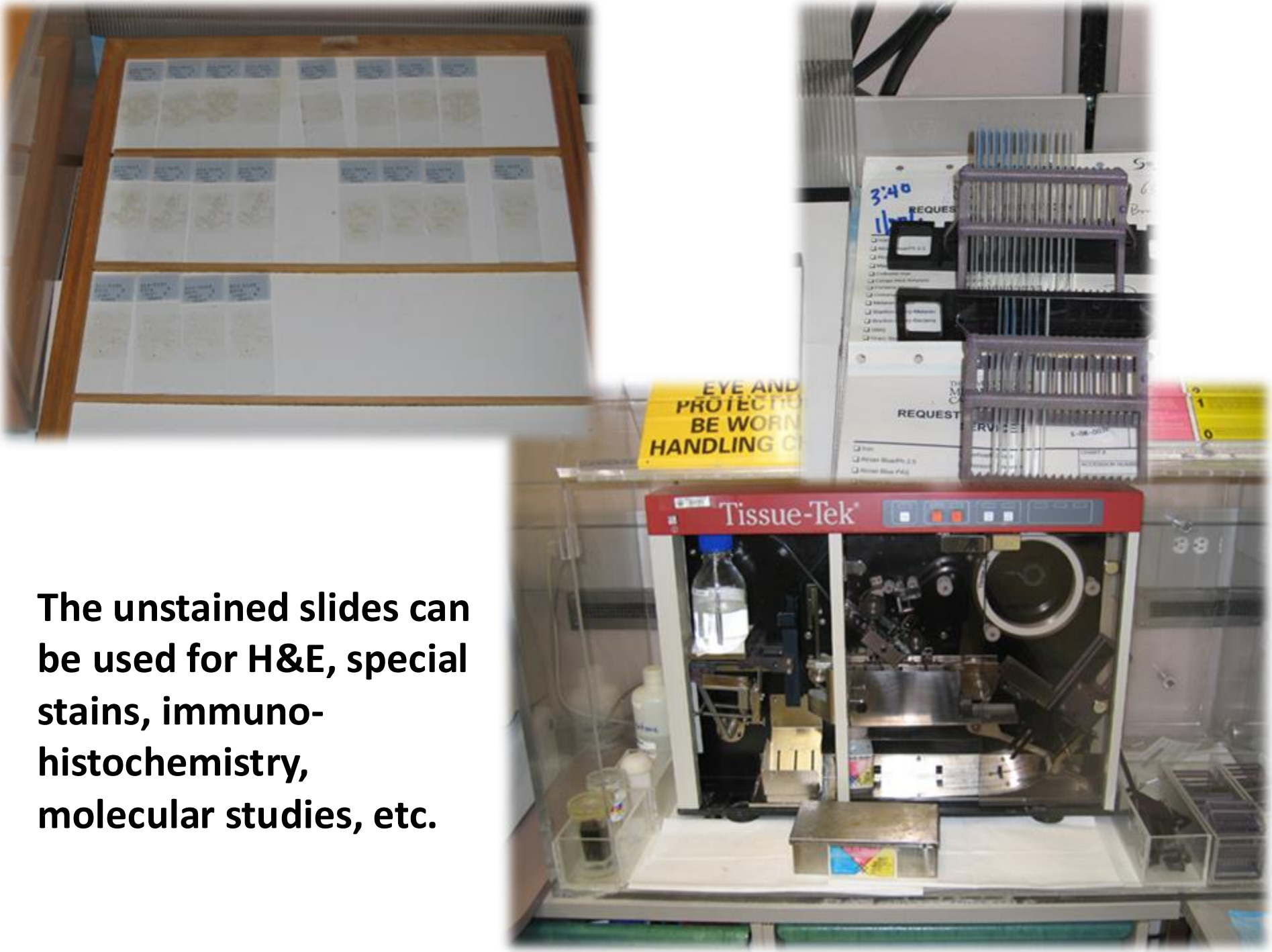
The tissue fragments are embedded in a paraffin mold and cooled – resulting in a tissue block.



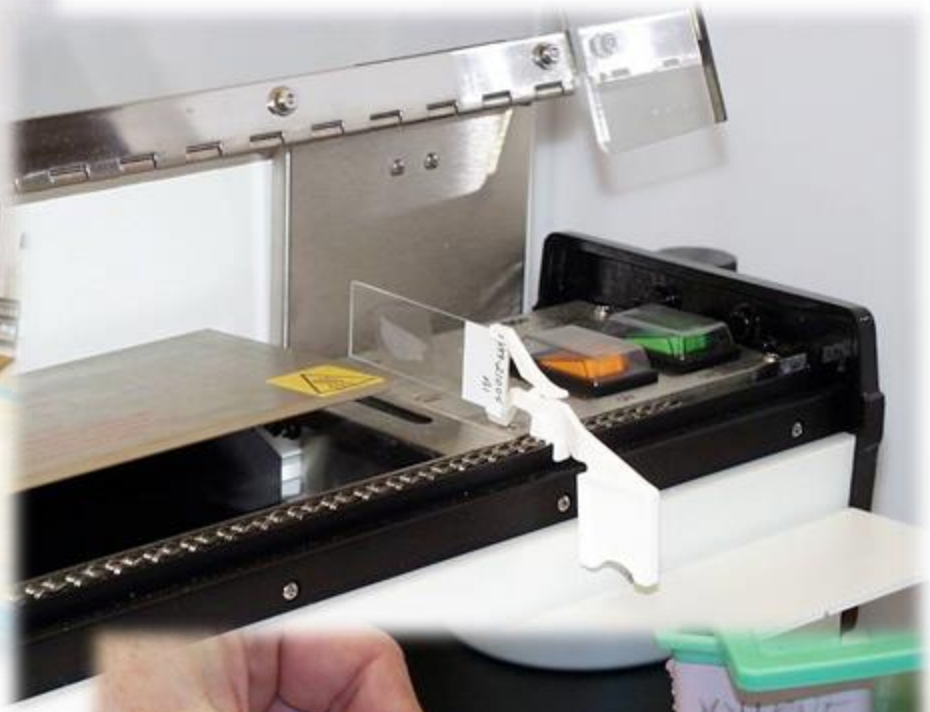


The paraffin-embedded blocks are loaded and cut using a microtome.

Tissue paraffin ribbons are placed in a warm waterbath and then picked up on glass slides.



The unstained slides can be used for H&E, special stains, immuno-histochemistry, molecular studies, etc.



Most slides are H&E (hemotoxlin & eosin) stained, given coverslips, organized and delivered to the proper pathologist.

Additional unstained slides can be cut at a later time.

After final diagnosis, both slides and the paraffin blocks from which they are cut are cataloged and stored for future use.

What information should be in my pathology report?

Protocol for the Examination of Specimens From Patients With Gastrointestinal Stromal Tumor (GIST)

Based on AJCC/UICC TNM, 7th edition
Protocol web posting date: June 2012

Procedures
- Biopsy
- Resection

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For the Members of the Cancer Committee, College of American Pathologists

* Denotes primary author. † Denotes senior author. All other contributing authors are listed alphabetically.

Surgical Pathology Cancer Case Summary

Protocol web posting date: June 2012

GASTROINTESTINAL STROMAL TUMOR (GIST): Resection

Select a single response unless otherwise indicated.

Procedure
___ Excisional biopsy
___ Resection
Specify type (eg, partial gastrectomy): _____
___ Metastasectomy
___ Other (specify): _____
___ Not specified

Tumor Site
Specify (if known): _____
___ Not specified

Tumor Size
Greatest dimension: ___ cm
+ Additional dimensions: ___ x ___ cm
___ Cannot be determined (see "Comment")

Tumor Focality
___ Unifocal
___ Multifocal
Specify number of tumors: _____
Specify size of tumors: _____

GIST Subtype
___ Spindle cell
___ Epithelioid
___ Mixed
___ Other (specify): _____

Mitotic Rate

Specify: ___ /50 HPF

Note: The required total count of mitoses is per 5 mm² on the glass slide section. With the use of older model microscopes, 50 HPF is equivalent to 5 mm². Most modern microscopes with wider 40X lenses/fields require only 20 HPF to embrace 5 mm². If necessary please measure field of view to accurately determine actual number of fields required to be counted on individual microscopes to count 5 mm².

+ Necrosis

+ ___ Not identified
+ ___ Present
    + Extent: ___%
+ ___ Cannot be determined

Risk Assessment (Note C)
___ None
___ Very low risk
___ Low risk
___ Intermediate risk
___ High risk
___ Overtly malignant/metastatic
___ Cannot be determined

Margins
___ Cannot be assessed
___ Negative for GIST
Distance of tumor from closest margin: ___ mm *or* ___ cm
___ Margin(s) positive for GIST
Specify margin(s): _____

Pathologic Staging (pTNM) (Note G)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT)
___ pTX: Primary tumor cannot be assessed
___ pT0: No evidence for primary tumor
___ pT1: Tumor 2 cm or less
___ pT2: Tumor more than 2 cm but not more than 5 cm
___ pT3: Tumor more than 5 cm but not more than 10 cm
___ pT4: Tumor more than 10 cm in greatest dimension

Regional Lymph Nodes (pN) (Note D)
___ Not applicable
___ pN0: No regional lymph node metastasis
___ pN1: Regional lymph node metastasis

Distant Metastasis (pM) (Note D)
___ Not applicable
___ pM1: Distant metastasis
+ Specify site(s), if known: _____

+ Additional Pathologic Findings
+ Specify: _____

Ancillary Studies (select all that apply) (Note E)

Immunohistochemical Studies
___ KIT (CD117)
    ___ Positive
    ___ Negative
___ Others (specify): _____
___ Not performed

Molecular Genetic Studies (eg, *KIT* or *PDGFRA* mutational analysis)
___ Submitted for analysis; results pending
___ Performed, see separate report: _____
___ Performed
    Specify method(s) and results: _____
___ Not performed

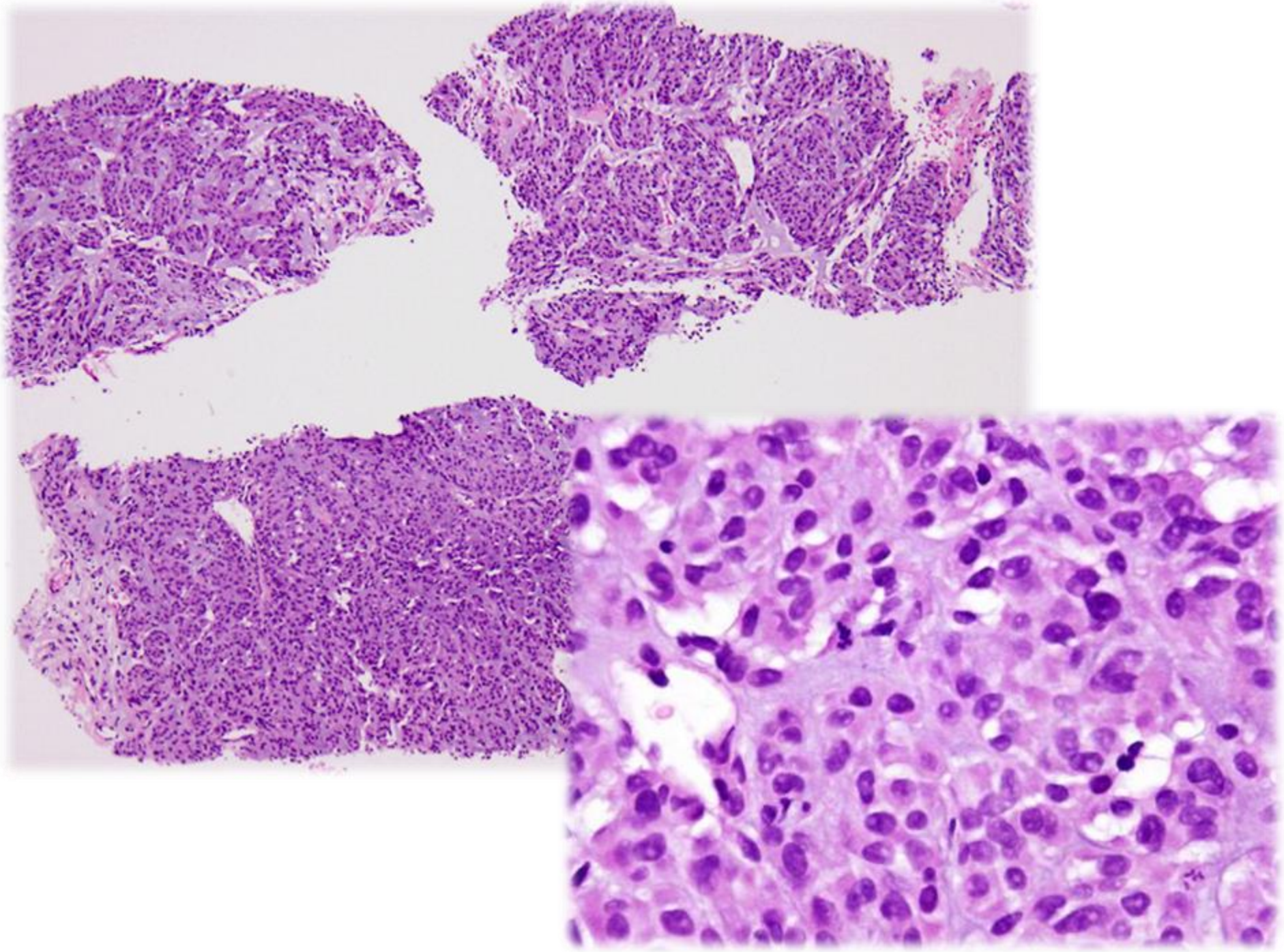
Preresection Treatment (select all that apply)
___ No therapy
___ Previous biopsy or surgery
    Specify: _____
___ Systemic therapy performed
    Specify type: _____
___ Therapy performed, type not specified
___ Unknown

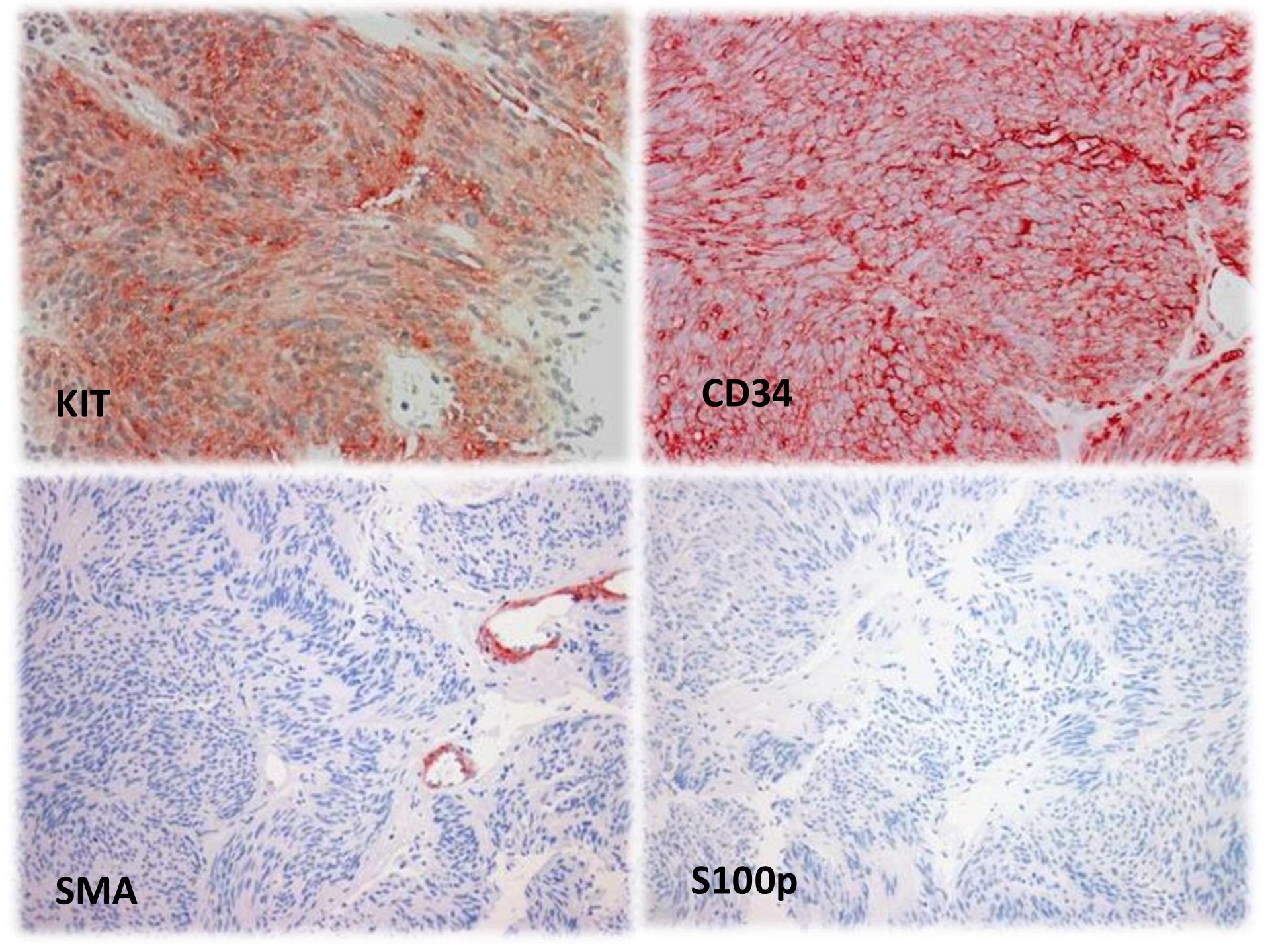
+ Treatment Effect (Note F)
+ Specify percentage of viable tumor: ___%

+ Comment(s)

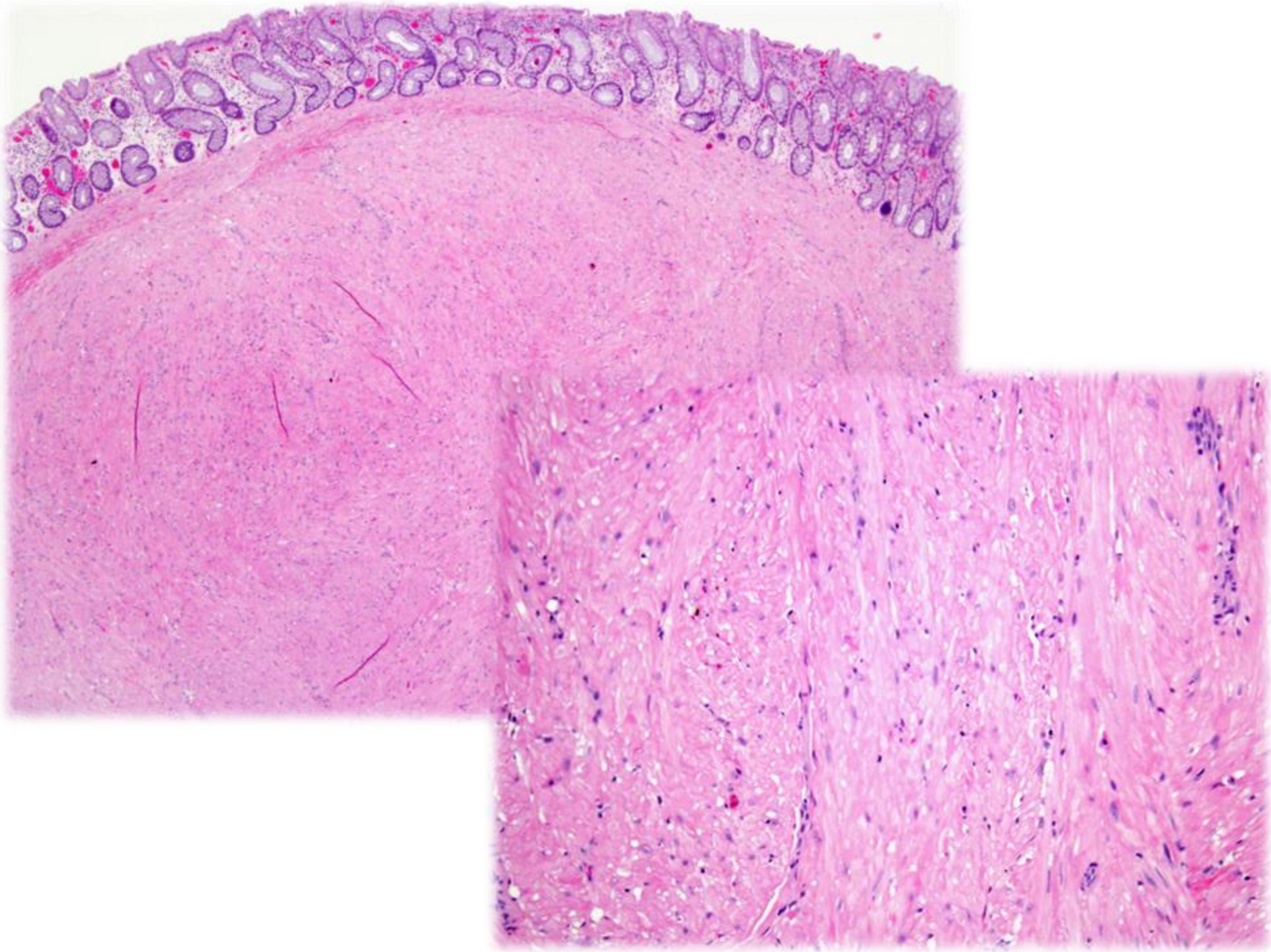
Getting the diagnosis right

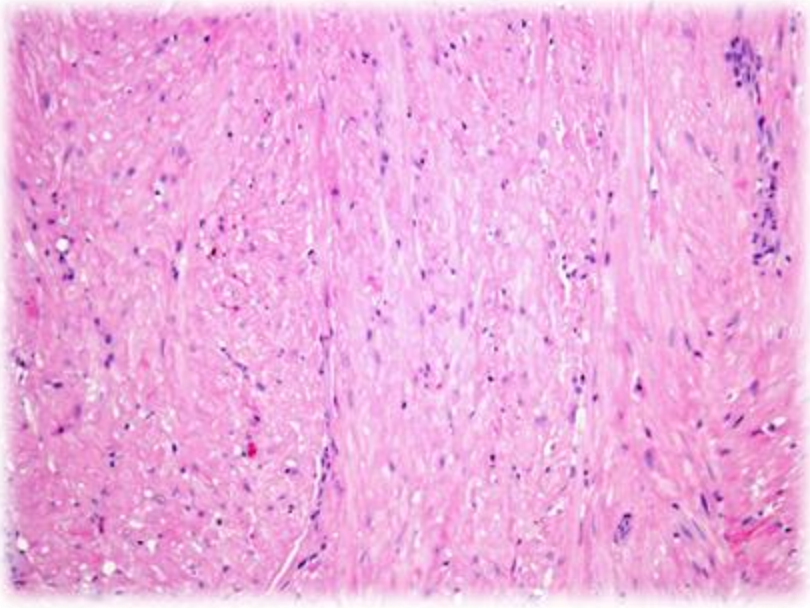
Case 1

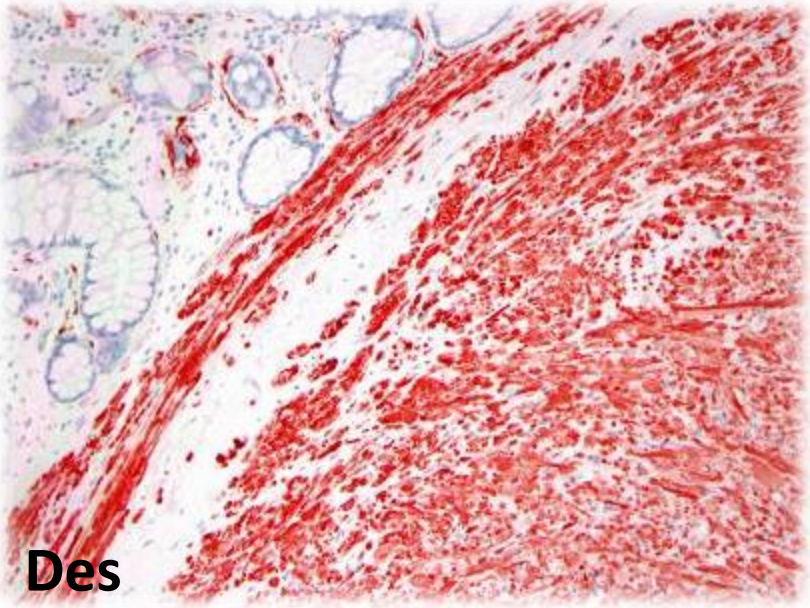


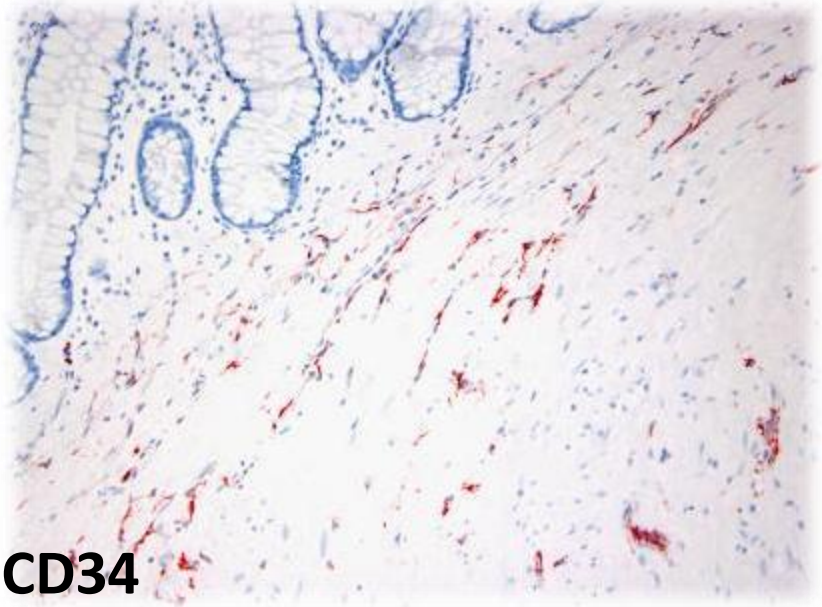

KIT
CD34
SMA
S100p

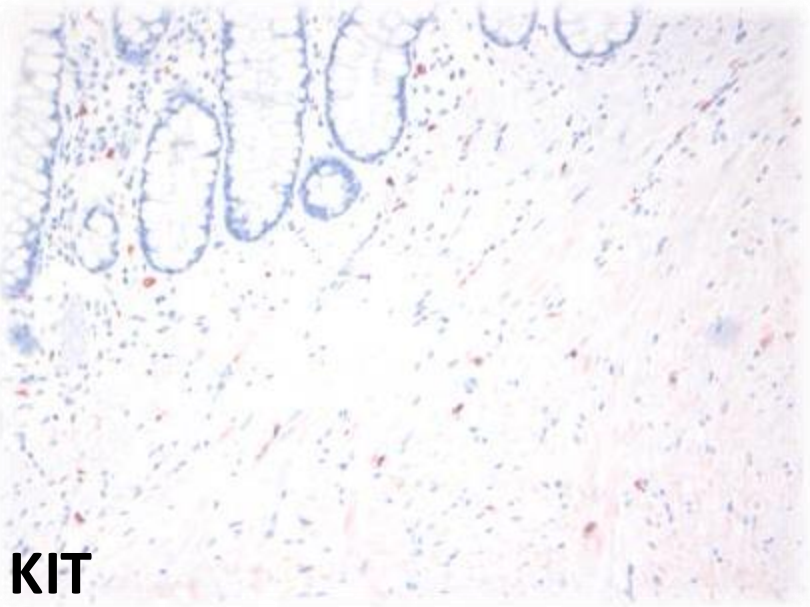
Case 2



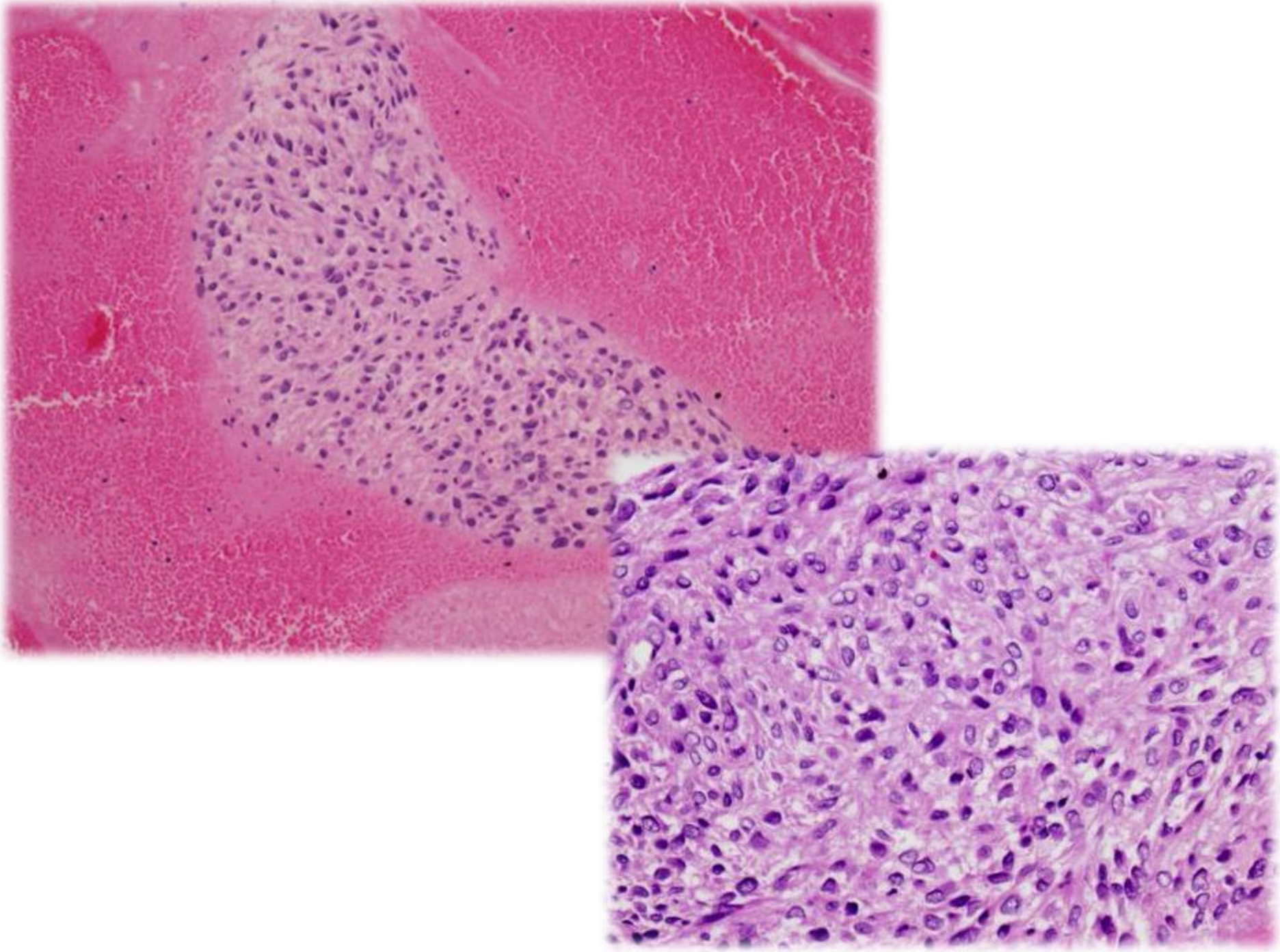


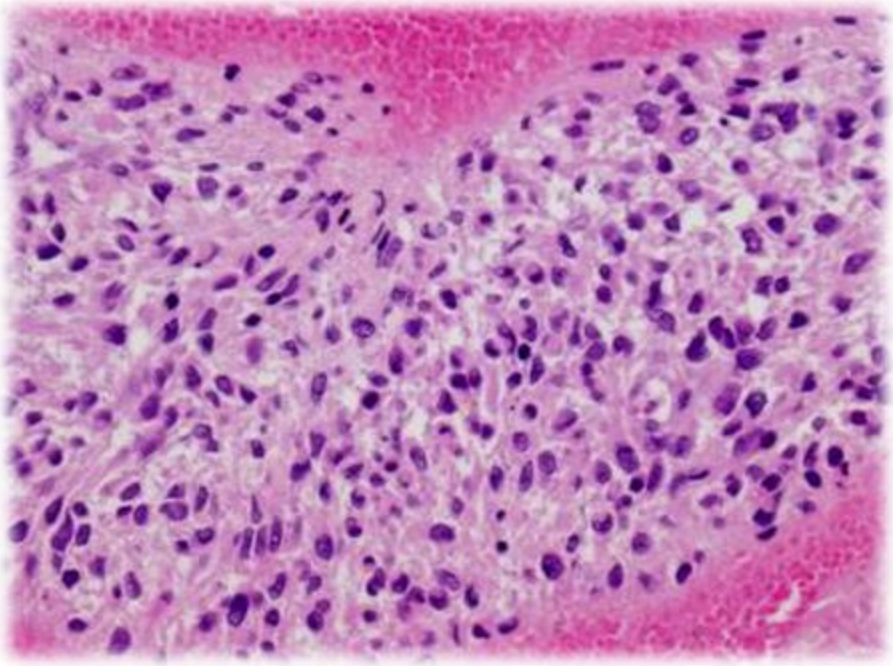

Des


CD34

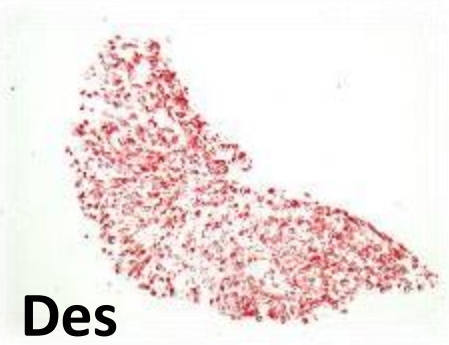

KIT

Case 3

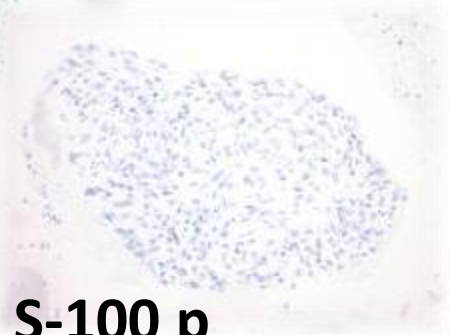




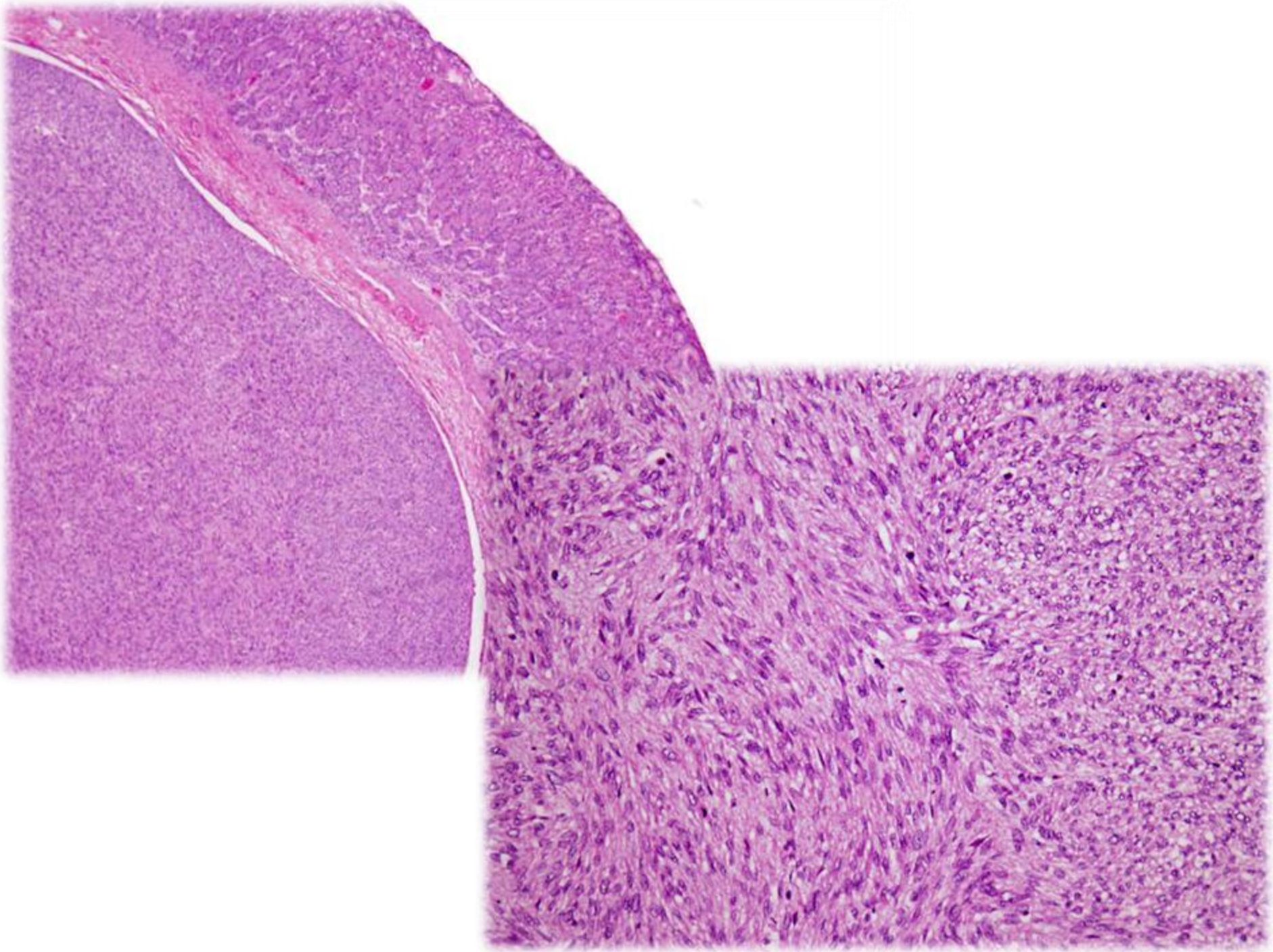

SMA

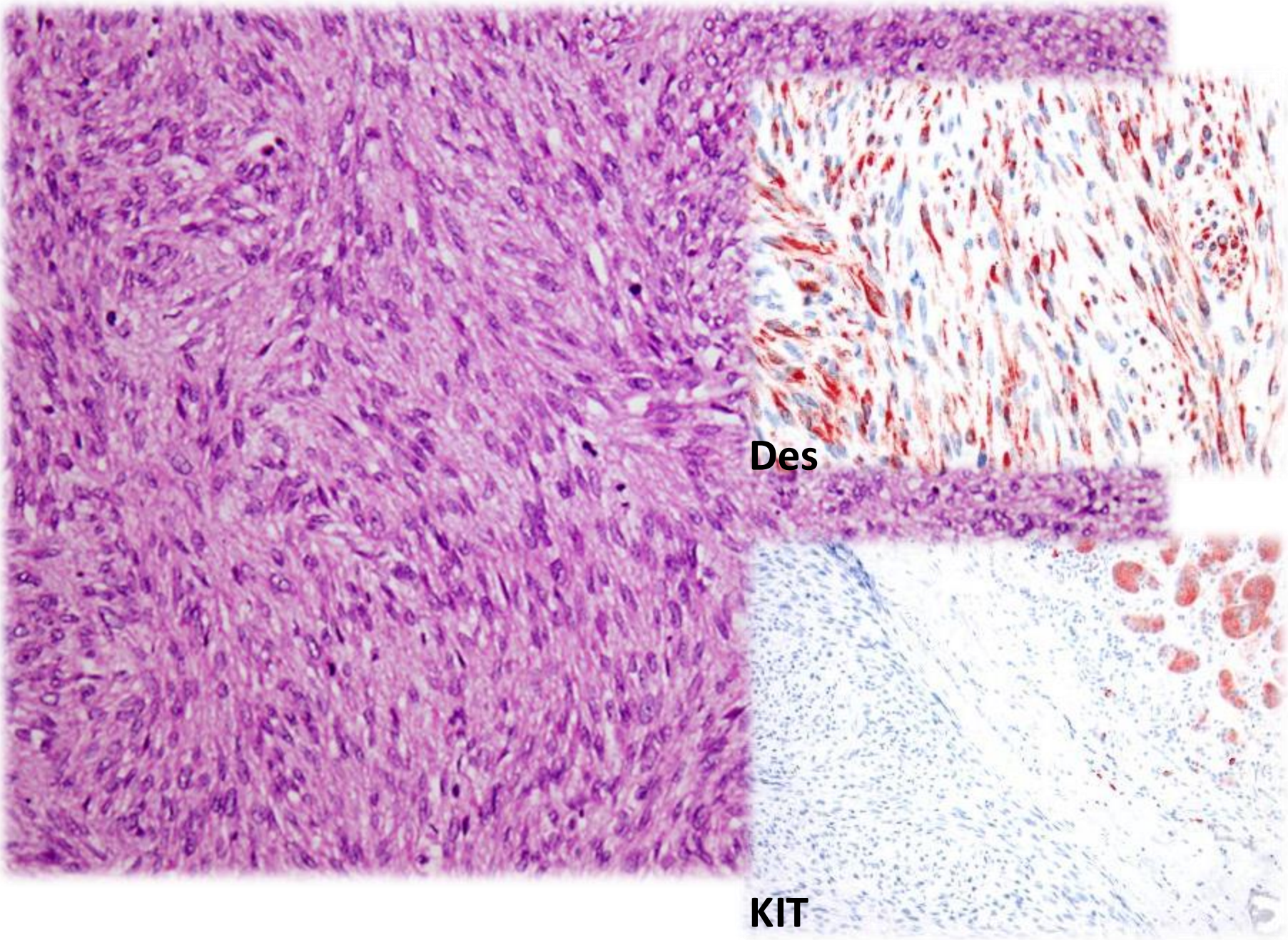

Des

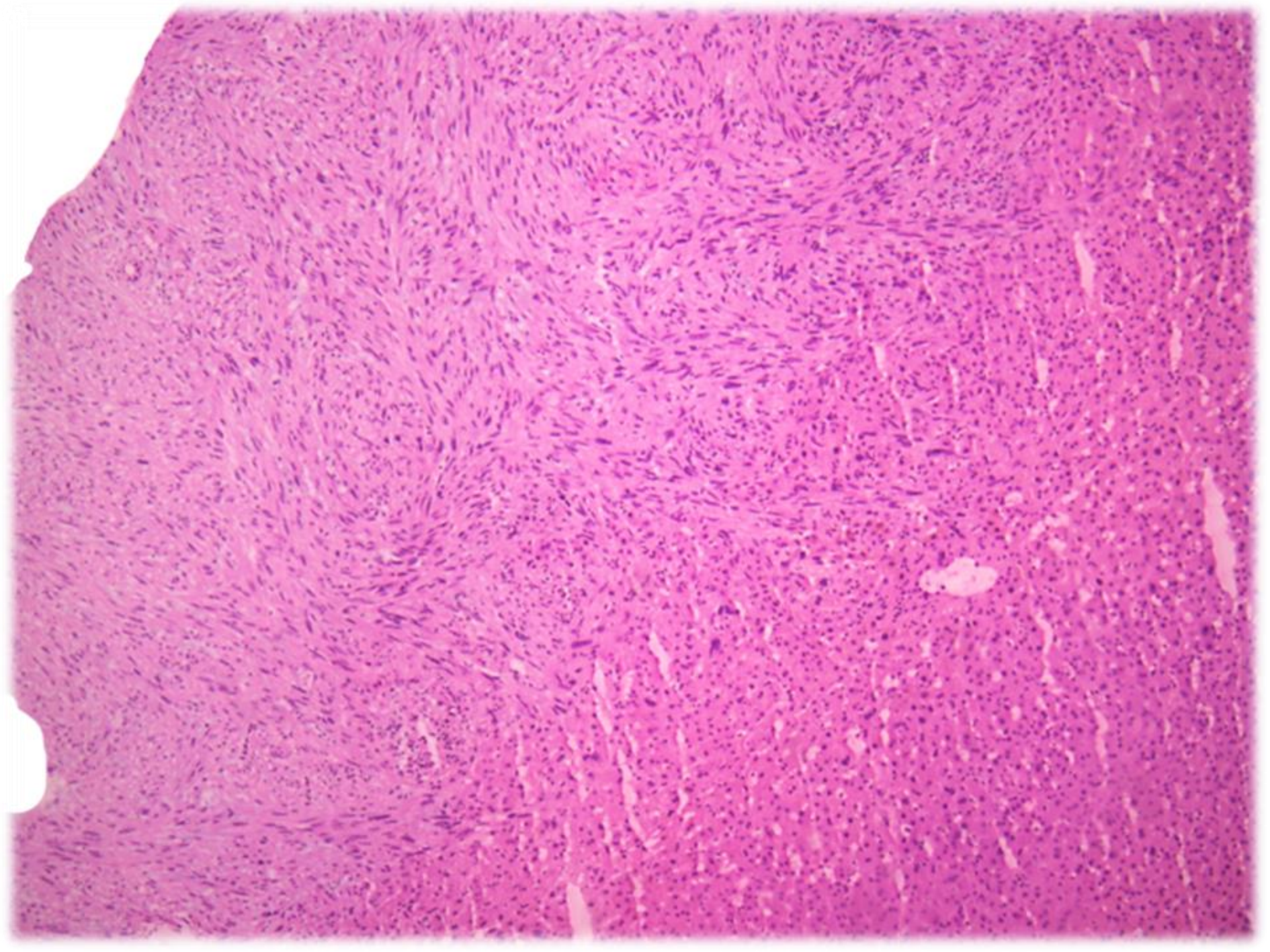

panK


S-100 p


KIT

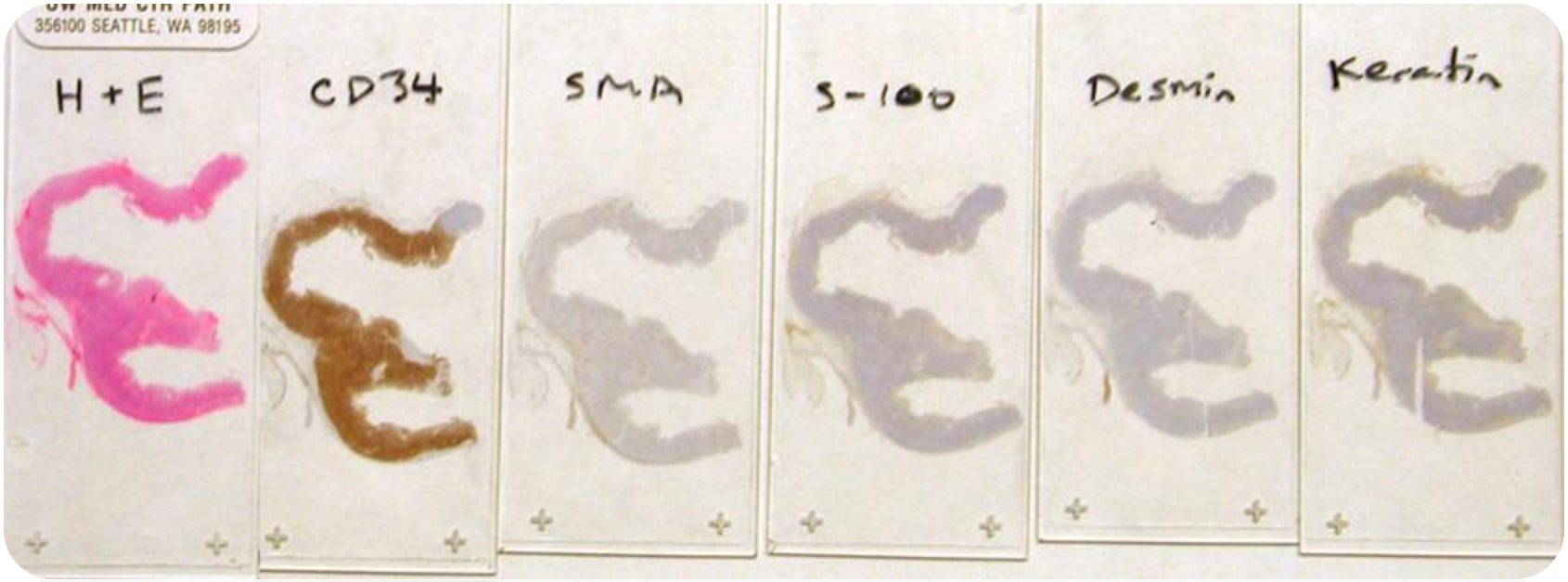



Des
KIT

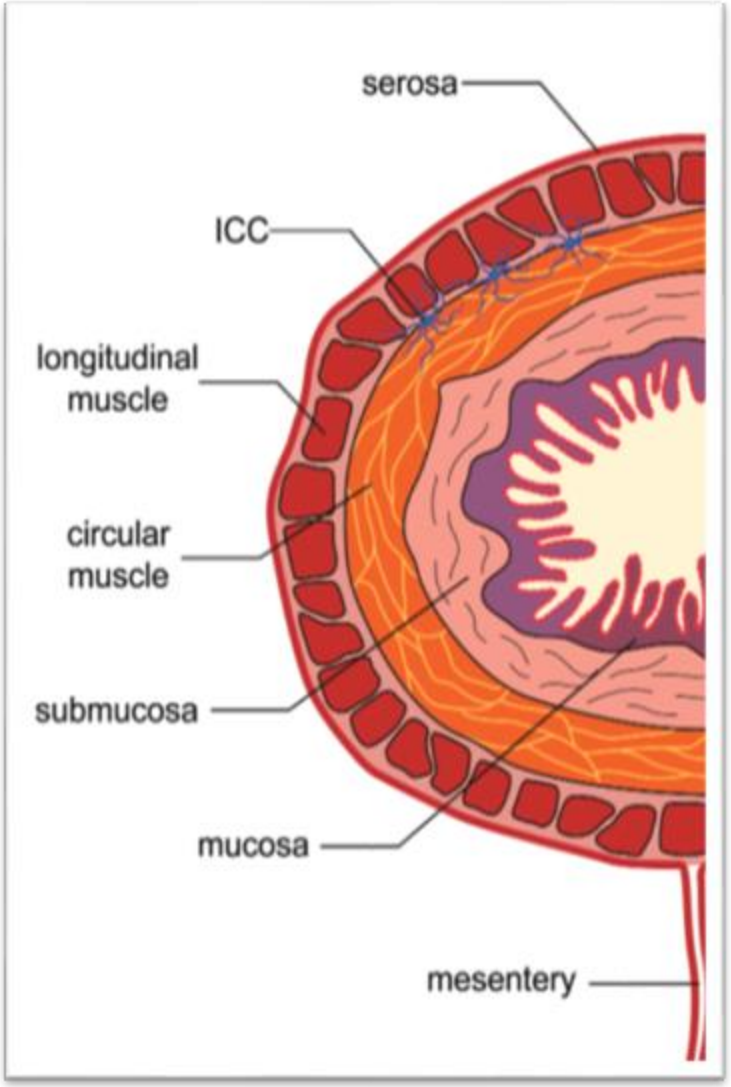


DIAGNOSIS	KIT	CD34	Ker	SMA	DES	S-100
GIST	+	+(70%)	-	+(40%)	-	-
Carcinoma	-	-	+	+(sar)	-	-
Melanoma	+/-	-	-	-	-	+
Leiomyoma	-	+/-	+/-	+	+	-
Leiomyosarcoma	-	+/-	+/-	+	+/-	-
Schwannoma	-	-	-	-	-	+
Fibromatosis	-	-	-	-	-	+/-

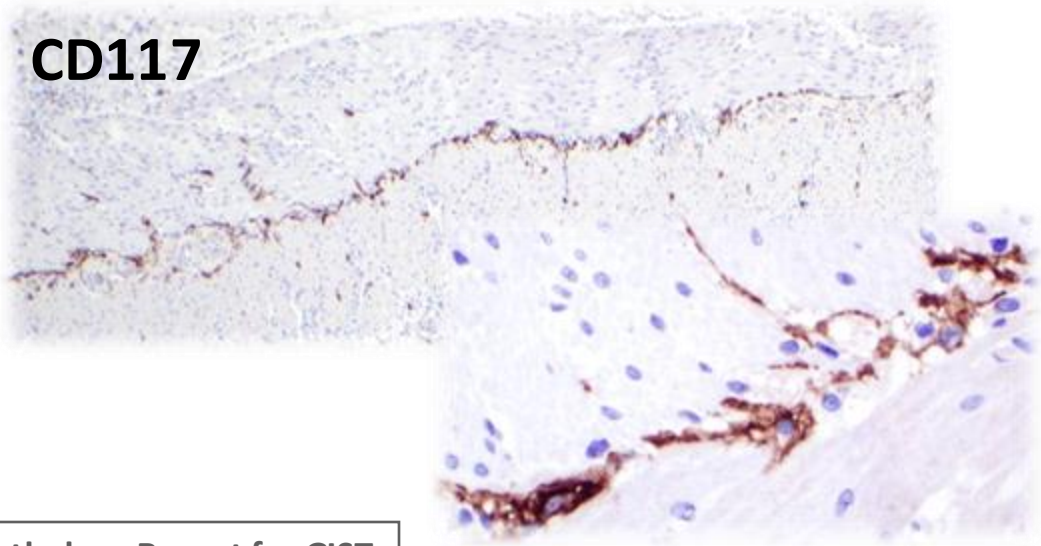
Immunohistochemical Profile of GISTs (Circa 1997 and prior)



Gastrointestinal Stromal Tumor



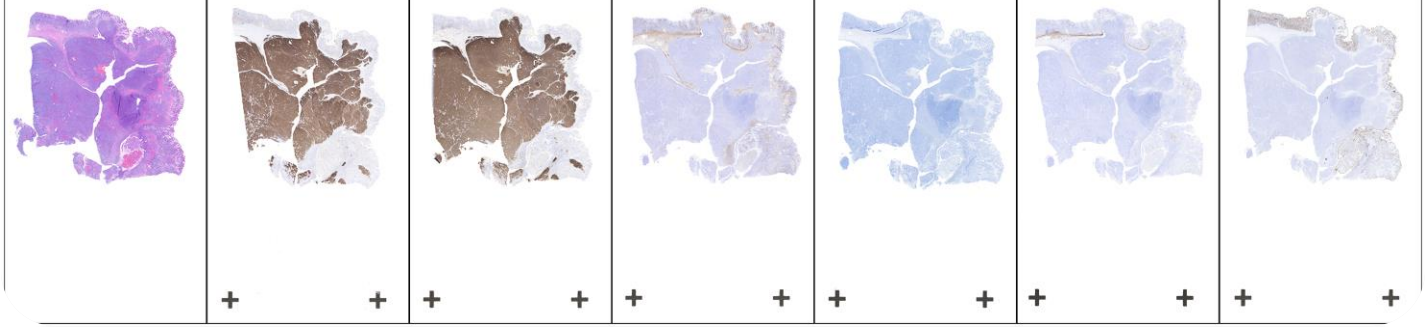
- **Arise from the interstitial cells of Cajal (ICC)**
- **ICC have a "pacemaker" function and are important in coordinating peristalsis**



Hornick & Lazar. GSI website: Understanding Your Pathology Report for GIST

Immunohistochemical Profile of GIST

H&E	CD117 (KIT)	CD34	Smooth muscle actin	S100 protein	Desmin	Pan-keratin
	95%	70%	30%	5%	2%	<1%
	+ +	+ +	+ +	+ +	+ +	+ +



KIT (CD117) +ve (95%)

CD34 +ve (70%)

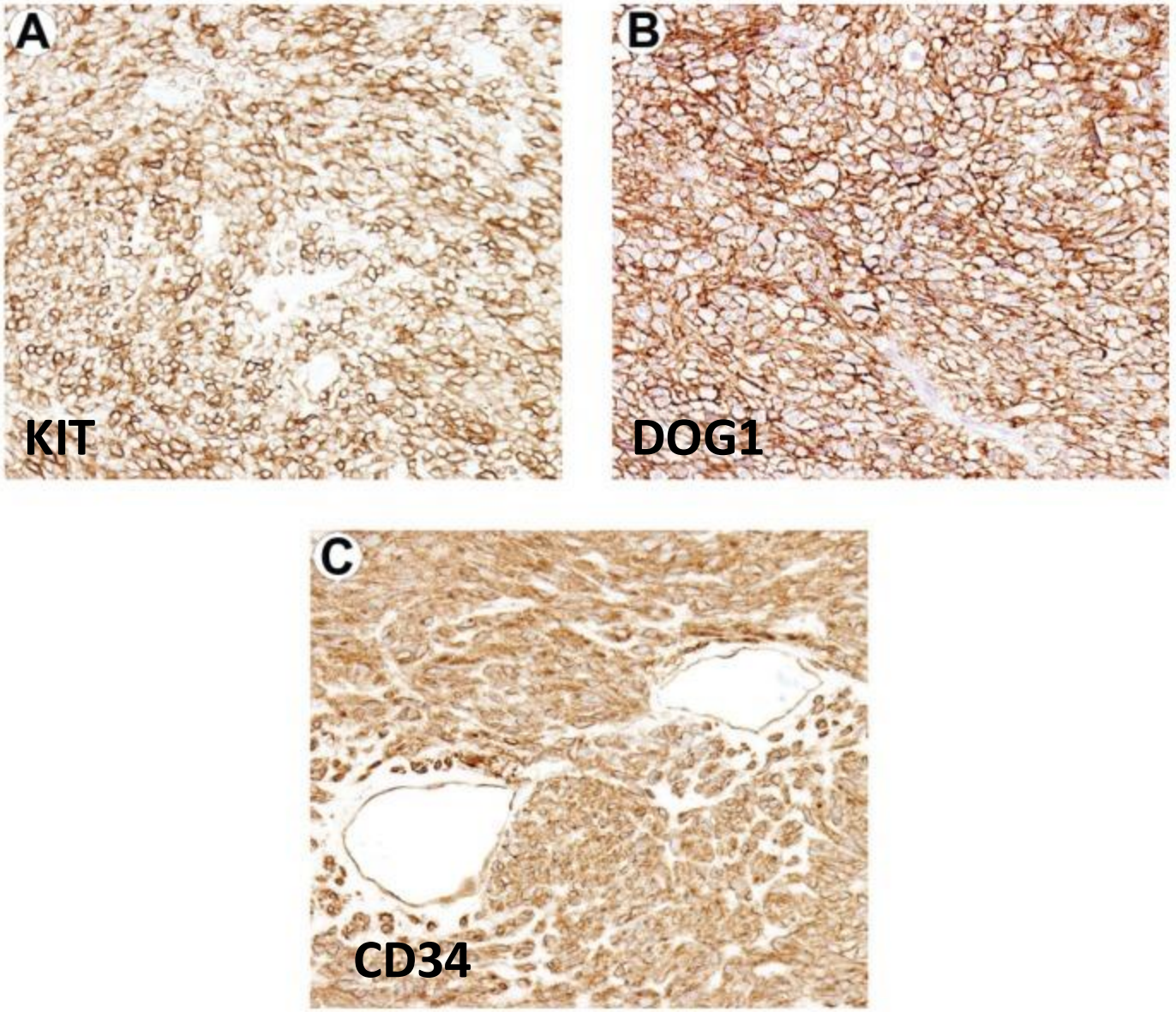
SMA +ve (30-40%)

Desmin –ve

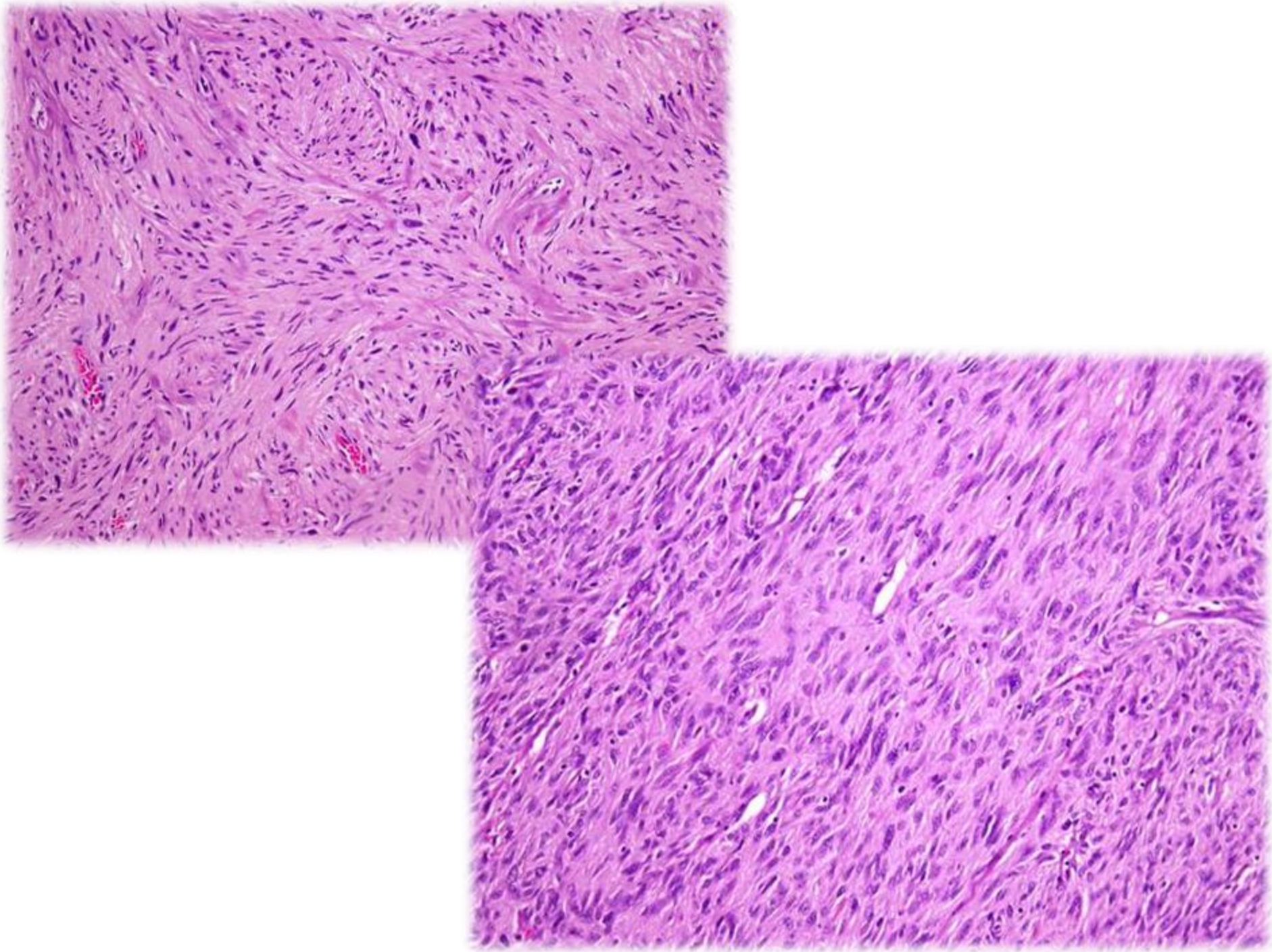
S-100 protein –ve

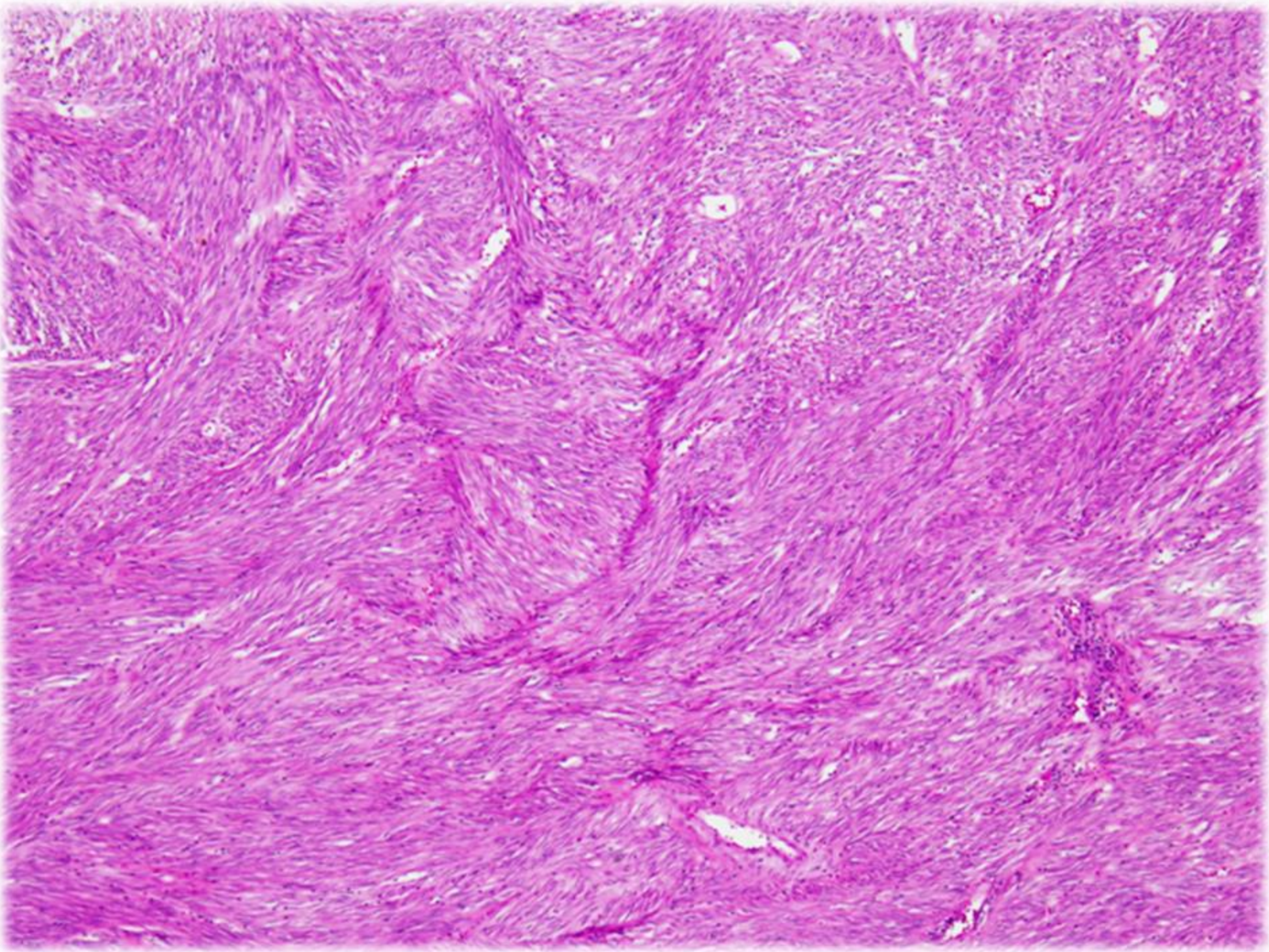
Keratin –ve

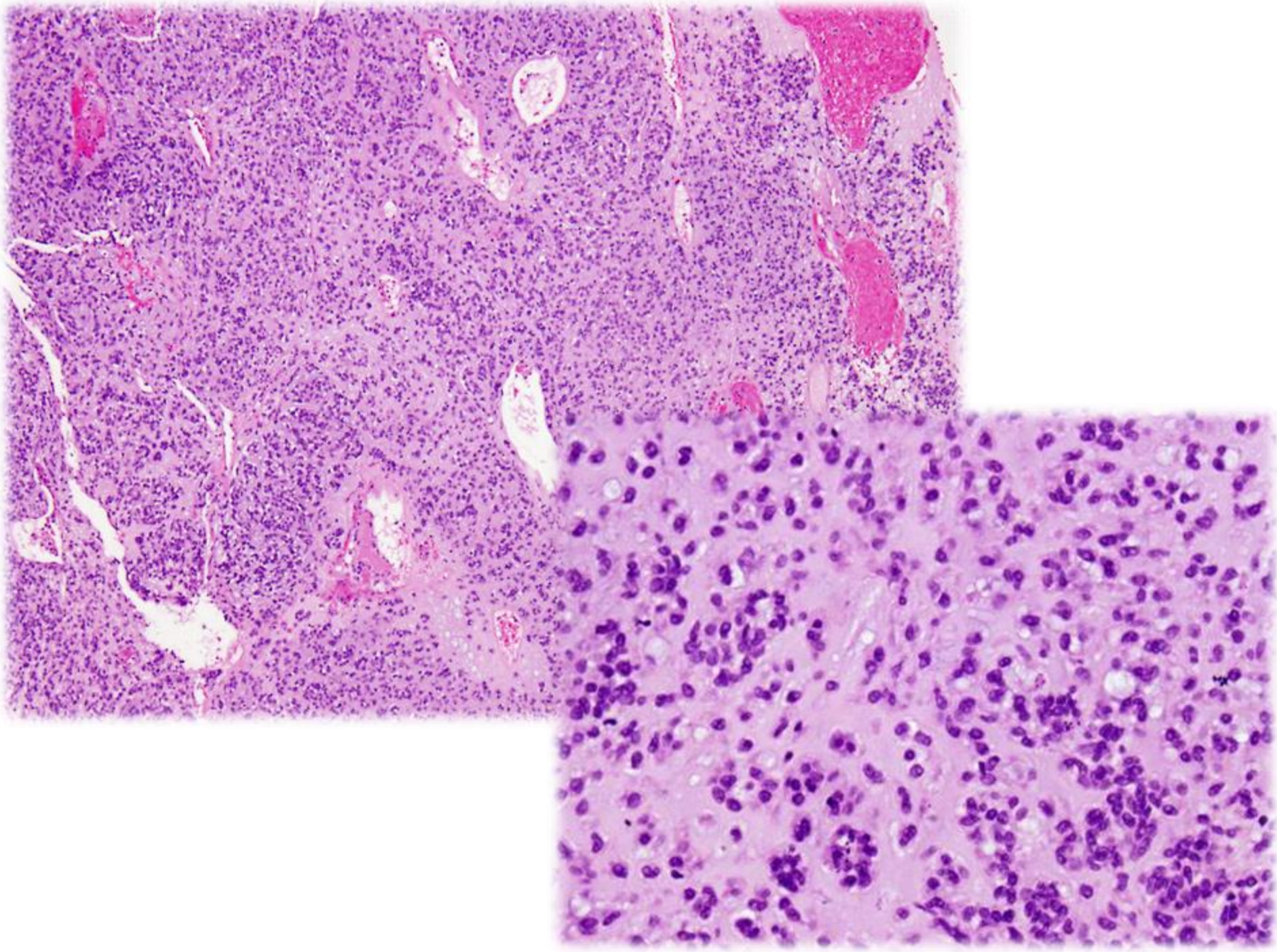
Liegl B et al. Hematol Oncol Clin North Am 2009; 23:49-68

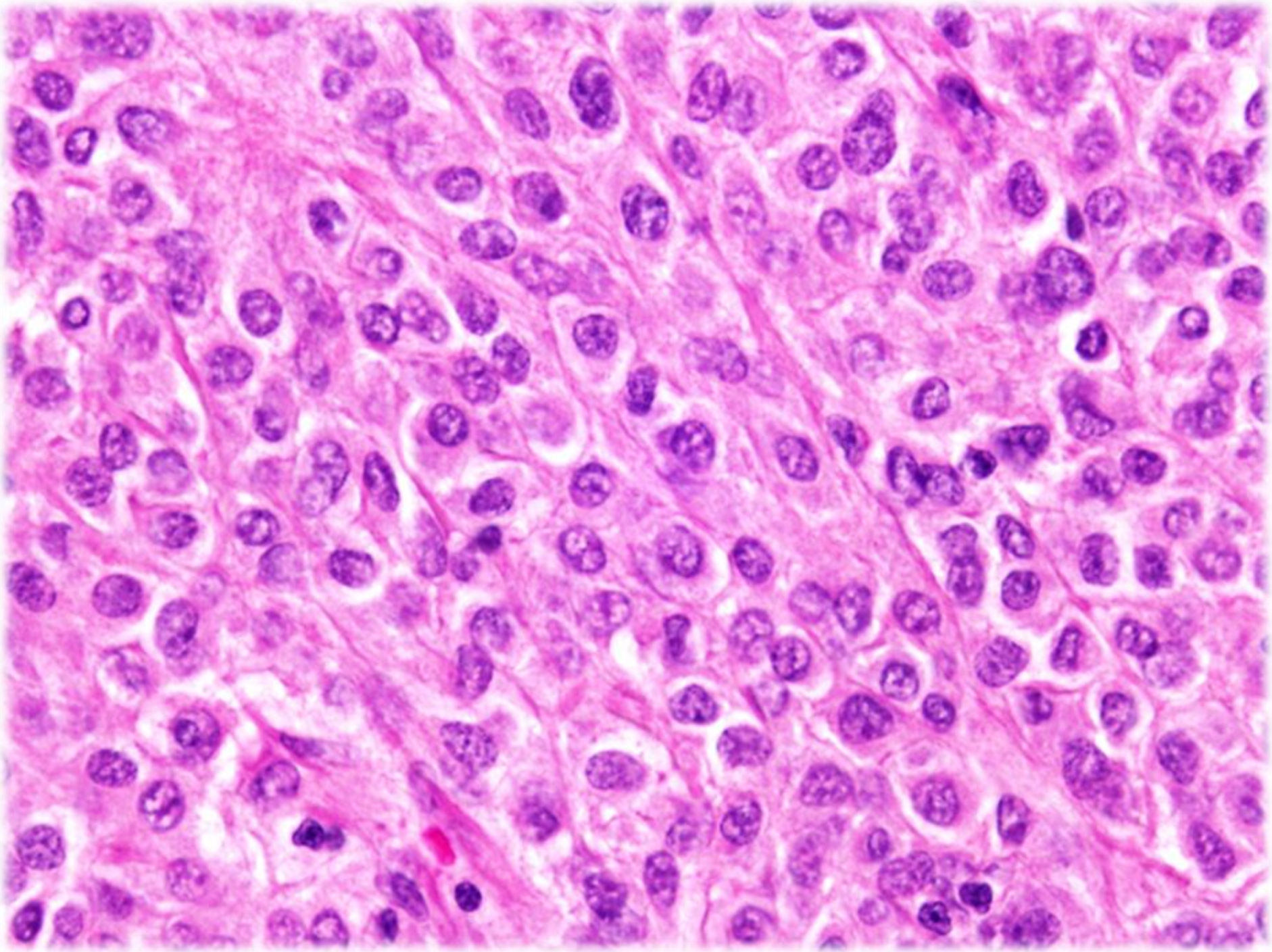

A
KIT
B
DOG1
C
CD34

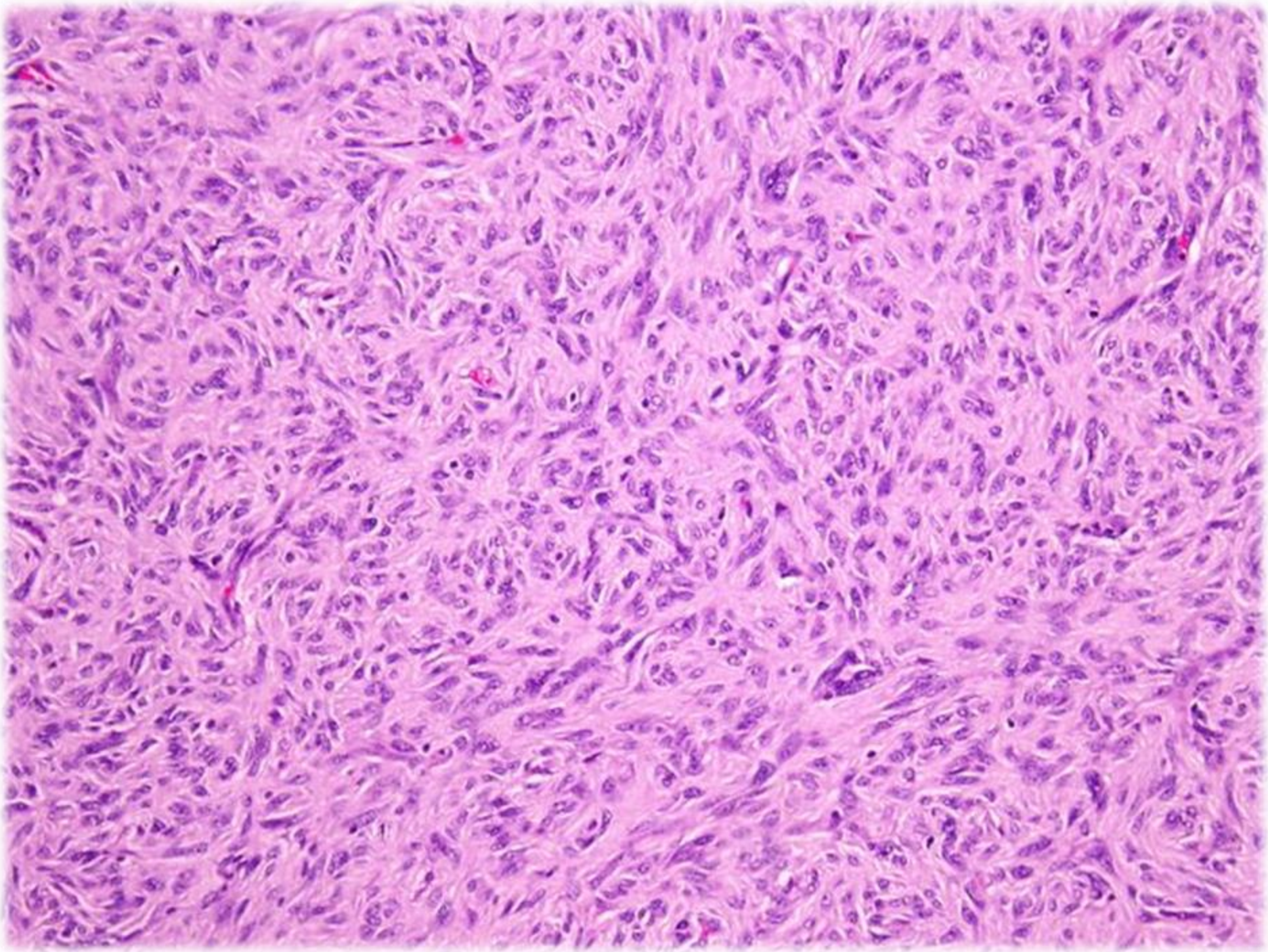
The many faces of GIST

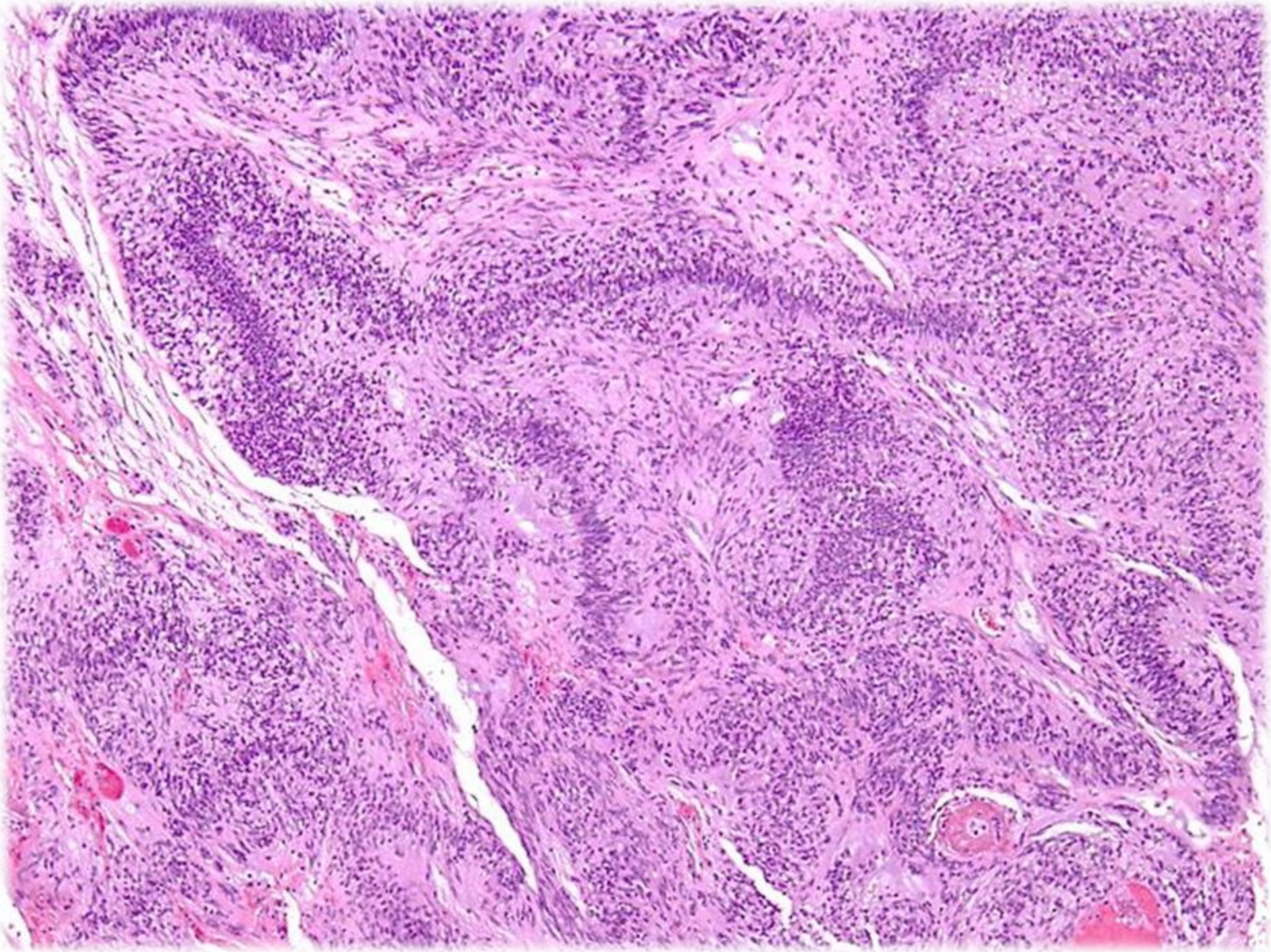


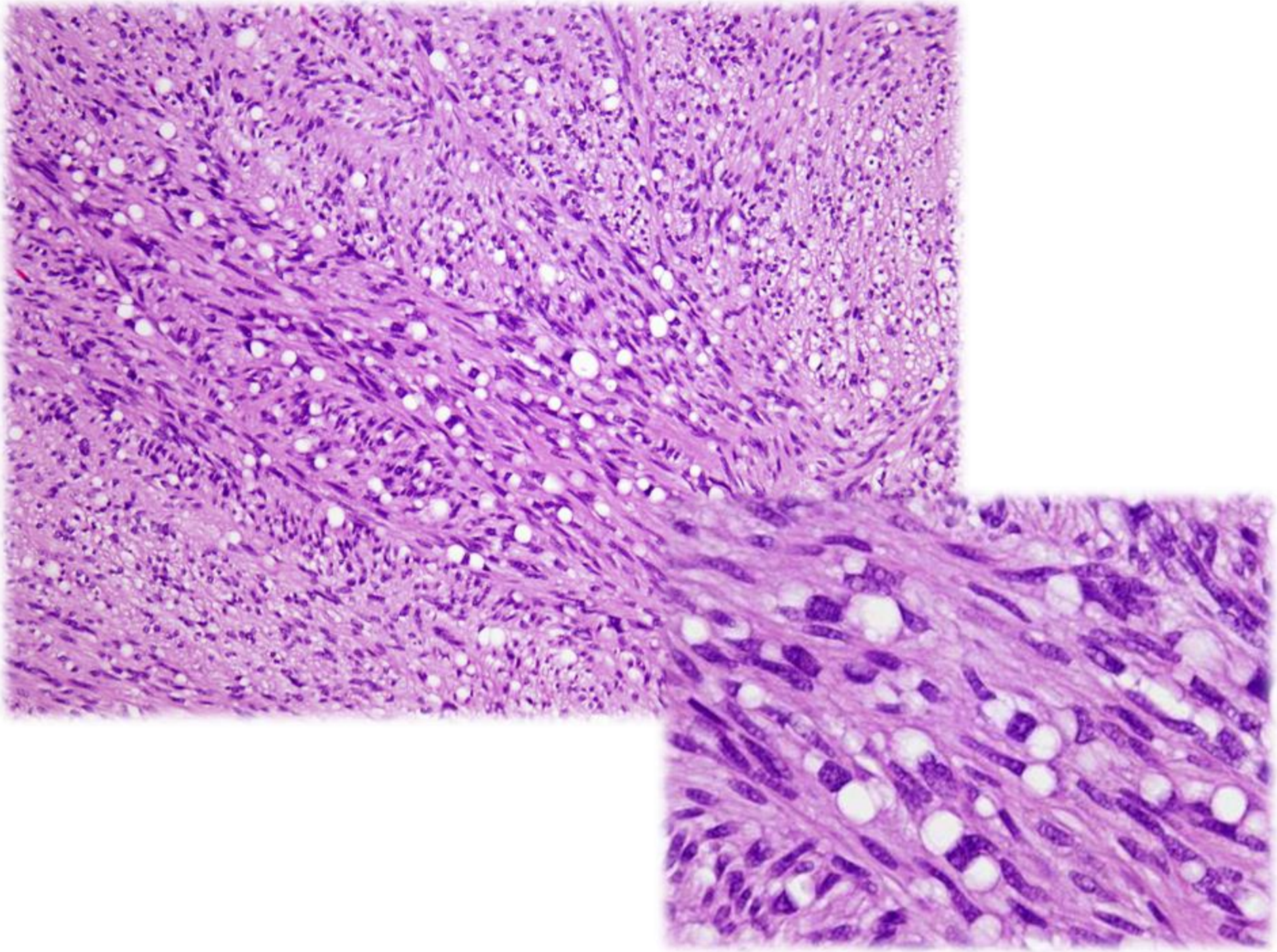


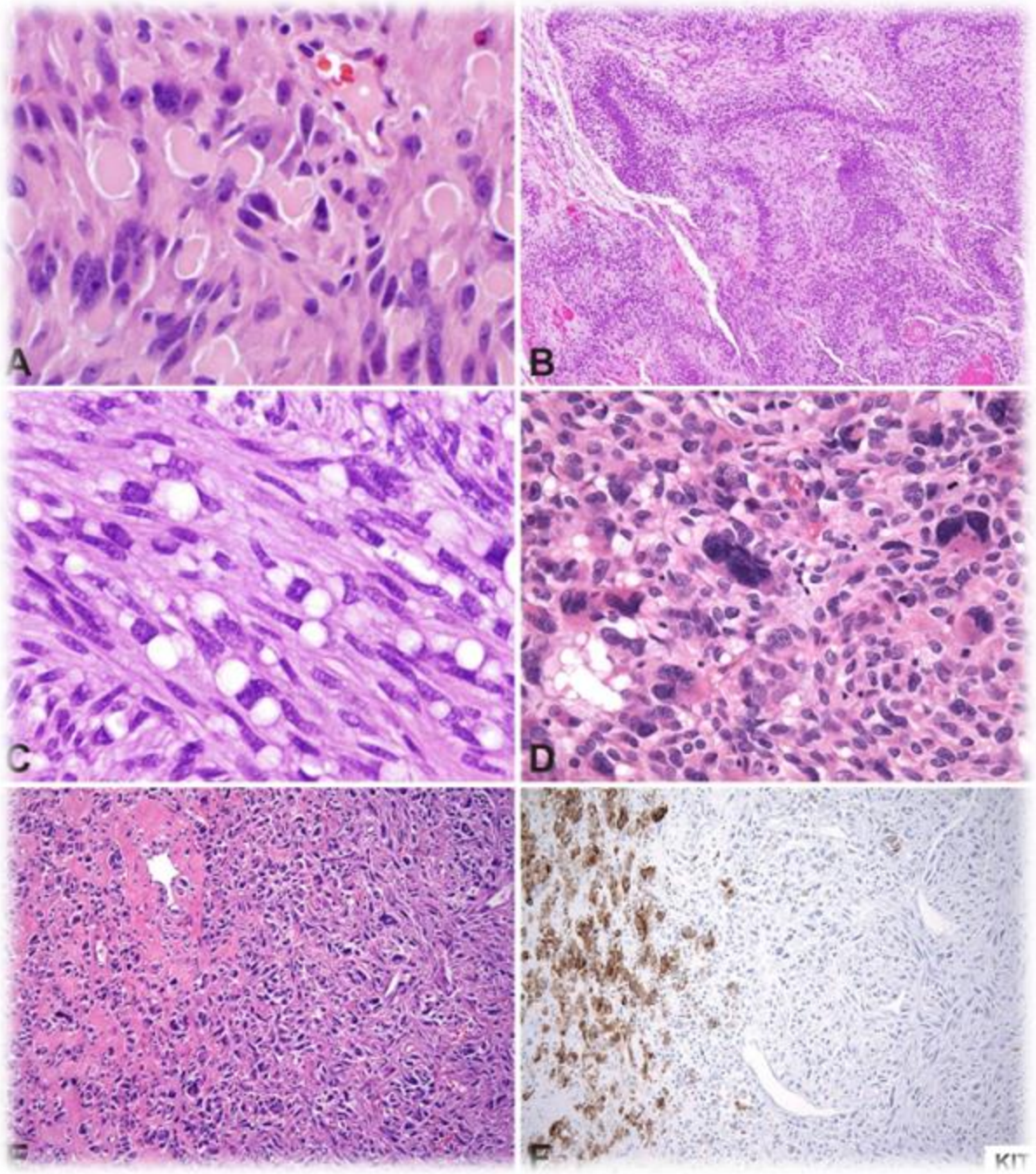


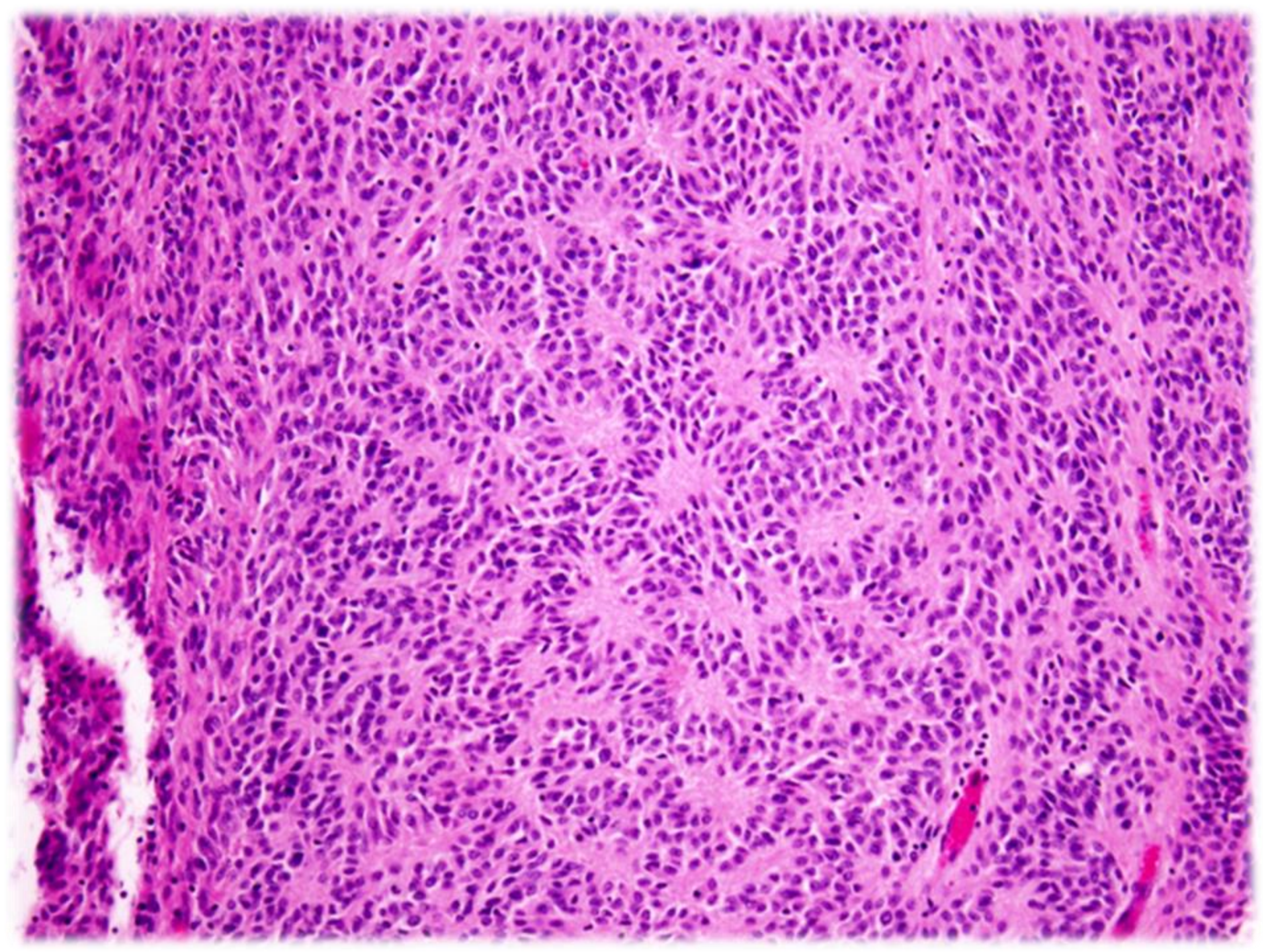









A
B
C
D
E
KIT



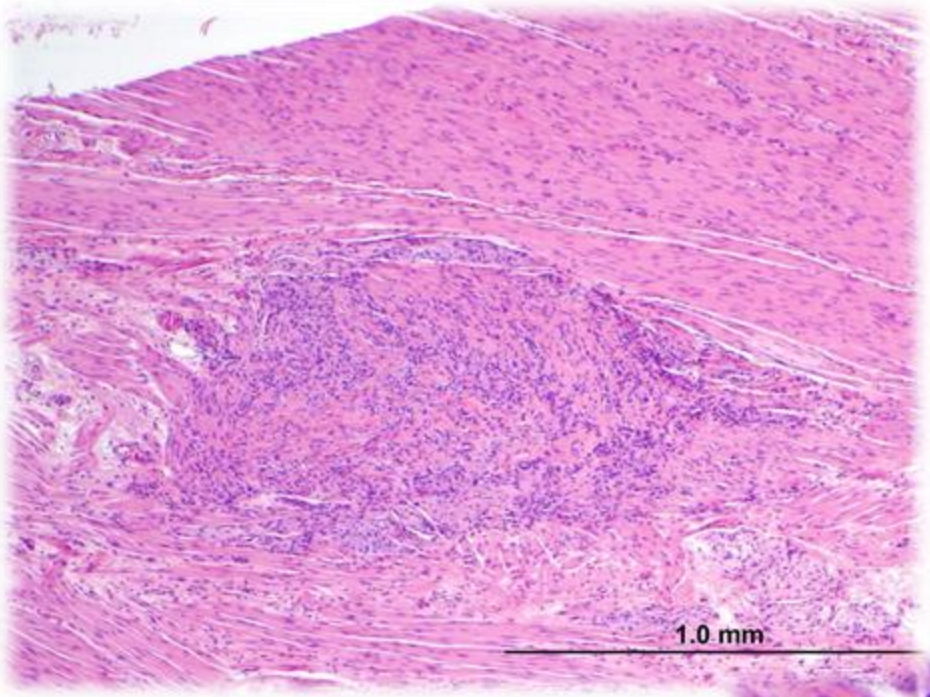
Clinical Characteristics of GIST

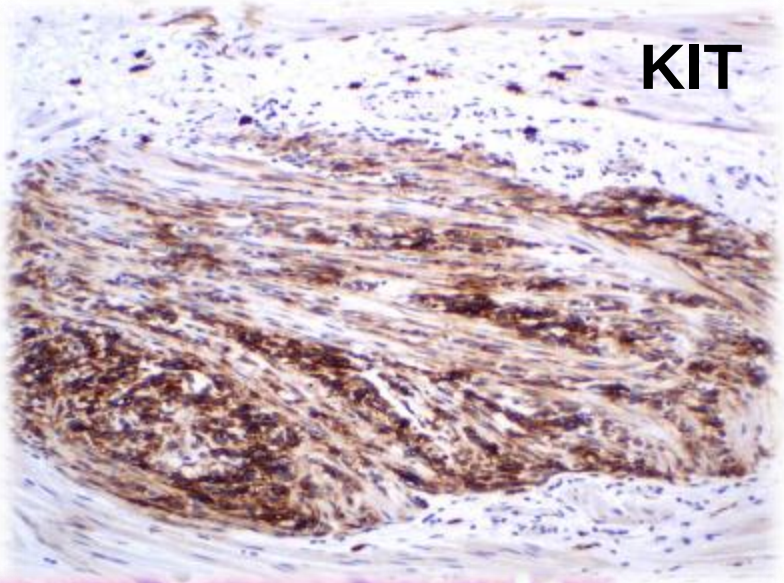
Wide age range – peak in 5^{th}-7^{th} decade

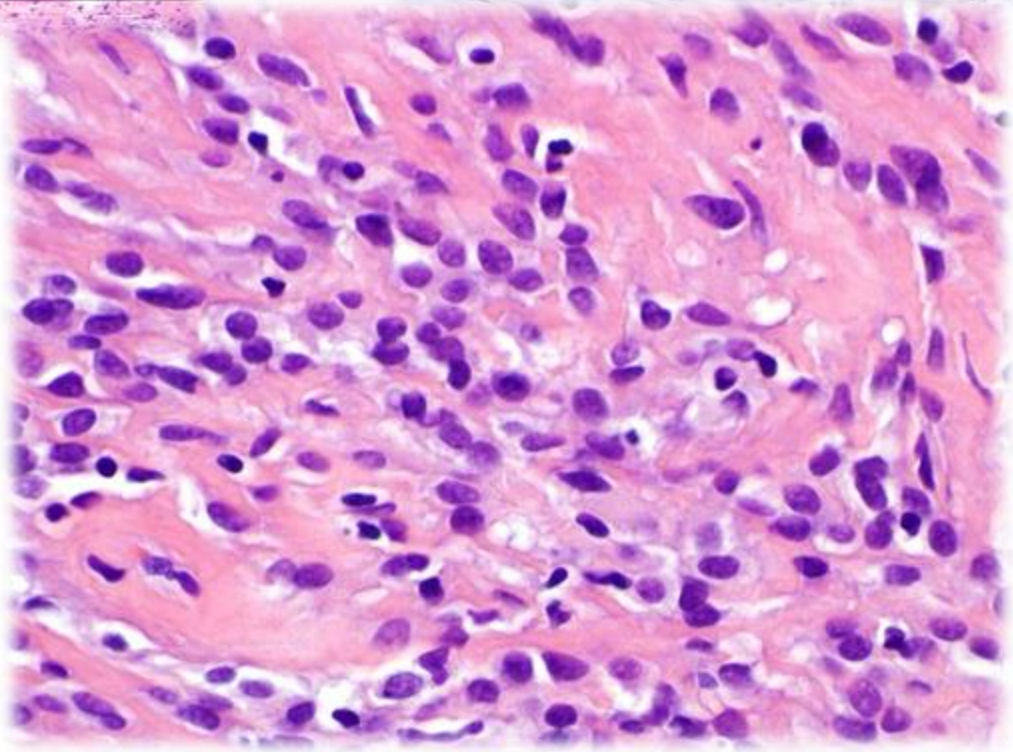
M = F

Small lesions = "incidentalomas"

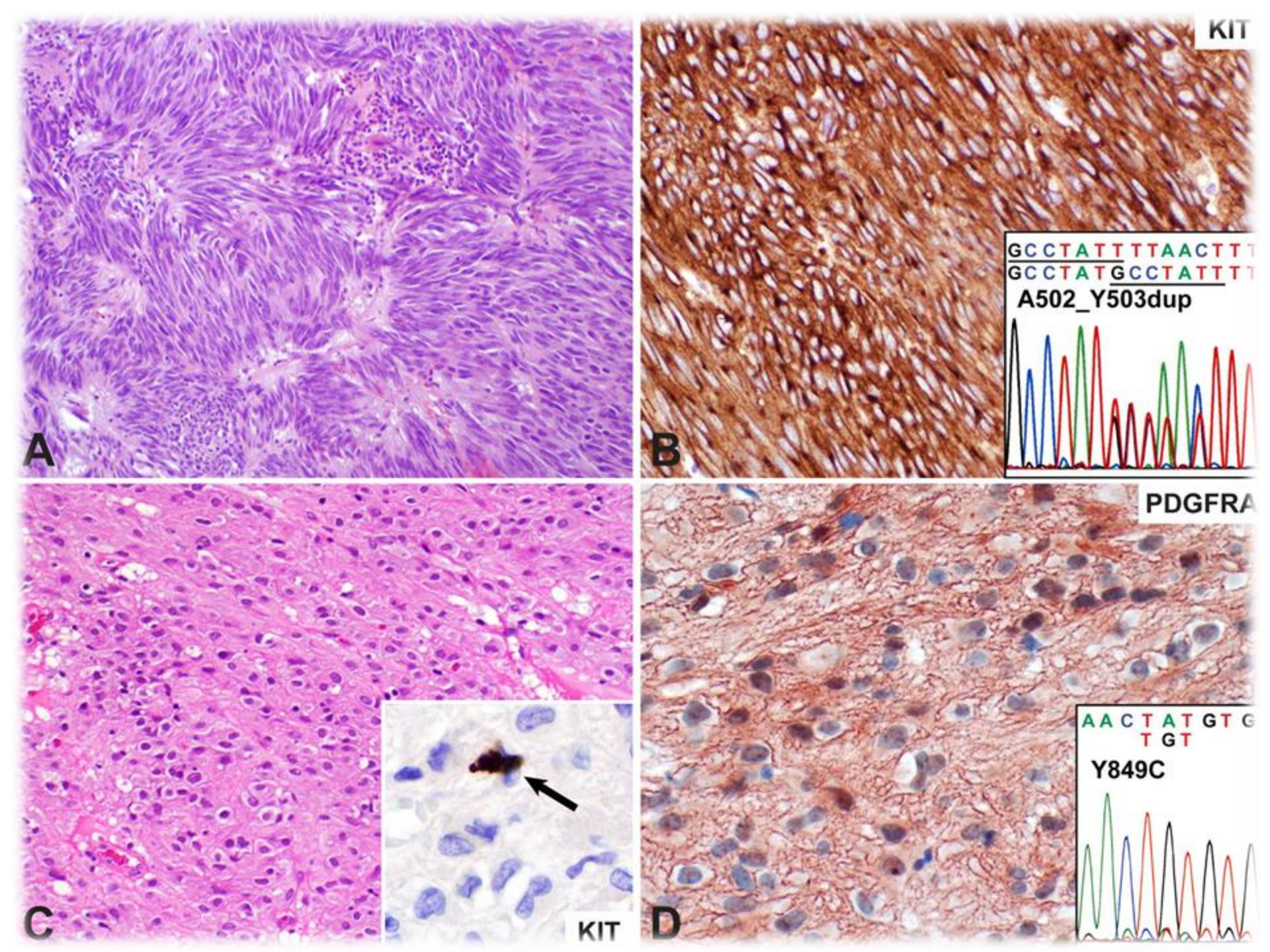
Presenting symptoms include:
abdominal pain,
gastrointestinal bleeding,
early satiety,
symptoms referable to a mass

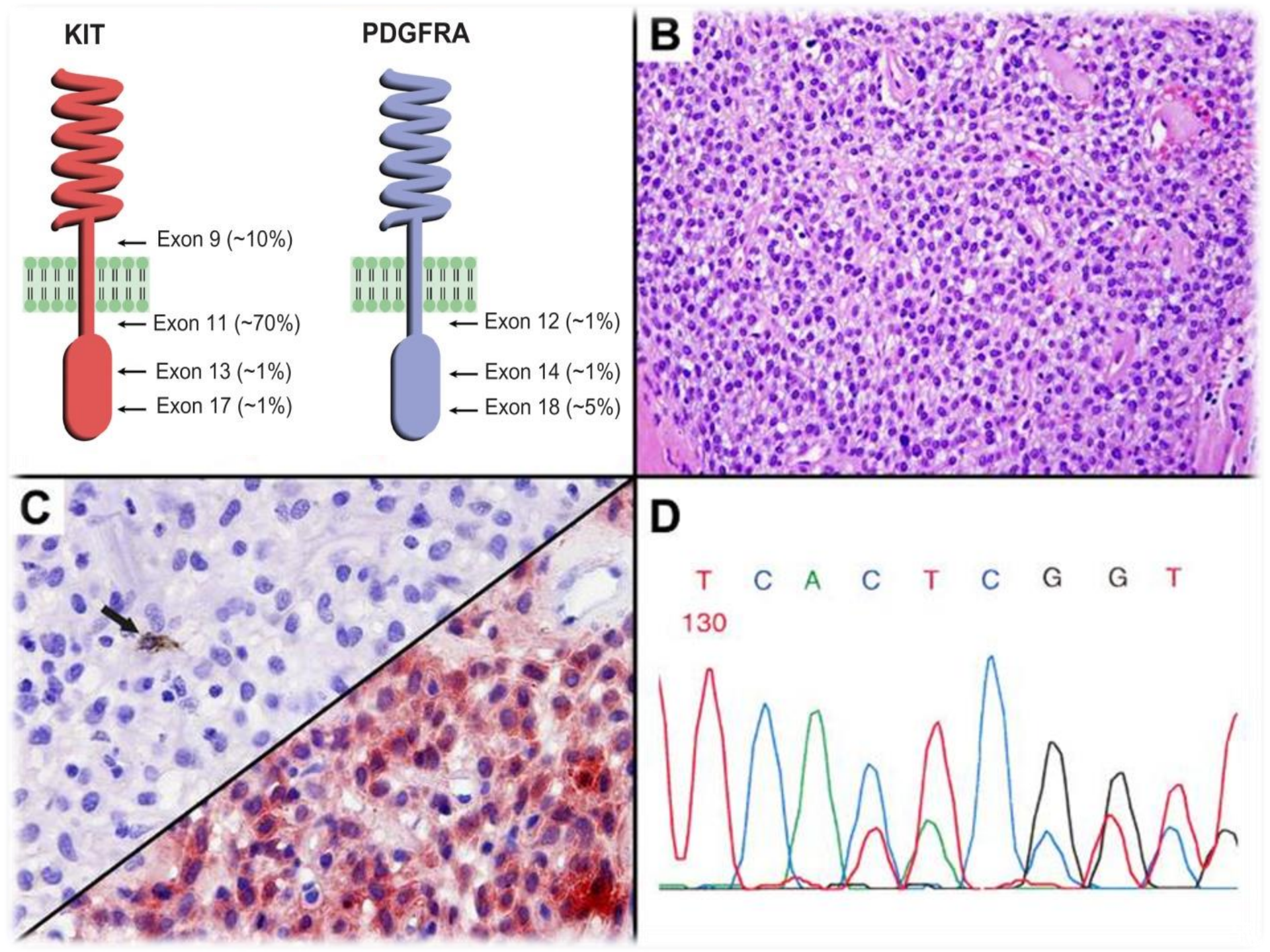


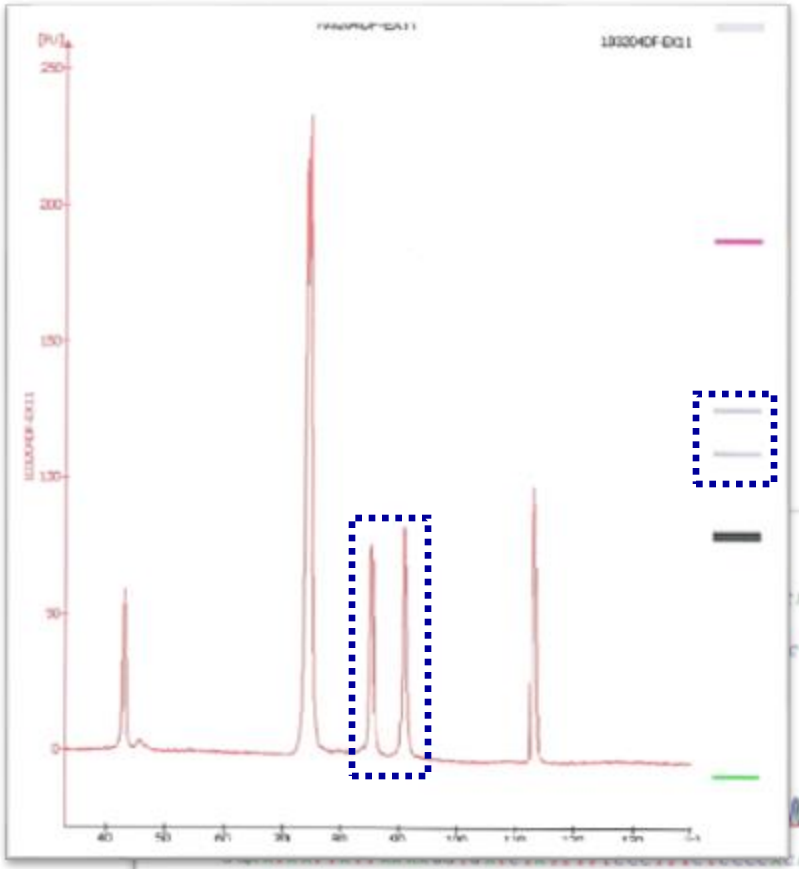




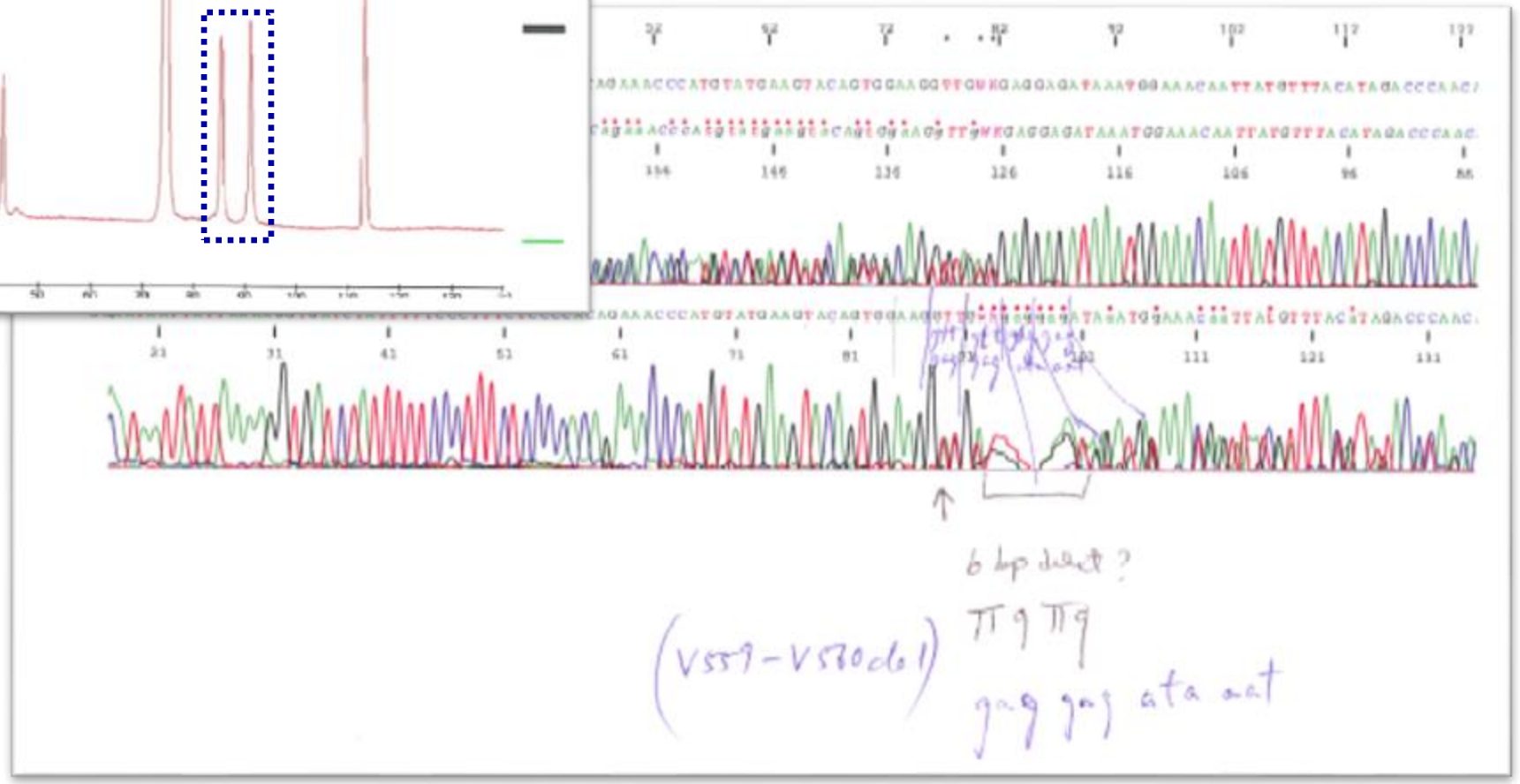
courtesy of Susan Abraham, UTMDACC, Houston, TX


A
KIT
B
GCCTATTTTAACTTT
GCCTATGCCTATTTT
A502_Y503dup
C
KIT
PDGFRA
D
AACTATGTG
TGT
Y849C


KIT
PDGFRA
Exon 9 (~10%)
Exon 11 (~70%)
Exon 13 (~1%)
Exon 17 (~1%)
Exon 12 (~1%)
Exon 14 (~1%)
Exon 18 (~5%)
B
C
D
T C A C T C G G T
130

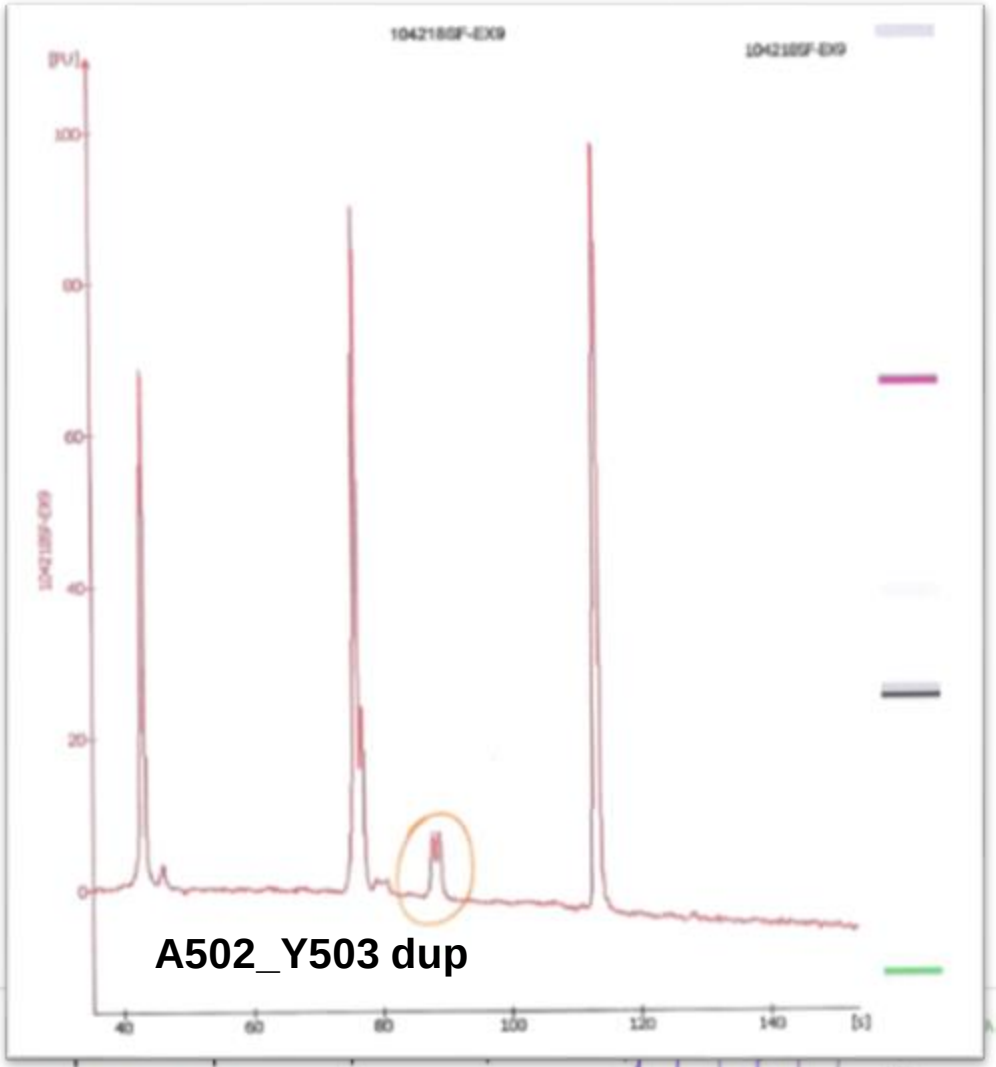


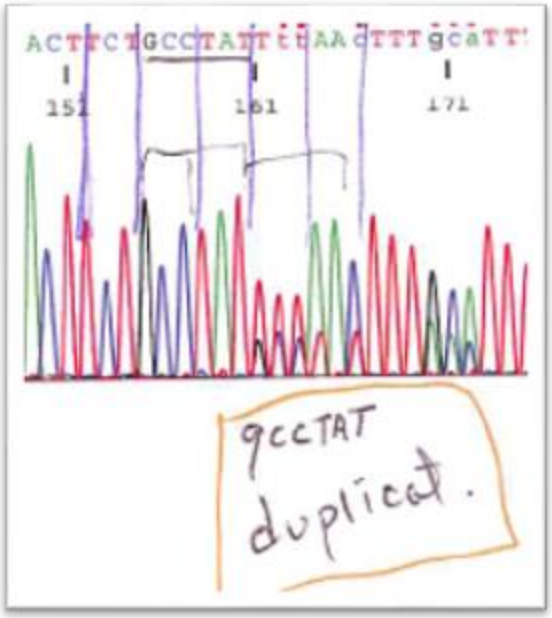
Exon 11
V559_V560del

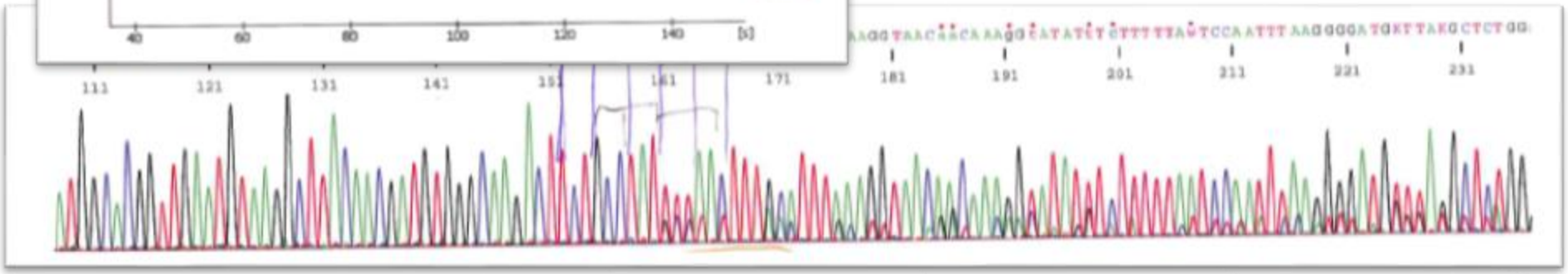


Exon 9

A502_Y503dup

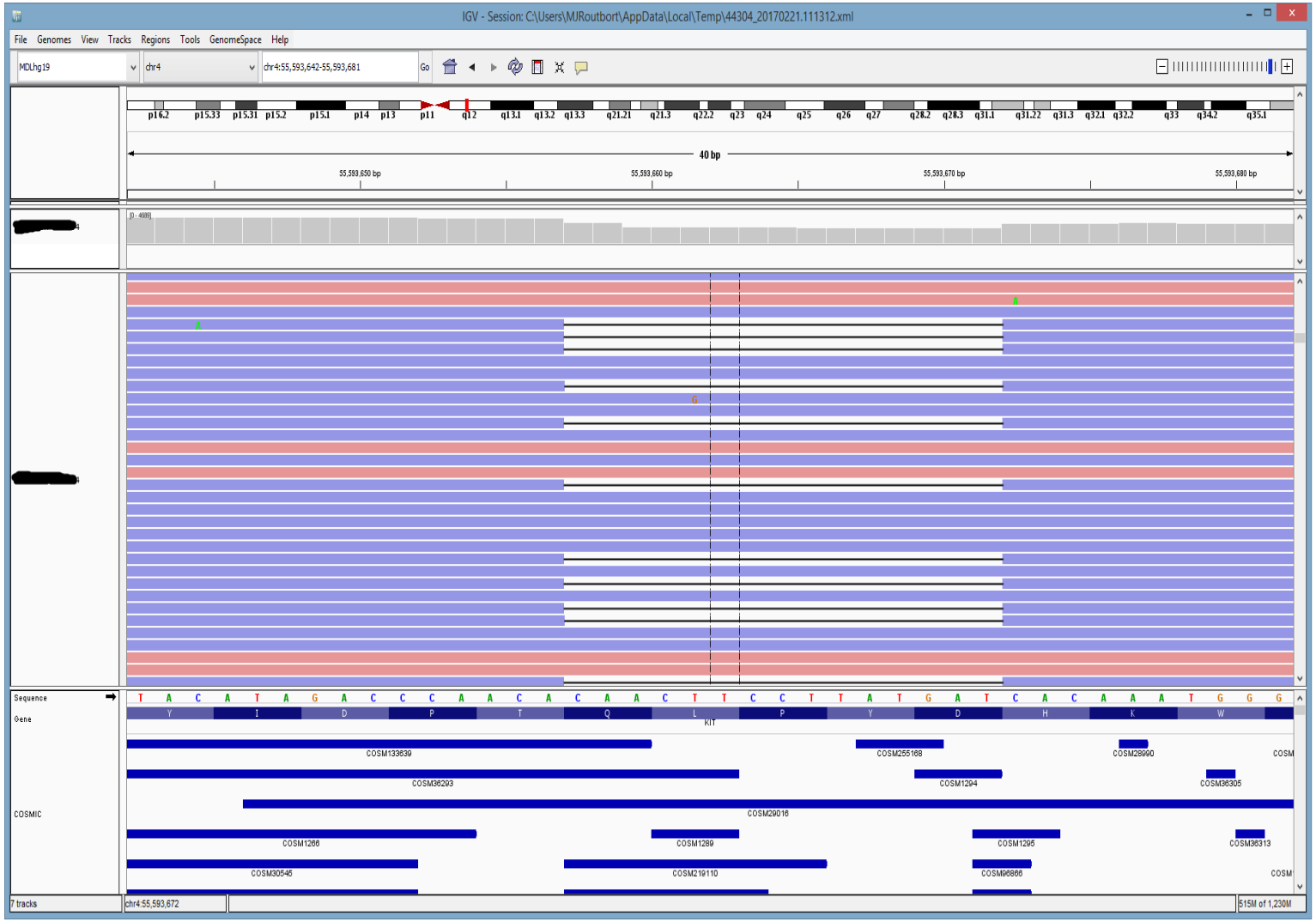




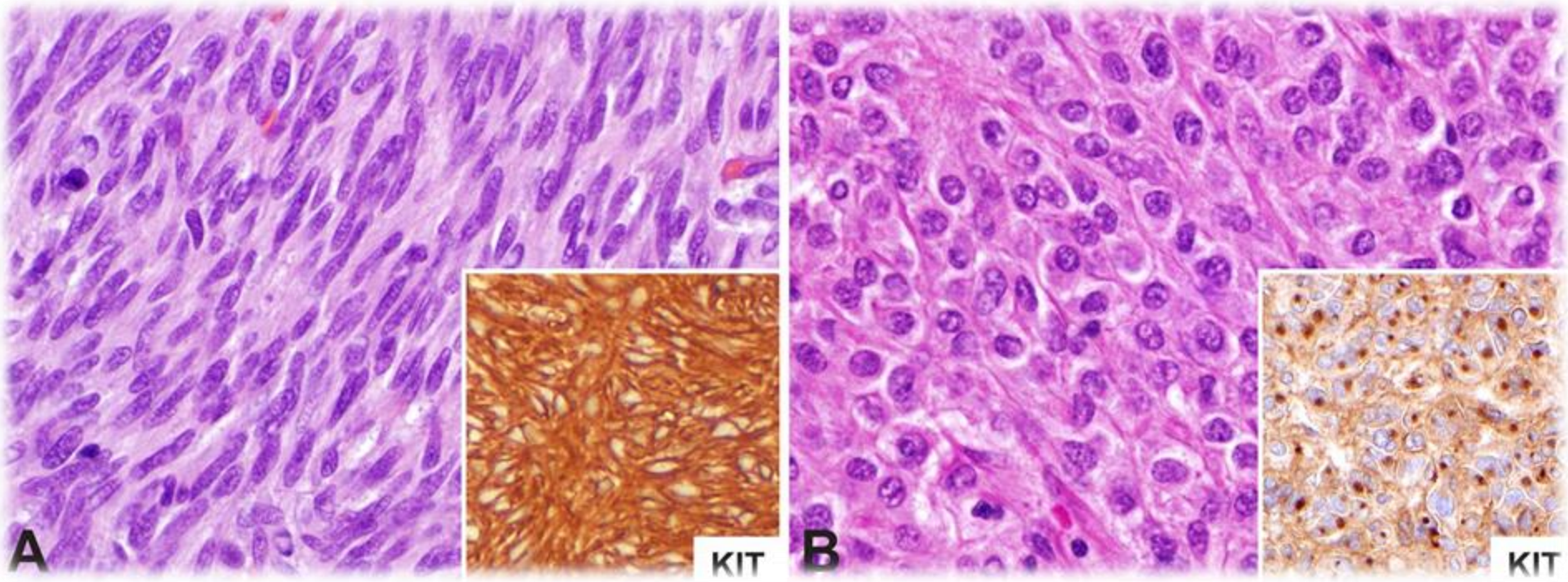


NM_000222.2(*KIT*):c.1725_1739del p.Q575_D579del

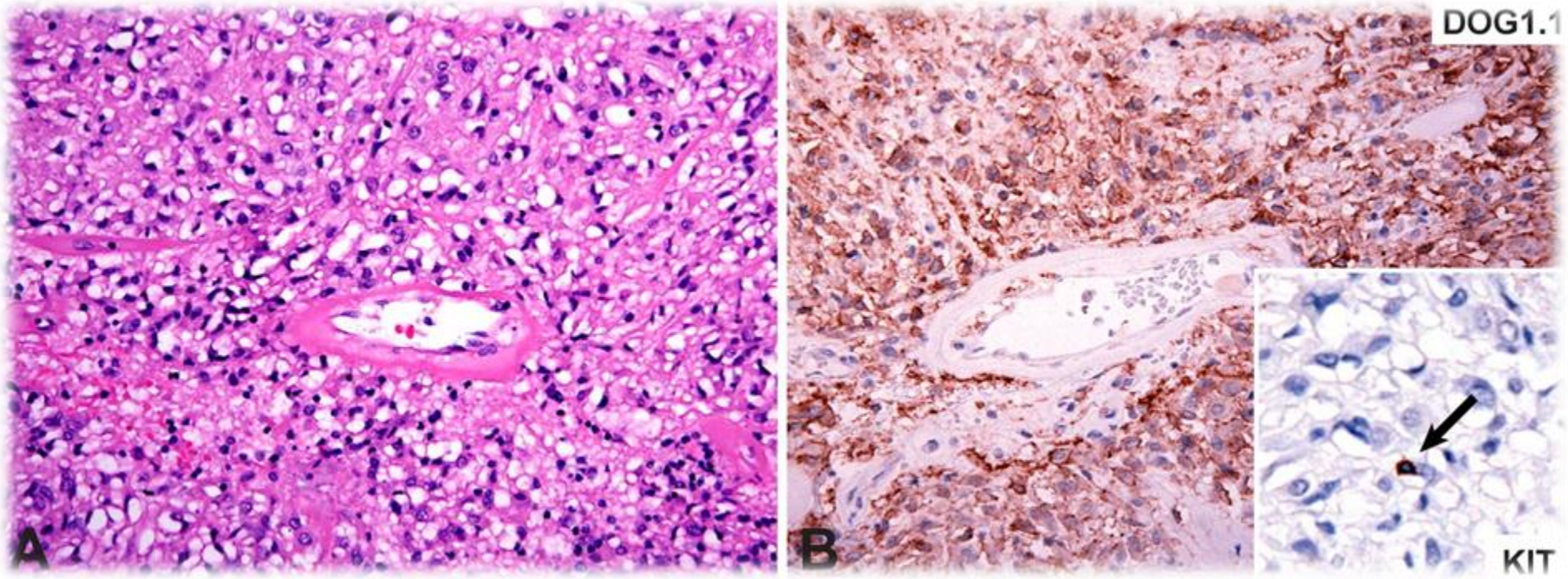
a 15-bp inframe deletion in exon 11 of KIT causing a loss of 5 amino acids.



KIT immunoreactivity in GIST



KIT-negative GIST



Gastric GISTs with Distinctive Histology (Multinodular/Plexiform)

- **Pediatric GISTs**
  - **Female predominance (peak 2nd decade)**
  - **Indolent, but late metastases common**
  - **Molecular genetic basis unknown**

Carney Triad

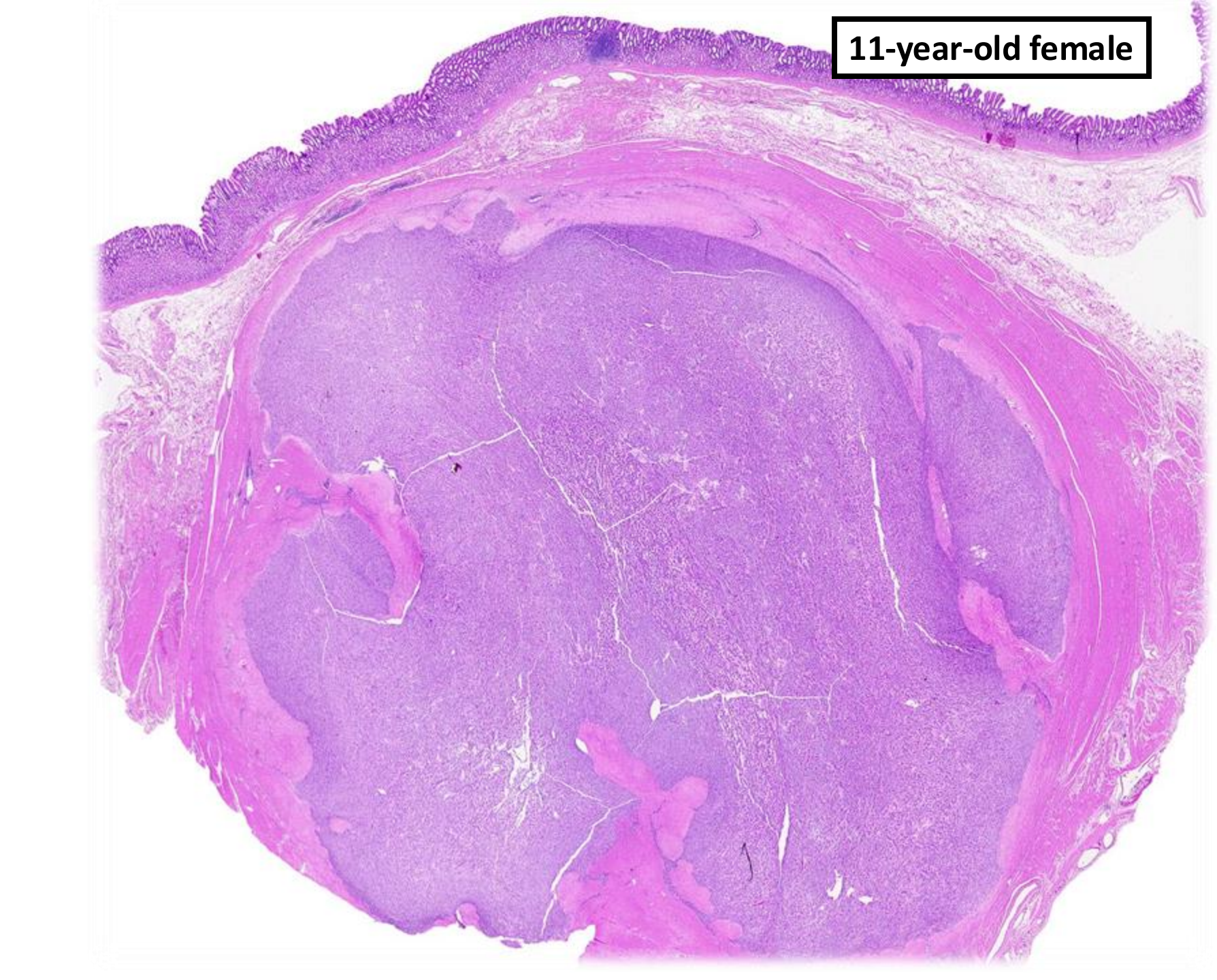
- **Gastric GIST, pulmonary chondroma, paraganglioma**
- **Molecular genetic basis unknown**

Carney-Stratakis Syndrome

- **Gastric GIST and paraganglioma**
- **Germline mutations in succinate dehydrogenase subunit genes (*SDHA*, *SDHB*, *SDHC*, or *SDHD*)**

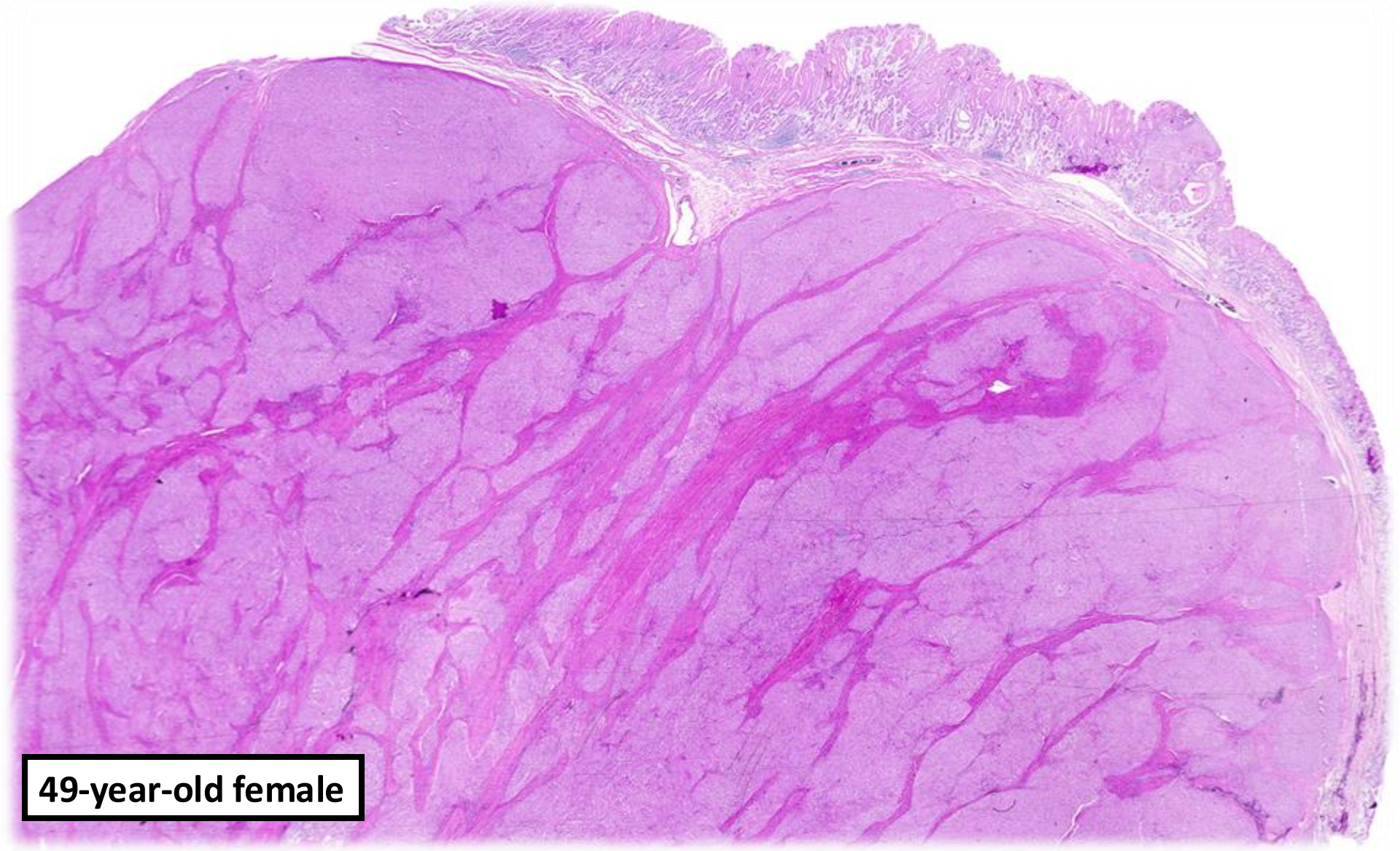
GIST with Distinctive Histology

- **Multinodular/plexiform growth pattern**
- **Epithelioid or mixed morphology**
- **“Pediatric-type” or “type 2” GISTs**
- **Loss of SDHB staining by IHC**
- **Lymph node metastases common**
- **Distant metastases common – clinically indolent**
- **Current risk assessment criteria do not reliably predict behavior**
- **No response to imatinib**

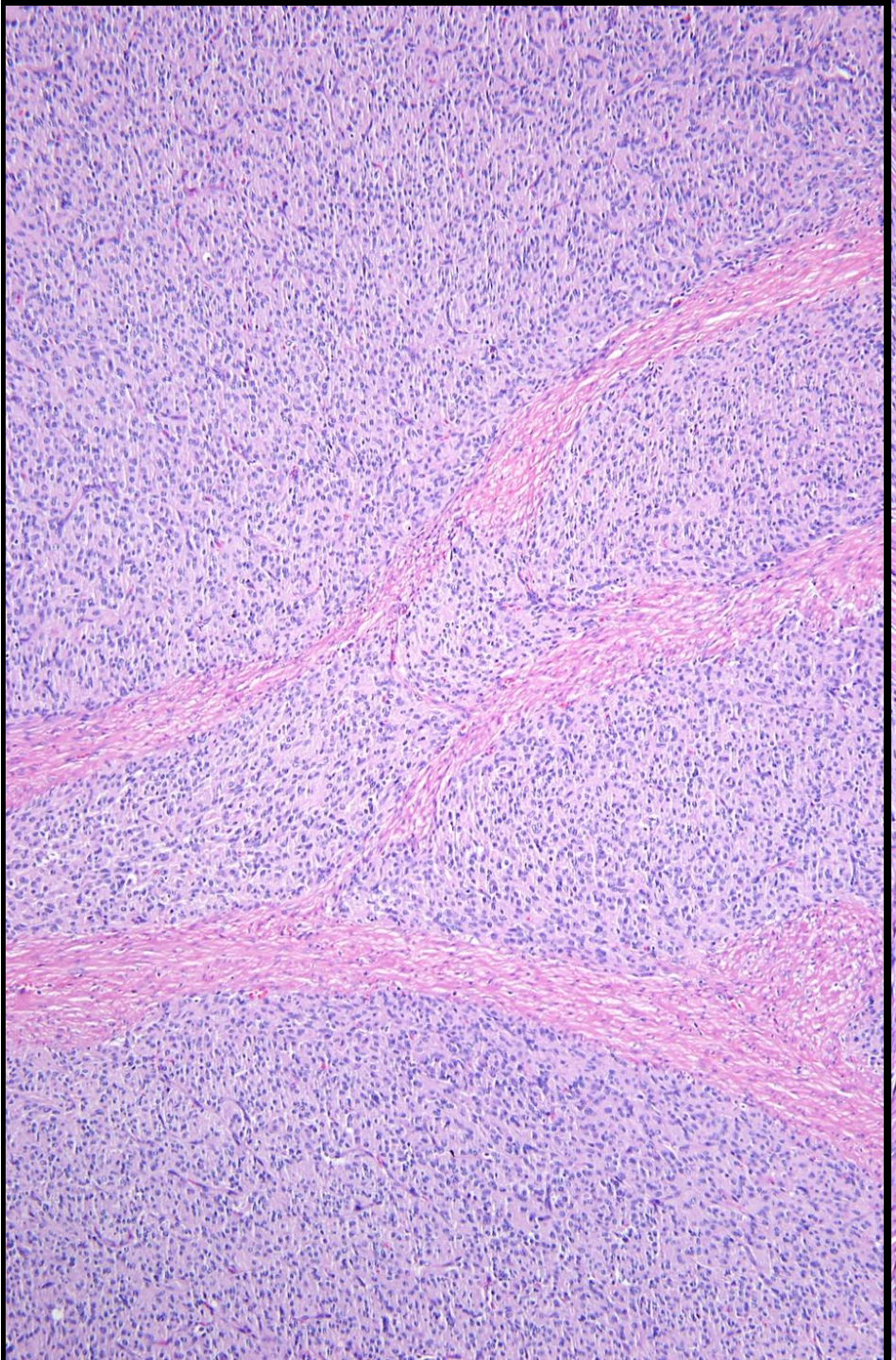
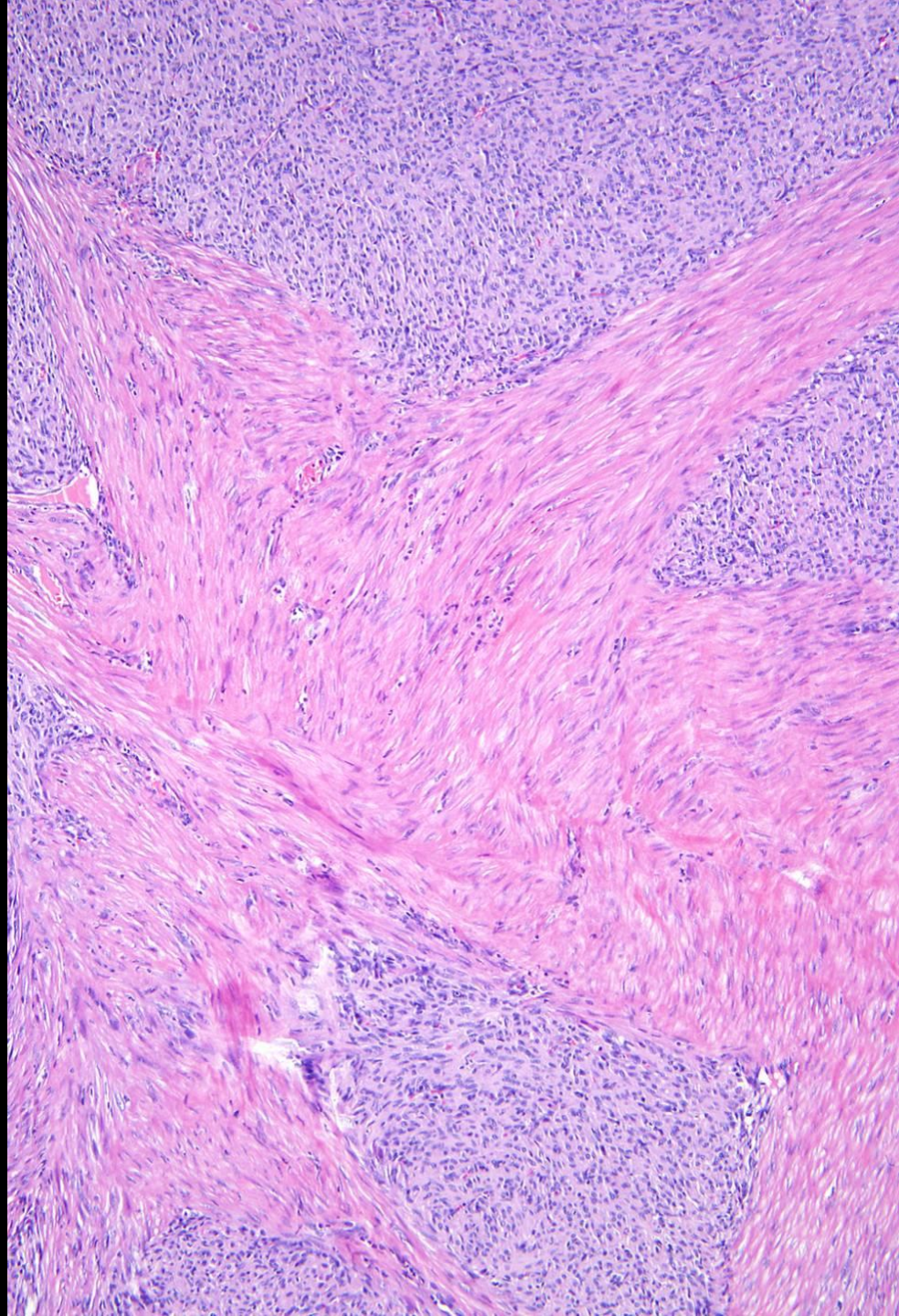


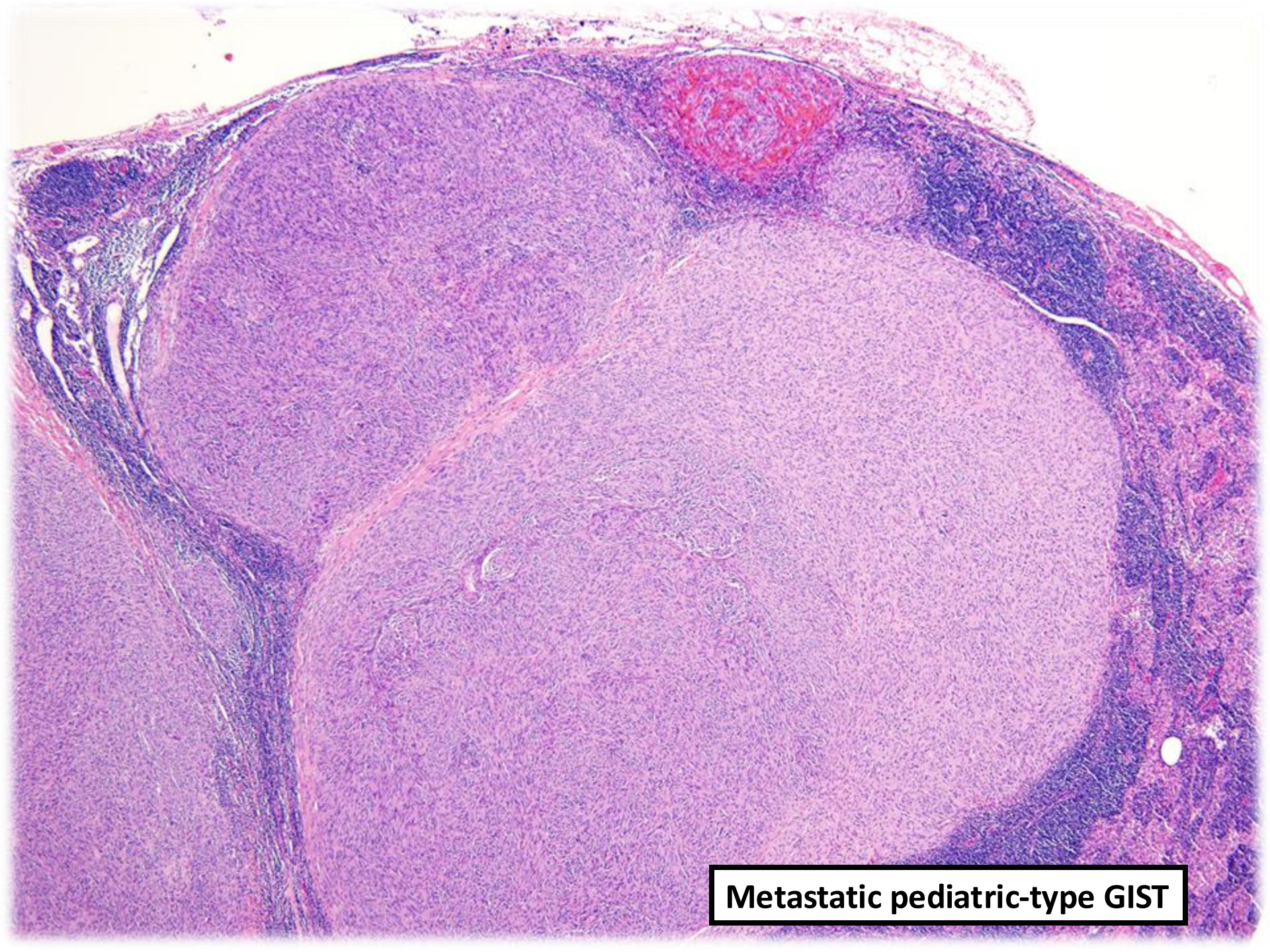
Courtesy of Jason Hornick, BWH/Harvard, Boston, MA

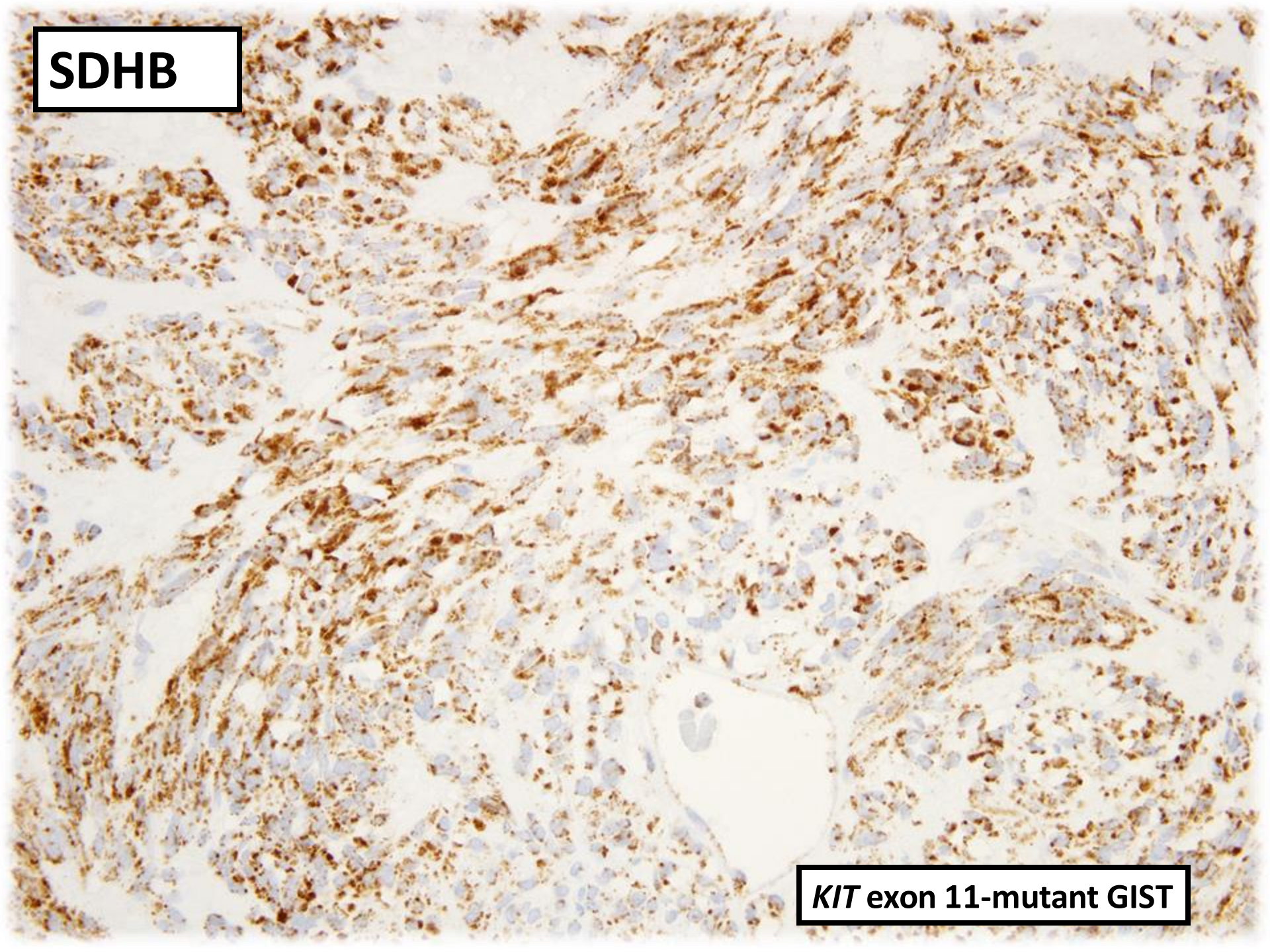
Pediatric-type GIST in an Adult

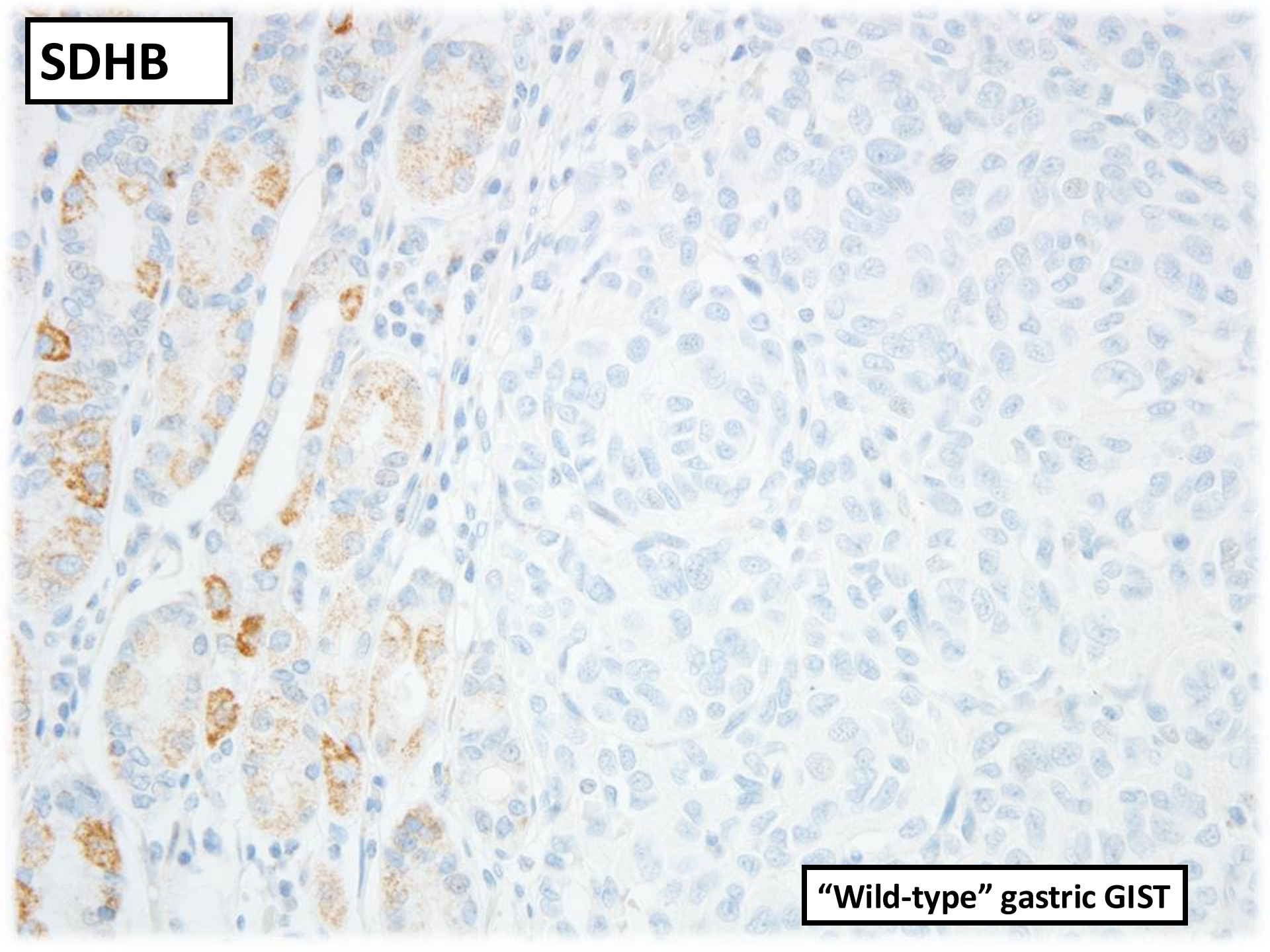


Courtesy of Jason Hornick, BWH/Harvard, Boston, MA


Metastatic pediatric-type GIST


SDHB
KIT exon 11-mutant GIST


SDHB
“Wild-type” gastric GIST

Risk assessment in GIST

GIST – Prognostic Factors

Size

Mitotic Rate

Anatomic Location

Pleomorphism

Cellularity

Necrosis

Mucosal Invasion

Proliferation Markers (Ki-67, Mib-1, PCNA, etc)

DNA Flow Cytometry

Image Analysis

Nuclear Organizer Regions

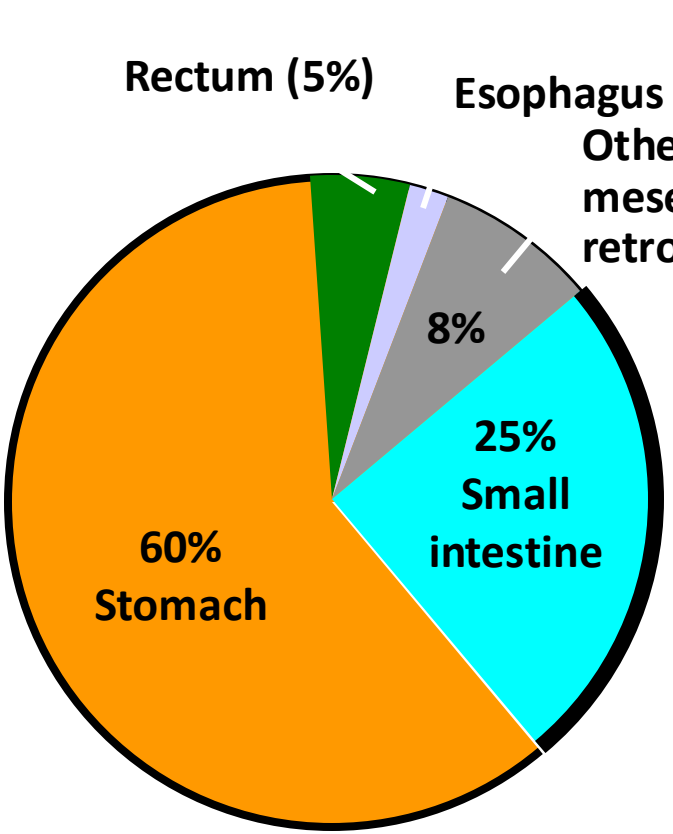
Problem – Small GISTs without mitoses can metastasize!

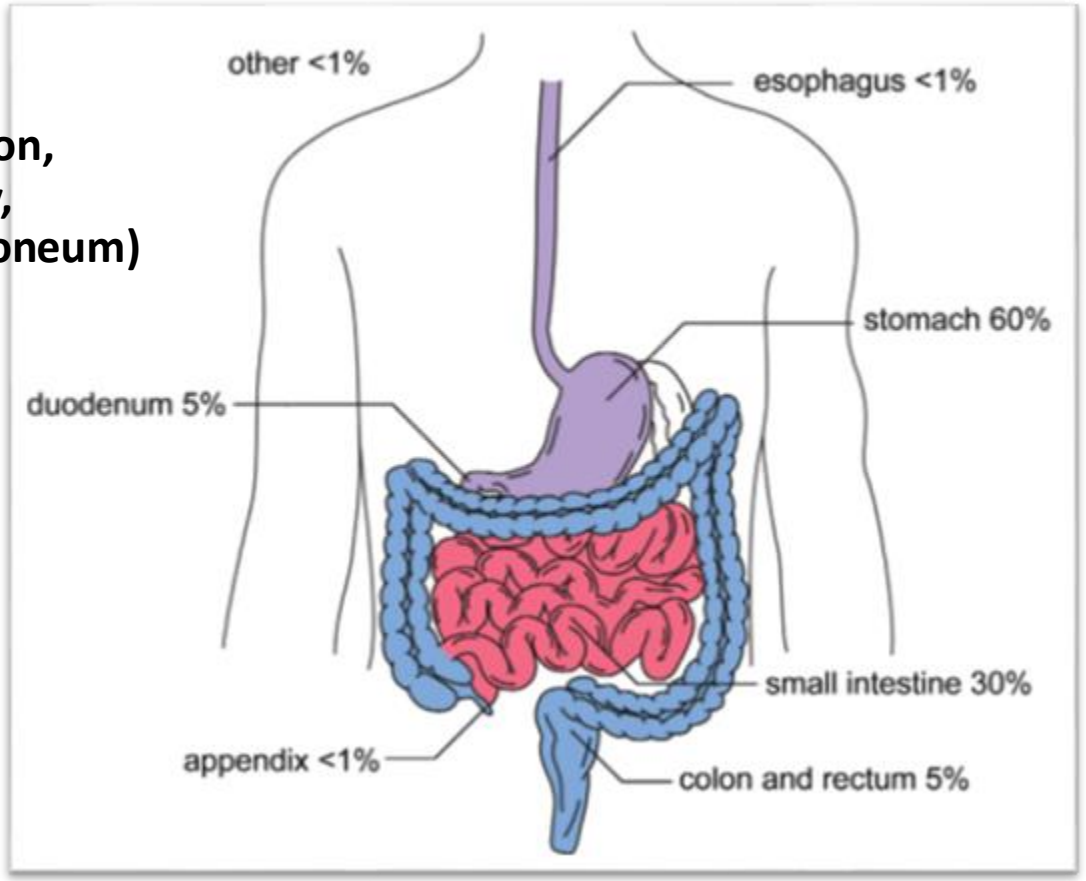
NIH Consensus Risk Assessment

	Size	Mitotic Count
Very Low Risk	< 2 cm	< 5/50 HPF
Low Risk	2-5 cm	< 5/50 HPF
Intermediate Risk	< 5 cm	6-10/50 HPF
	5-10 cm	< 5/50 HPF
High Risk	> 5 cm	> 5/50 HPF

Fletcher et al., Hum Pathol, 2002

GIST: Sites of Involvement





Omentum, mesentery, pelvis and retroperitoneum = EGIST (<1%)

Hornick & Lazar. GSI website: Understanding Your Pathology Report for GIST.

2007/2010/2014 NCCN GIST Risk Assessment Guidelines***

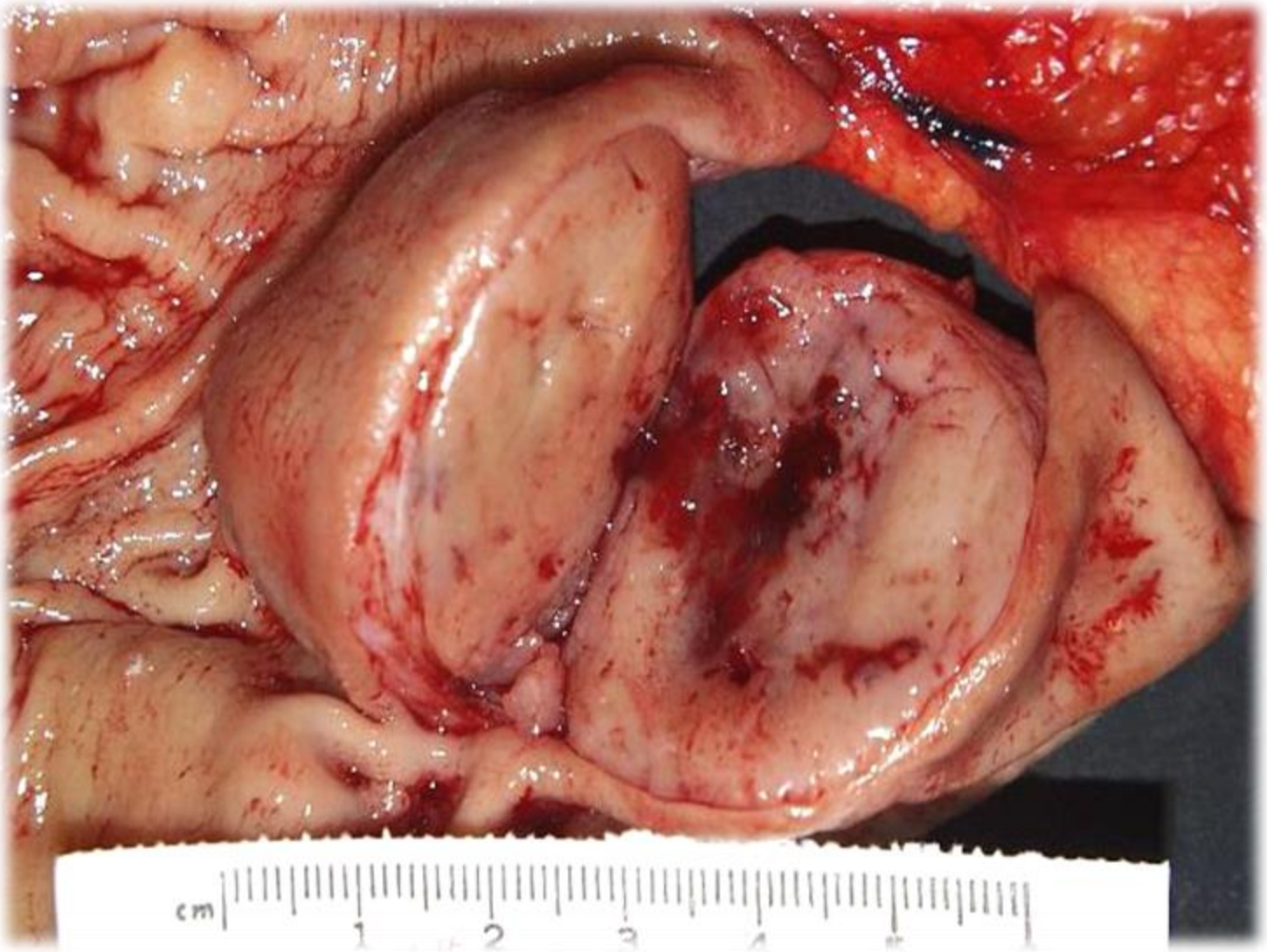
Tumor	Parameters	Risk of	Progressive	Disease# (%)	
	Size	Gastric	Duodenum	Jejunum/Ileum	Rectum
Mitotic	≤ 2 cm	None (0%)	None (0%)	None (0%)	None (0%)
Index	> 2 ≤ 5 cm	Very low (1.9%)	Low (8.3%)	Low (4.3%)	Low (8.5%)
≤ 5 per 50 hpf	> 5 ≤ 10 cm	Low (3.6%)	(Insuff. data)	Moderate (24%)	(Insuff. data)
	> 10 cm	Moderate (10%)	High (34%)	High (52%)	High (57%)
Mitotic	≤ 2 cm	None*	(Insuff. data)	High*	High (54%)
Index	> 2 ≤ 5 cm	Moderate (16%)	High (50%)	High (73%)	High (52%)
> 5 per 50 hpf	> 5 ≤ 10 cm	High (55%)	(Insuff. data)	High (85%)	(Insuff. data)
	> 10 cm	High (86%)	High (86%)	High (90%)	High (71%)

Miettinen *et al.* 2005 and 2006

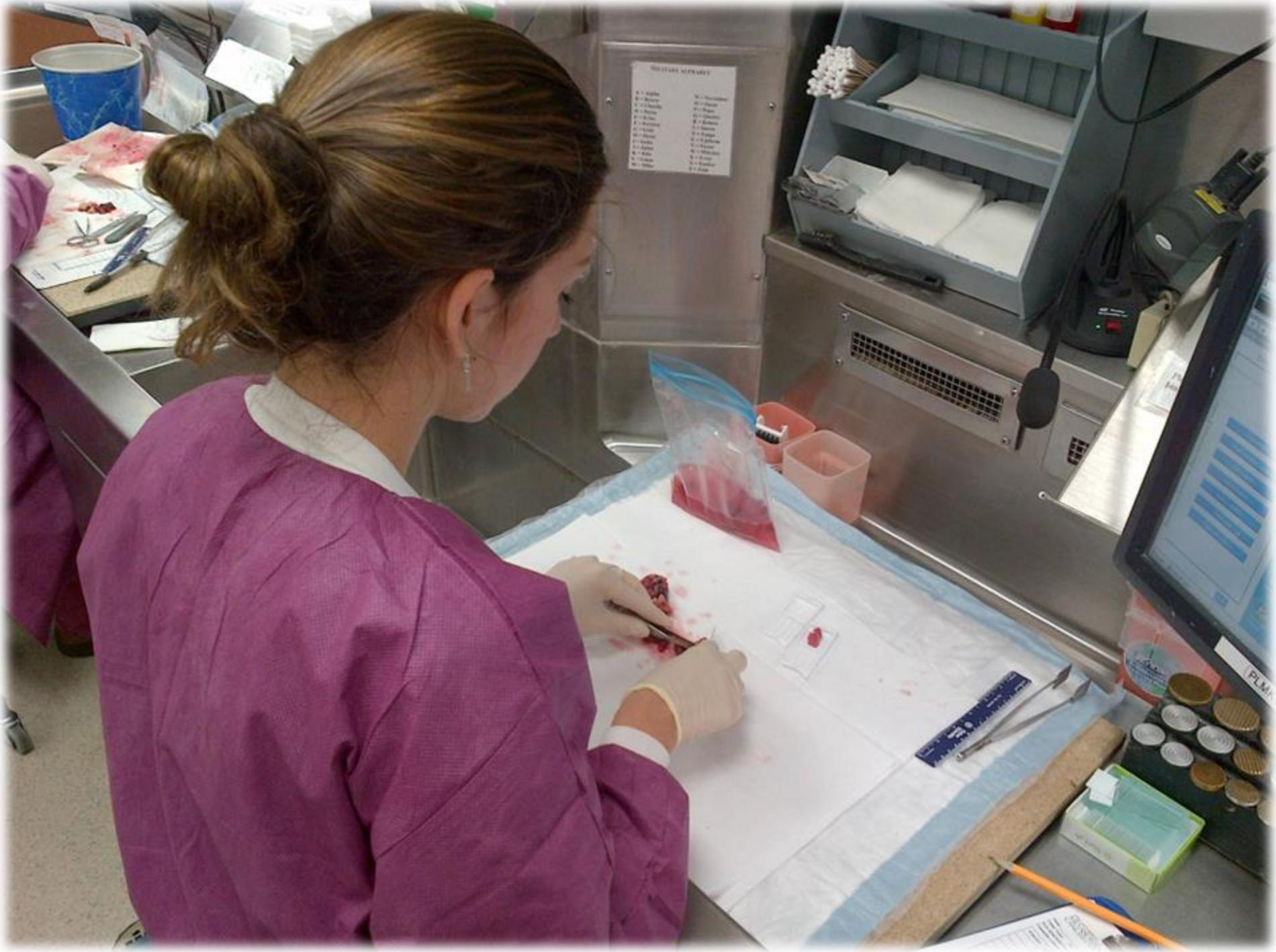
***Modified from Miettinen & Lasota, *Semin Diagn Pathol*, 2006 by Dr. Chris Corless, OHSU

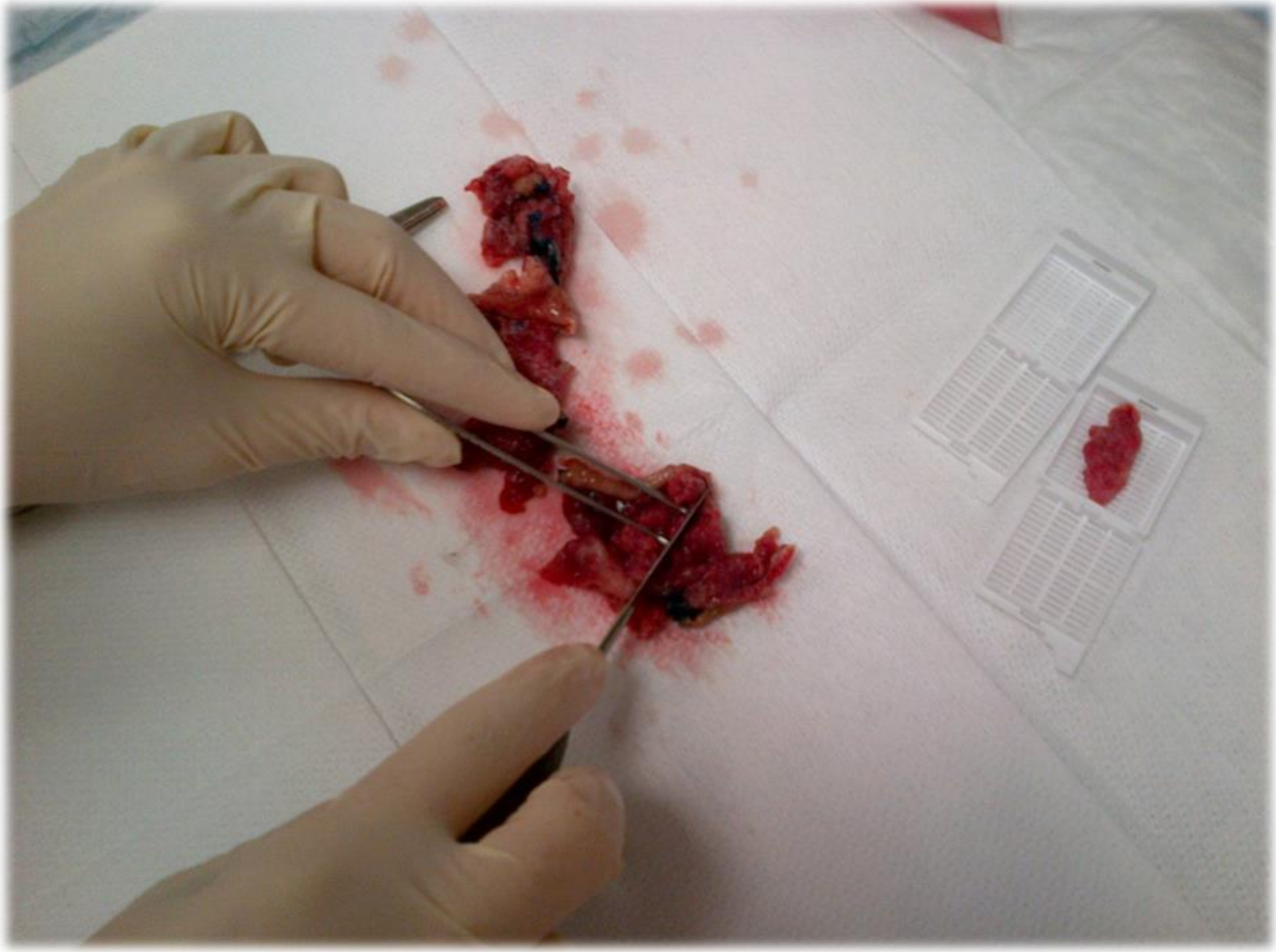
Data based on long-term follow-up of 1055 gastric, 629 small intestinal, 144 duodenal and 111 rectal GIST

GIST - Gross Appearance



Courtesy of Brian Rubin, Cleveland Clinic





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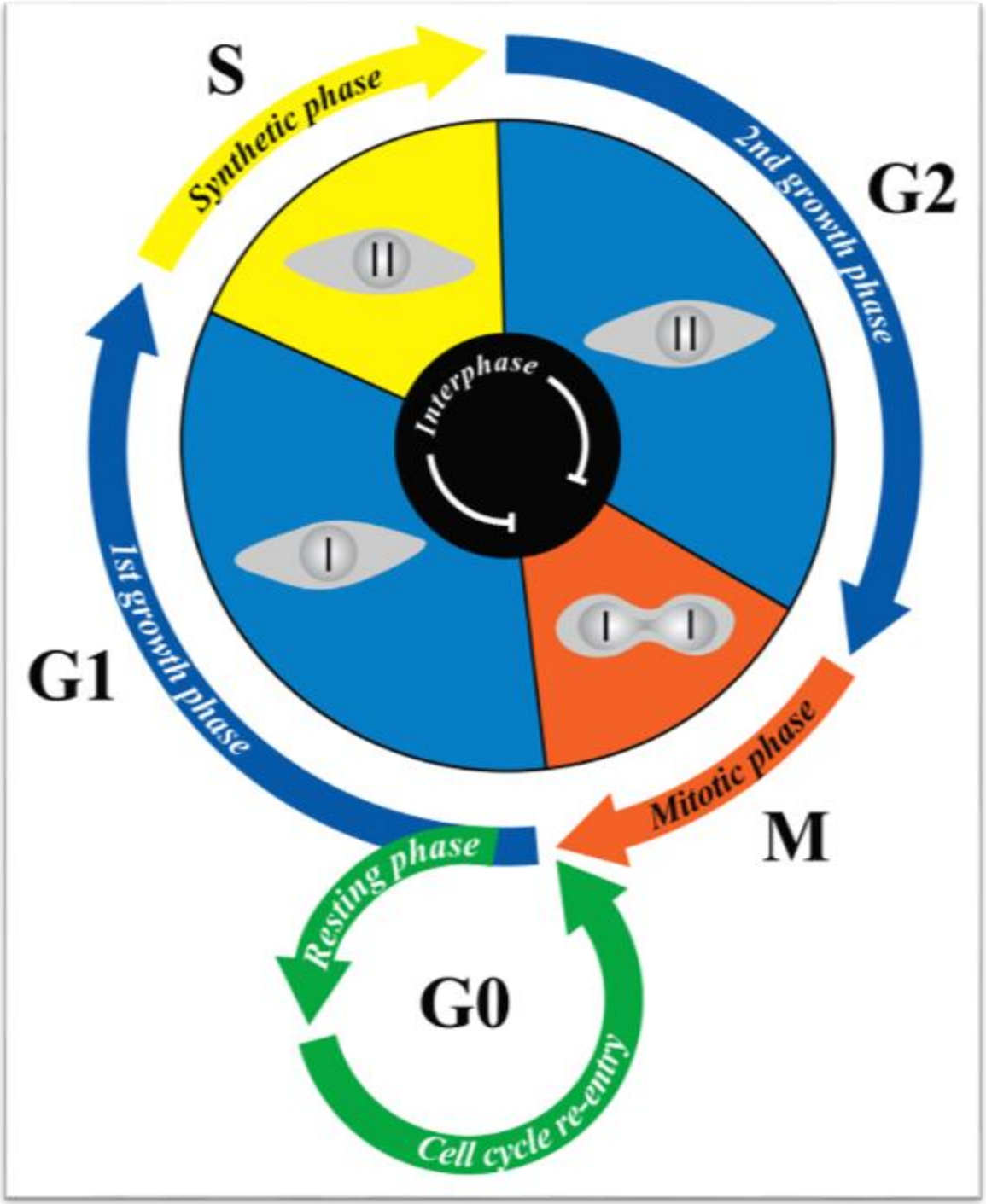
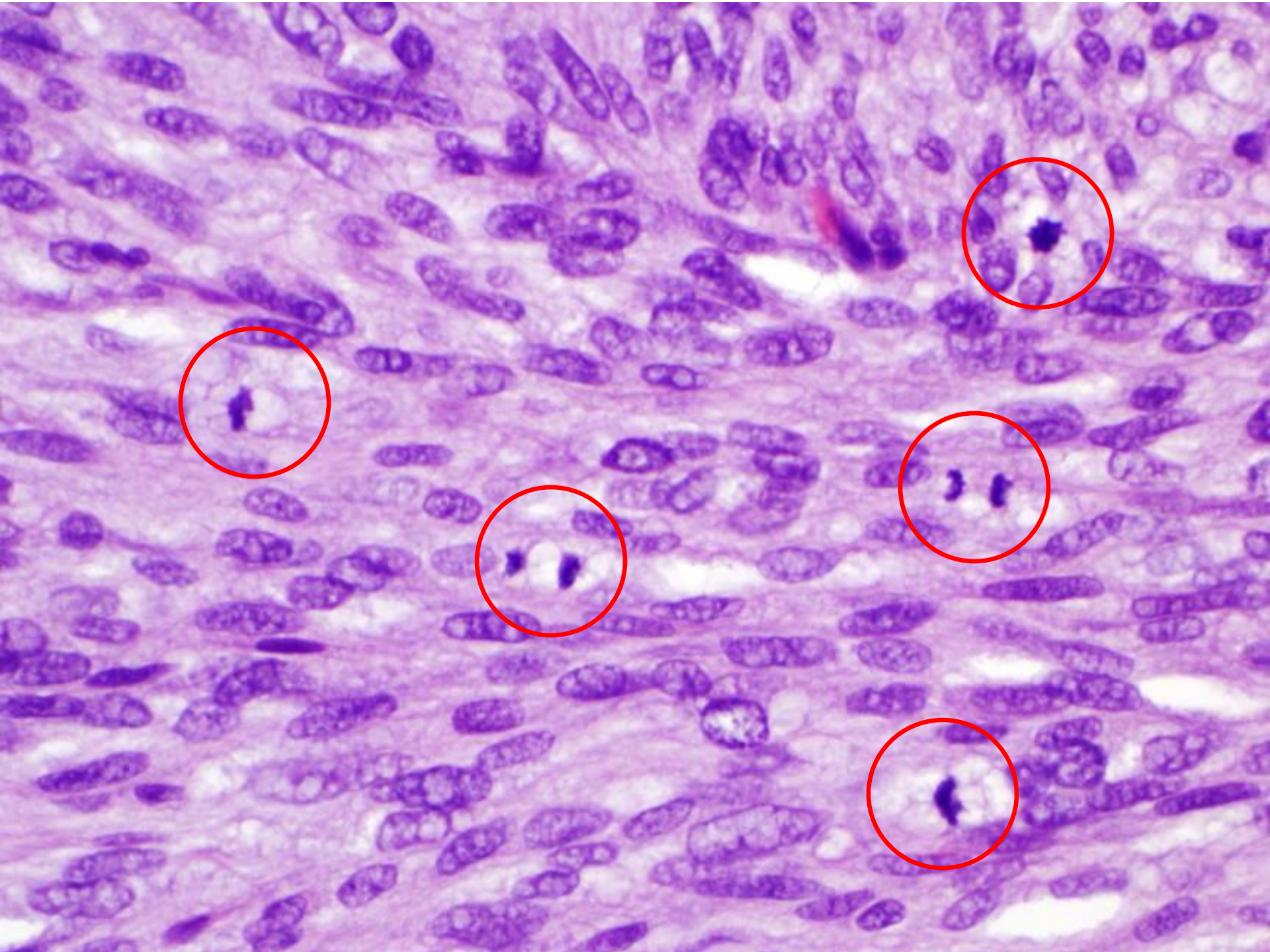
≤ 5 per 50 hpf	> 5 ≤ 10 cm	Low (3.6%)	(Insuff. data)	Moderate (24%)	(Insuff. data)
	> 10 cm	Moderate (10%)	High (34%)	High (52%)	High (57%)
Mitotic	≤ 2 cm	None*	(Insuff. data)	High*	High (54%)
Index	> 2 ≤ 5 cm	Moderate (16%)	High (50%)	High (73%)	High (52%)
> 5 per 50 hpf	> 5 ≤ 10 cm	High (55%)	(Insuff. data)	High (85%)	(Insuff. data)
	> 10 cm	High (86%)	High (86%)	High (90%)	High (71%)

***Modified from Miettinen & Lasota, *Semin Diagn Pathol*, 2006 by Dr. Chris Corless, OHSU
Data based on long-term follow-up of 1055 gastric, 629 small intestinal, 144 duodenal and 111 rectal GIST

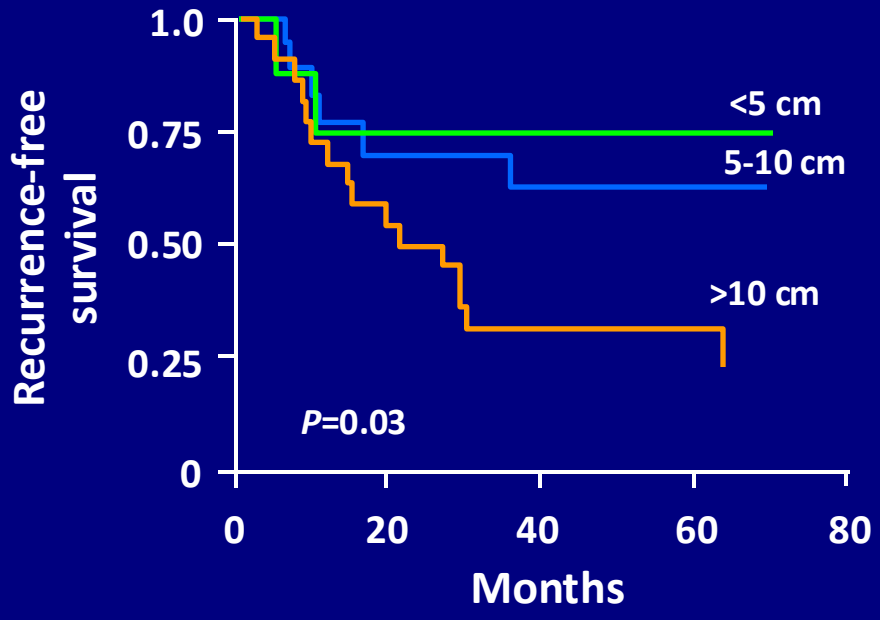
Miettinen *et al.* 2005 and 2006

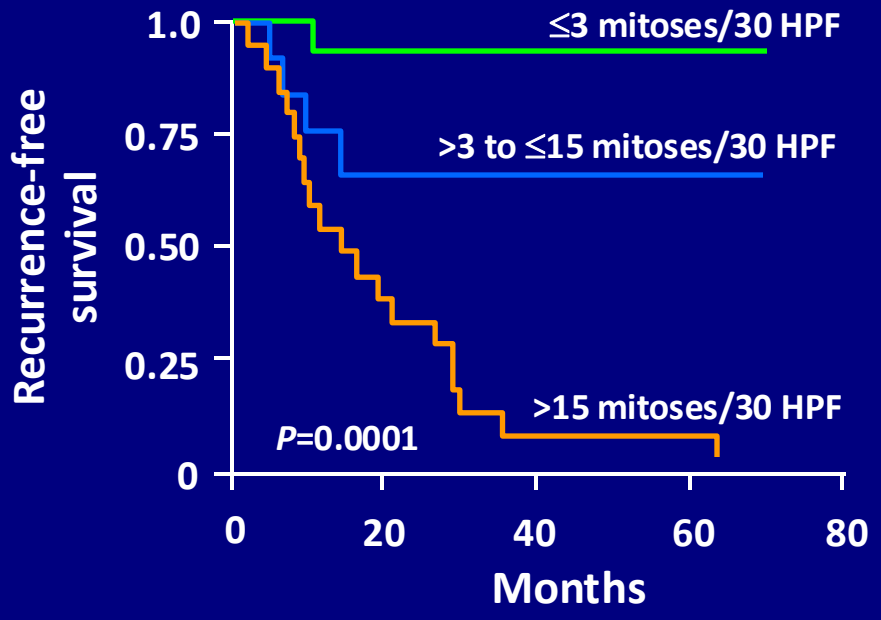

S
Synthetic phase
2nd growth phase
G2
Interphase
G1
1st growth phase
Mitotic phase
M
Resting phase
G0
Cell cycle re-entry



GIST - Recurrence-Free Survival Following Surgical Treatment of Primary GIST

- **Recurrence-free survival is predicted by tumor size and mitotic index**





Singer et al. *J Clin Oncol*. 2002;20:3898

FNCLCC Grading

- **All three numbers are summated to determine degree of differentiation**

Grade 1 : 2-3

Grade 2 : 4-5

Grade 3 : 6-8

- **Proven to correlated well with survival**

- ***Mitotic Count.*** **In the most mitotically active area, ten successive high-power fields (at 400x magnification=0.1734 mm^2) using a 40x objective.**

1 **0-9 mitoses per 10 HPFs**

2 **10-19 mitoses per 10 HPFs**

3 **>20 mitoses per 10 HPFs**

- ***Tumor necrosis.*** **Evaluated on gross examination and validated with histological sections**

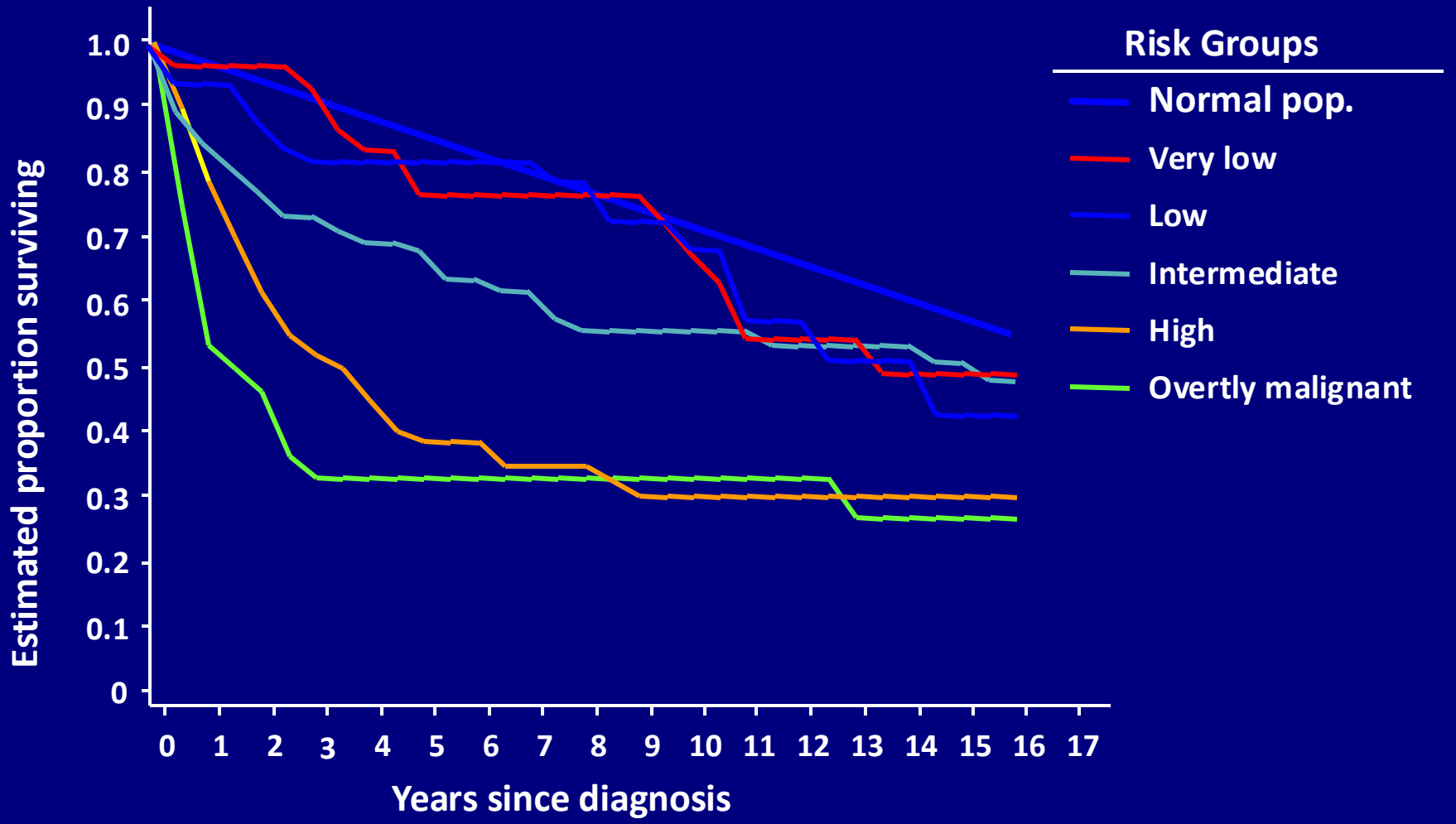
0 **No tumor necrosis**

1 **<50% tumor necrosis**

2 **>50% tumor necrosis**

- ***Degree of Differentiation.*** **1-3**

GIST - Overall Survival by Risk Group



Kindblom. at: http://www.asco.org

Prediction Tools

Gastrointestinal Stromal Tumor Prediction Tools

Share

Our gastrointestinal stromal tumor prediction tools are designed to help patients and their physicians calculate the likelihood of tumor recurrence following the complete resection (surgical removal of all cancerous tissue) of the gastrointestinal stromal tumor. They are designed for patients who have not received tyrosine kinase inhibitors before or after surgery.

Survival Without Recurrence Following Surgery

Our gastrointestinal stromal tumor nomogram is a tool designed to predict the likelihood of tumor recurrence two years and five years following the complete resection (surgical removal of all cancerous tissue) of the gastrointestinal stromal tumor. It is appropriate for patients who have not received tyrosine kinase inhibitors before or after surgery.

Artificial Intelligence Calculator for Recurrence Following Surgery

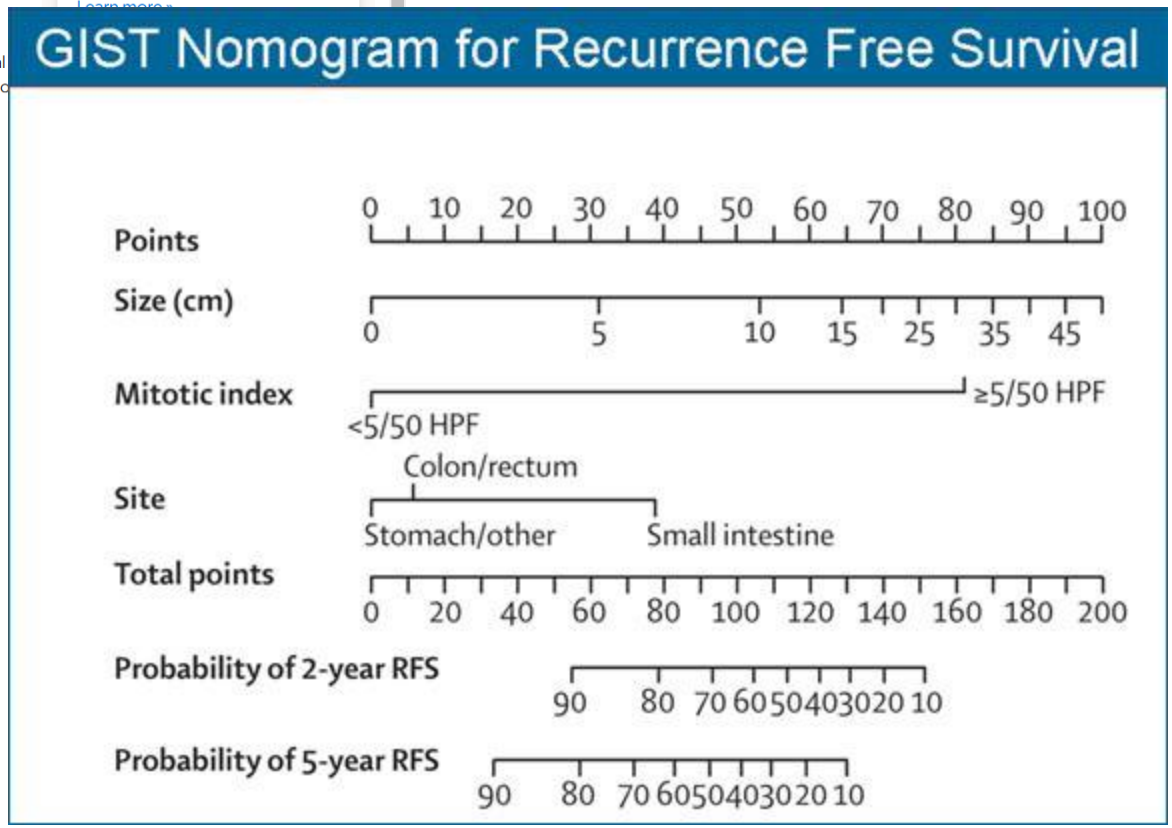
Using new machine-learning classifiers called optimal classification trees, our artificial intelligence (AI)-based calculator is designed to predict the probability of gastrointestinal stromal tumor recurrence five years following the complete resection (surgical removal of all cancerous tissue) of the gastrointestinal stromal tumor. It is designed for patients who have not received tyrosine kinase inhibitors before or after surgery.

Change Prediction Tool

Stomach (Gastric) Cancer Information

The most common type of stomach cancer (gastric cancer) is called adenocarcinoma. Learn more about the different types and how Memorial Sloan Kettering gastric cancer experts can help.

Learn more »

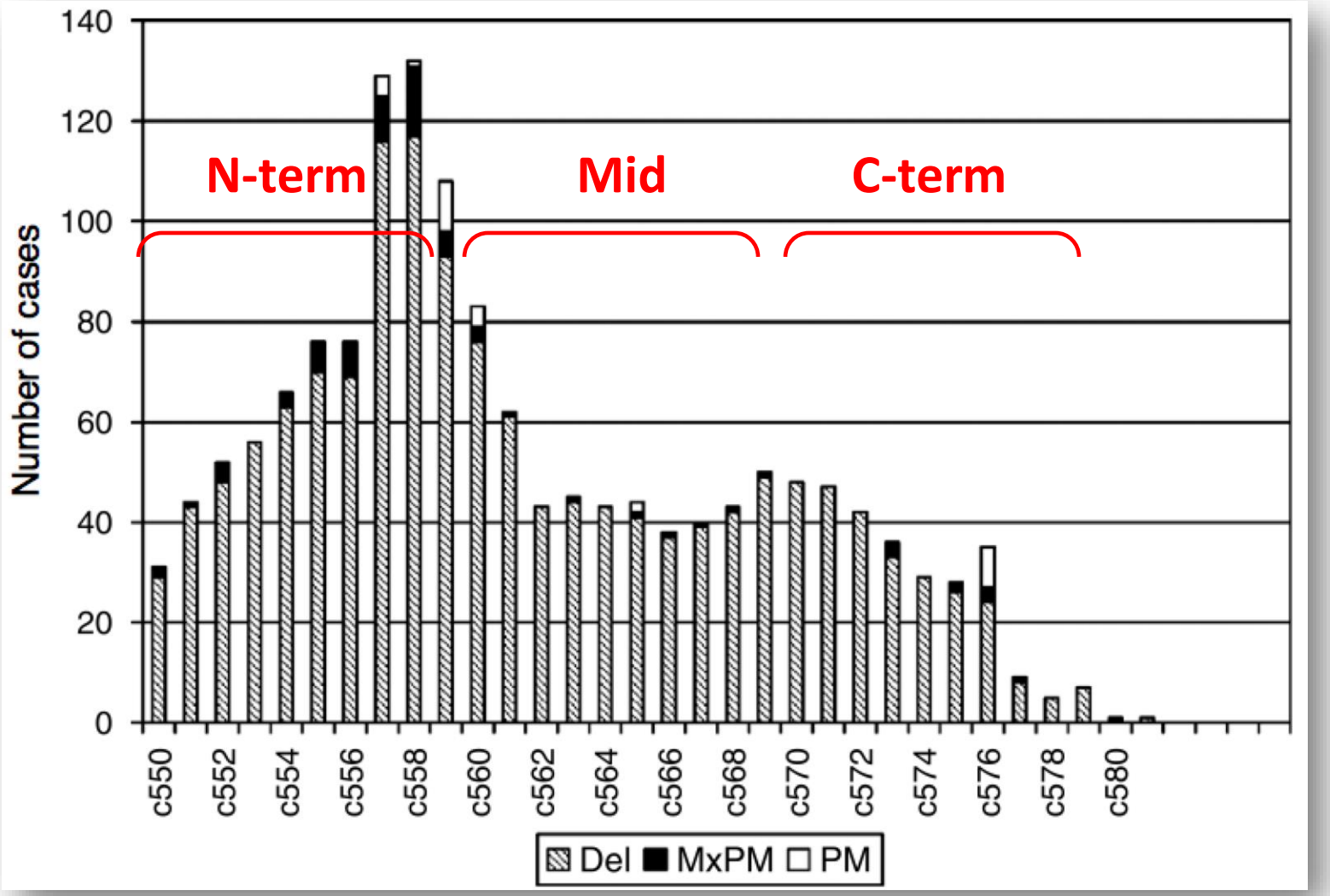


Genomic complexity and prognosis
Possible approaches

- **(Histological grading)**
- **Risk assessment +:**
  - **Array-CGH**
  - **Carter signature**
  - **Next generation Sequencing**

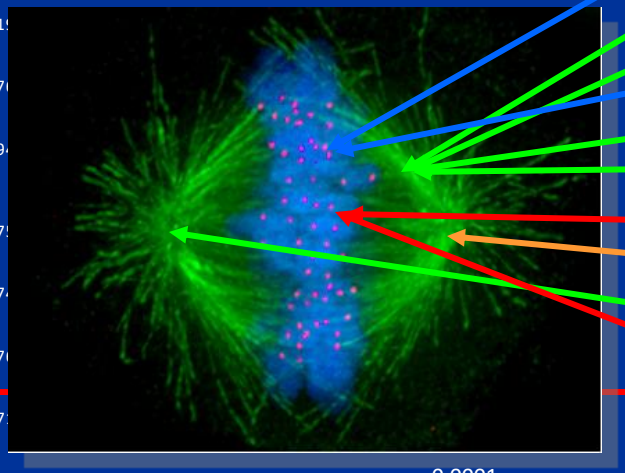
Courtesy of J-M Coindre & F Chibon, Bordeaux, France (Fresch Sarcoma Group)

Spectrum of KIT Exon 11 Mutations



Debiec-Rychter et al., J Pathol, 2004.

CINSARC : GO analysis of the 67 significant genes



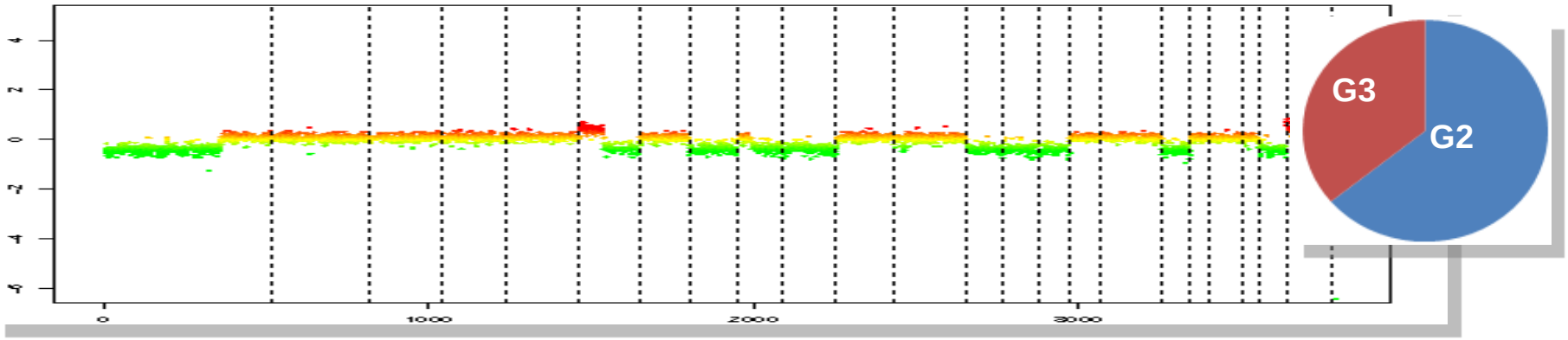
GO.ID	selection	array	pValue	Z-Score	GO.Term
GO:0000775	10	37	1,06E-14	23,58	chromosome, pericentric region
GO:0005819				21,03	spindle
GO:0005876				25,62	spindle microtubule
GO:0005694				12,73	chromosome
GO:0005875				11,42	microtubule associated complex
GO:0005874				7,88	microtubule
GO:0000776				12,42	kinetochore
GO:0005871				10,67	kinesin complex
GO:0005813	4	48	0,0001	7,96	centrosome
GO:0000940					some
GO:0030496					
GO:0005657					
GO:0005814	2	9	0,0012	9,52	centriole
GO:0015630	2	13	0,0022	7,84	microtubule cytoskeleton
GO:0000922	2	16	0,0032	7,02	spindle pole
GO:0000785	3	75	0,0059	4,47	chromatin
GO:0000786	2	32	0,0111	4,77	nucleosome
GO:0001939	1	3	0,0187	8,30	female pronucleus
GO:0005816	1	3	0,0187	8,30	spindle pole body

CINSARC is a signature related to chromosome management and mitosis control associated with genome complexity

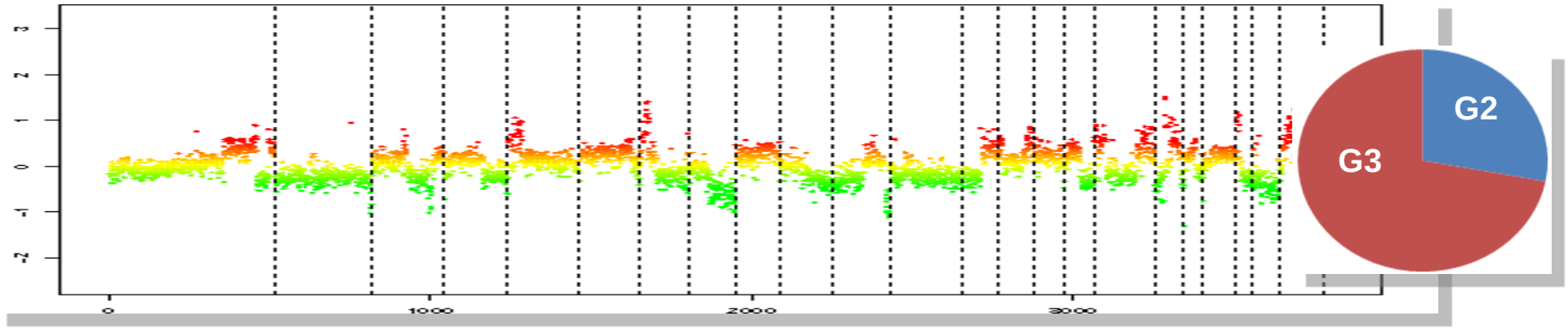
Courtesy of J-M Coindre & F Chibon, Bordeaux, France (Fresch Sarcoma Group)

CINSARC : arrayCGH analysis and correlation with FNCLCC grading

« Arm » Profile



« Rearranged » Profile

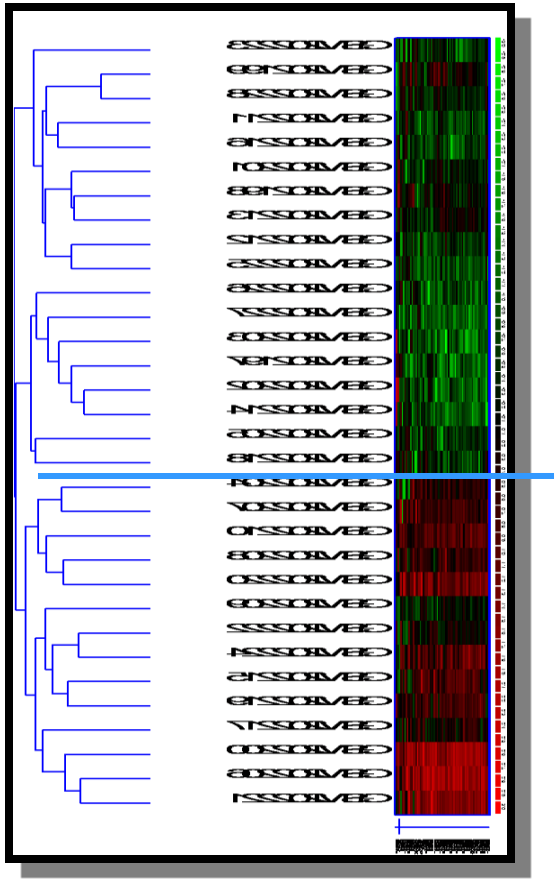


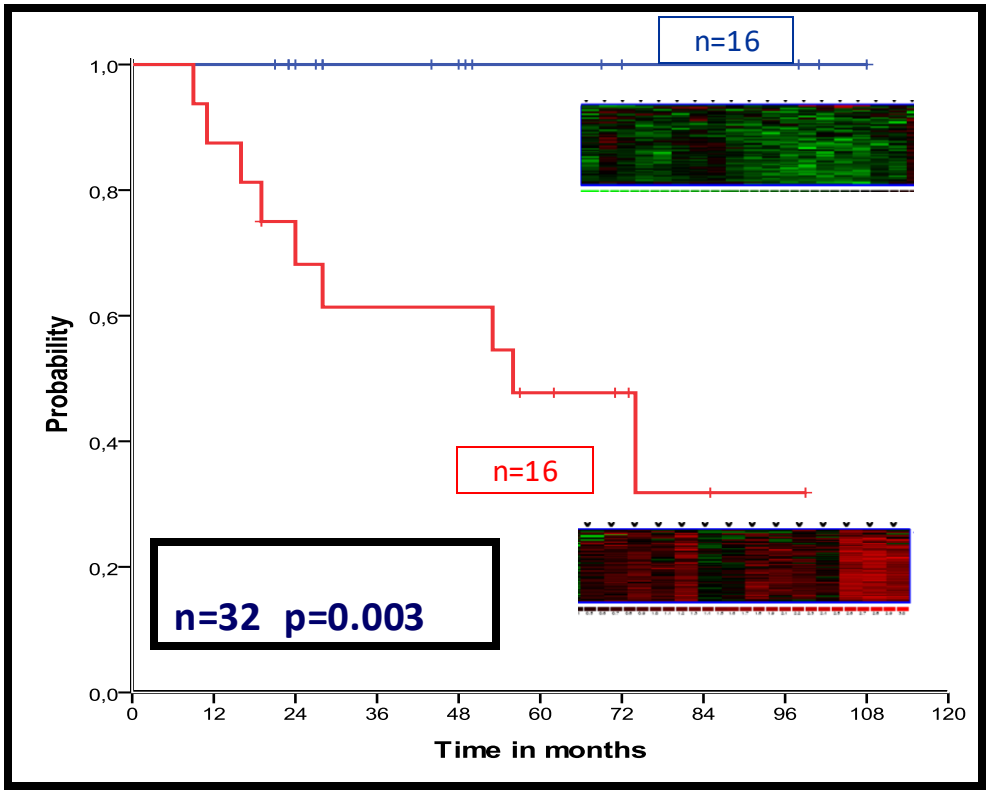
Courtesy of J-M Coindre & F Chibon, Bordeaux, France (Fresch Sarcoma Group)

CINSARC and GIST

In-silico study of 32 GISTs

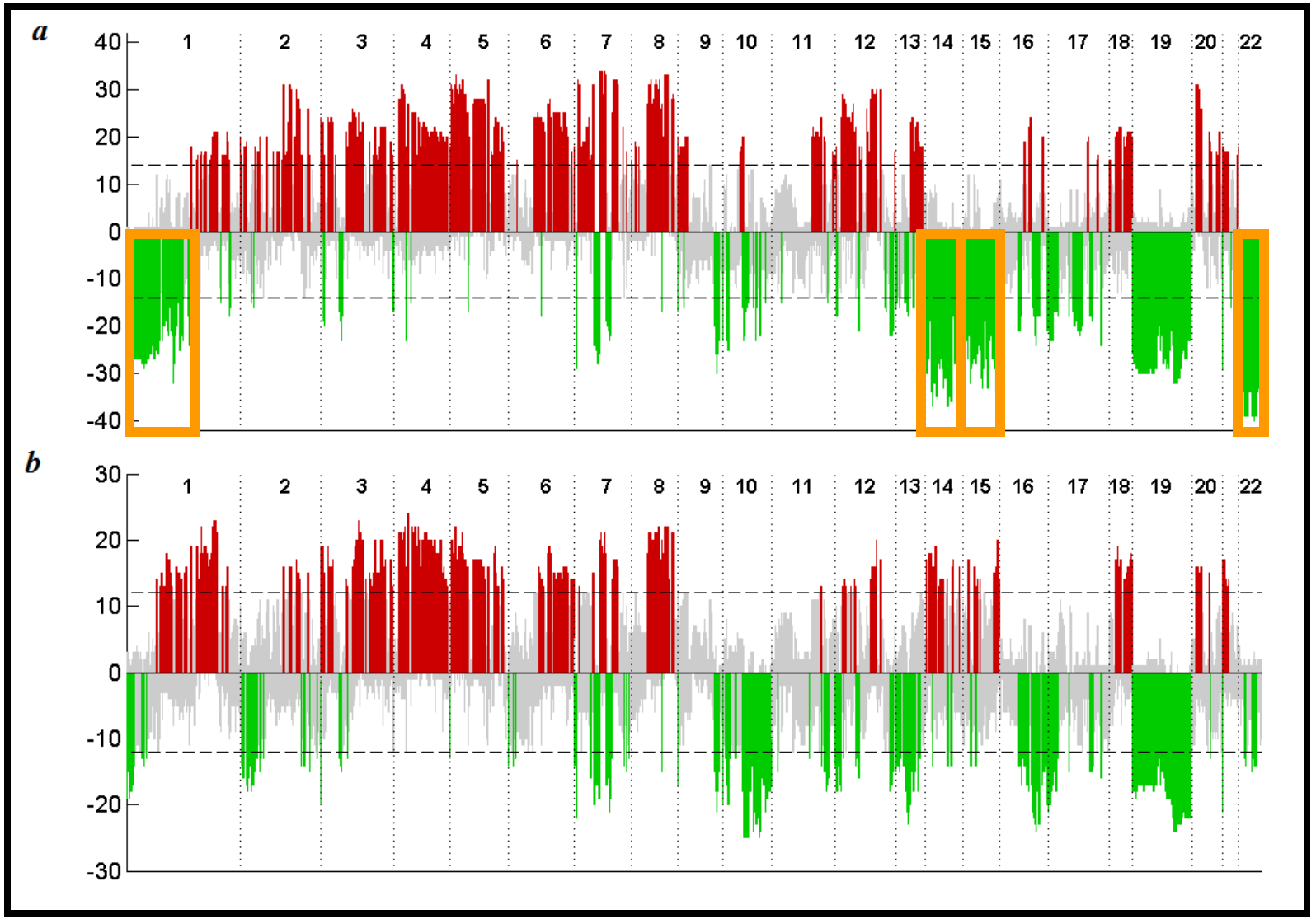
(Yamaguchi *et al* 2008)





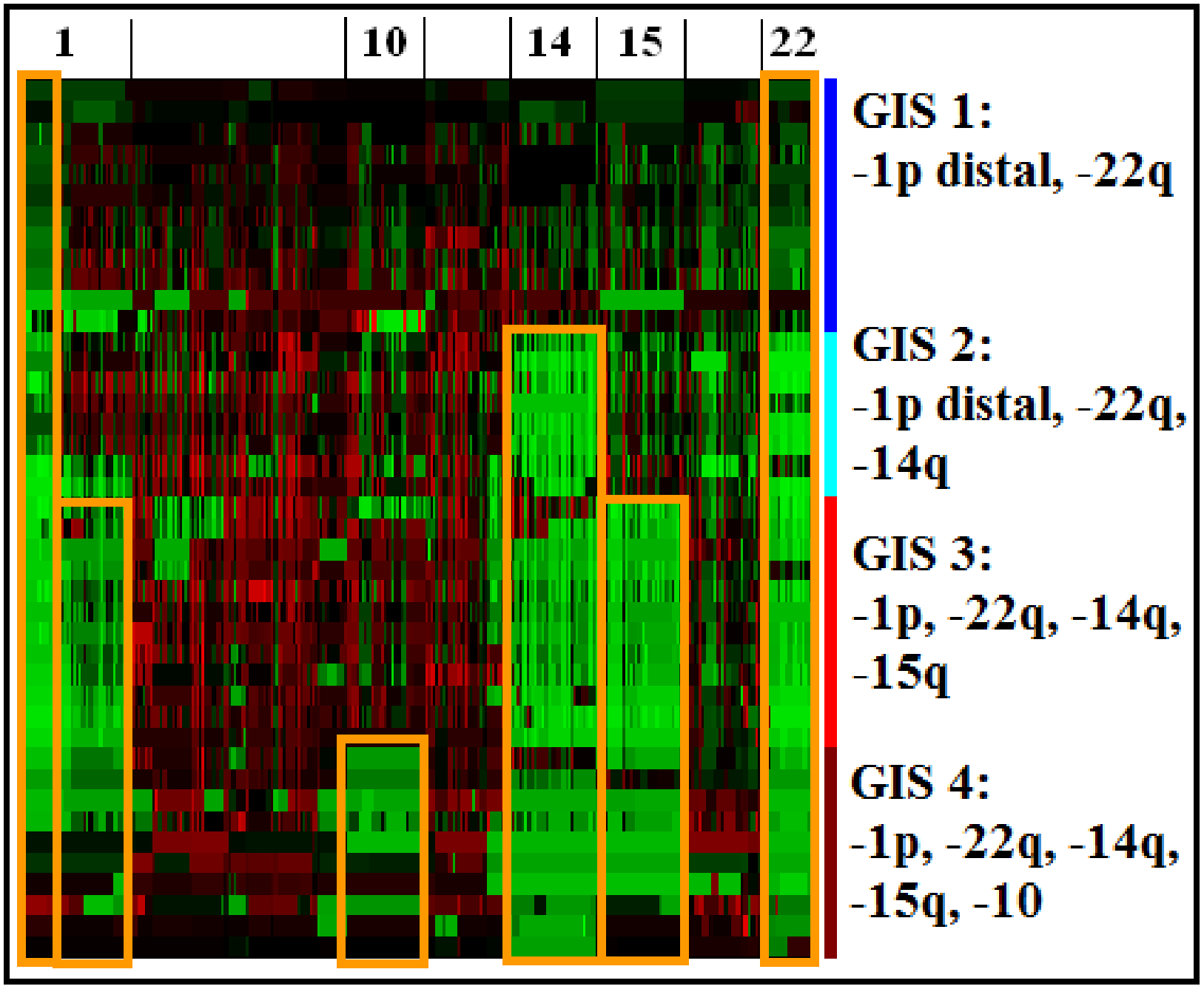
Courtesy of J-M Coindre & F Chibon, Bordeaux, France (Fresch Sarcoma Group)

GIST (n=42)

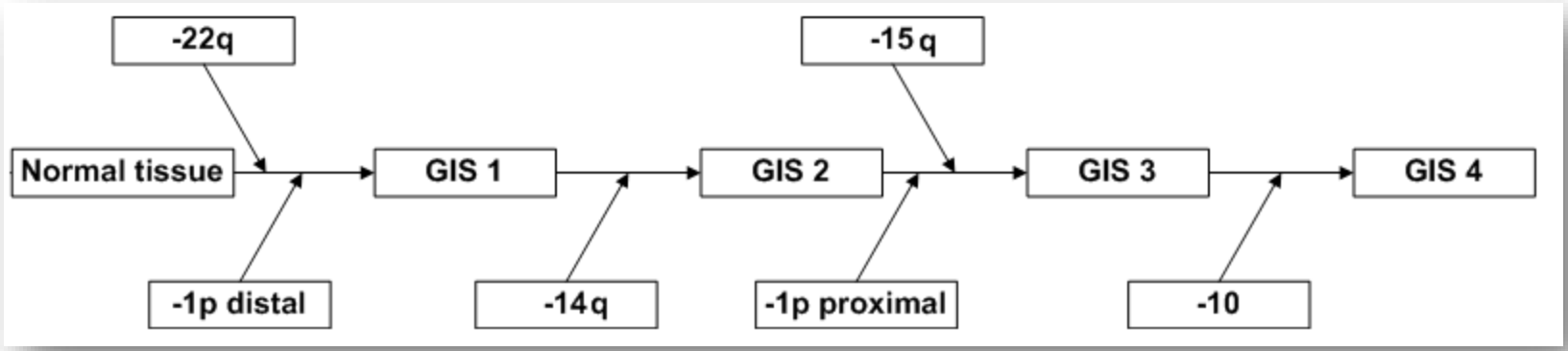


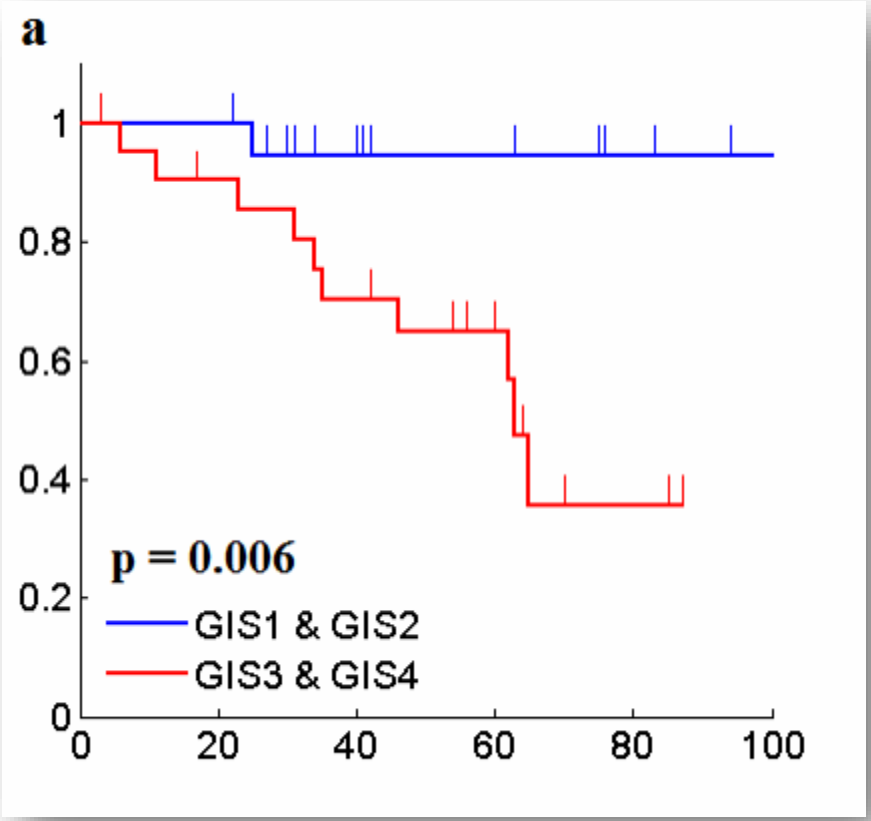
LMS (n=30)

Ylipää A, et al. Cancer 2011 117(2)380-9, 2011



Ylipää A, et al. Cancer 2011 117(2)380-9, 2011

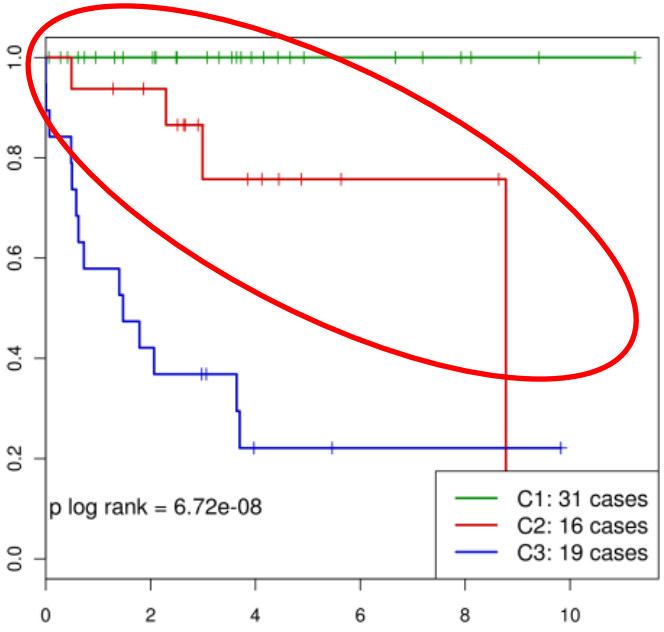


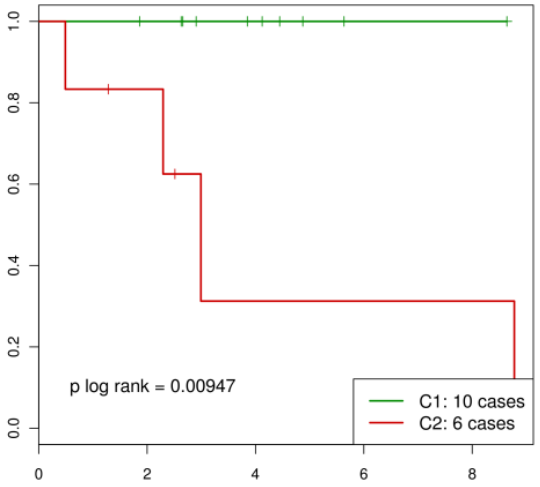


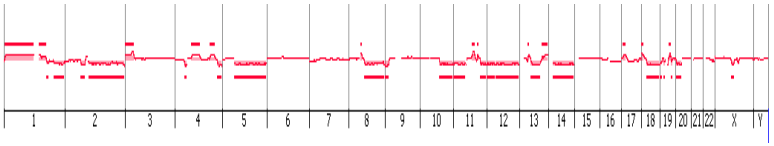
Ylipää A, et al. Cancer 2011 117(2)380-9, 2011

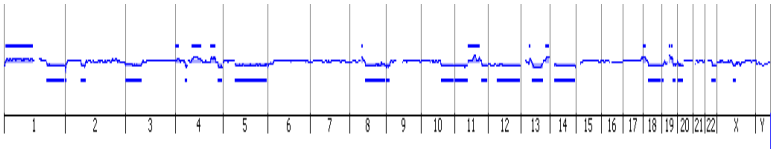
GIST and molecular signature

(Lagarde et al. Clin Cancer Res 2012;18: 826-838)





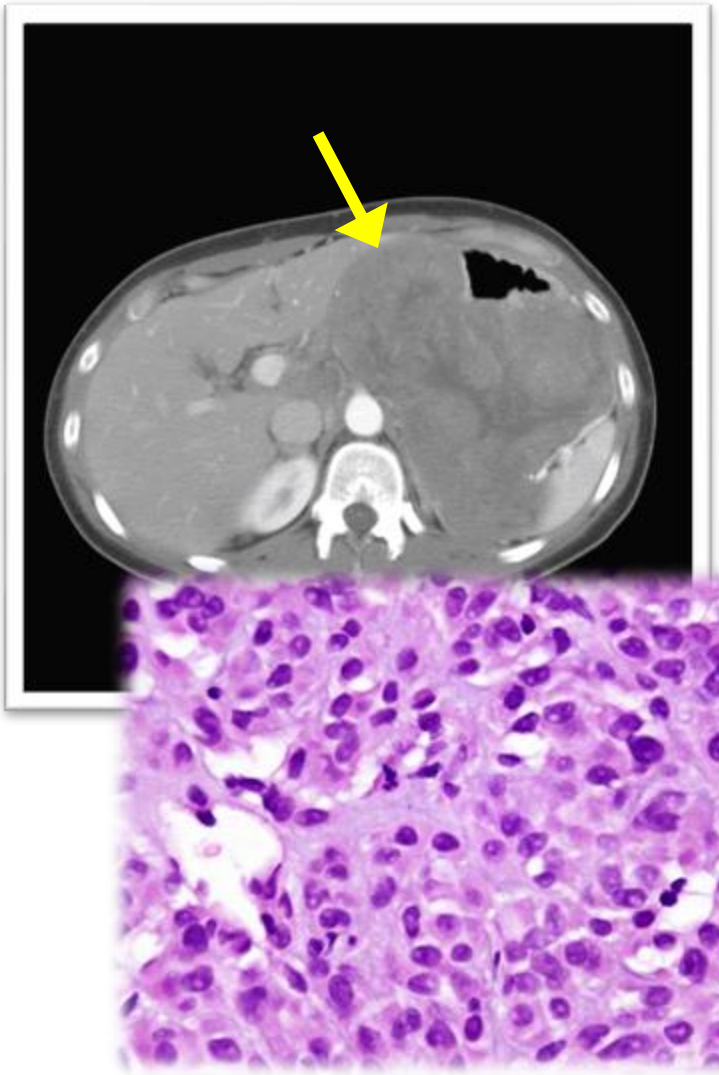


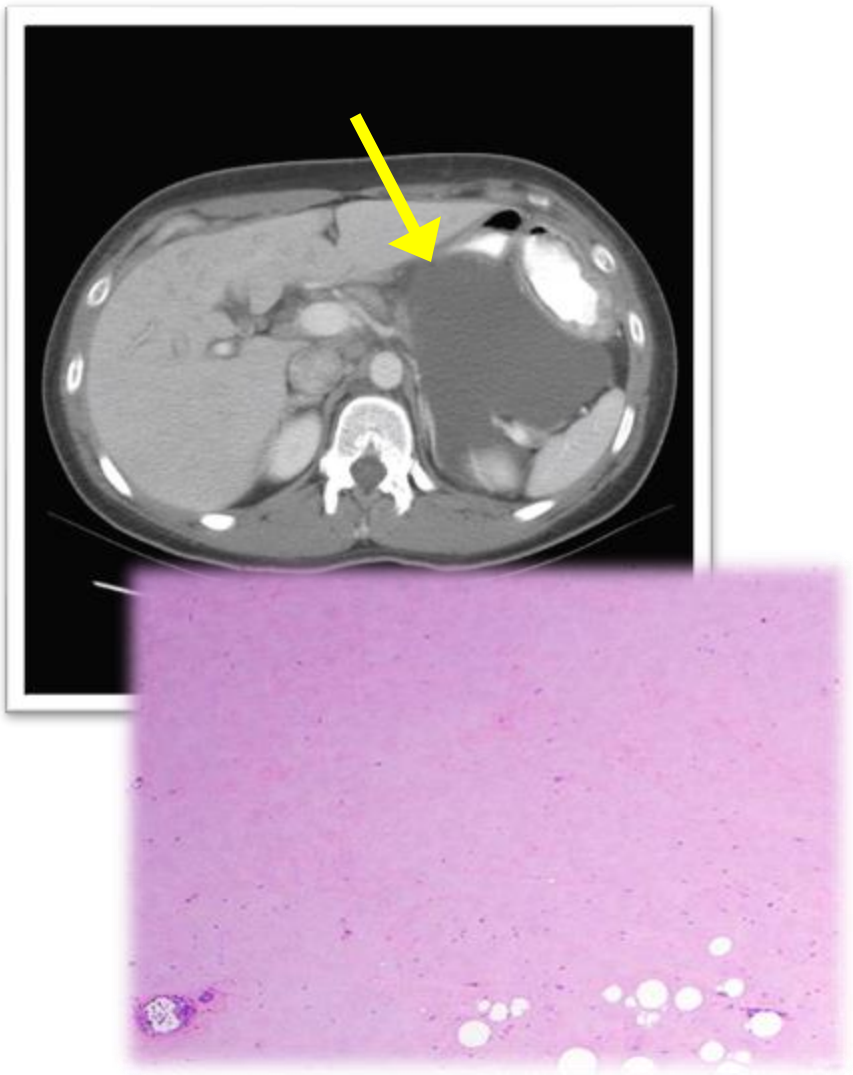


Courtesy of J-M Coindre & F Chibon, Bordeaux, France (Fresch Sarcoma Group)

Treatment can cause big changes.

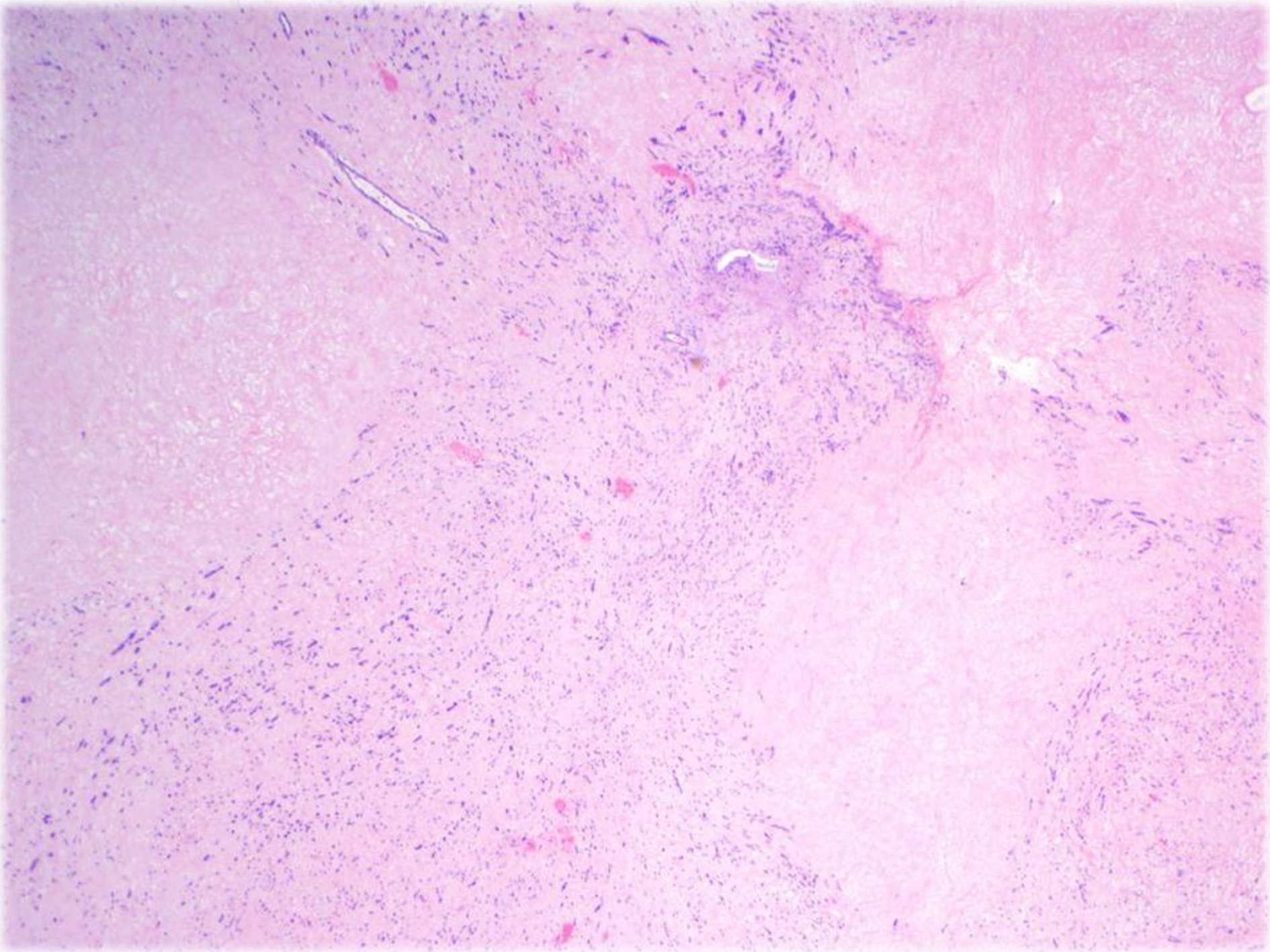
Treatment effect

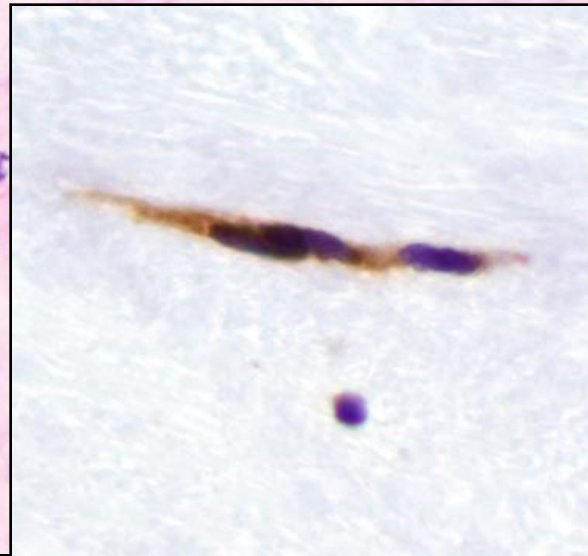




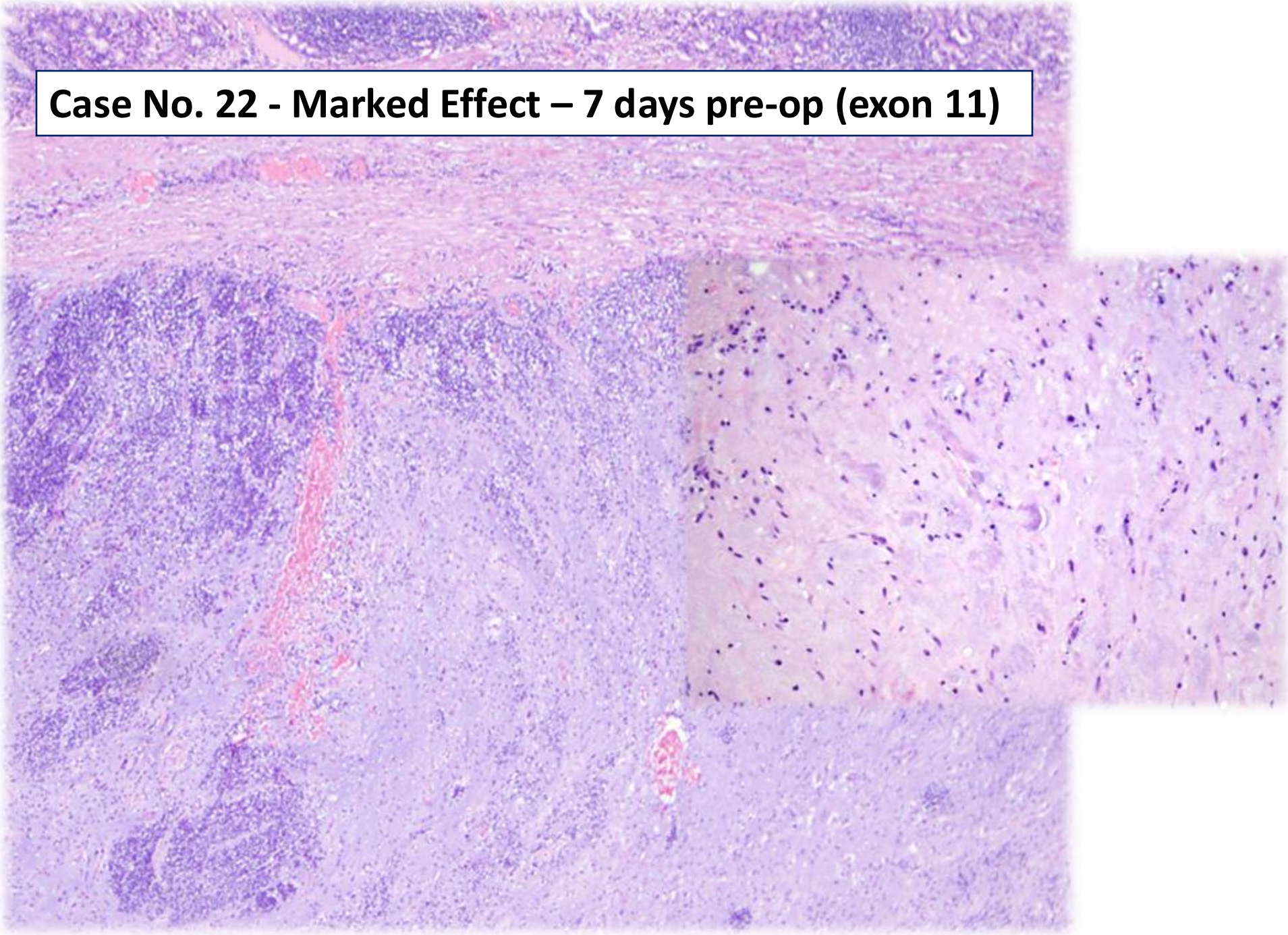
Pre-Imatinib

Post-Imatinib (8 weeks therapy)

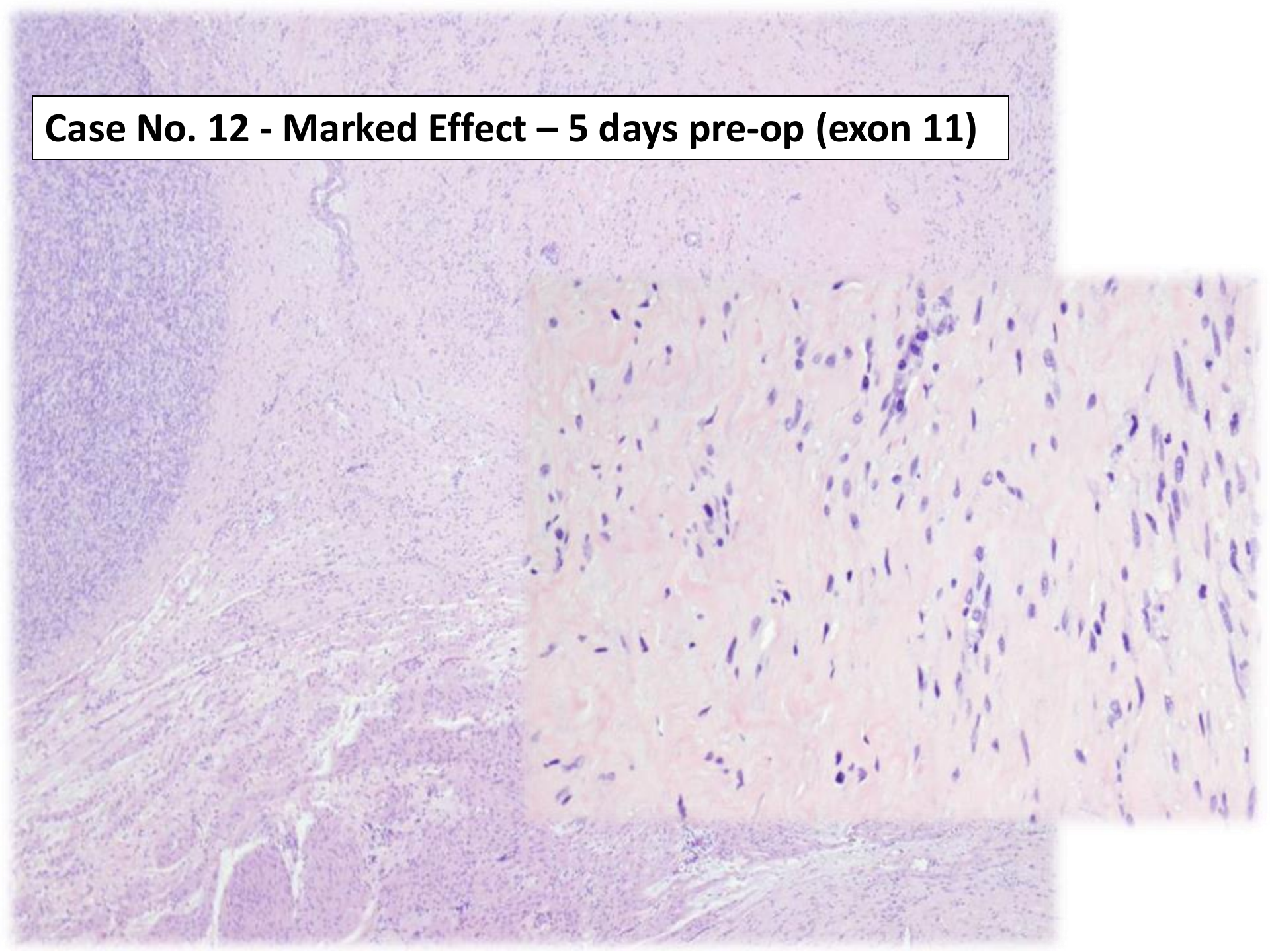




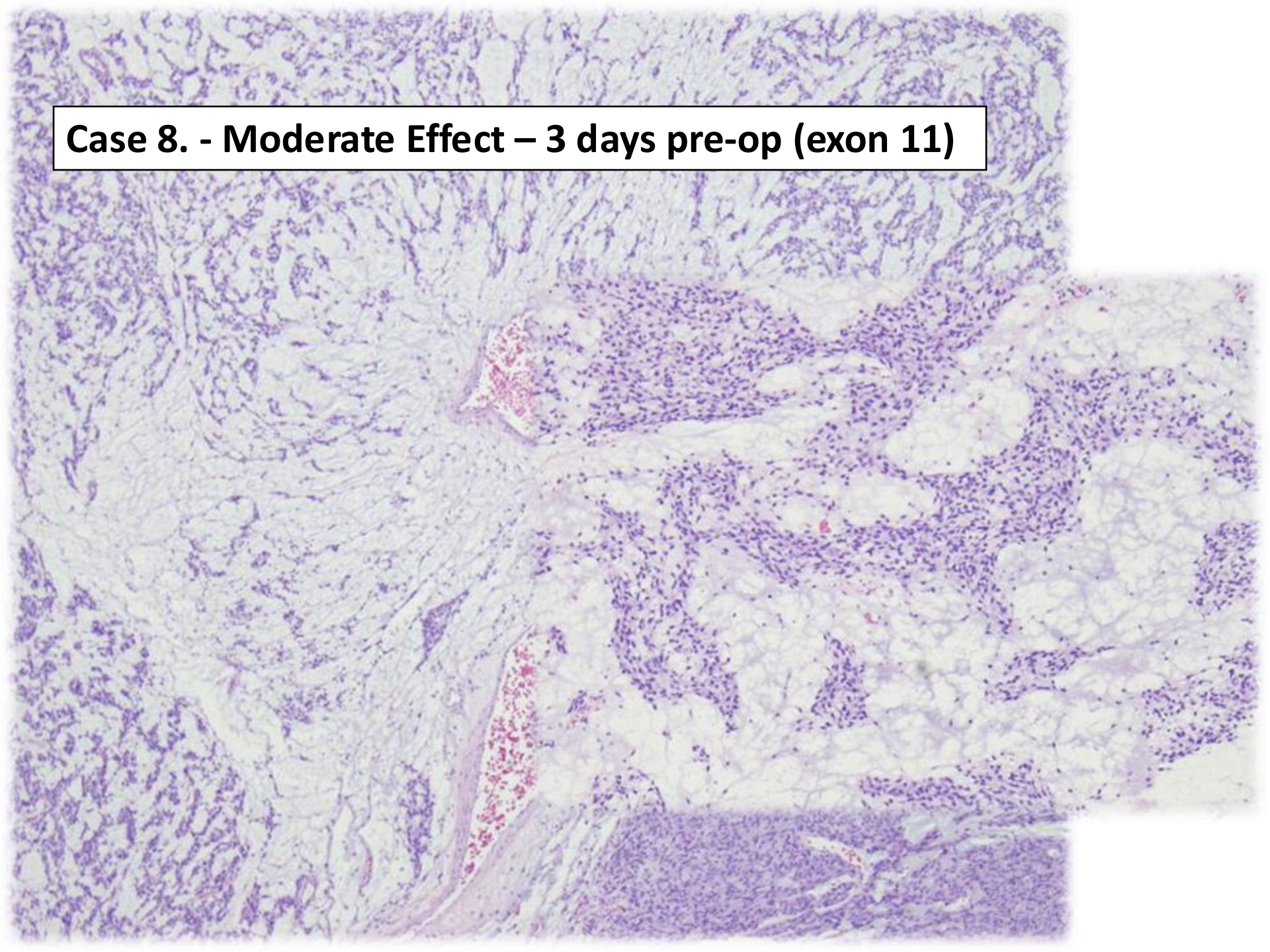
Case No. 22 - Marked Effect – 7 days pre-op (exon 11)

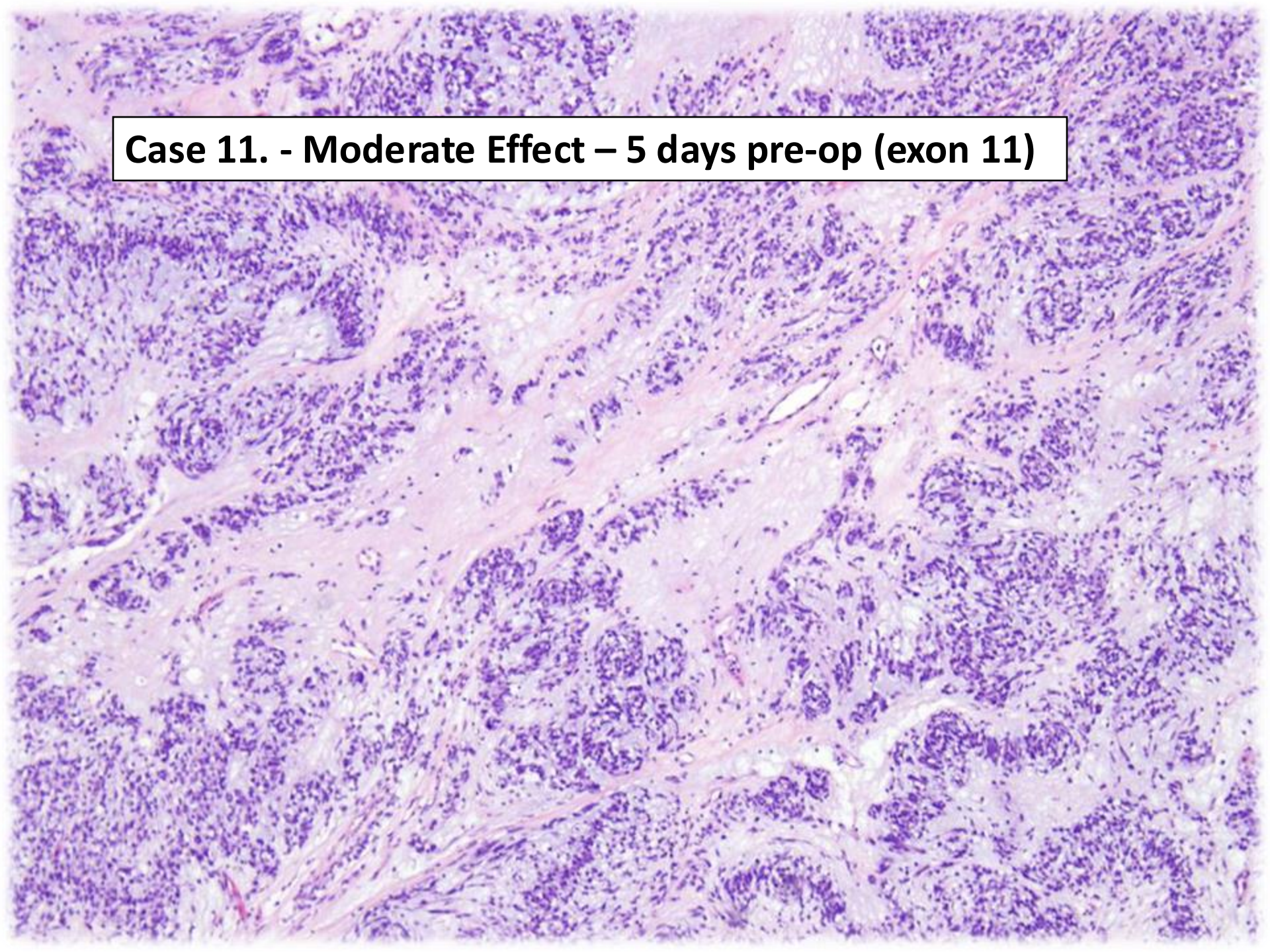


Case No. 12 - Marked Effect – 5 days pre-op (exon 11)

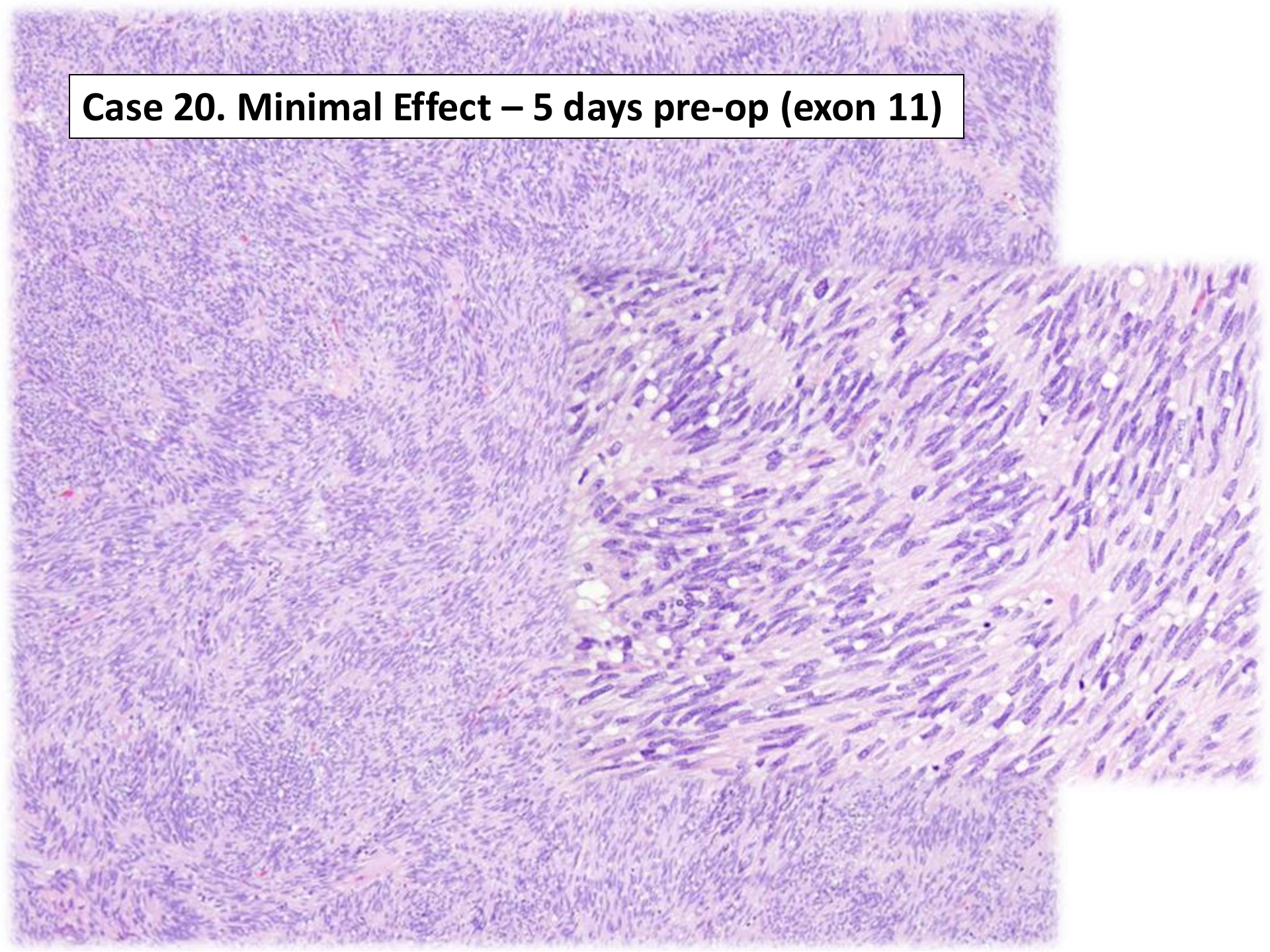


Case 8. - Moderate Effect – 3 days pre-op (exon 11)

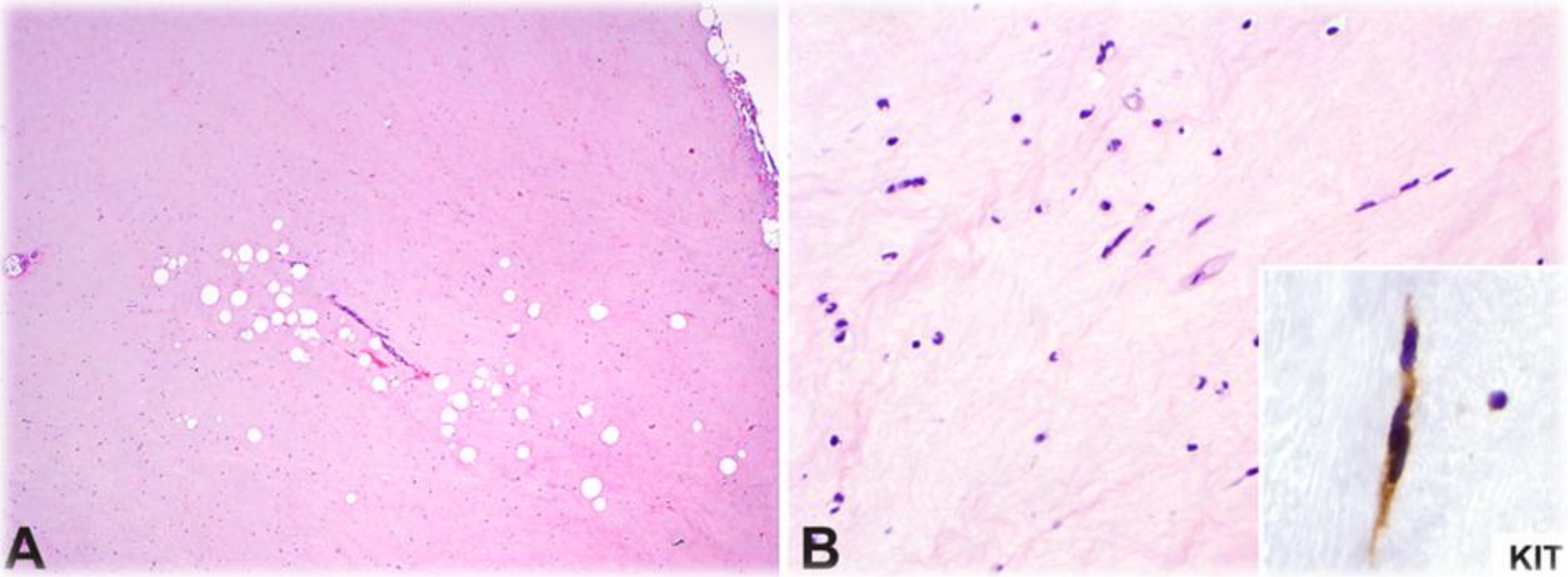



Case 11. - Moderate Effect – 5 days pre-op (exon 11)

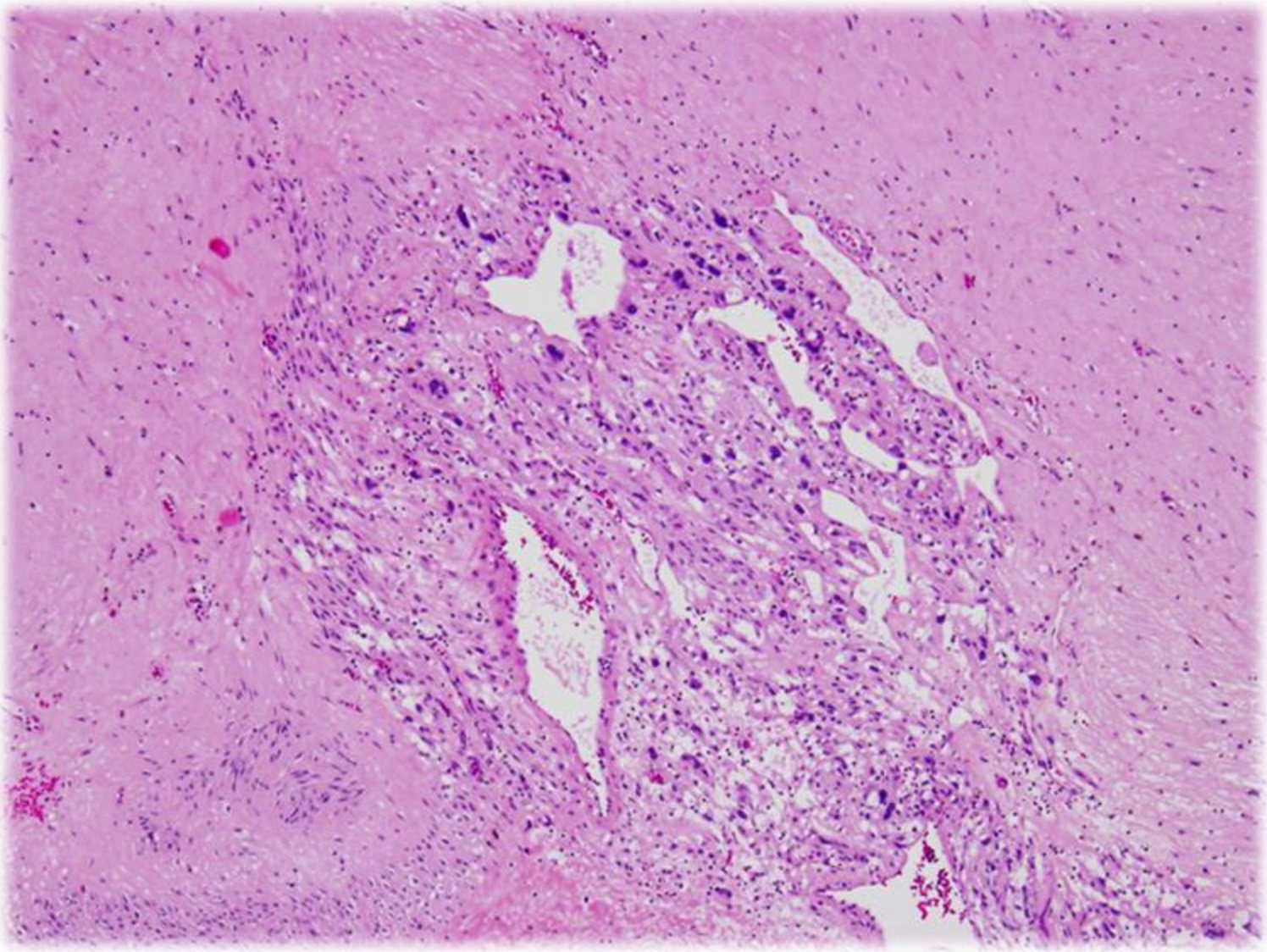
Case 20. Minimal Effect – 5 days pre-op (exon 11)

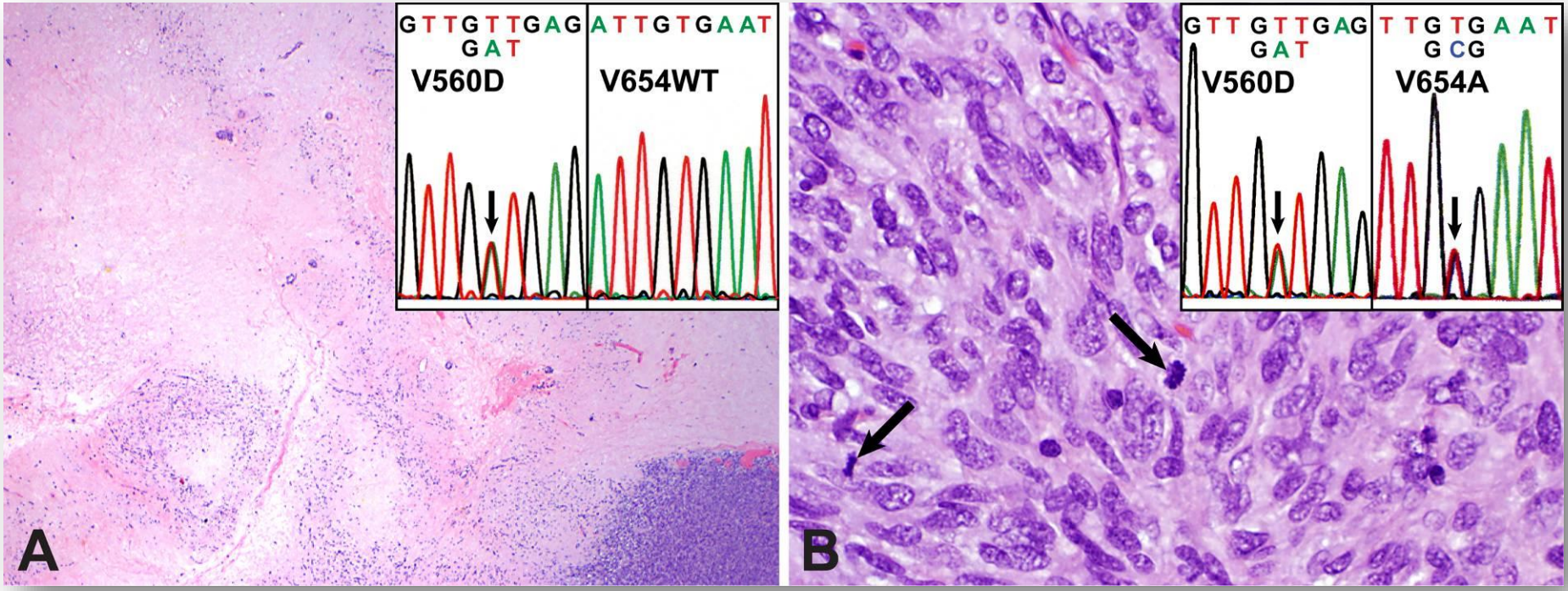


Long term Imatinib Tx



Long term Imatinib Tx

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V560D
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V654A
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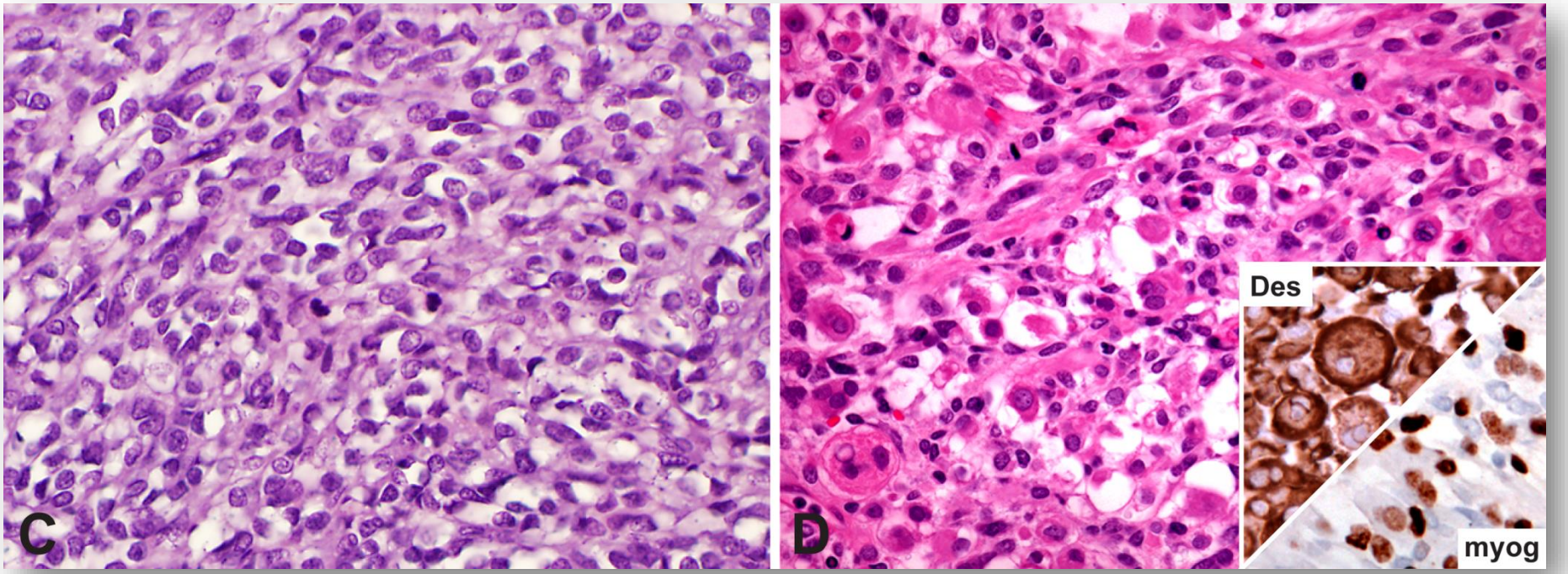
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Thanks!

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- **Jon Trent, University of Miami.**
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