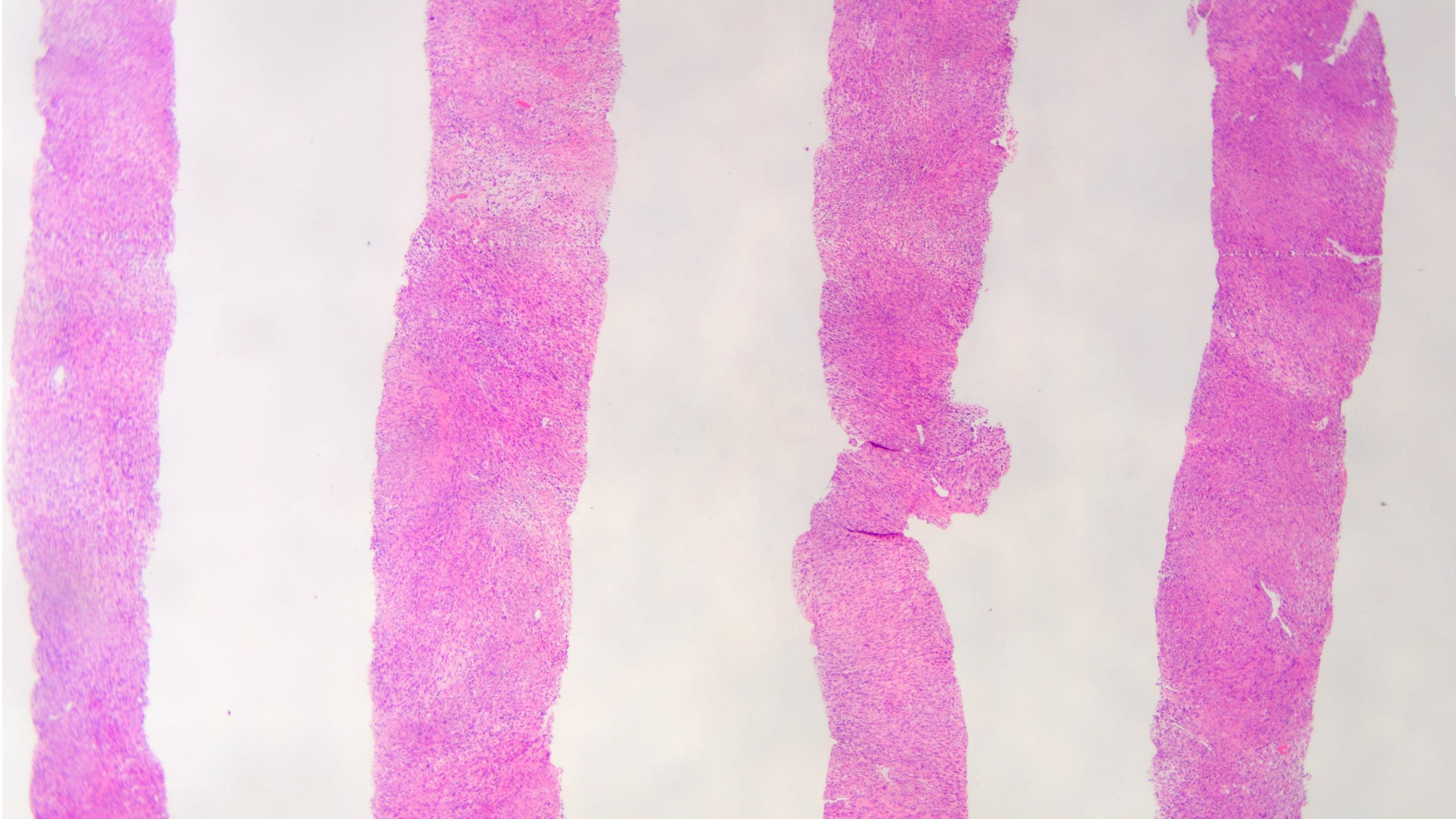
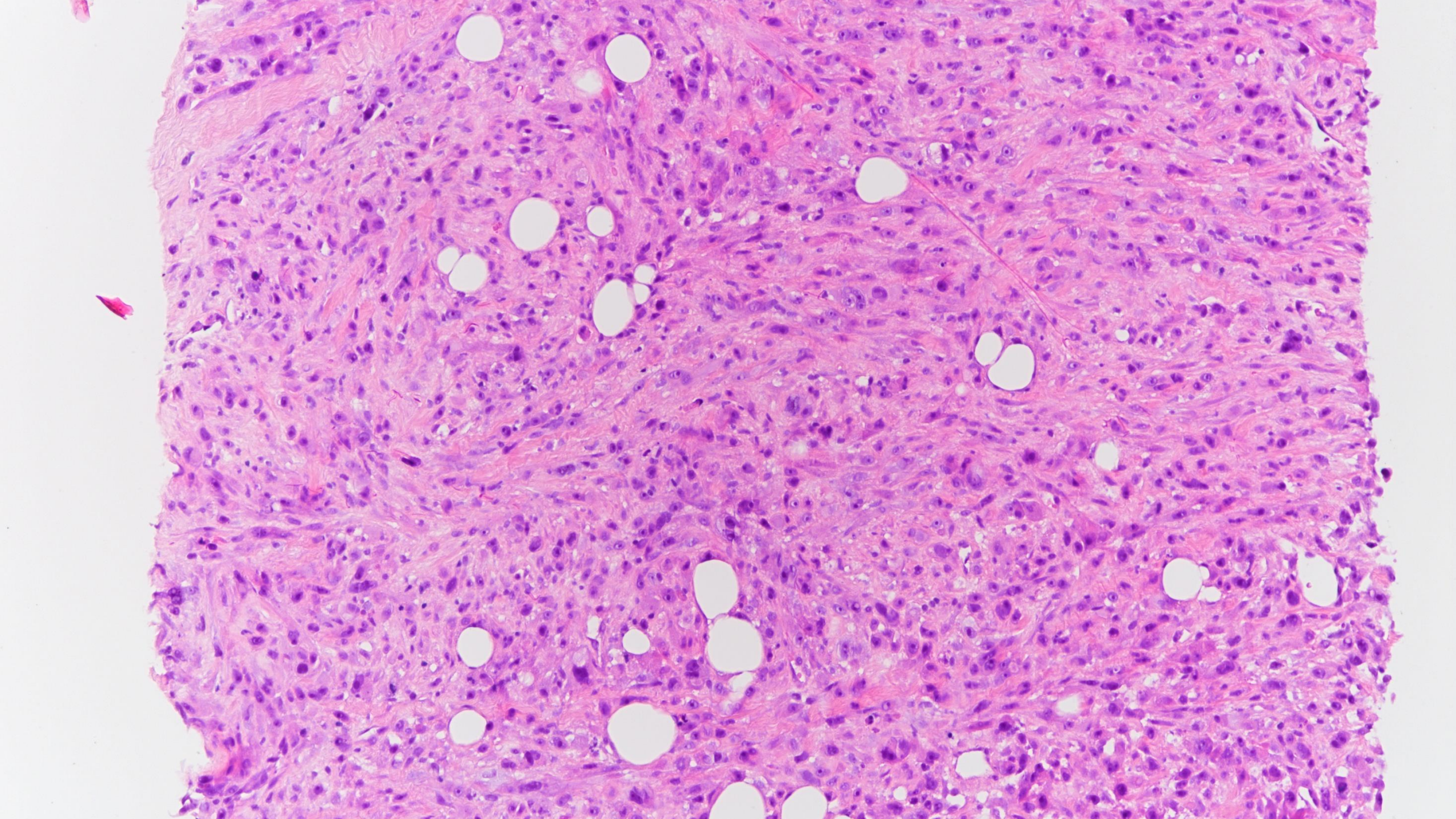
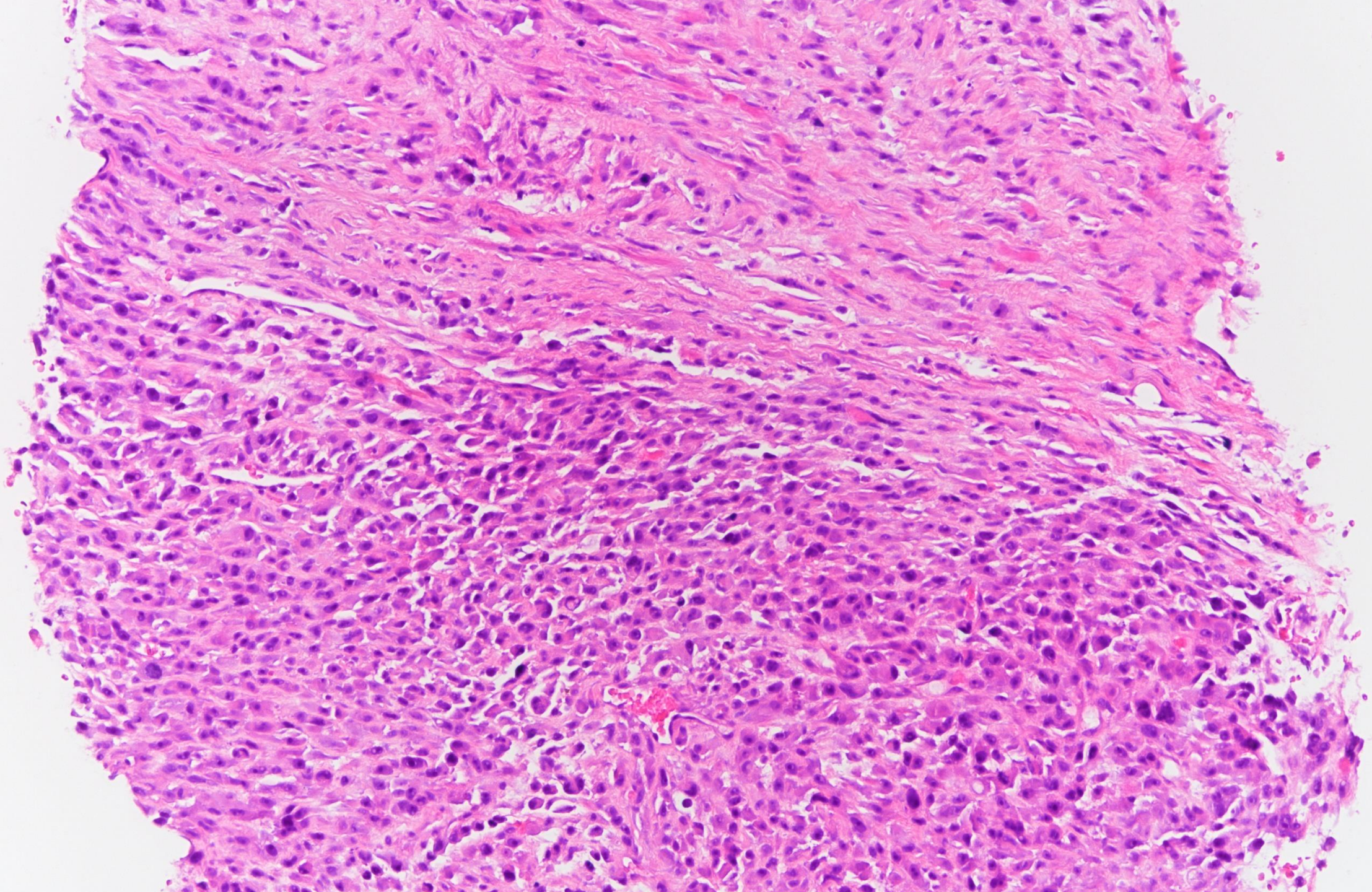
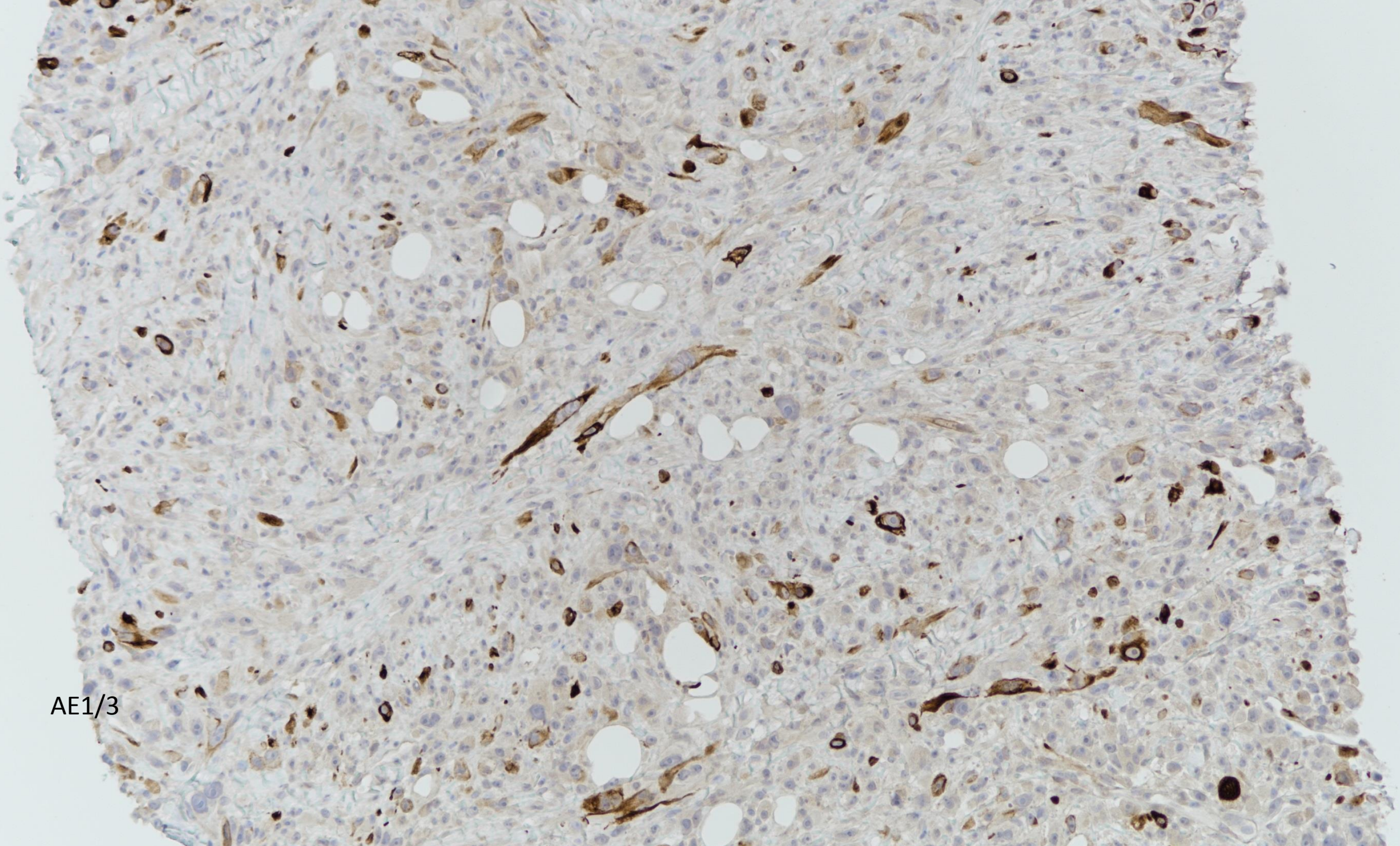
Brief clinical history case 1

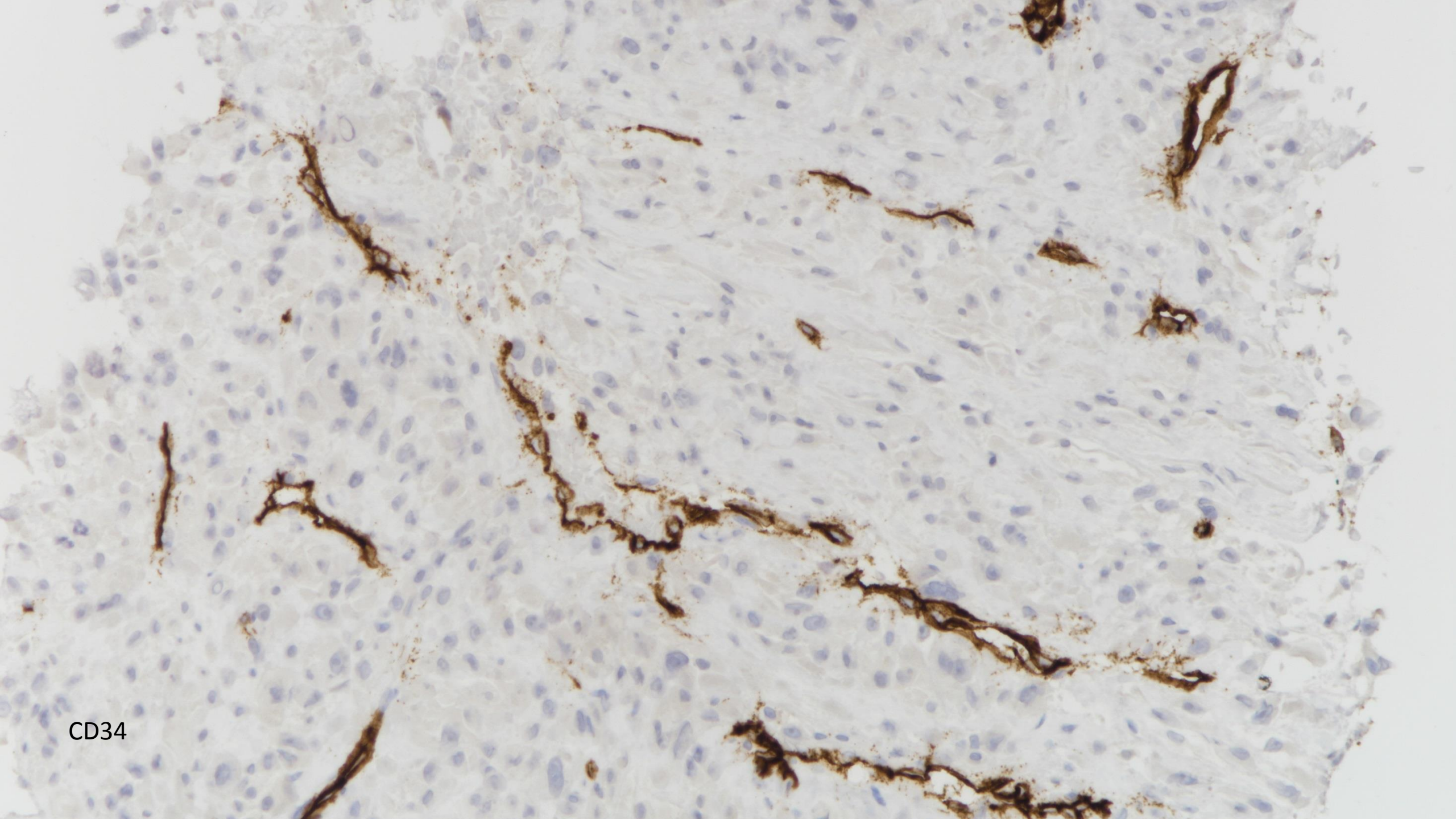
- A 54 years old female with a history of mastectomy for phyllodes tumor 3 years ago and had radiotherapy afterwards
- She presented with a mass at the site of the TRAM flap
- Biopsy was done








AE1/3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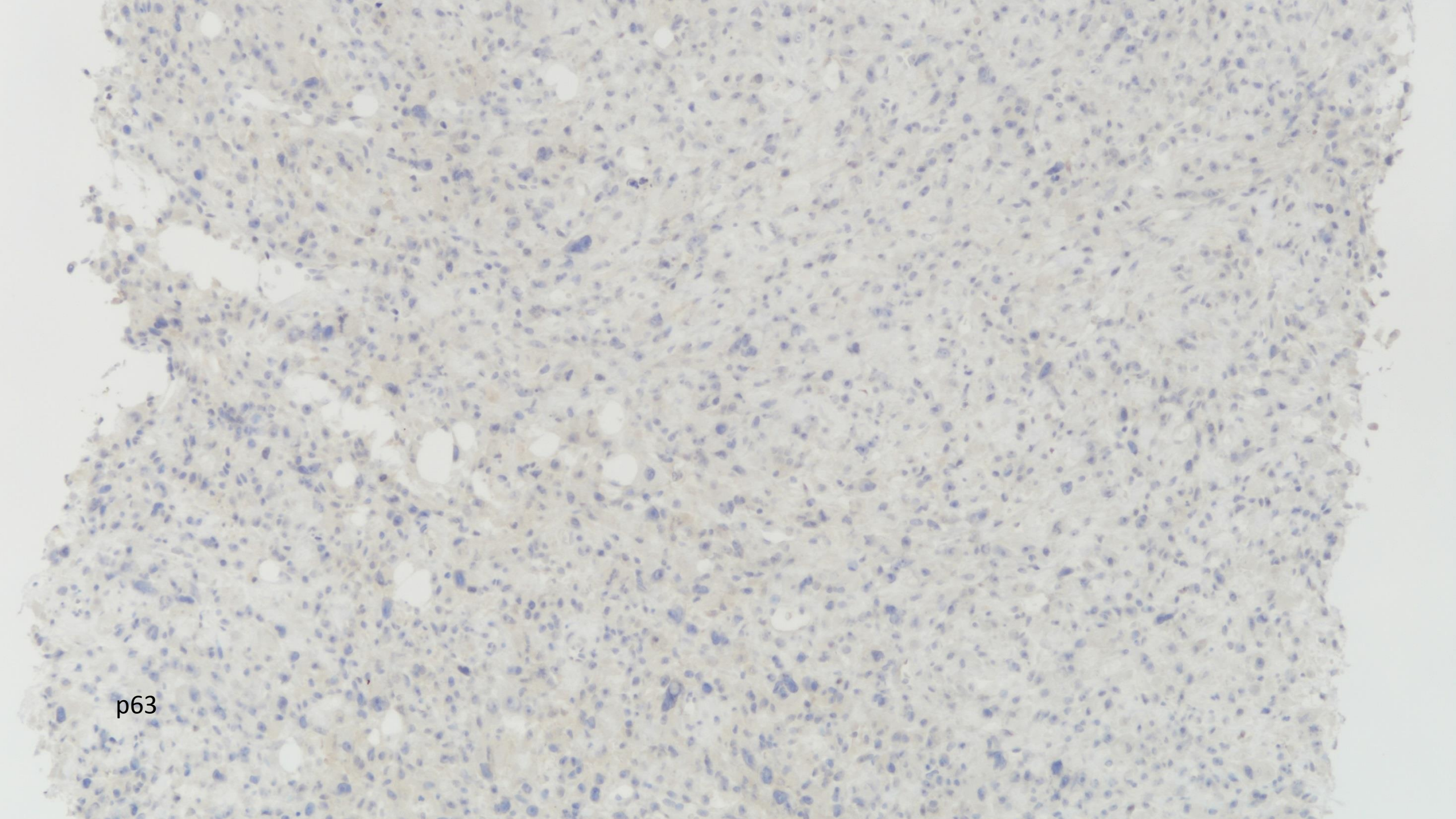
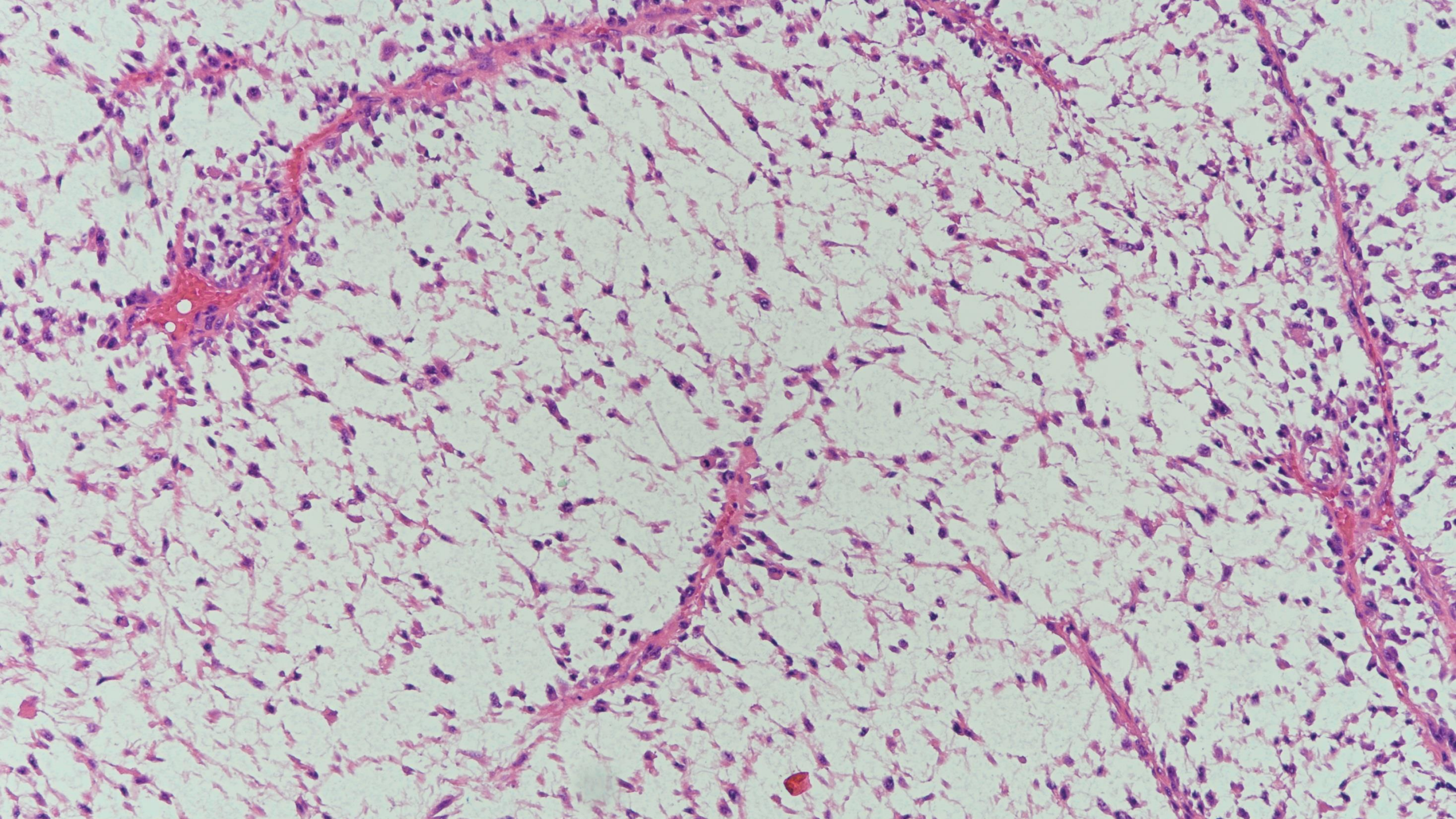
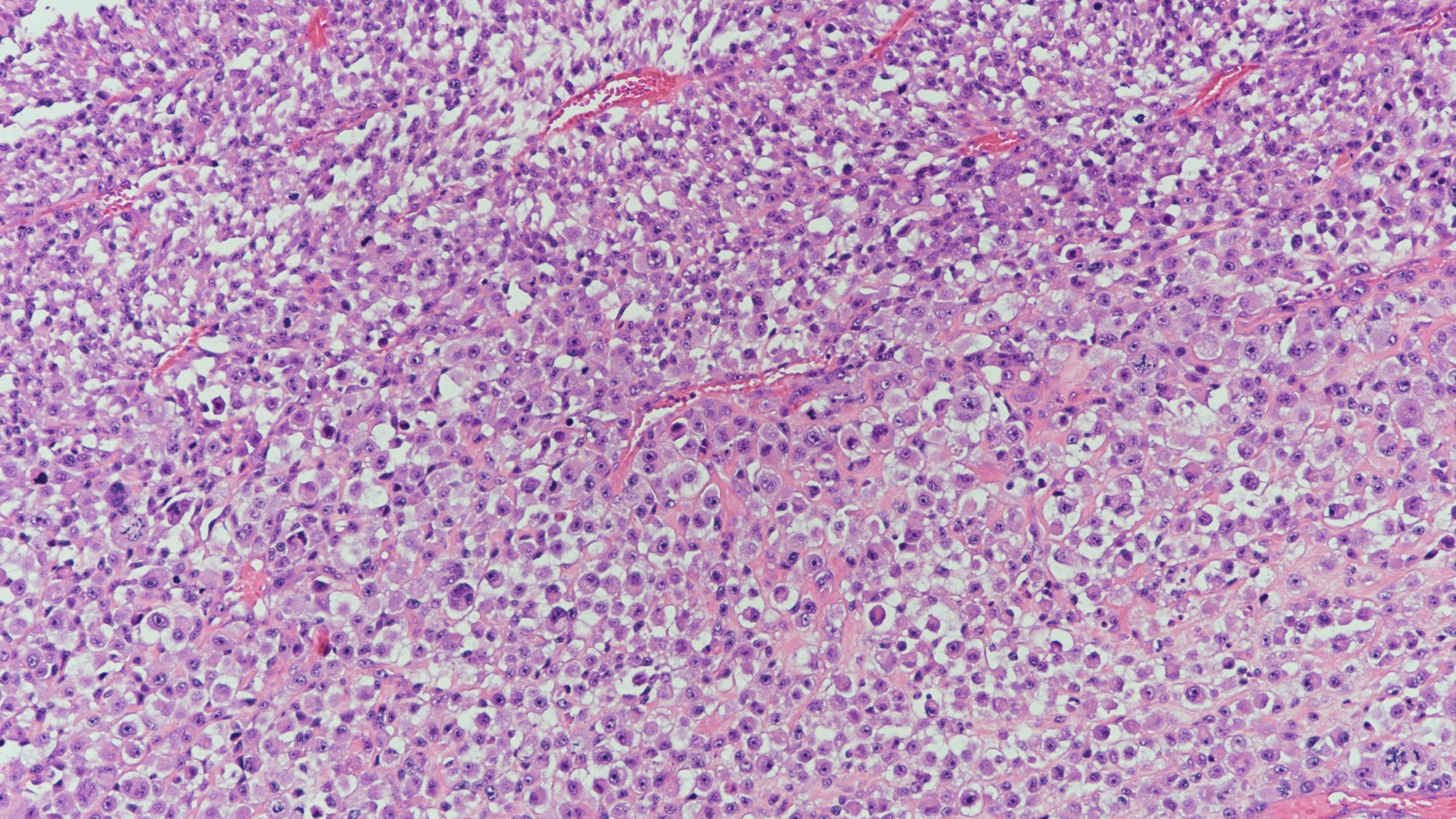
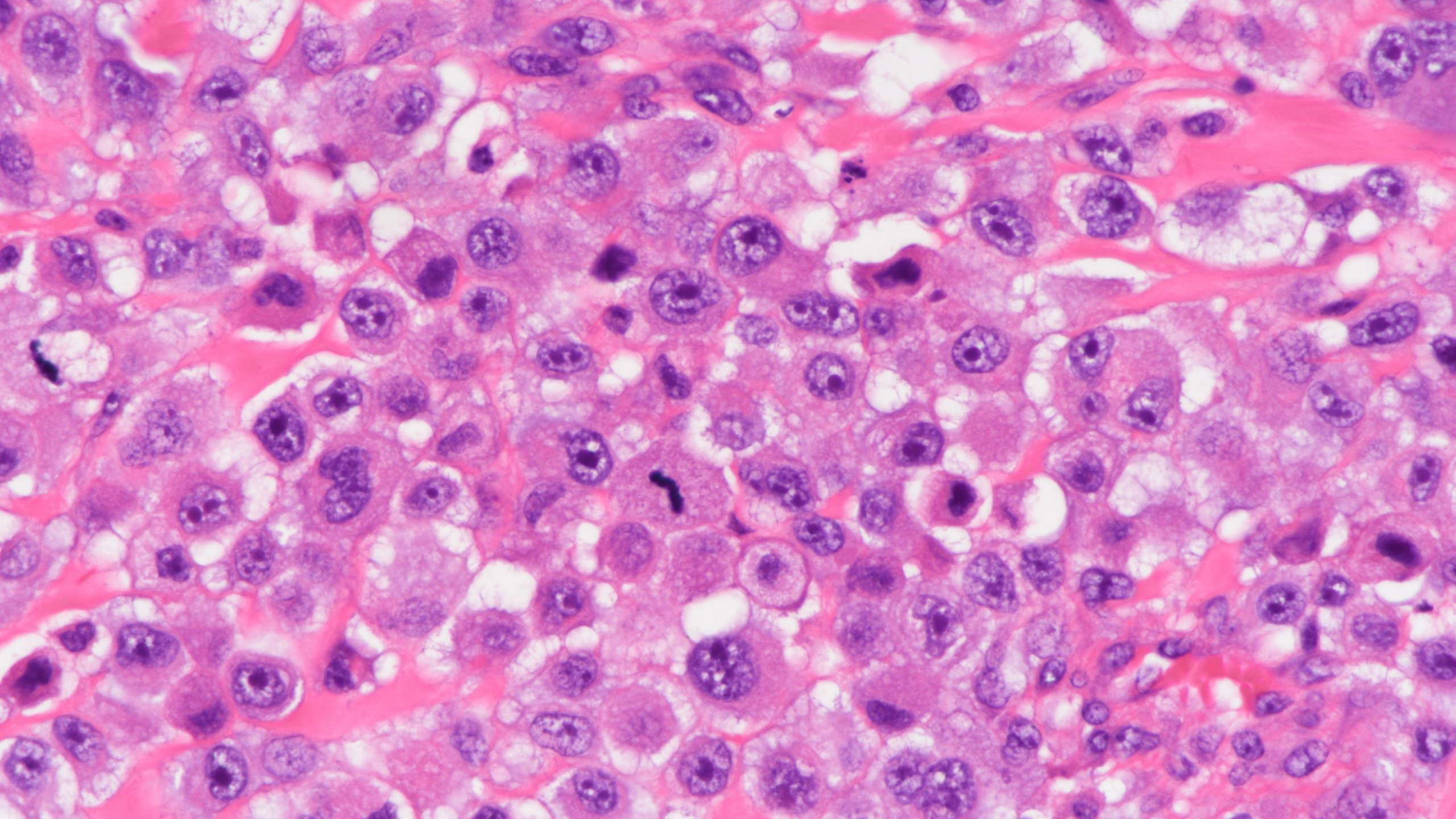
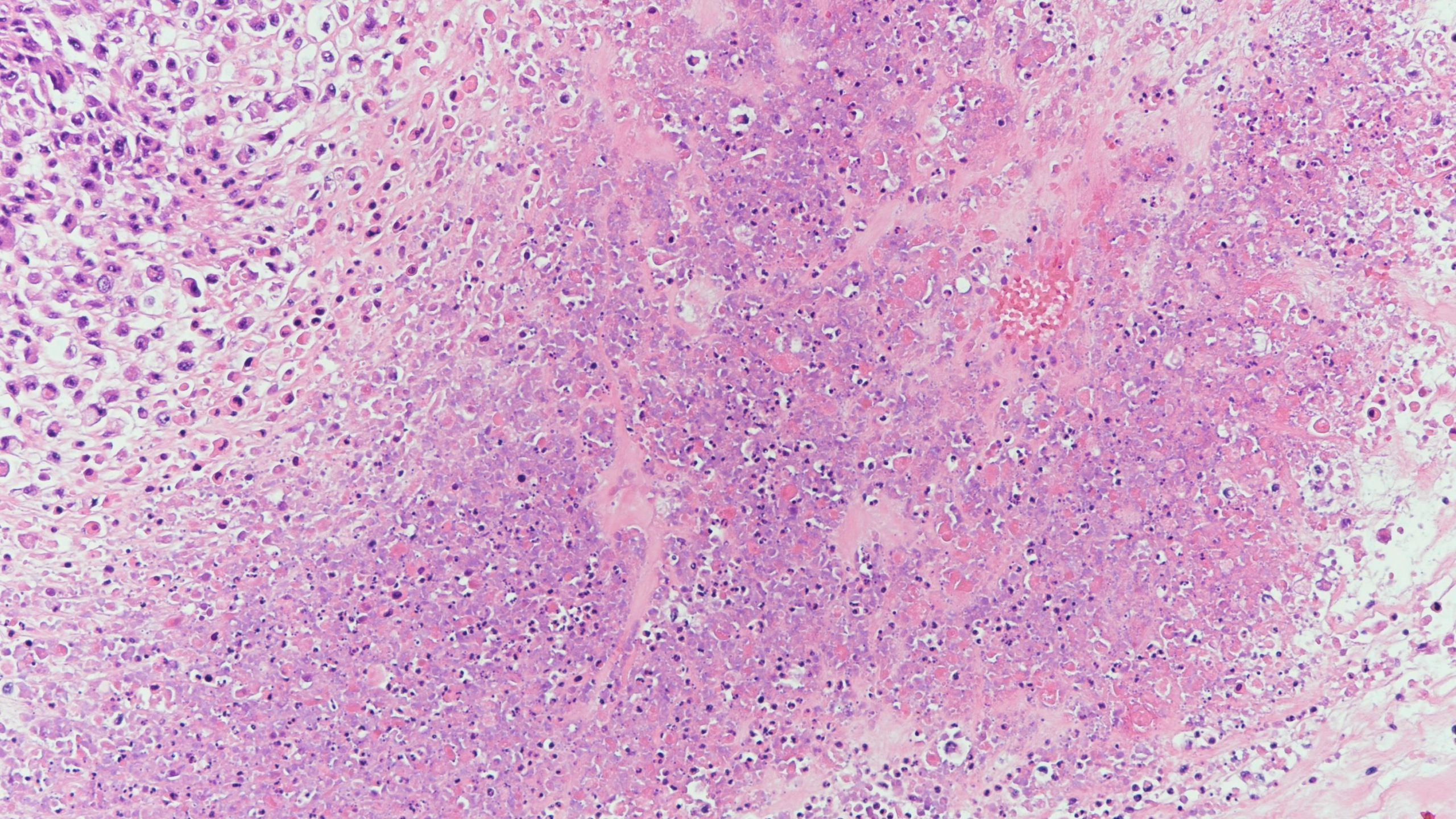

p63

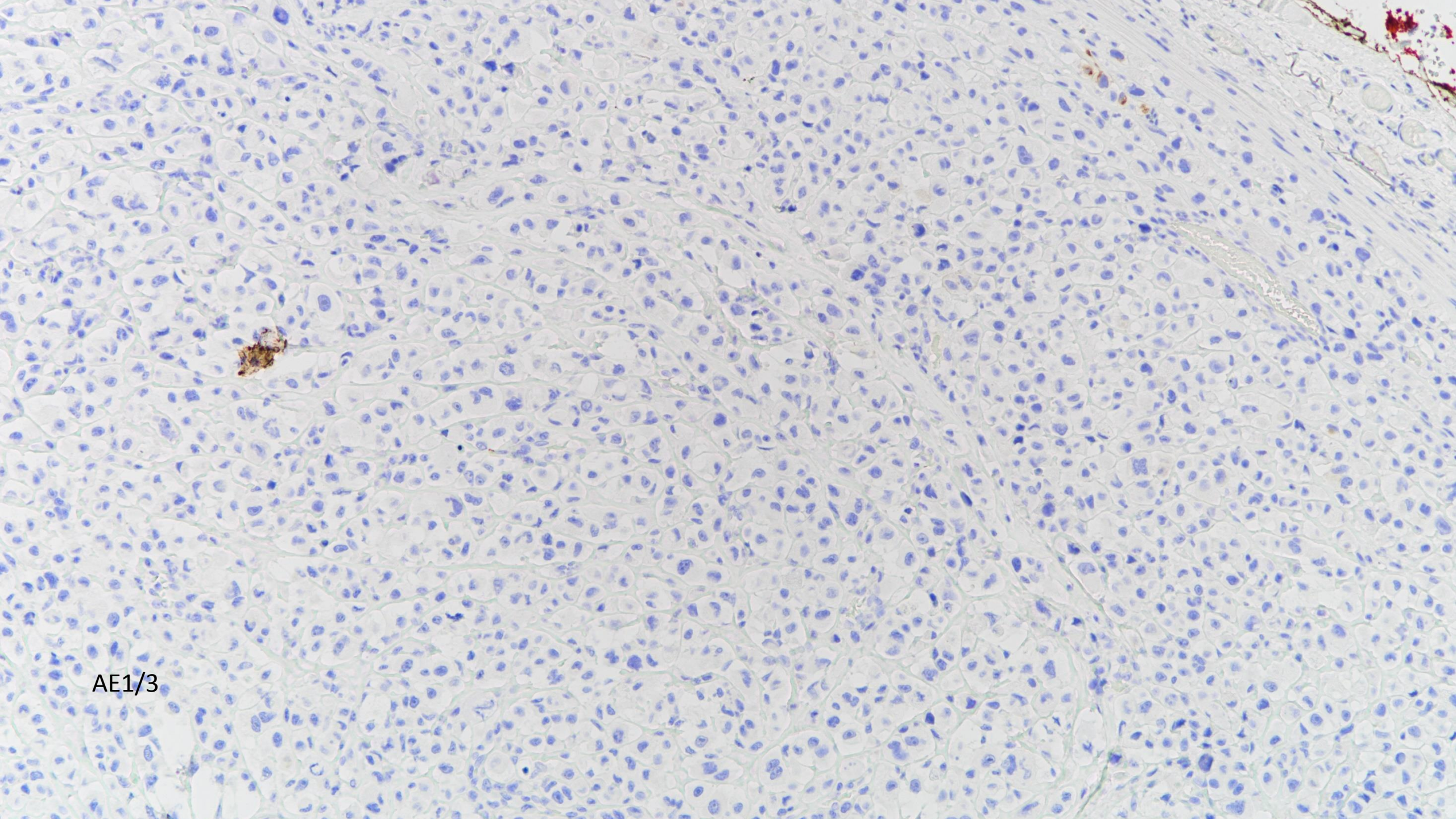
- The previous tumor










AE1/3

Spindle cell tumors

Epithelial cell

Spindle cells of UEH
Spindle cell DCIS
Metaplastic carcinoma

Myoepithelial cell

Spindle cell adenomyoepithelioma
Myoepithelial carcinoma

Mesenchymal cell

Fasciitis
Fibromatosis
PASH
Myofibroblastoma
Fibrous tumor
Sarcomas
Phyllodes tumors

Approach

- Clinical history
  - Recurrence? Complication of irradiation? New primary?
- Histology
  - Grade of spindle cells
  - Epithelial element
- Immunohistochemistry
  - Cytokeratins
  - Myoepithelial markers
  - p63
- Molecular tests

Major differential diagnoses

- Malignant PT (recurrence)
- Primary breast sarcomas (radiation induced?)
- Sarcomatoid carcinoma (primary)

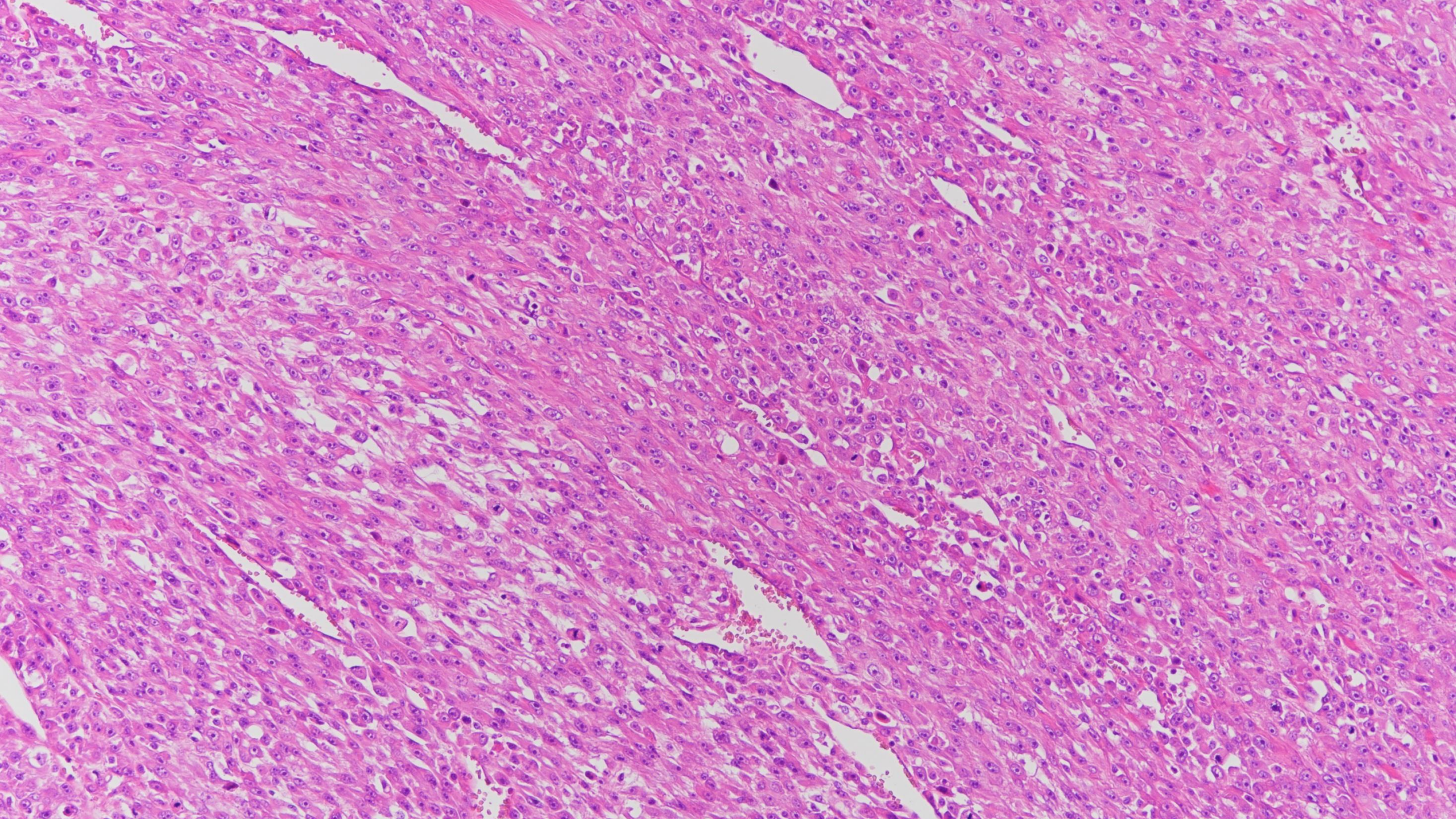
Potentially useful markers

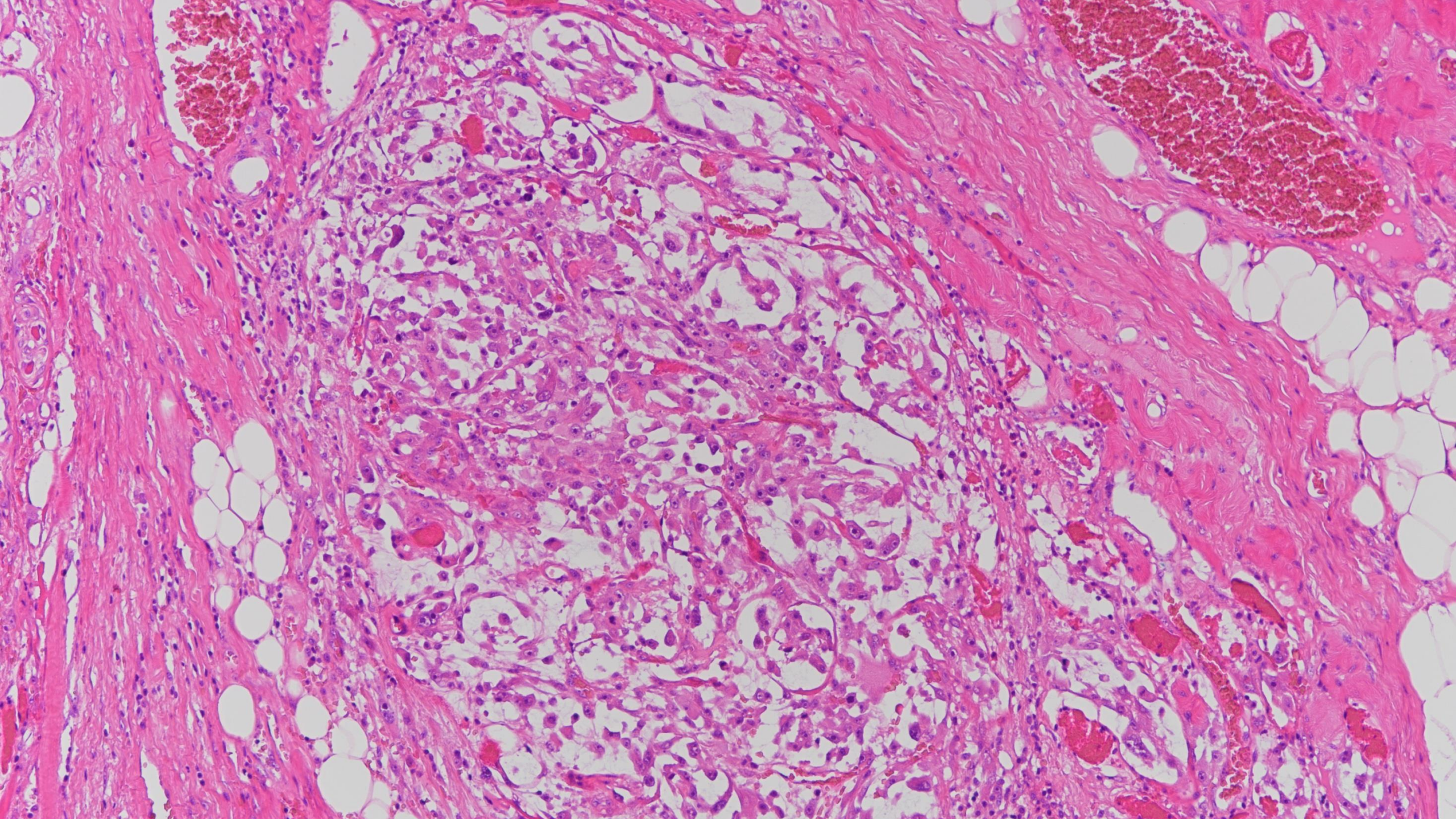
Cytokeratins (Pan CK)

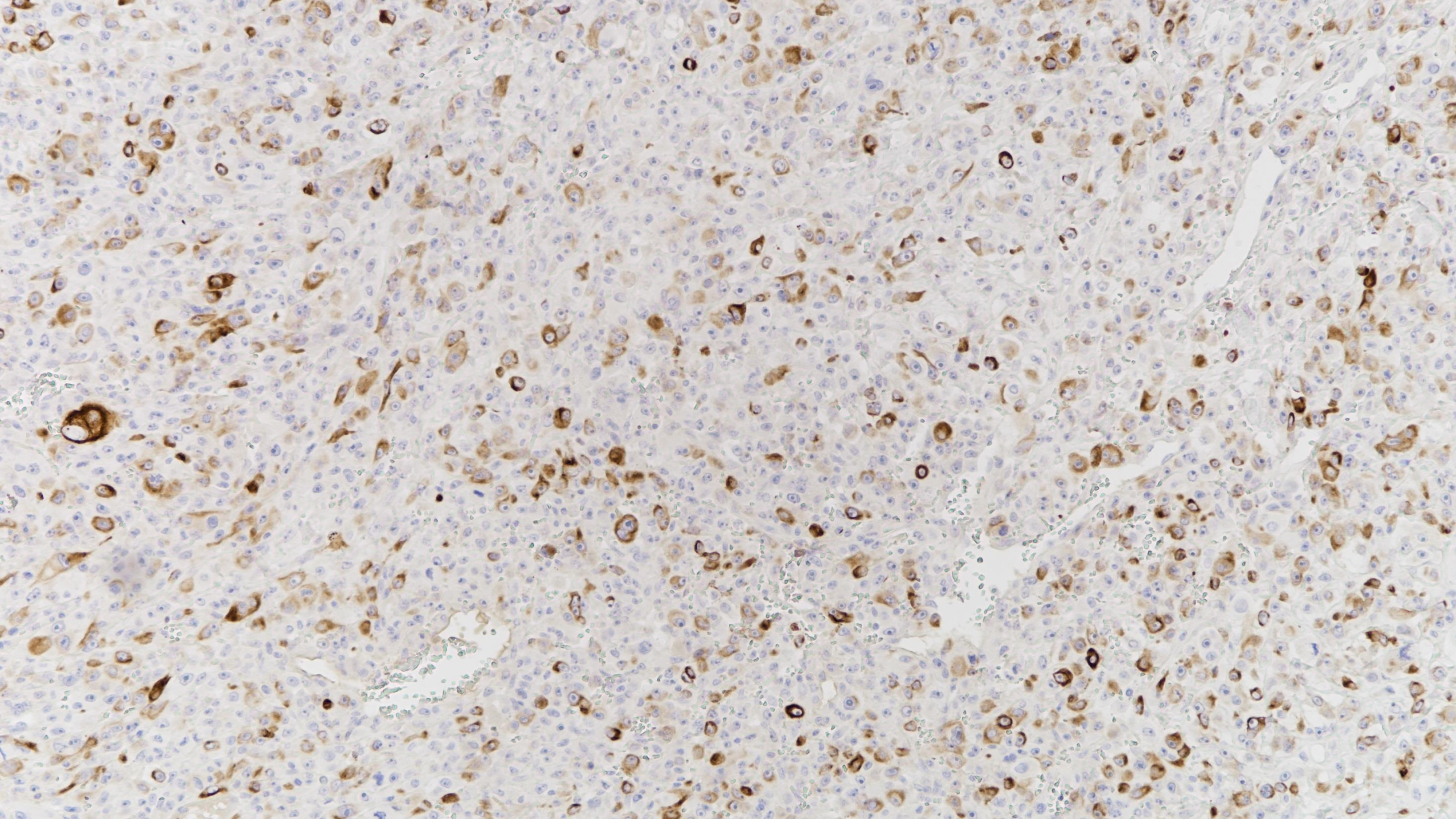
- Malignant PT - negative
- Sarcomatoid carcinoma – positive
- Primary breast sarcomas - negative

p63

- Malignant PT - negative
- Sarcomatoid carcinoma - positive
- Primary breast sarcomas - negative







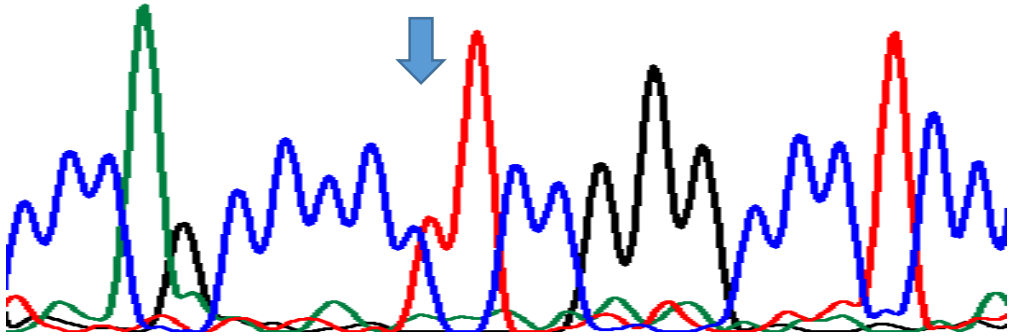
TERT promoter

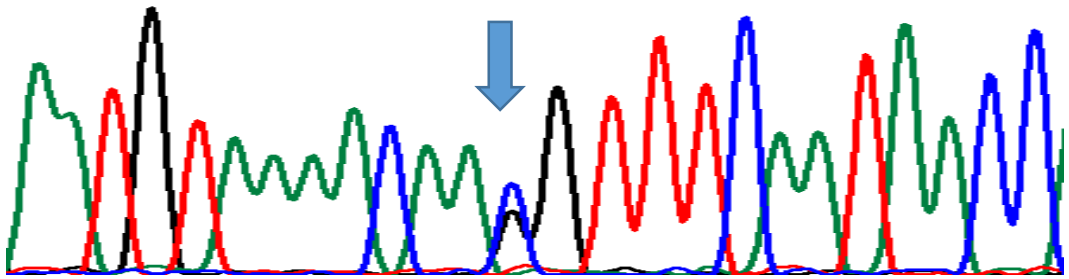
MED12 exon 2 hot spot

C>T

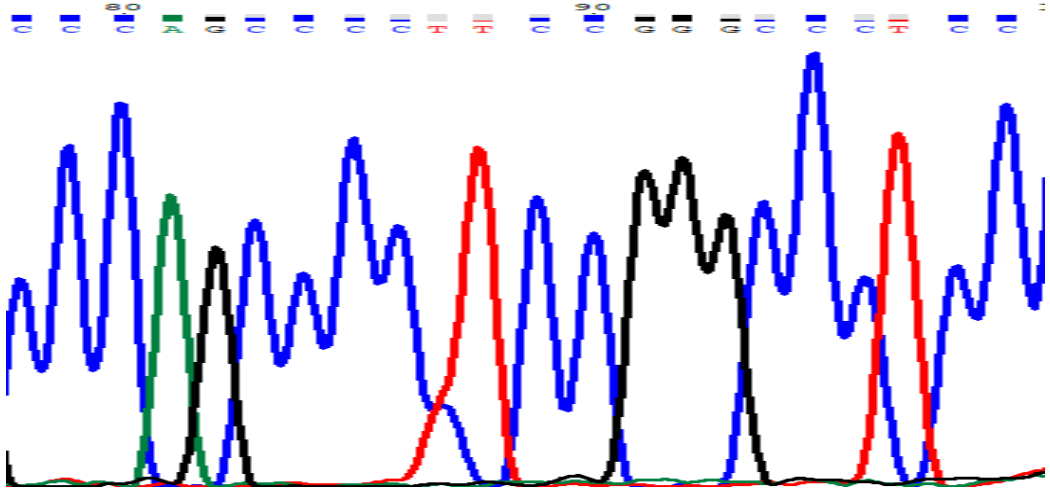
G>C

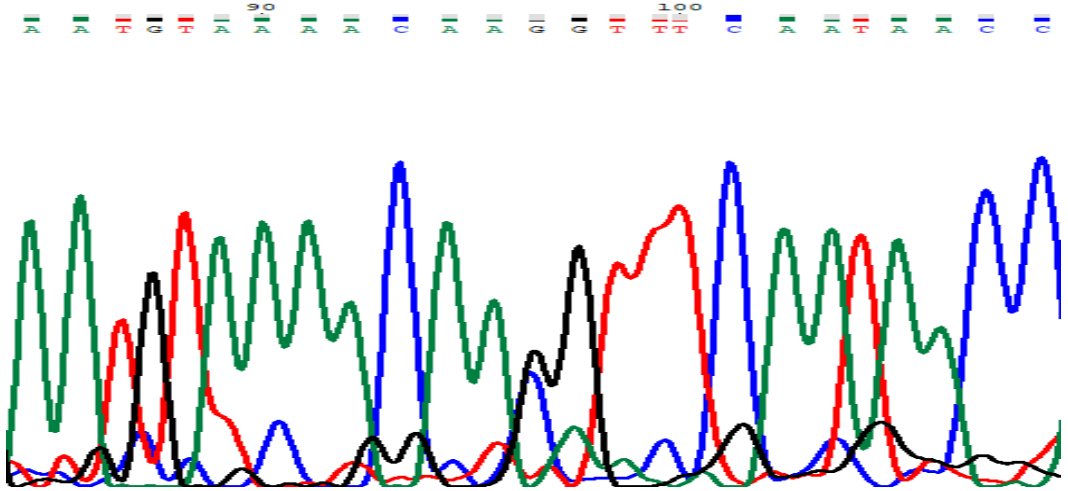
Primary





recurrent





MED12 exon 2

Table 1. Summary of *MED12* exon 2 mutations in SNB, including MBCs, PTs, PNSs and Fibromatoses, and in squamous MCB

Tumour type	*MED12* exon 2 mutation		Total
	+	–	
MBC	0	33	33
Bs	0	20	20
Bh	0	6	6
Sq	0	7	7
PT[1]	35 (71.4)	14 (28.6)	49 (100)
Benign	16 (72.7)	6 (27.3)	22 (100)
Borderline	12 (70.6)	5 (29.4)	17 (100)
Malignant	7 (70.0)	3 (30.0)	10 (100)
PNS	0	2	2
Fibromatosis	0	8	8

Bs, biphasic with spindle metaplasia; Bh, biphasic with heterologous mesenchymal metaplasia, including osteoid, chondroid or matrix metaplasia; Sq, squamous MBC of pure epithelial type.

Distinguish PT from other spindle cell neoplasms

Lien HC et al 2016 APIMS 124:356

TERT promoter mutations

- Mutations in TERT promoter lead to overexpression of TERT (melanomas, HCC, urothelial carcinoma)
- Frequent in PT but rare in FA
- 35.5% (27/76) Vs 0% (0/100); 3 malignant cases with TERT amplification
- 65% (30/46) Vs 7% (4/58)
- 27.1% in PT with the highest frequency in borderline tumors
- Mutations were present in stromal component
- TERT promoter mutations associated with older age, MED12 mutations and stromal cellularity

Piscuoglio S et al 2016 J Pathol 238:508
Yoshida M et al 2015 Br J Cancer 113:1244
Tsang JY et al 2018 Sci Rep 8:3881