



Mass General Brigham



HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

A 57-year-old woman with incidental infiltrative mediastinal mass

Miekan Stonhill, MD

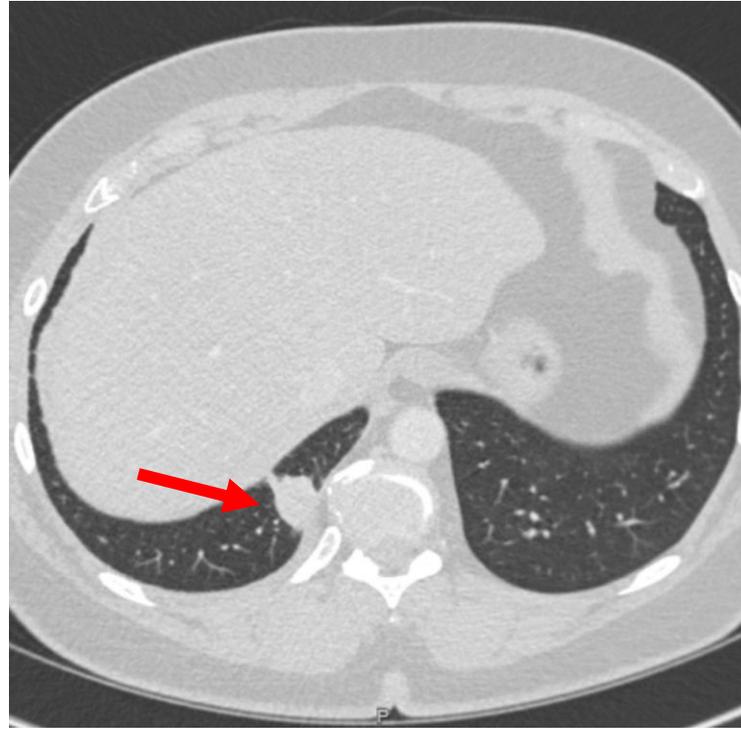
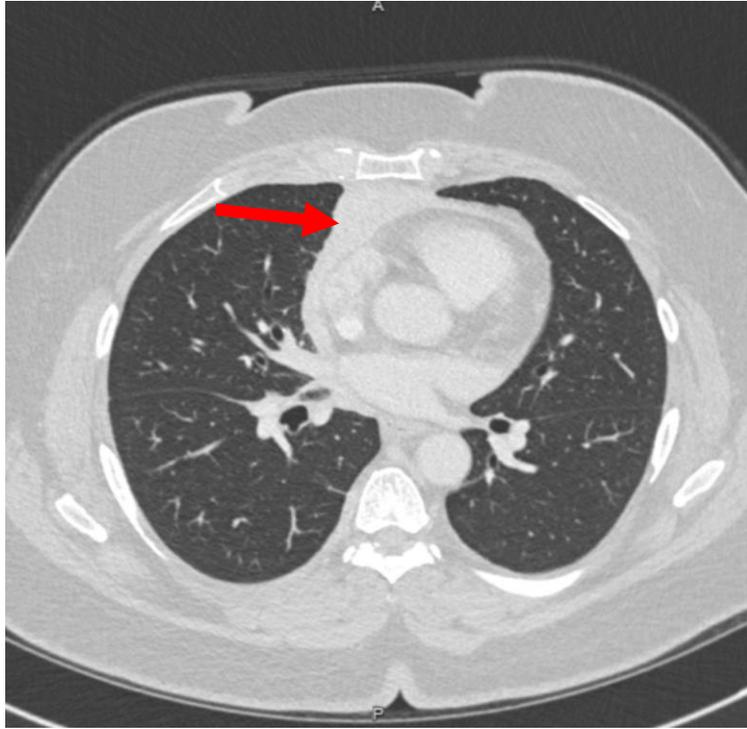
Hematopathology Fellow, Mass General Brigham

History and clinical presentation

- 57-year-old woman, nonsmoker, with no significant past medical history
- Presented to the ED with acute abdominal pain
- CT abdomen was obtained and showed no intraabdominal process, but did show thoracic adenopathy and lung nodules
- CT chest was obtained



CT Chest (with contrast)



“Infiltrative prevascular mediastinal process, foci of enhancing right pleural thickening, right lower lobe nodule, and enlarged anterior diaphragmatic lymph node. These findings are favored to represent a nonmalignant process such as IgG4 disease or non-Langerhans' cell histiocytosis. The imaging appearance would be unusual for lymphoma.”

VATS wedge resection and pleural biopsies

Intraoperative findings:

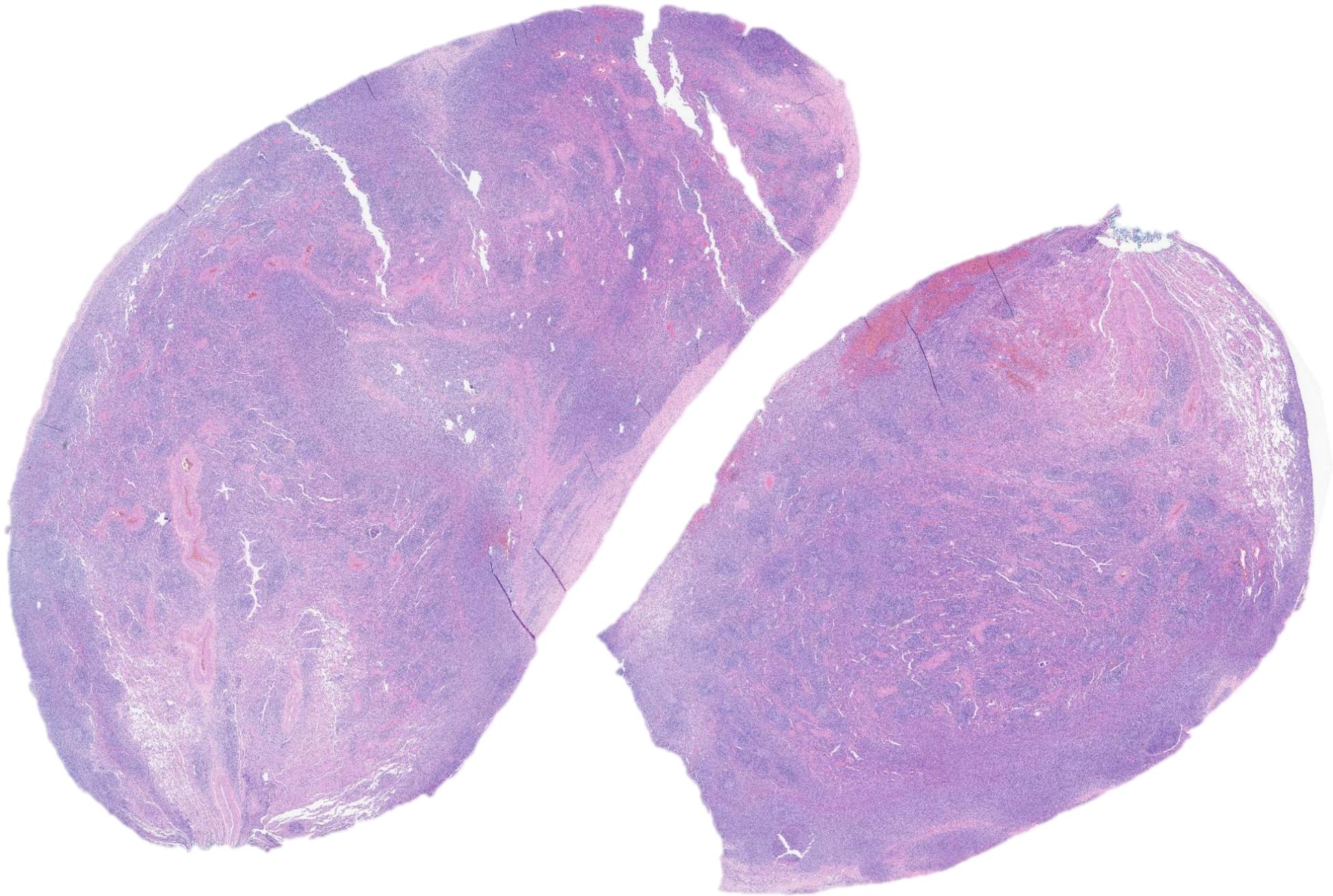
“Mediastinum inspected with diffuse matted appearance encasing great vessels”

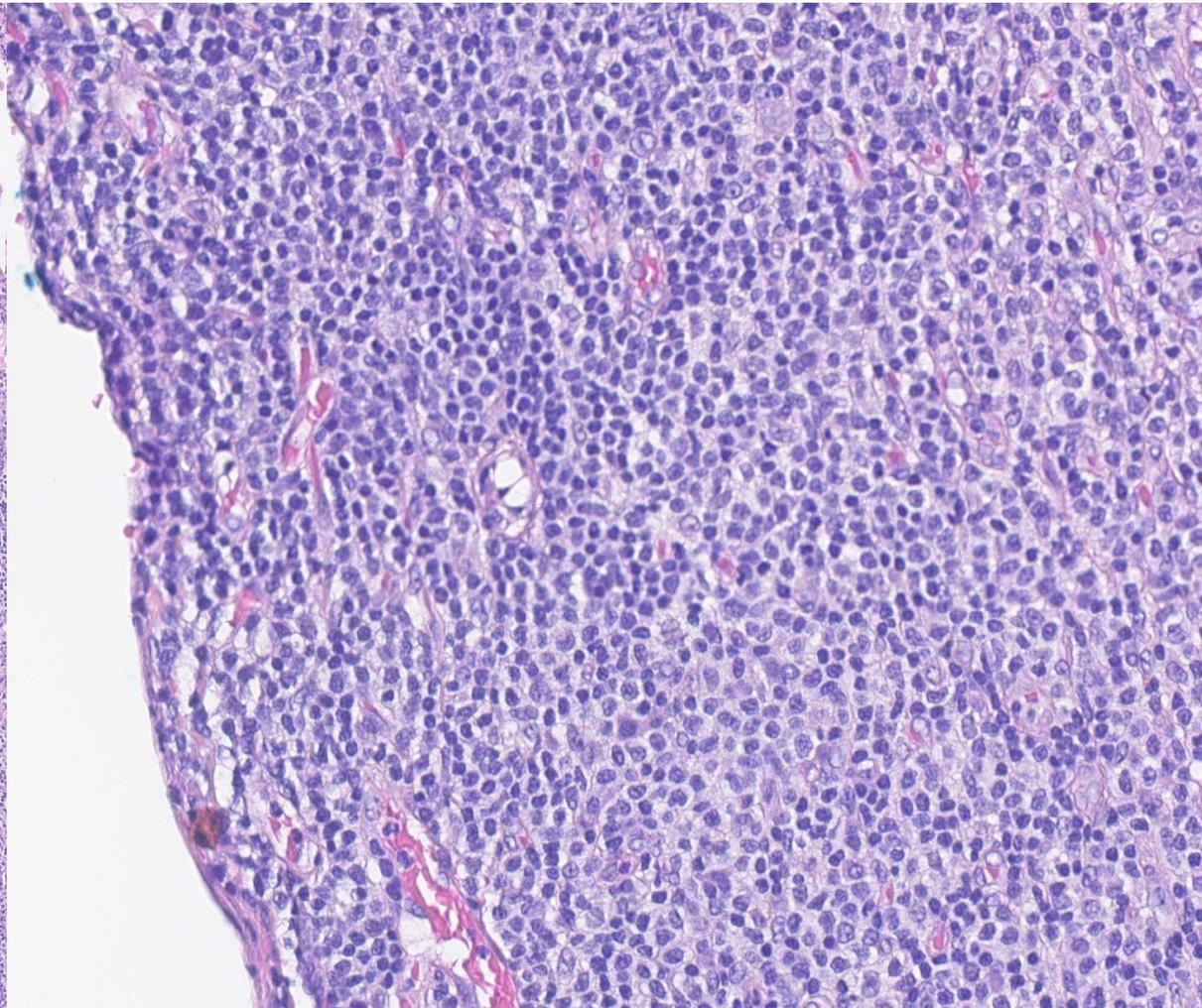
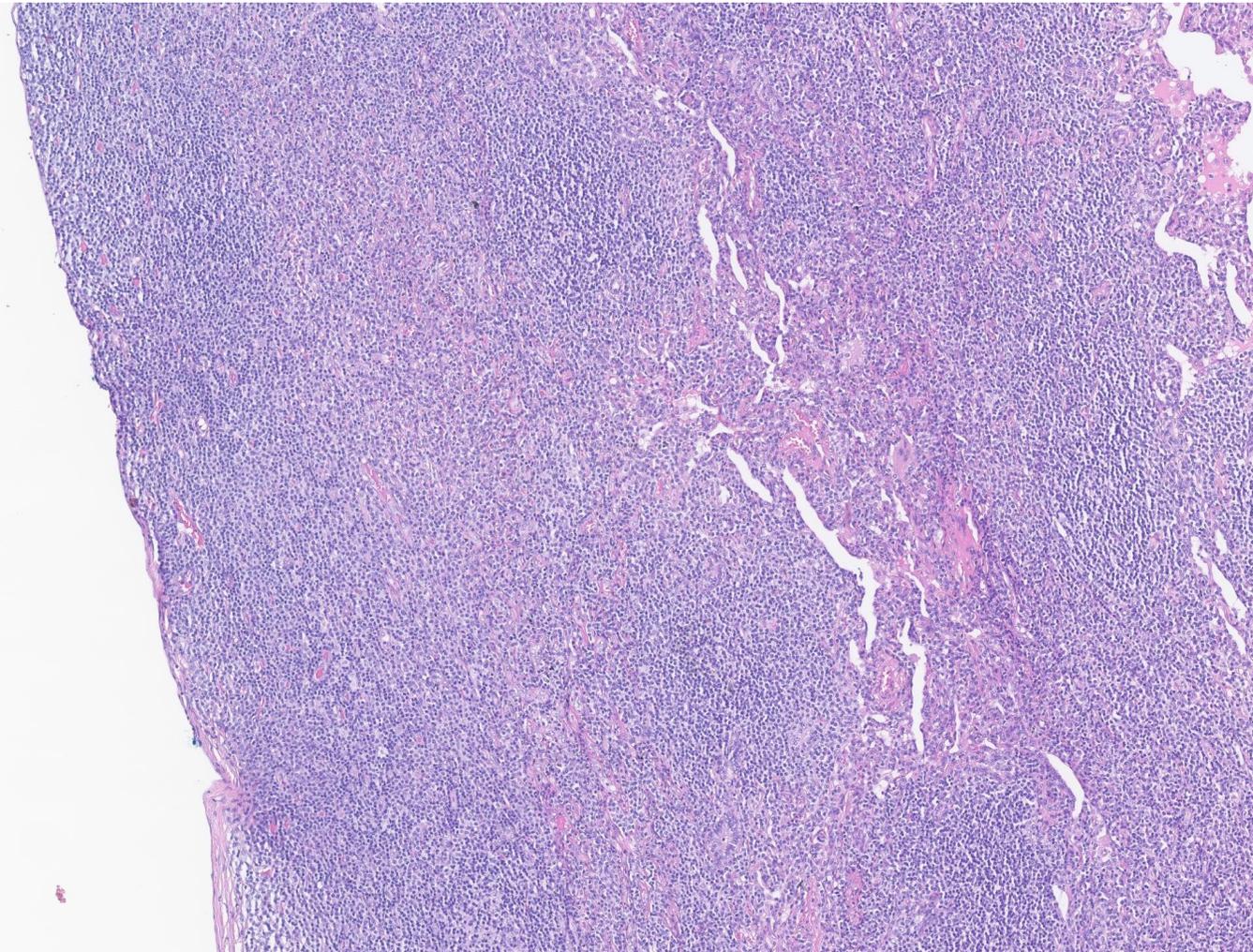
Intraoperative frozen section diagnosis (pleural biopsy):

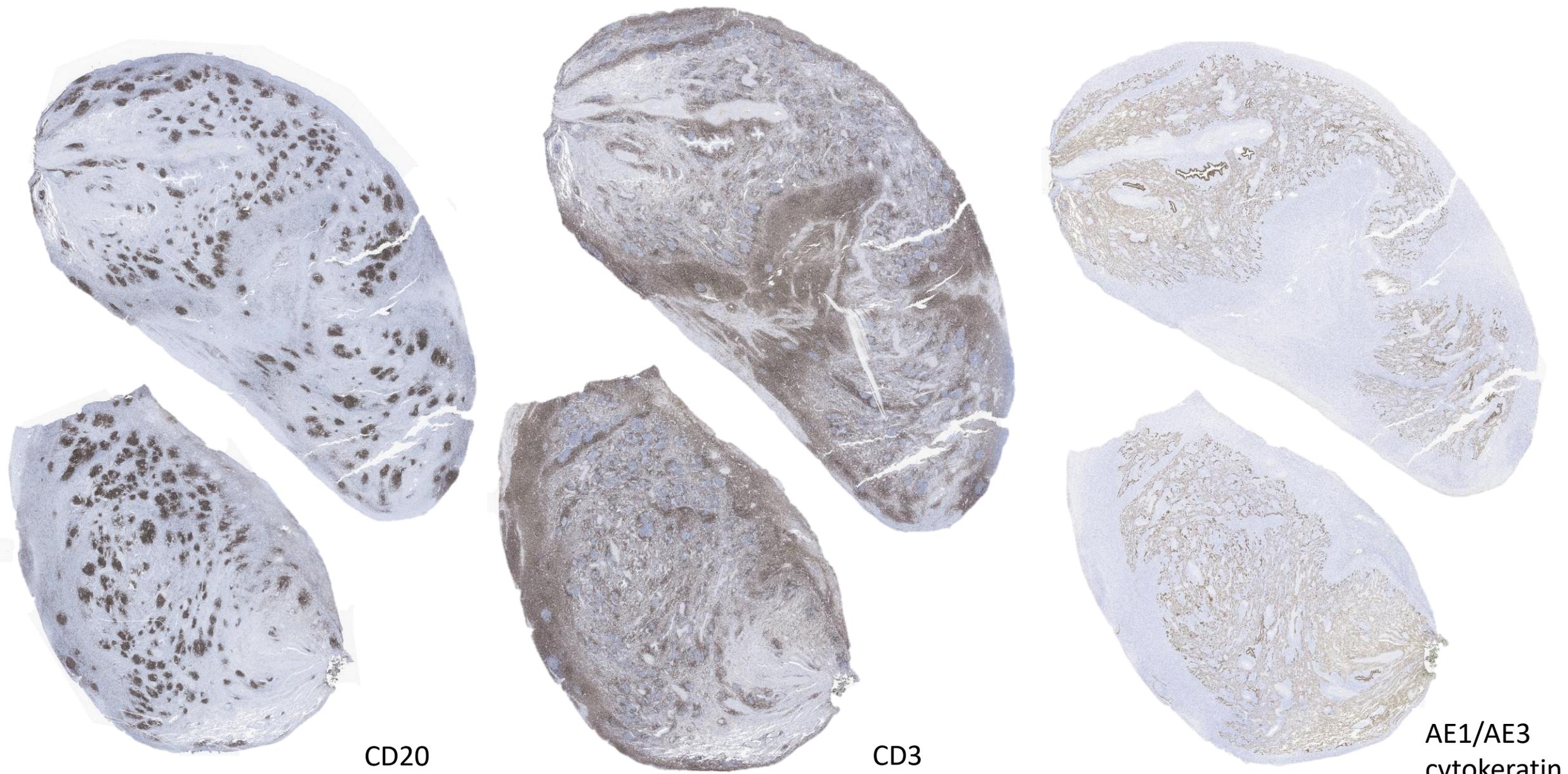
“Atypical lymphoid infiltrate. More tissue requested for hematopathology work up.”

Pleural biopsies (x2) and right lower lobe wedge resection obtained









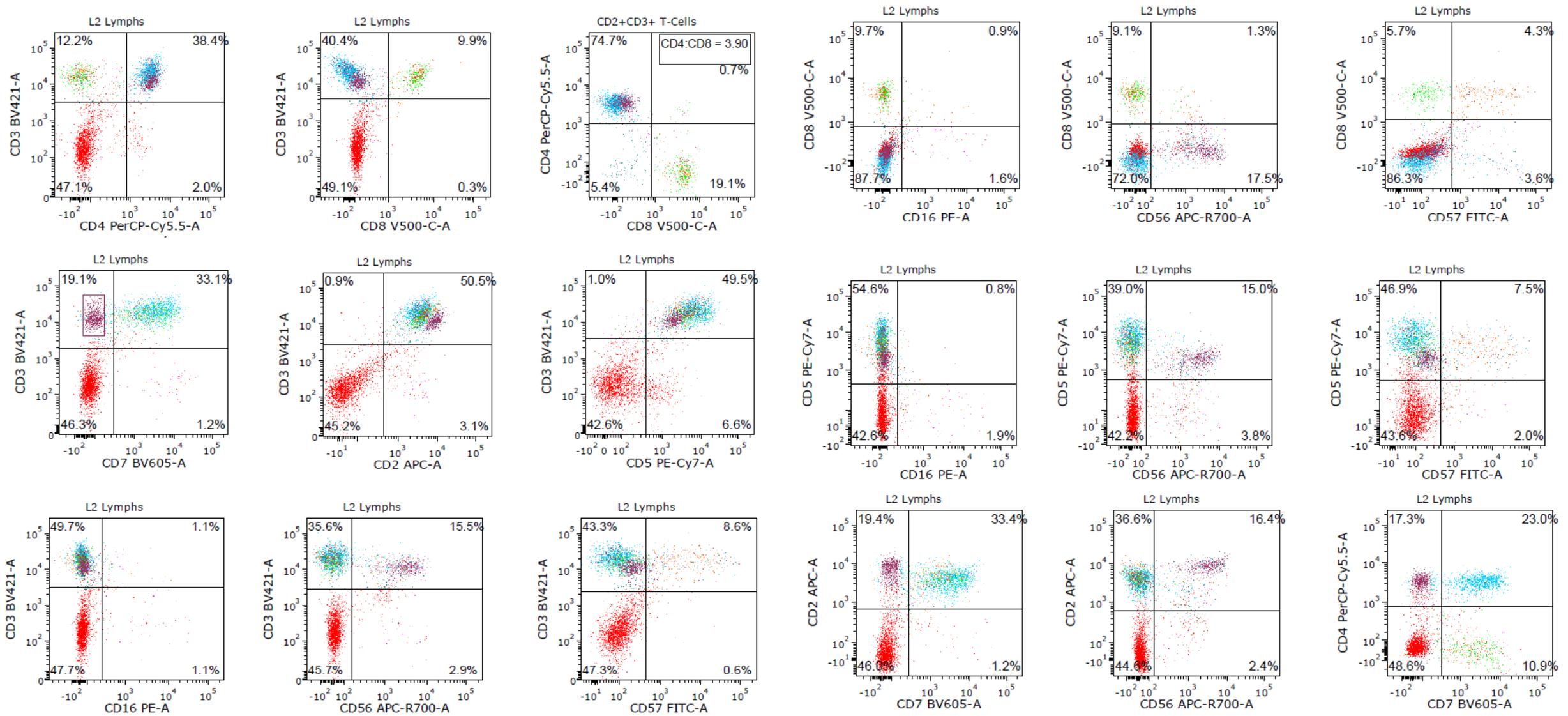
CD20

CD3

AE1/AE3
cytokeratin



Intrdepartmental consult to Hematopathology requested: "Please sign this case out"



Purple population: 19% T cells with unusual immunophenotype
 (CD3+ CD2bright CD5dim CD7- CD4+ CD8- CD56+ CD16- CD57-)



 CD2



CD5



CD7



CD4

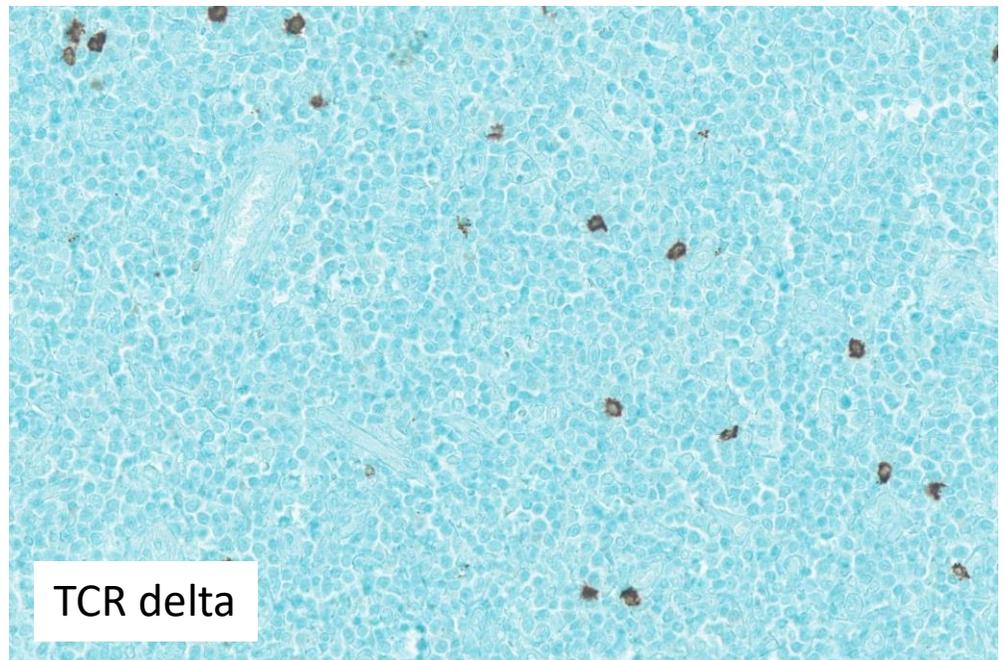
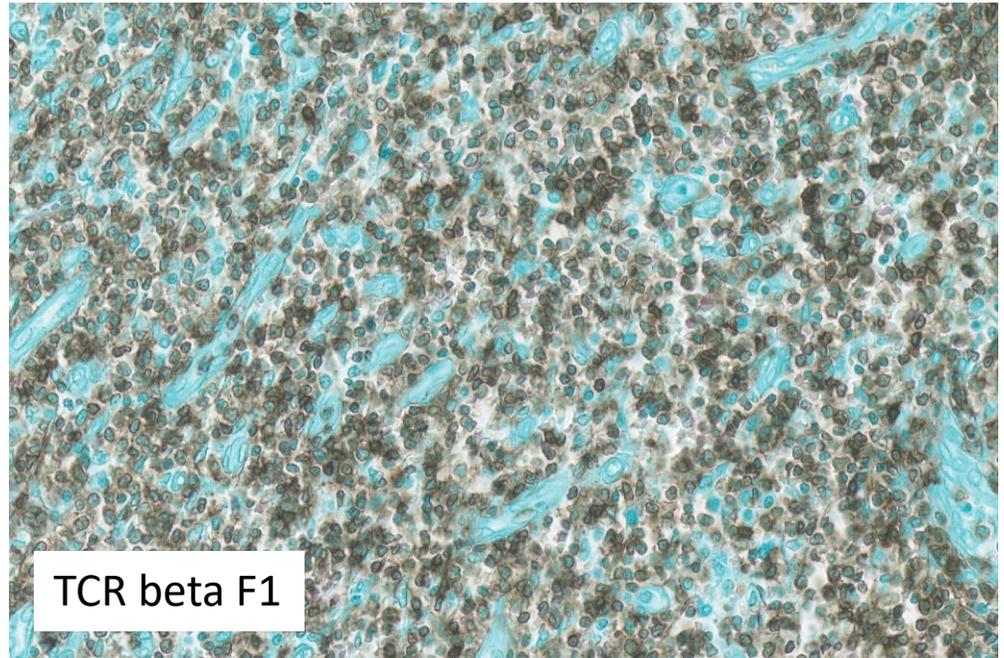
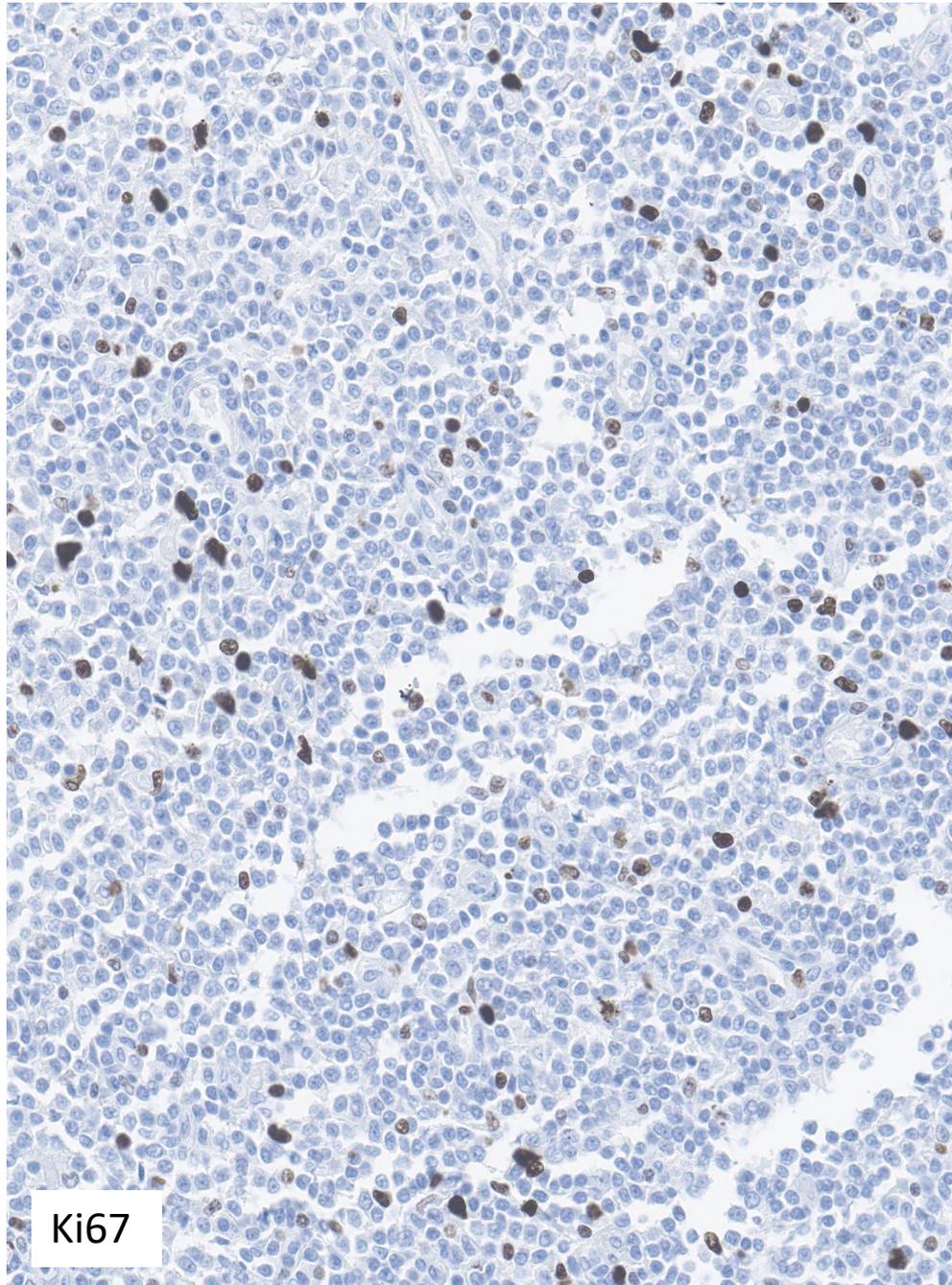


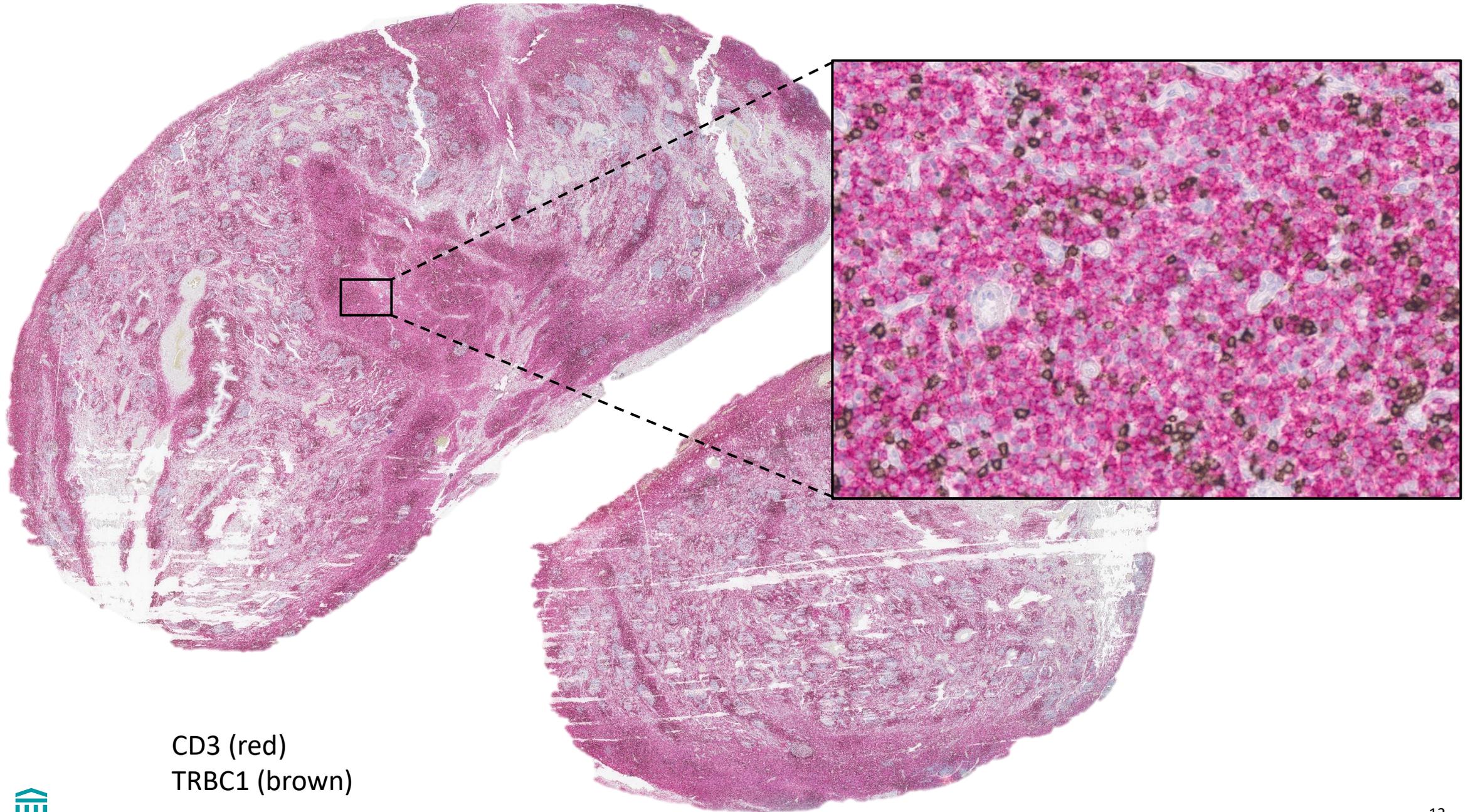
CD8



CD56

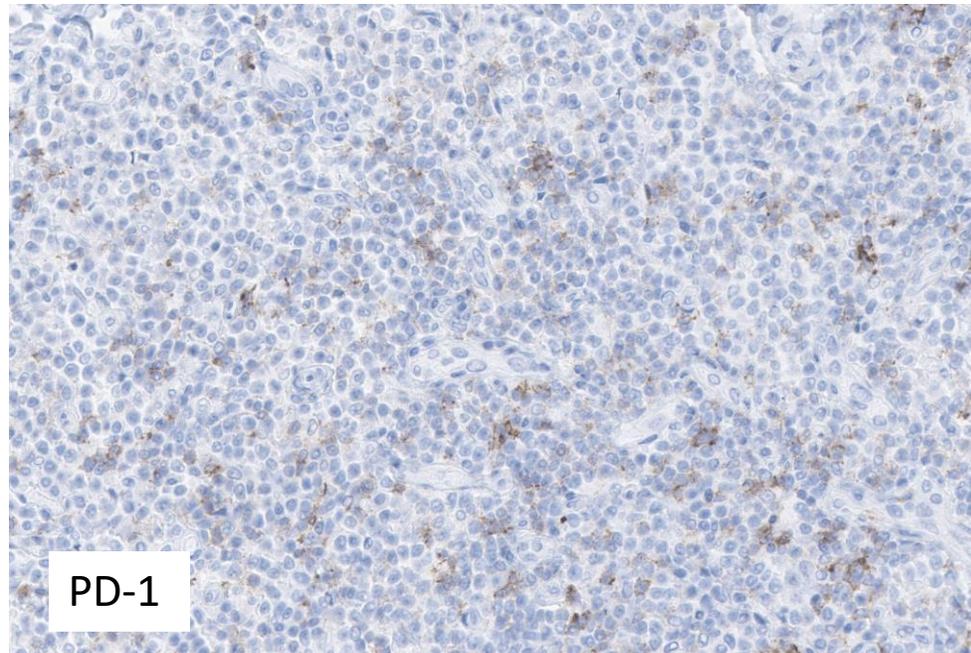
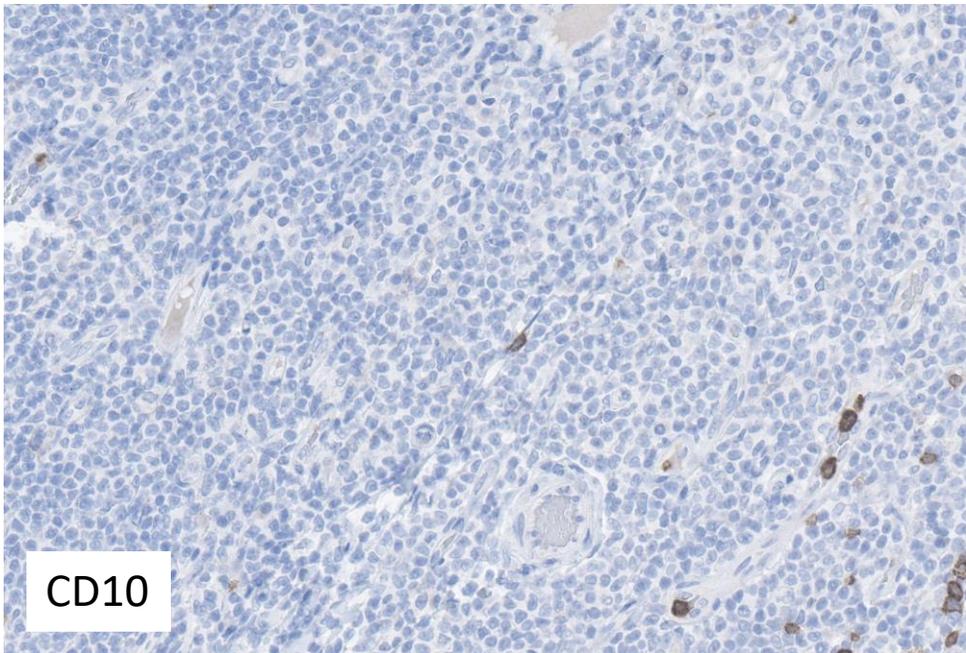
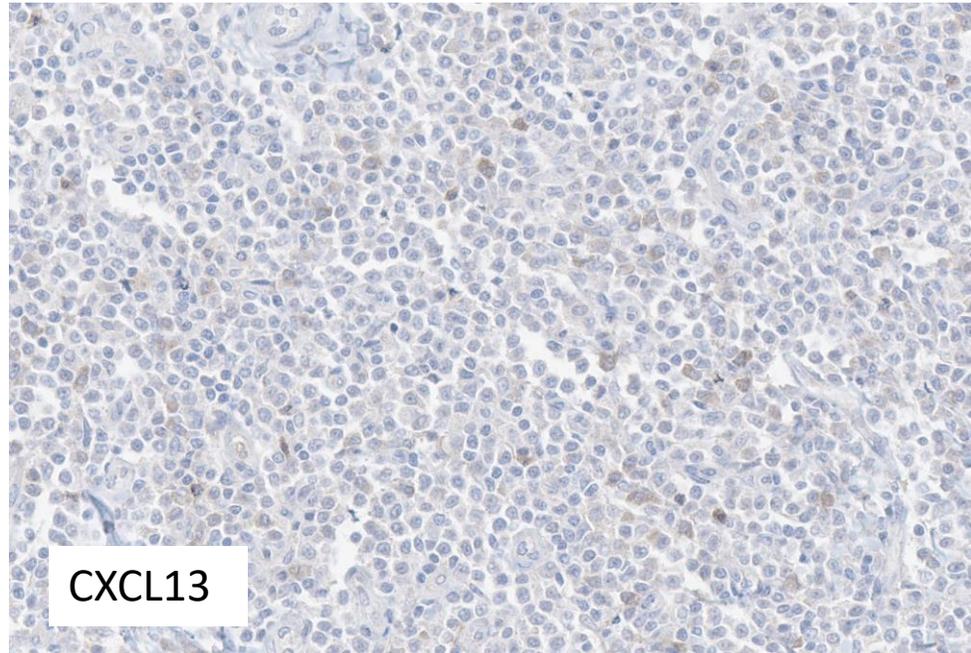
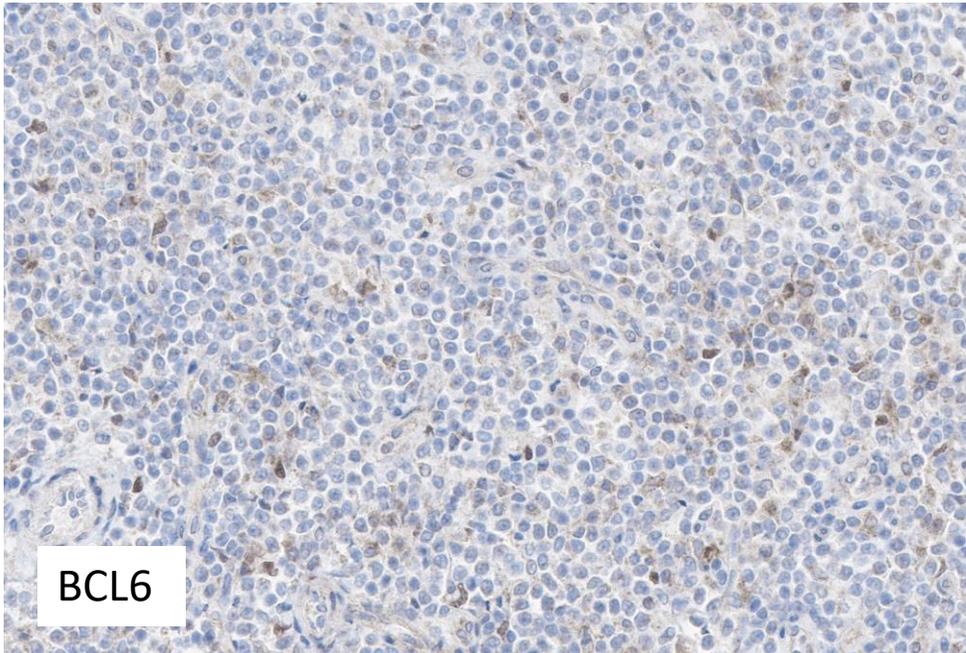


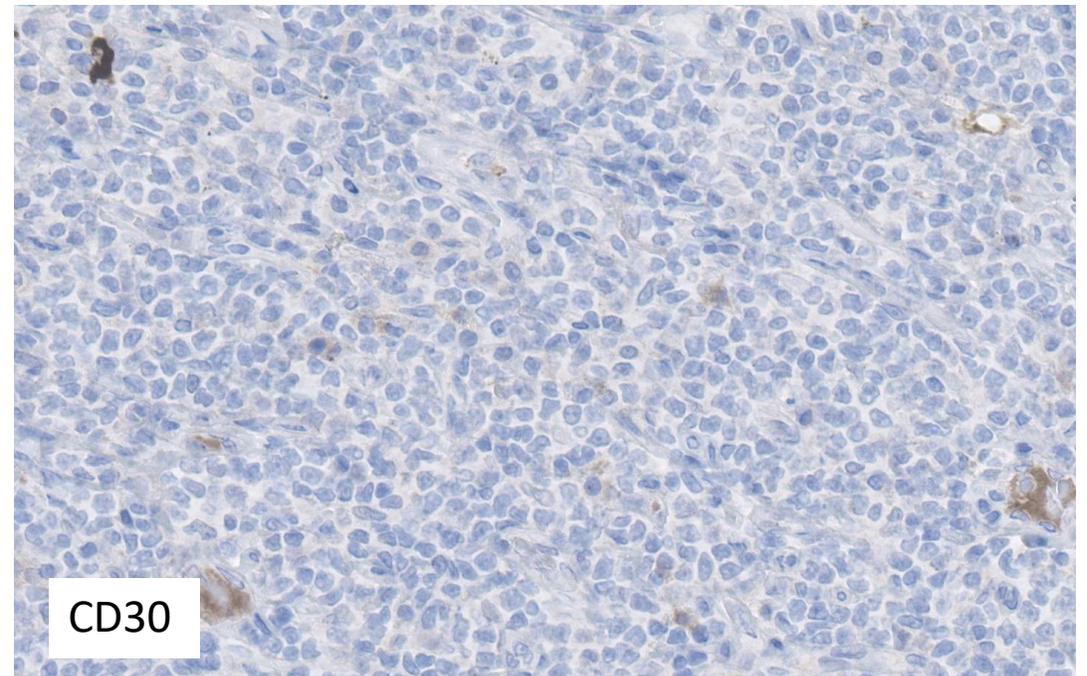
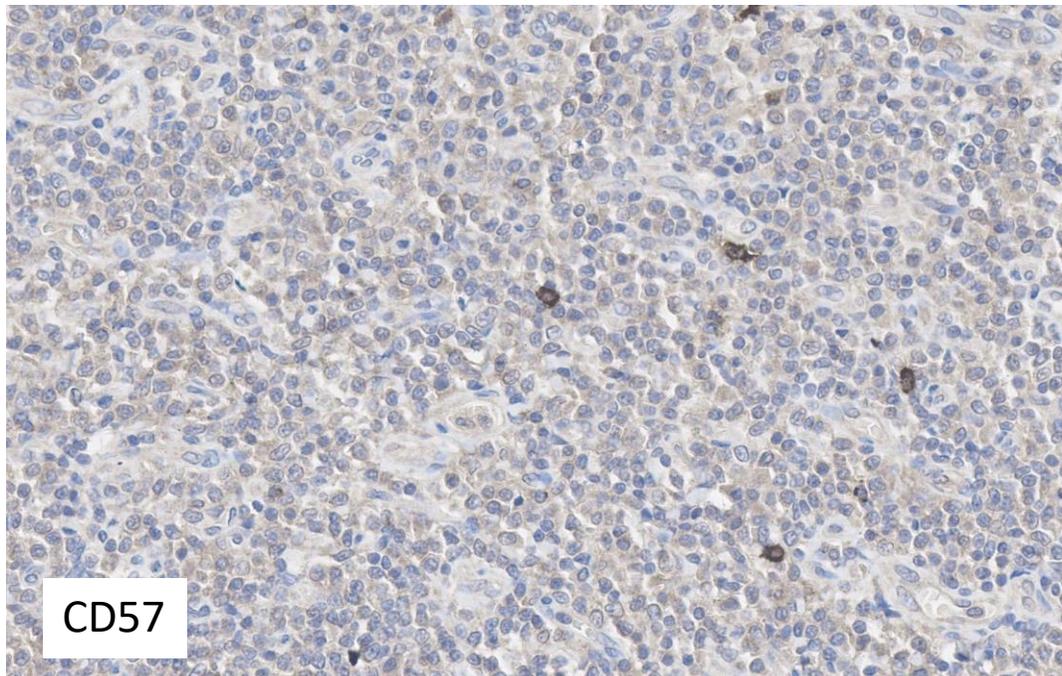
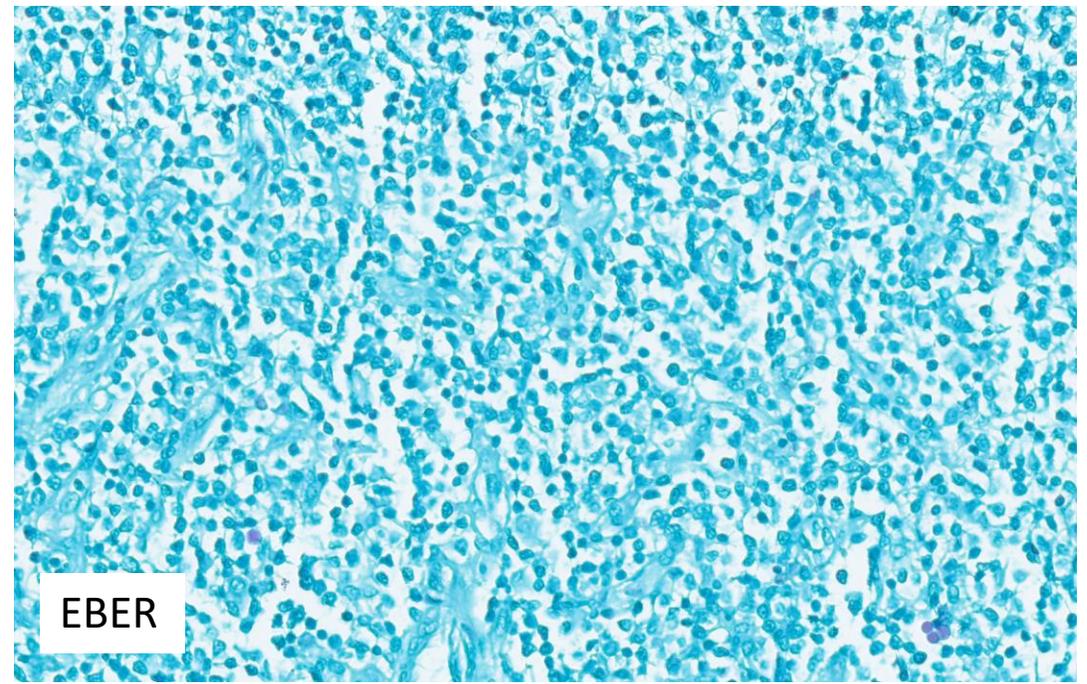
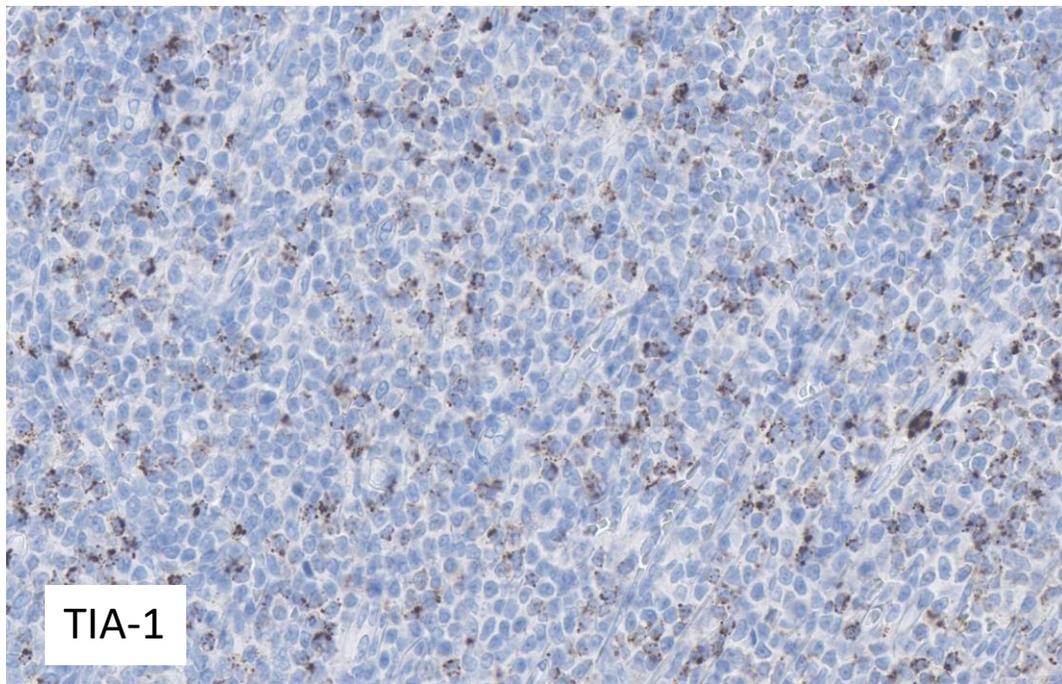




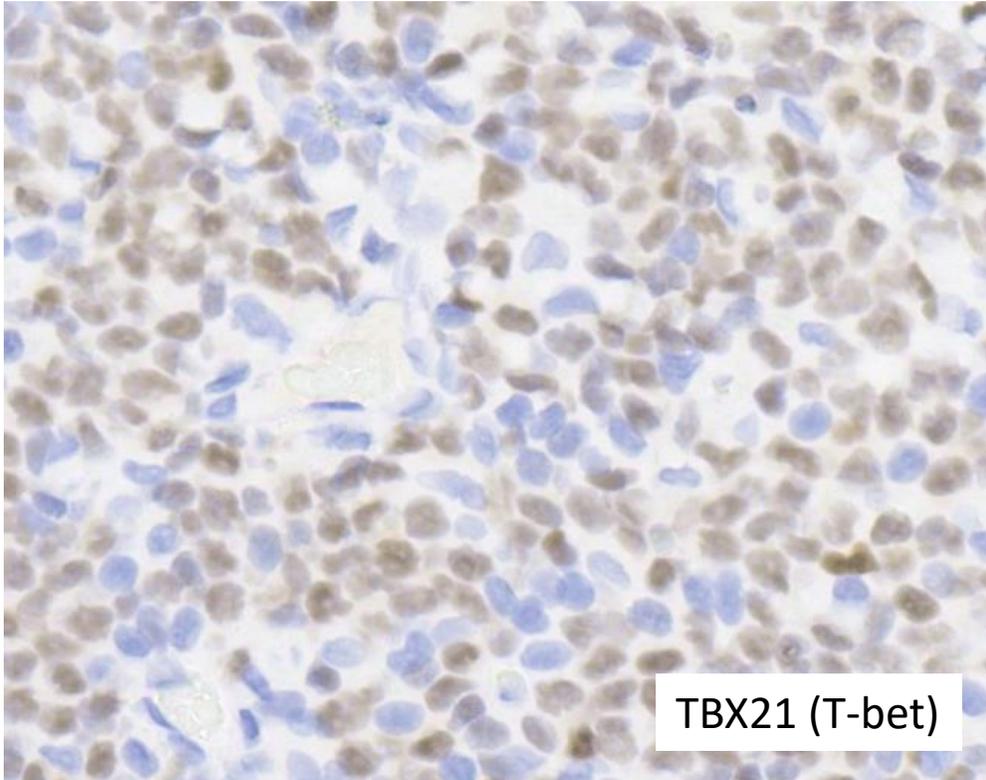
CD3 (red)
TRBC1 (brown)







What is this entity?



TBX21 (T-bet)

Other positive stains:

- CD43

Other negative stains:

- ALK
- p53
- TCL1
- CD25
- GATA3

What it is:

CD4+ T-cell lymphoma with low proliferation index

What it isn't:

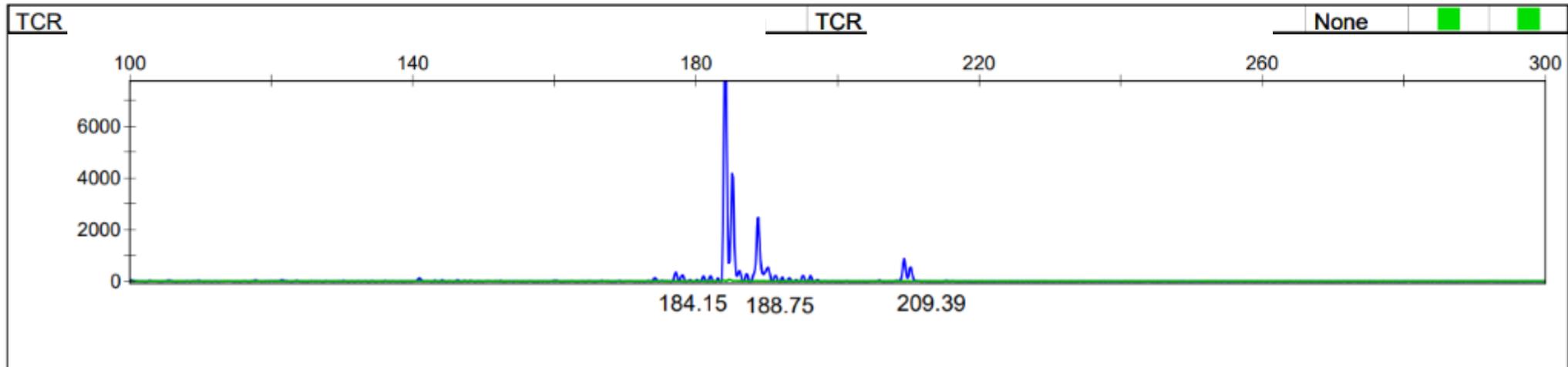
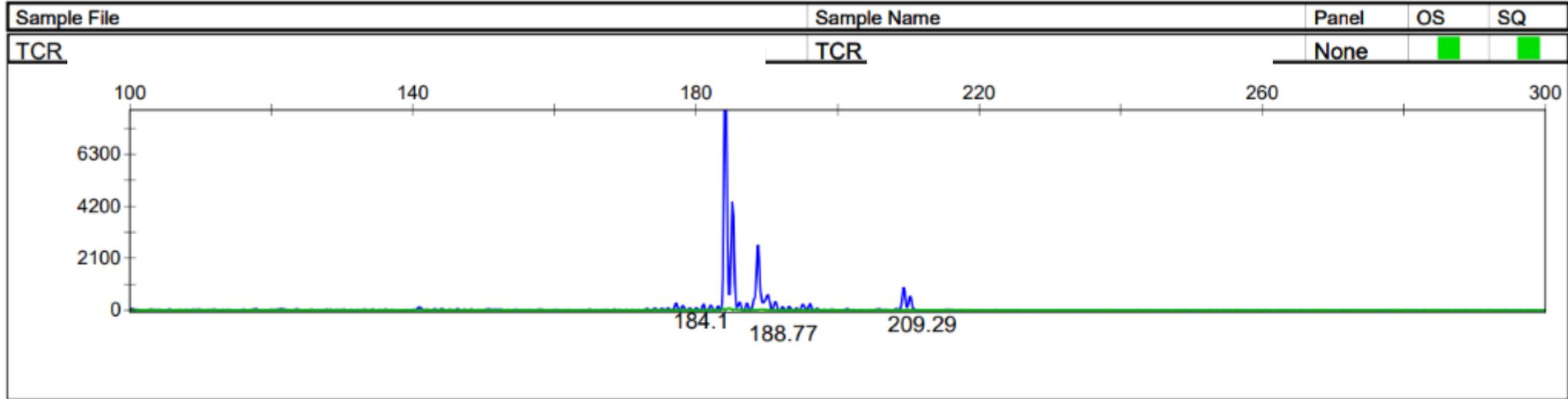
- T-follicular helper cell lymphoma
- EBV+ NK/T cell lymphoma
- CD30+ T-cell lymphoproliferative disorder
- Hepatosplenic T cell lymphoma

What is left?

- Indolent T-cell lymphoma ~~of the gastrointestinal tract~~
- PTCL-NOS?



Additional ancillary testing

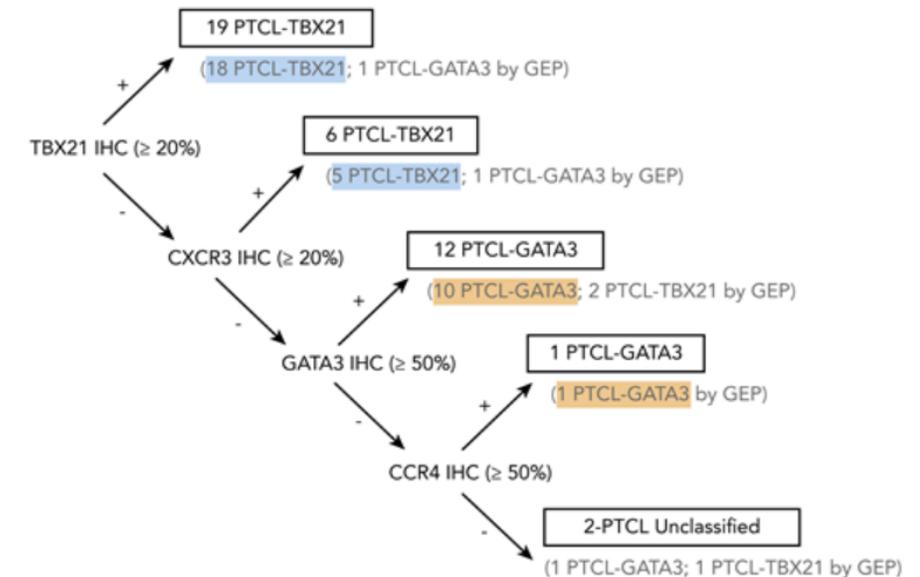
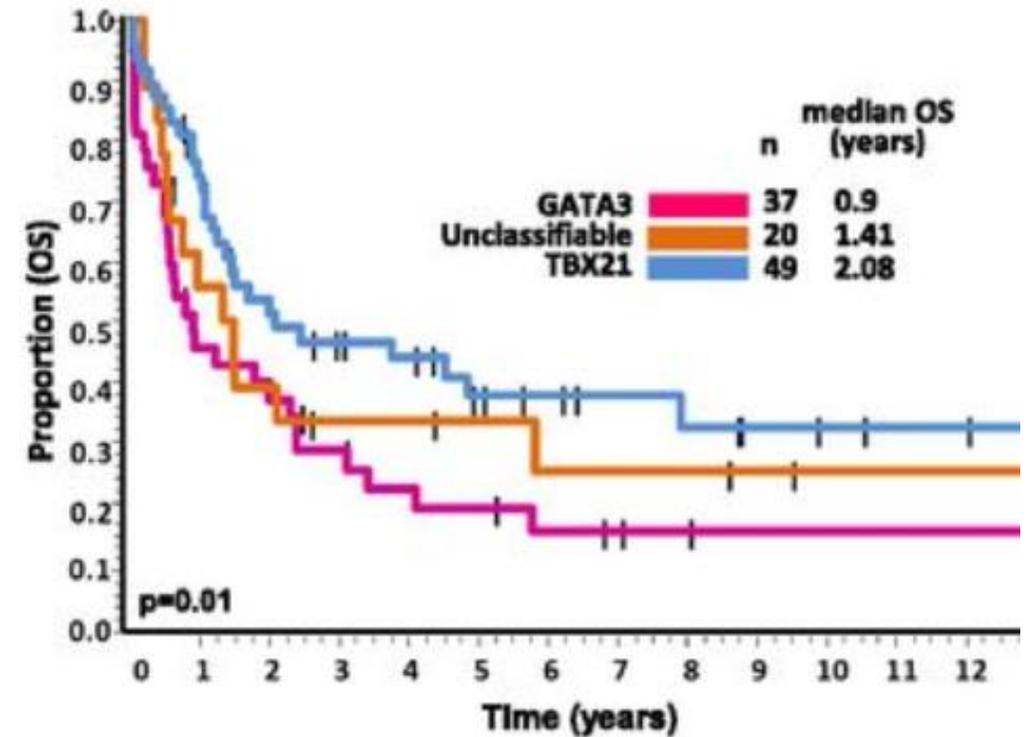


Molecular subtyping of PTCL-NOS

Two molecular subgroups of PTCL-NOS have been described (PMID: 24632715)

- 1) GATA3 subtype: increased expression of GATA3 and its target genes
 - 19% 5-year overall survival
 - High MYC expression, high proliferation, and aberrant PI3K activation
- 2) TBX21 subtype: increased expression of T-bet and its target genes
 - 38% 5-year overall survival
 - NF-κB pathway enrichment

These subtypes can be distinguished by an IHC algorithm (PMID: 31562134)



NGS findings

Rearrangement - FGFR1 intron 10 (chr8:38276329) :: SATB1 intron 7 (chr3:18433570)

A similar *SATB1::FGFR1* fusion was recently reported in a case of primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma (PCAECTL), which shows robust initial response to pemigatinib (FGFR2 inhibitor, FDA-approved for cholangiocarcinoma)

SETD2 c.1023delinsCC (p.S342Lfs*5), exon 3 - in 9% of 581 reads Predicted inactivating mutation, associated with high-risk disease- similar to mutations previously seen in hepatosplenic T-cell lymphoma and monomorphic epitheliotropic intestinal T-cell lymphoma

BCOR c.4345A>G (p.M1449V), exon 10 - in 47% of 435 reads
DAXX c.980G>A (p.R327Q), exon 3 - in 45% of 651 reads
EME1 c.380A>G (p.N127S), exon 2 - in 52% of 655 reads
ENG c.*202_*210dup (), exon 14 - in 56% of 73 reads
NSD1 c.72C>T (p.A24A), exon 2 - in 47% of 709 reads
PDGFRA c.2075G>A (p.S692N), exon 15 - in 48% of 633 reads
PTK2B c.2671G>A (p.V891M), exon 34 - in 48% of 340 reads
SDHAF2 c.496C>T (p.R166C), exon 4 - in 48% of 558 reads
ZNRF3 c.1243G>A (p.V415M), exon 7 - in 49% of 403 reads

1q43 Gain
7p Arm Loss
7q34 Loss
8p11.23 Loss

Final diagnosis

T-CELL LYMPHOPROLIFERATIVE DISORDER (see comment)

Comment: The lung and pleura are involved by a mature, small CD4+ T-cell lymphoproliferative disorder composed predominantly of small atypical lymphoid cells with a very low proliferation index (<5%). There is no significant expression of T-follicular helper cell markers or cytotoxic markers, and EBV is negative. Based on these immunophenotypic findings, this case may be classified as a peripheral T-cell lymphoma, NOS, TBX21 subtype; however, the morphology and very low Ki-67 proliferation index are suggestive of a relatively indolent process. Careful clinical correlation is recommended. Correlation with pending NGS studies and HTLV-1 serology is also advised.



Clinical followup

- Patient is currently on observation
 - No plans for usual PTCL-NOS treatment (CHOP, CHOEP, allo-HSCT)
 - Possible role for pemigatinib?
- Mediastinal mass is stable on follow-up imaging



References

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