



The Curveball of Follicular Lymphoma: A Journey from Refractory to Remission

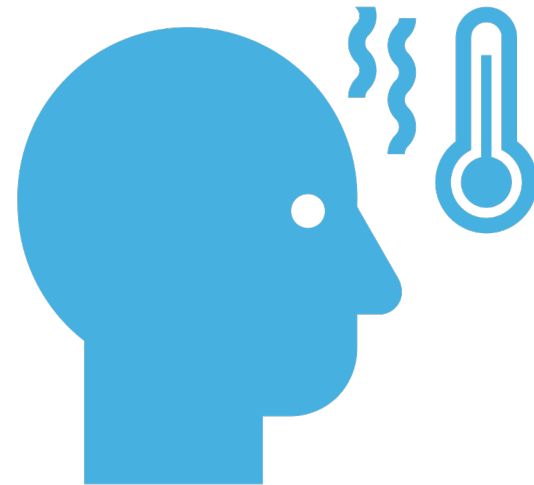
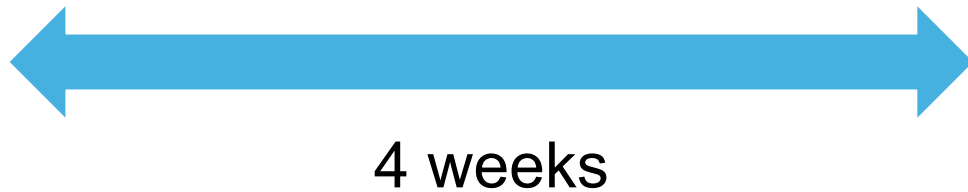
Dr Devin Fitzgerald, Haematology Registrar

08/11/2024

Dr James Meeke, Histopathology SHO

Case

- 60 year old male
- Night sweats
- Weight loss
- Painful splenomegaly



Investigations

- WCC 27.3, Lymphocytes 23.21, Neutrophils 2.46
- Hb 11.3, MCV 88, Platelets 96
- LDH 1466
- Blood film – circulating lymphoid cells with follicular appearance

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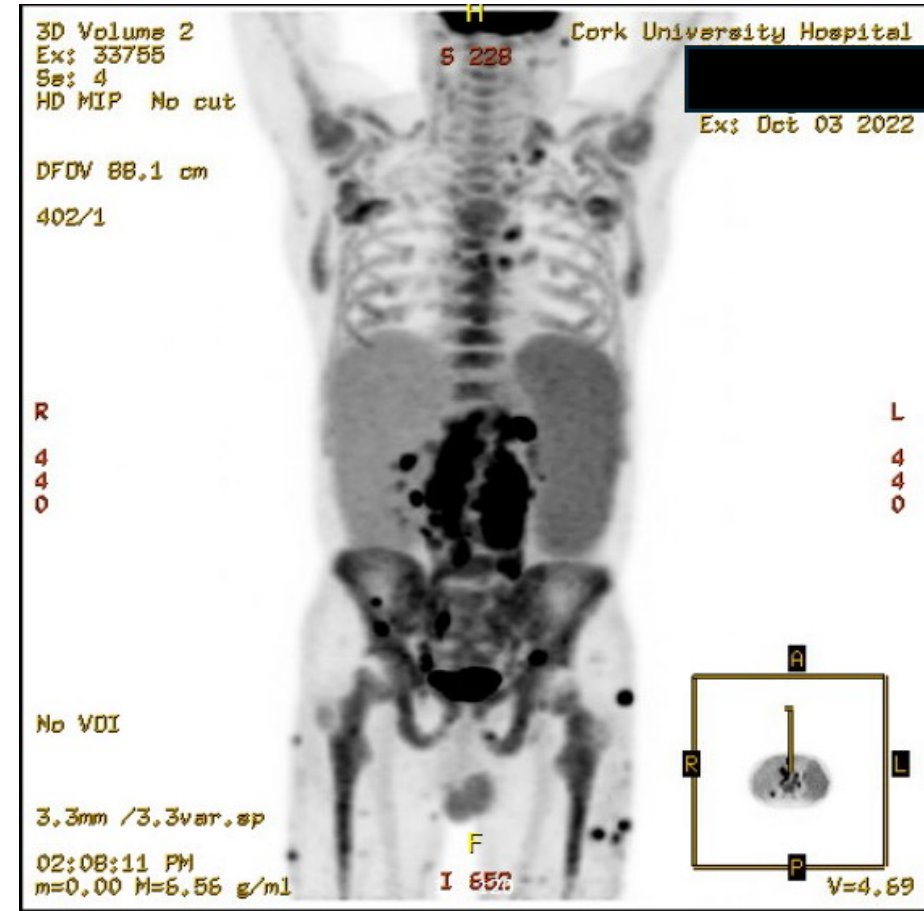
Initial PET CT

FDG avid disease above and below the diaphragm.

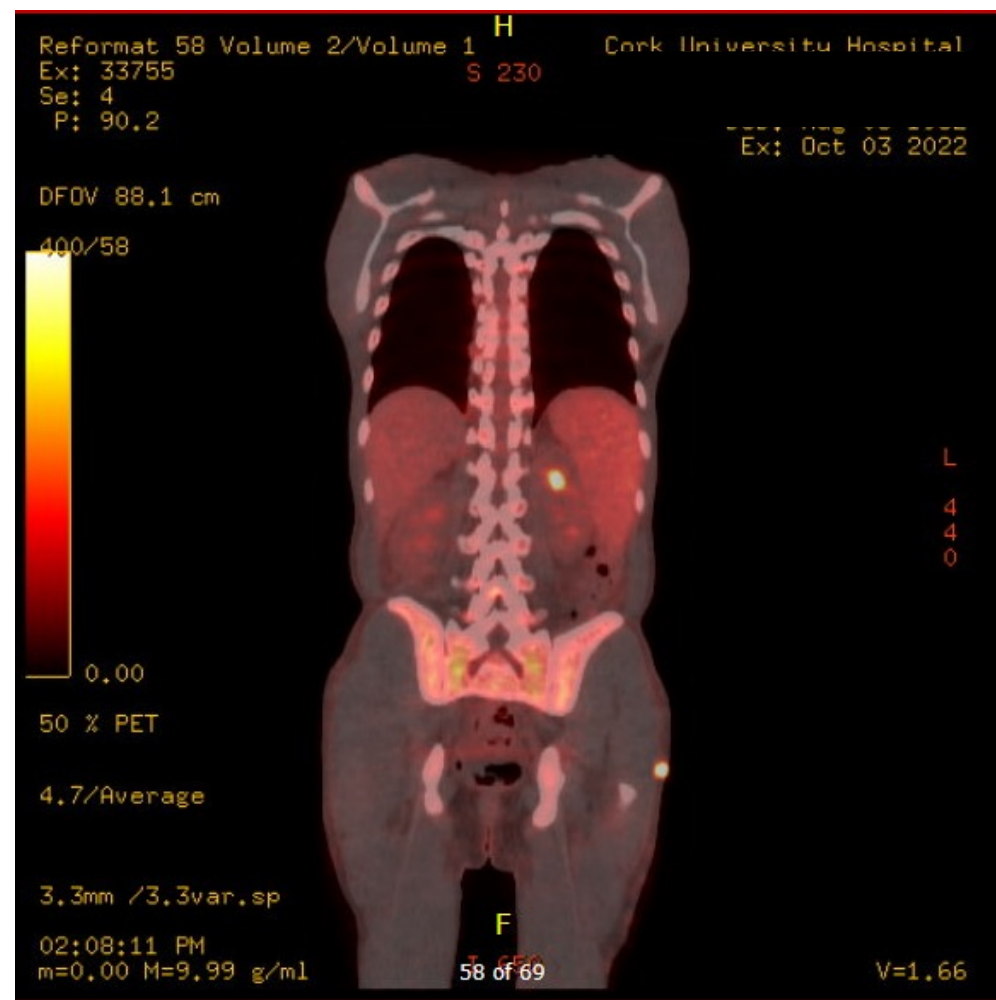
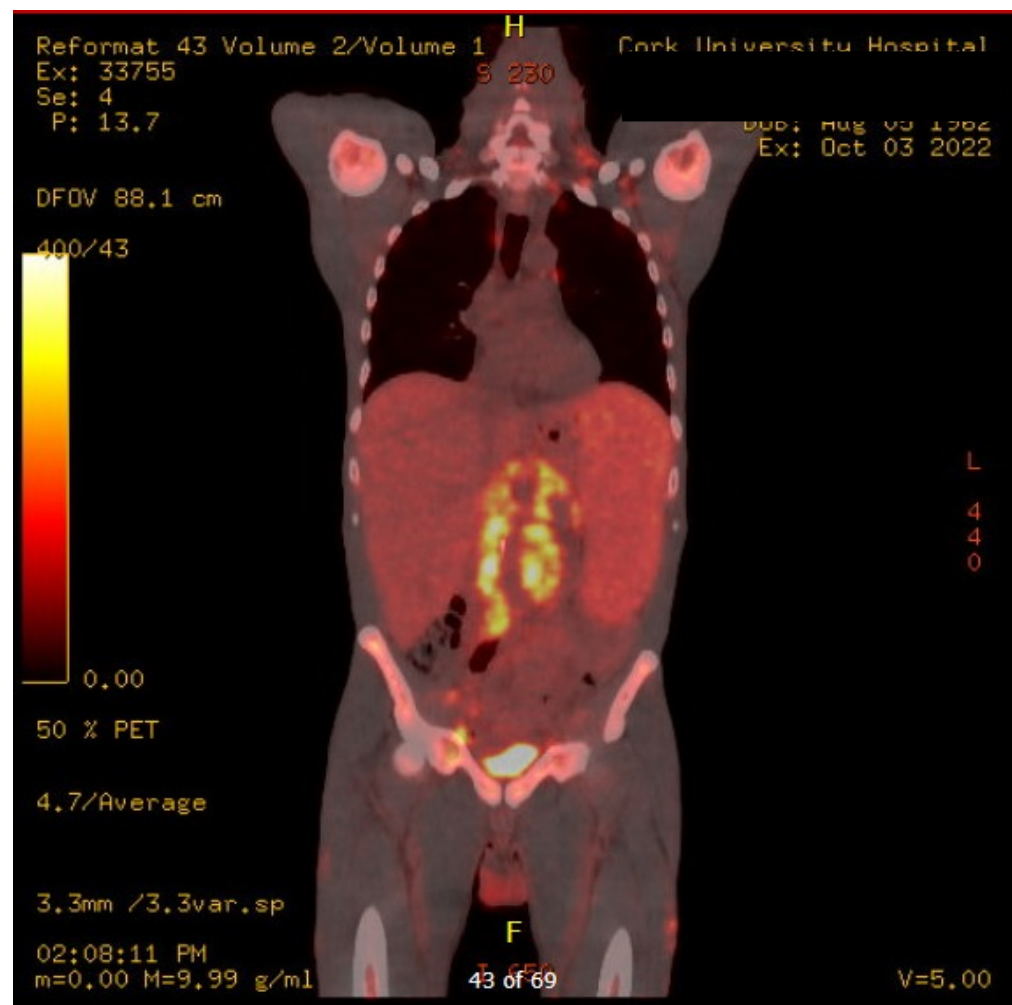
Splenic involvement with enlarged spleen.

Subcutaneous nodules overlying left hip.

Diffuse uptake throughout the marrow

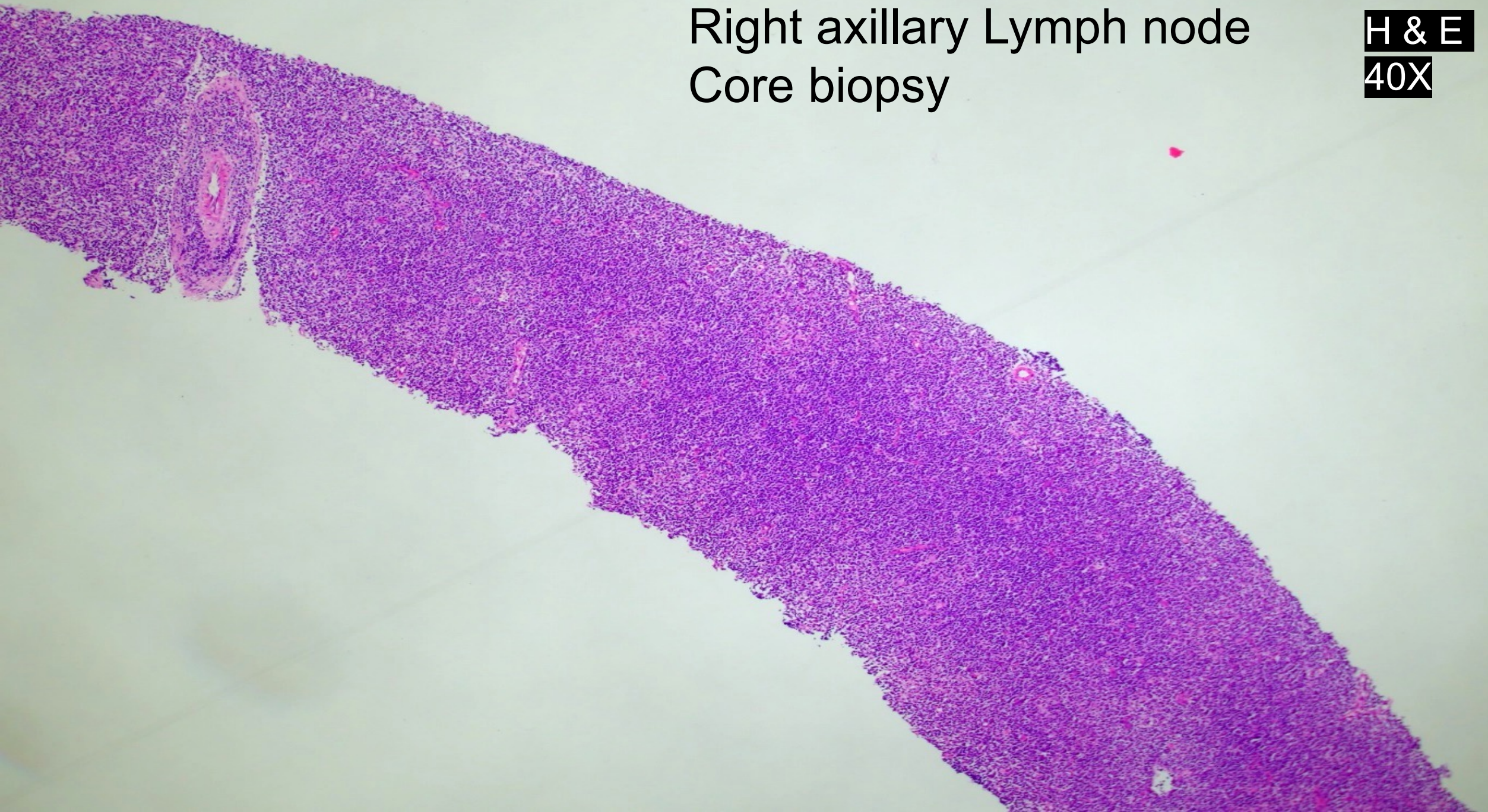


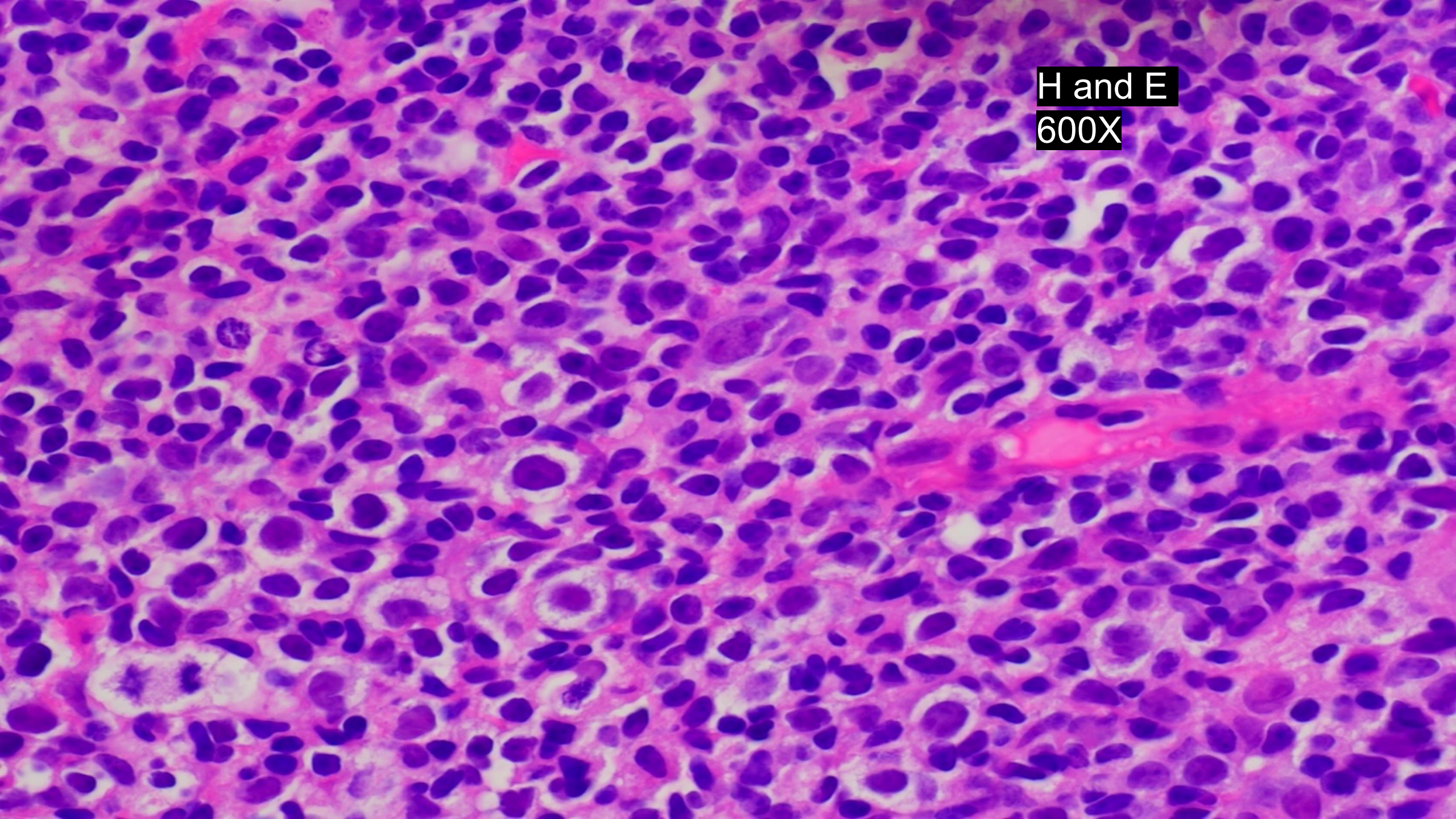
Initial PET CT



Right axillary Lymph node
Core biopsy

H & E
40X



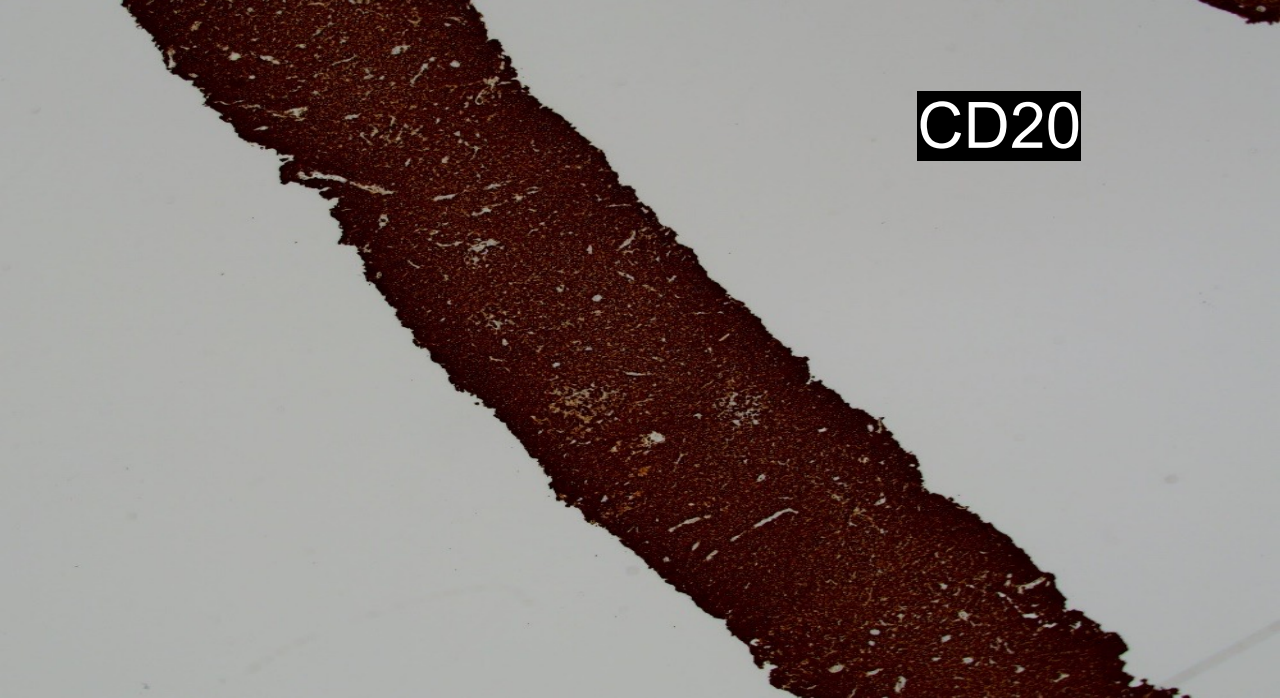


H and E
600X



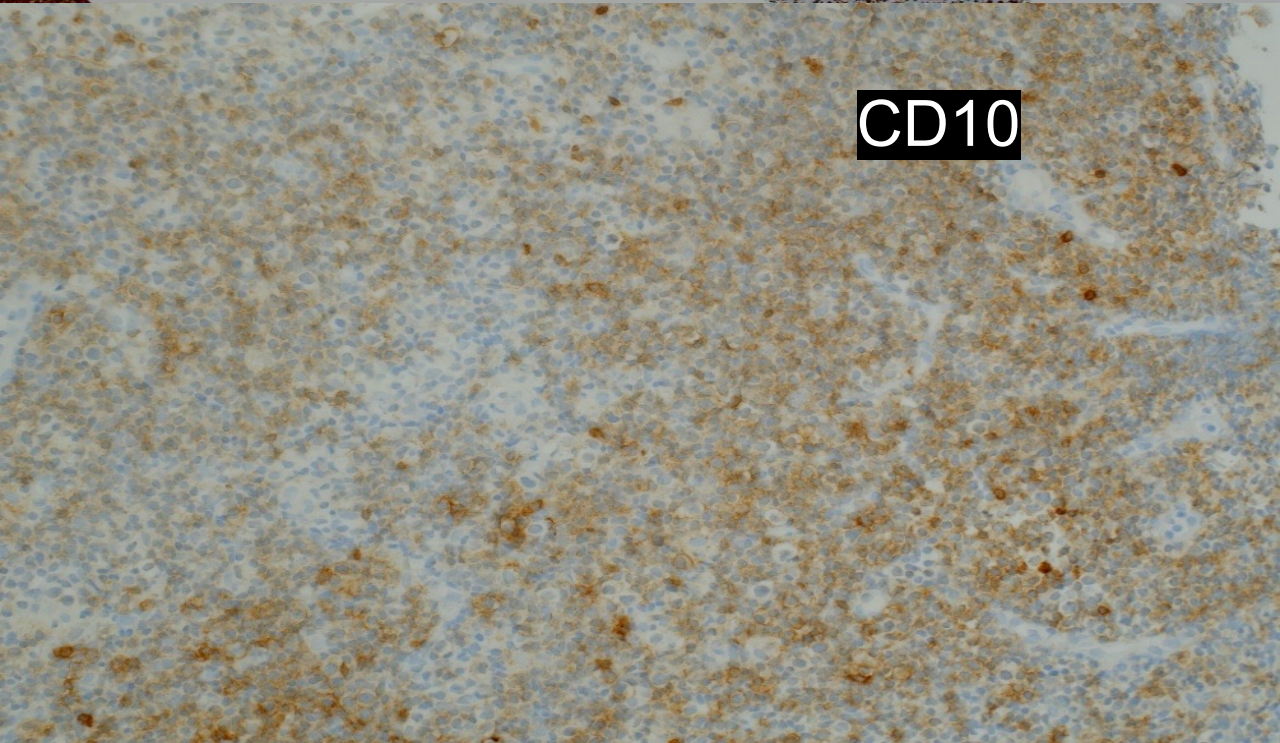
CD3

Immunohistochemistry (IHC) for CD3. The image shows a tissue section with a dense population of brown-stained cells, indicating positive CD3 expression. The staining is localized to a specific area of the tissue.



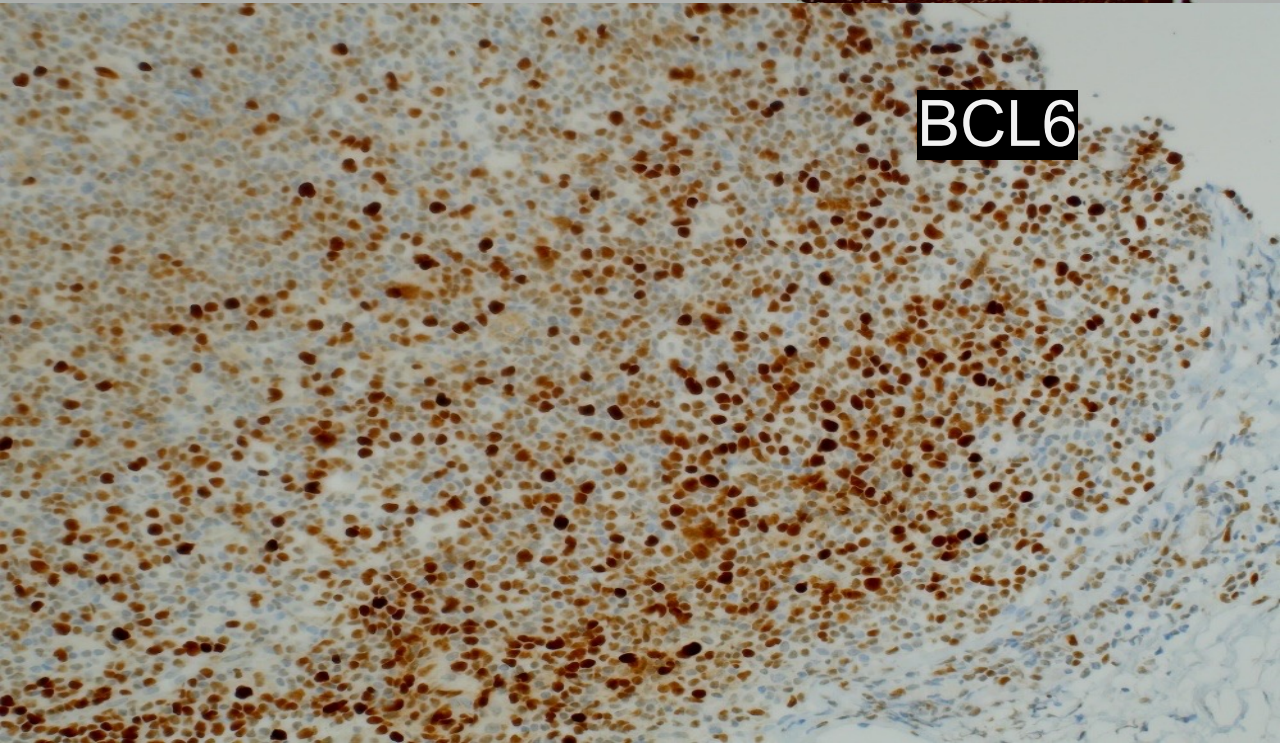
CD20

Immunohistochemistry (IHC) for CD20. The image shows a tissue section with a dense population of brown-stained cells, indicating positive CD20 expression. The staining is localized to a specific area of the tissue.



CD10

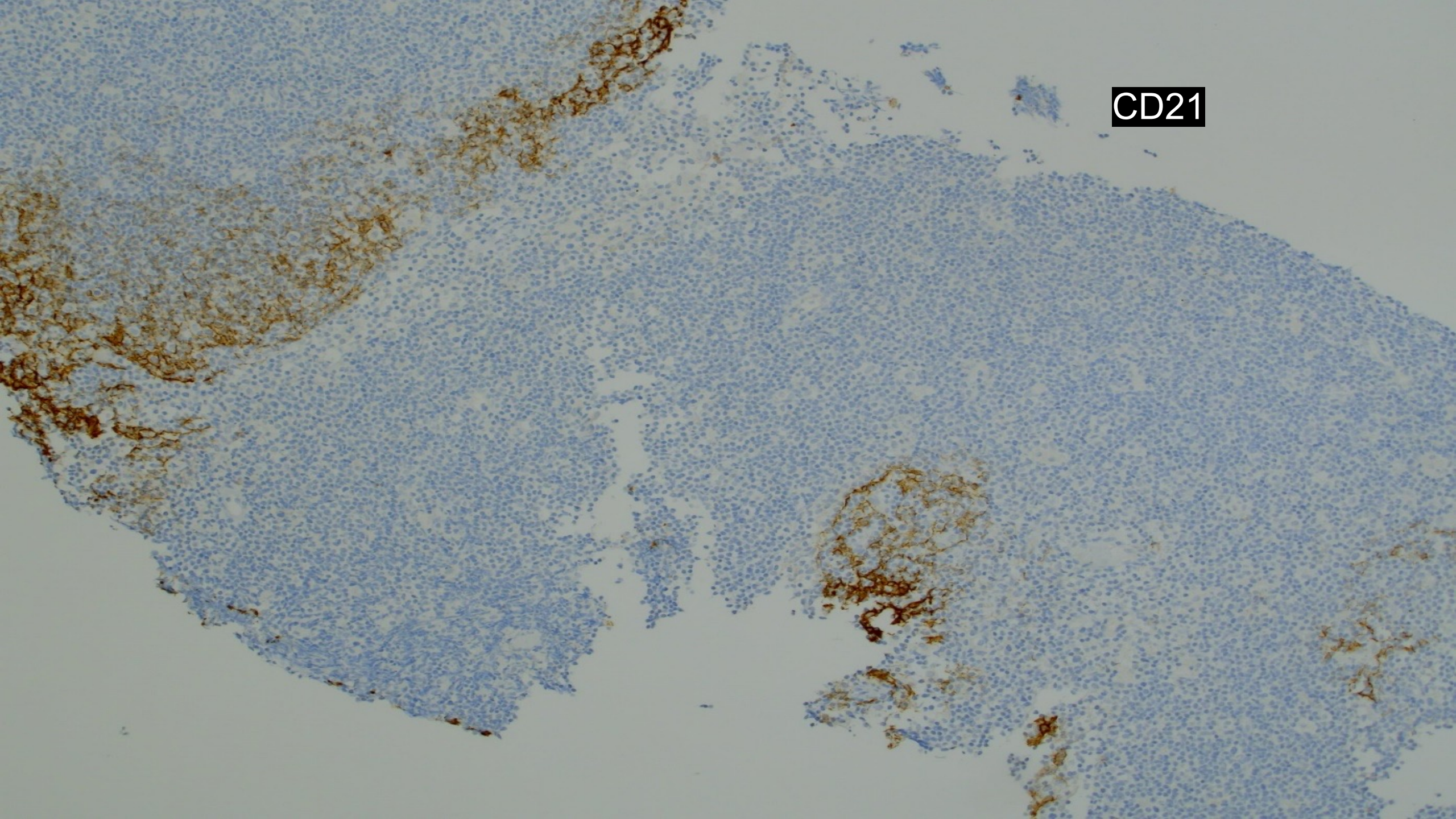
Immunohistochemistry (IHC) for CD10. The image shows a tissue section with a dense population of brown-stained cells, indicating positive CD10 expression. The staining is localized to a specific area of the tissue.



BCL6

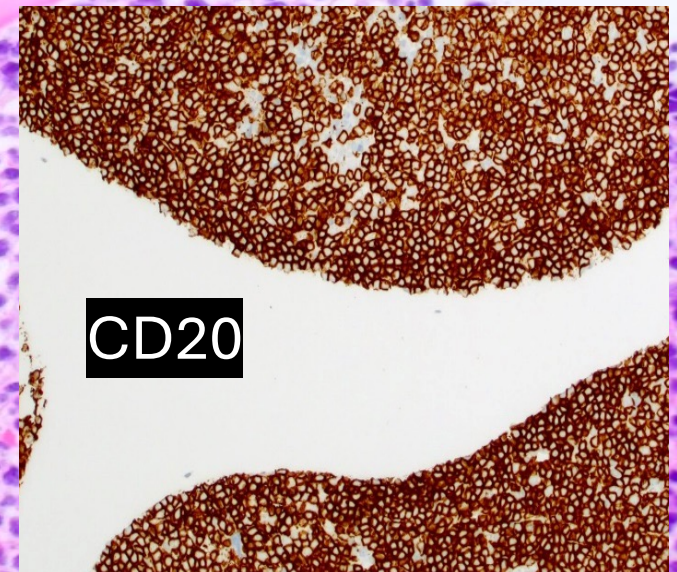
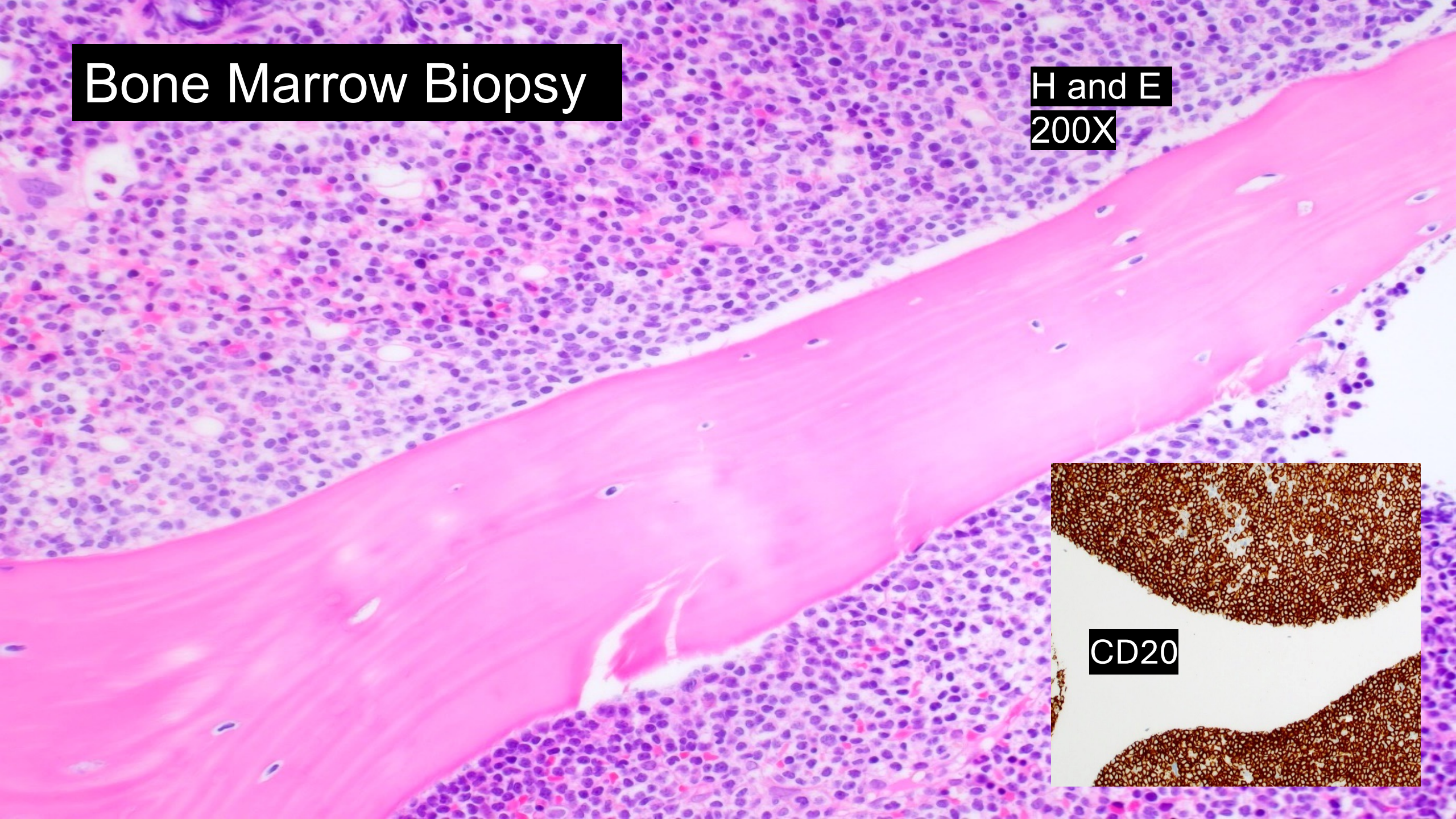
Immunohistochemistry (IHC) for BCL6. The image shows a tissue section with a dense population of brown-stained cells, indicating positive BCL6 expression. The staining is localized to a specific area of the tissue.

CD21

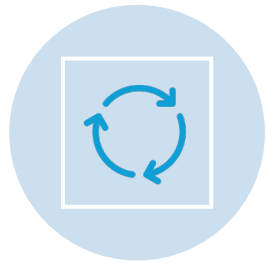


Bone Marrow Biopsy

H and E
200X



Initial Therapy



R-CHOP



Significant Red
Cell Transfusion
requirement

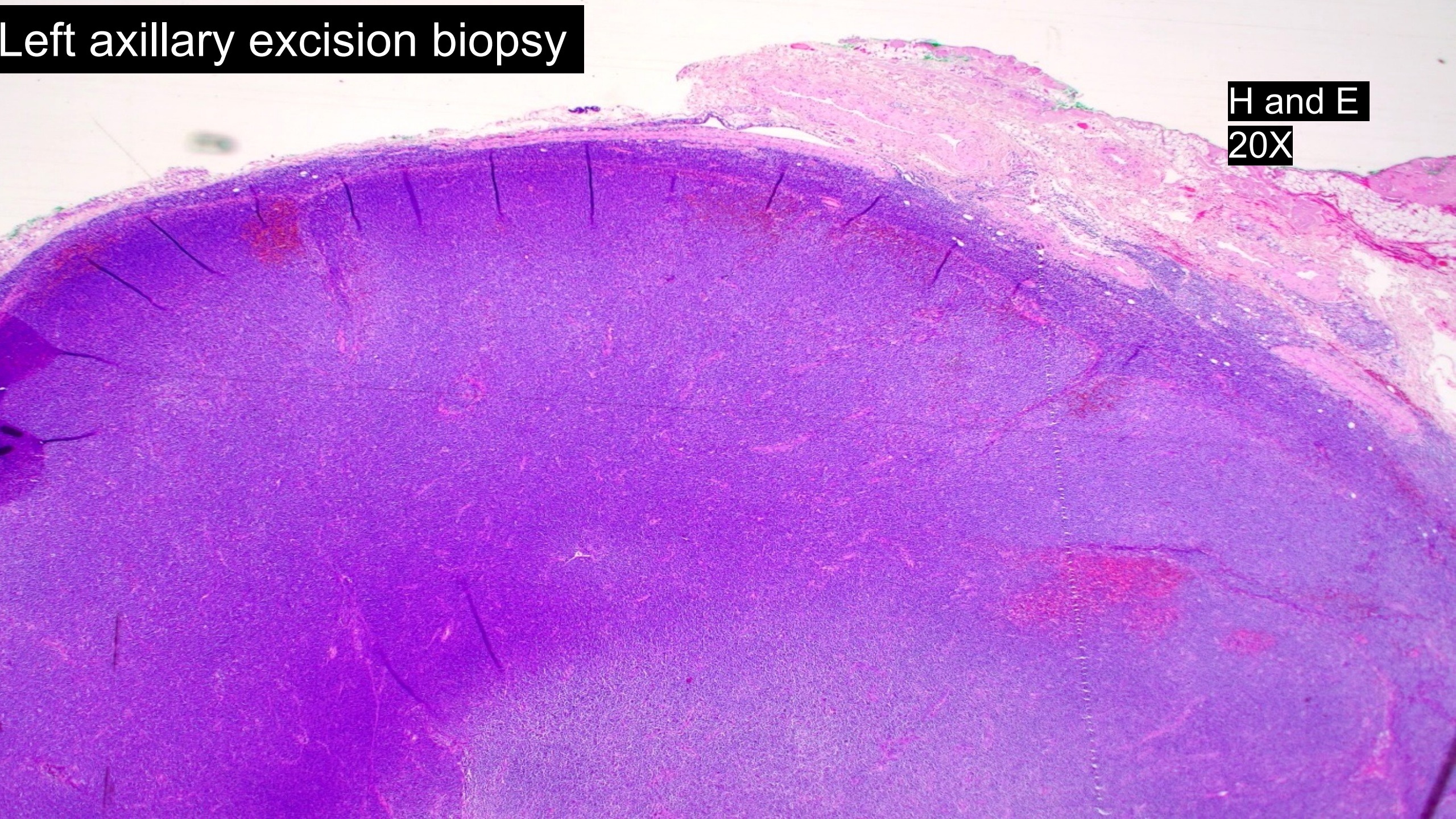
R-CHOP x2 Cycles

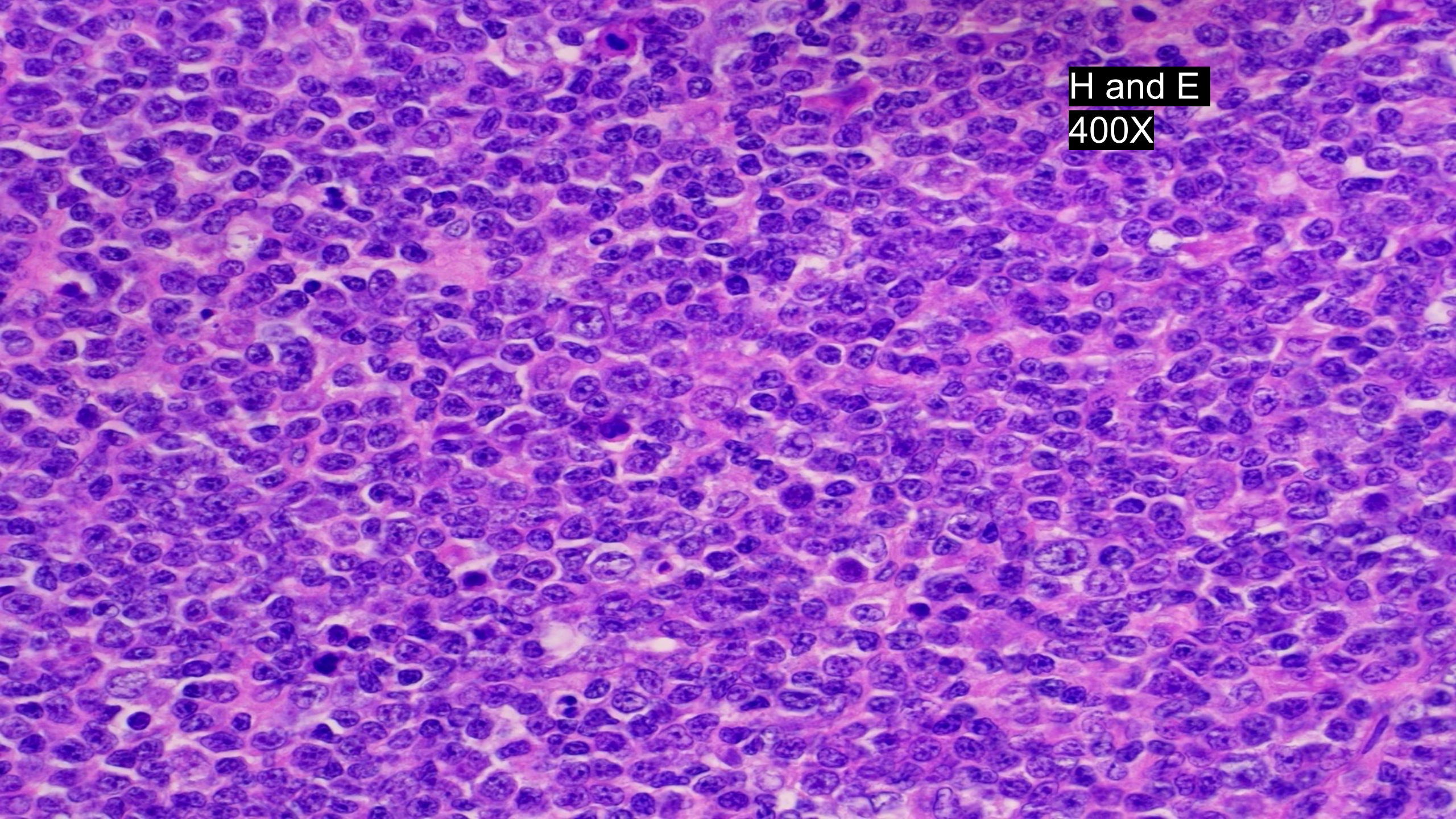


Left axillary excision biopsy

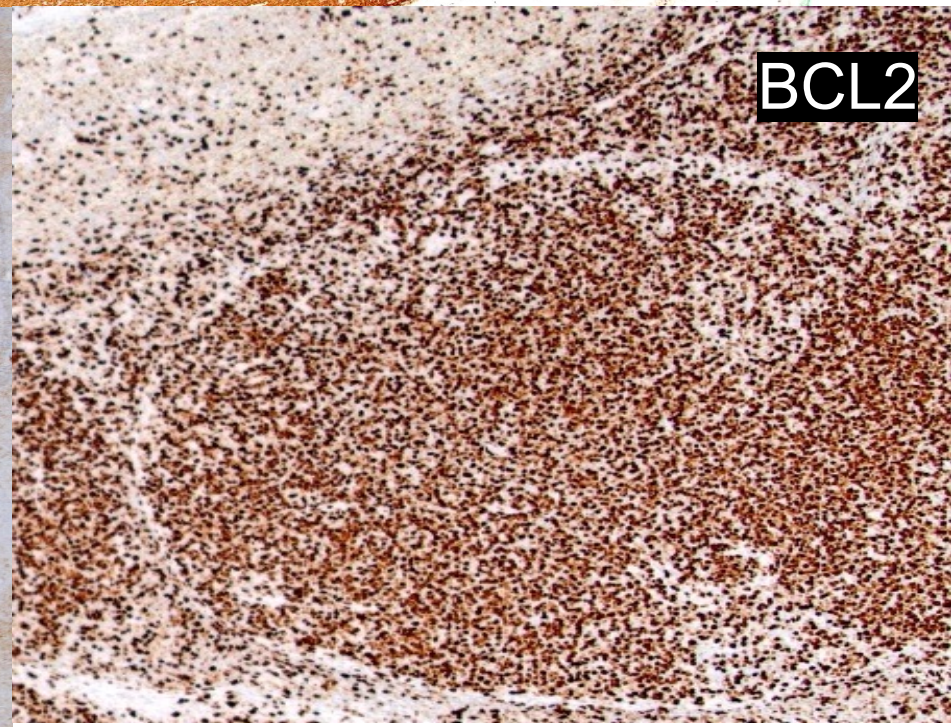
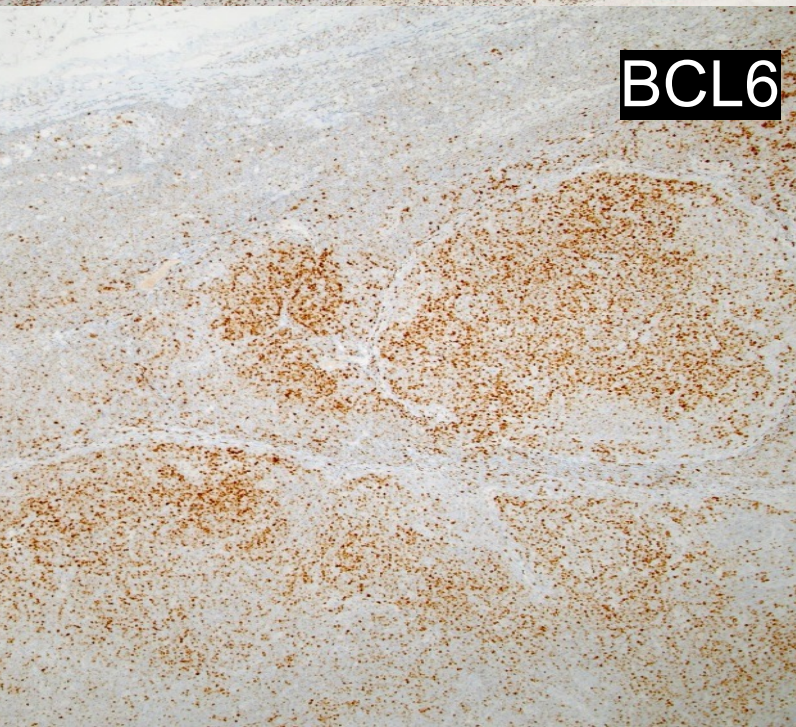
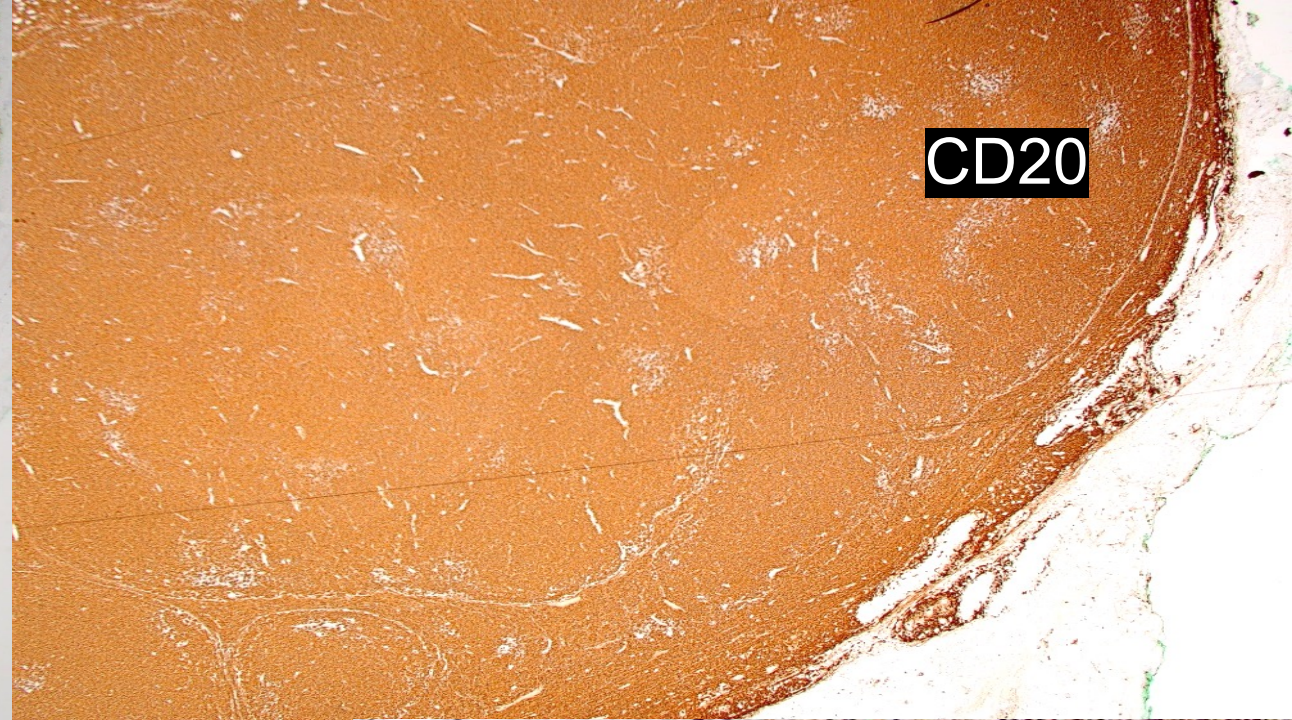
H and E

20X





H and E
400X



CD21

Ki67

FISH Analysis

- BCL2 (18q21)-Rearrangement Present

- BCL2/IGH t(14;18) Fusion-Translocation Observed

- MYC (8q24)-No Rearrangement Present

- MYC/IGH t(8;14) Fusion-No Translocation Observed

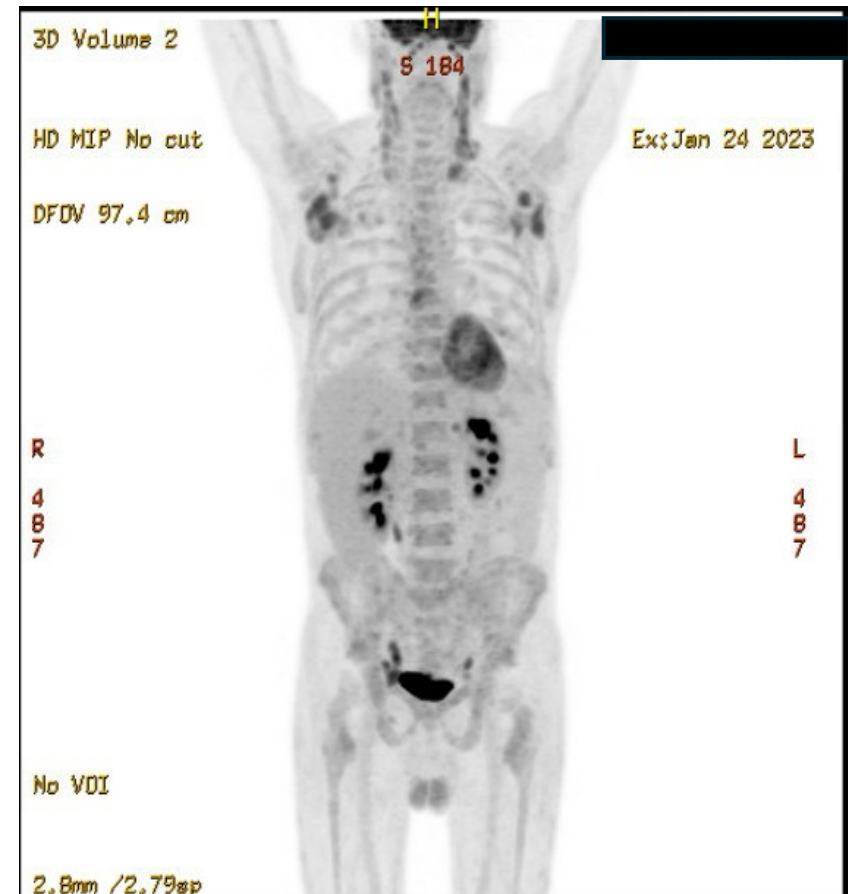
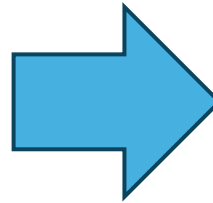
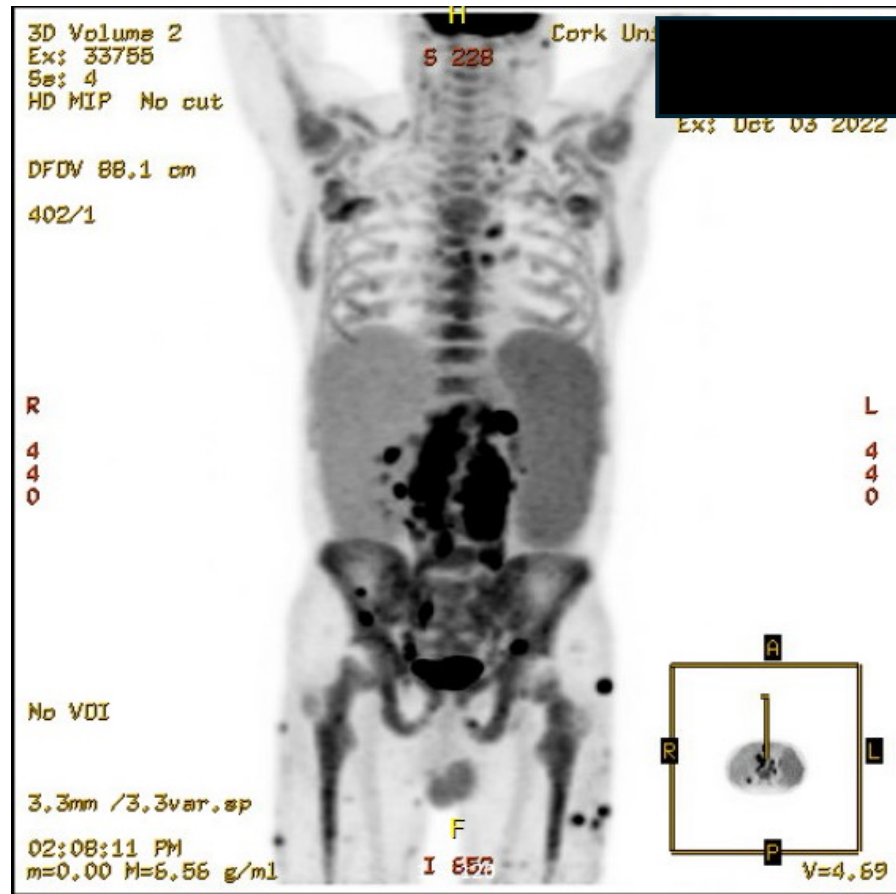
- BCL6 (3q27)-No Rearrangement Present

- DUSP22/IRF4-No Rearrangement Present

R-ICE

- Reduction in lymphadenopathy and splenomegaly
- Reduction in transfusion dependence

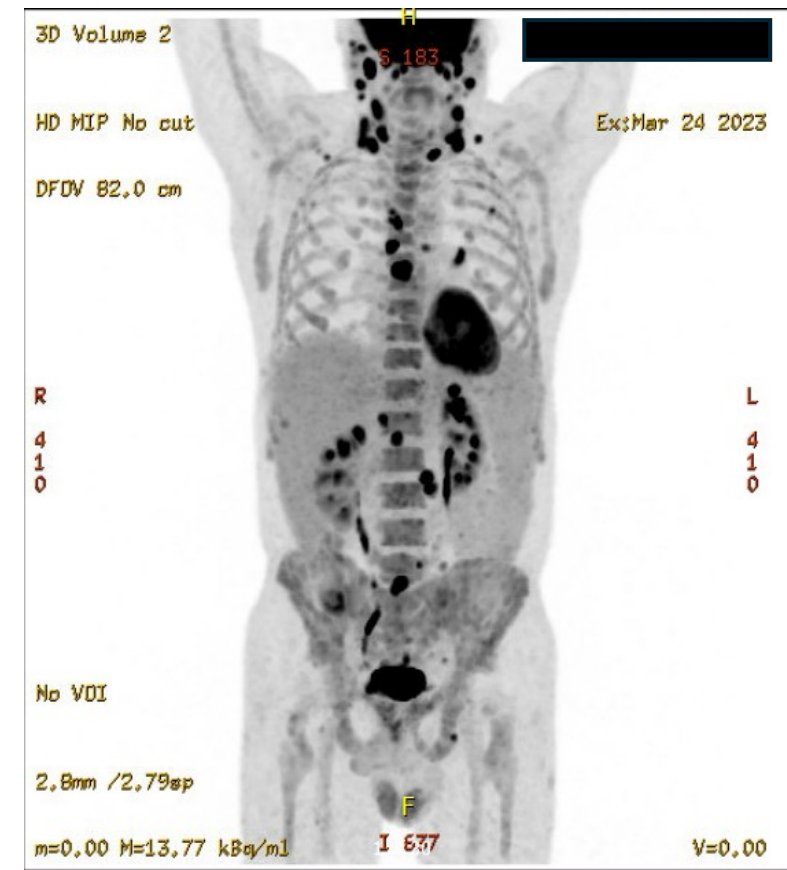
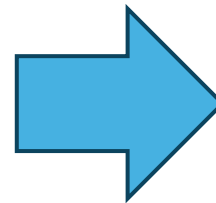
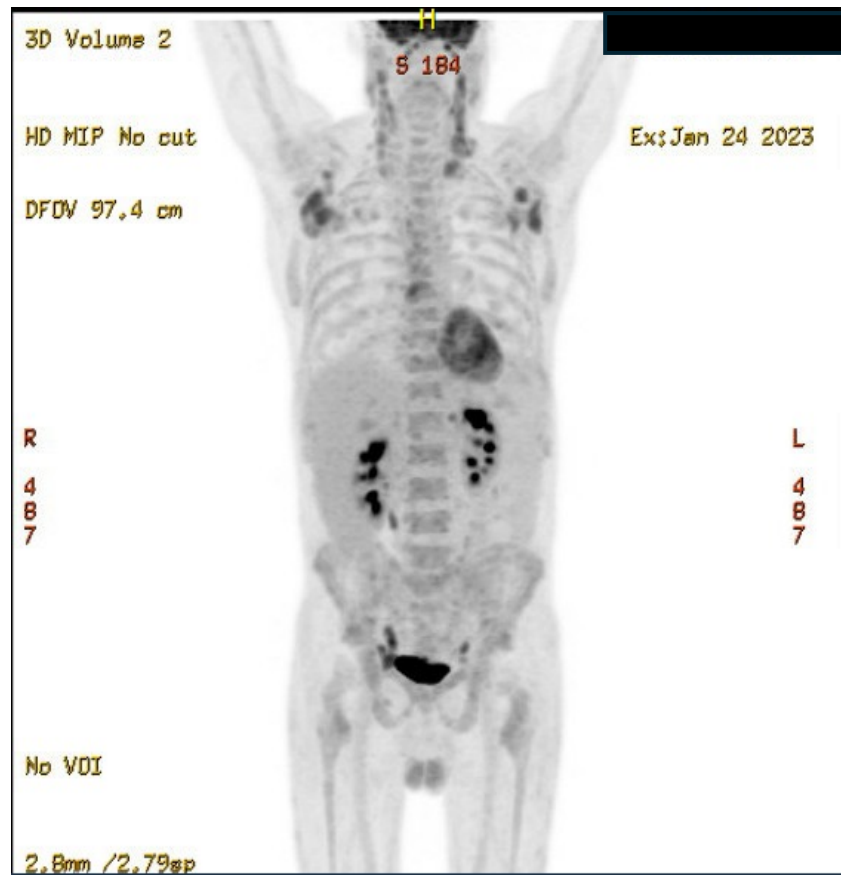
Initial PET vs PET Post Cycle 2 R-ICE



Post Cycle 4 R-ICE

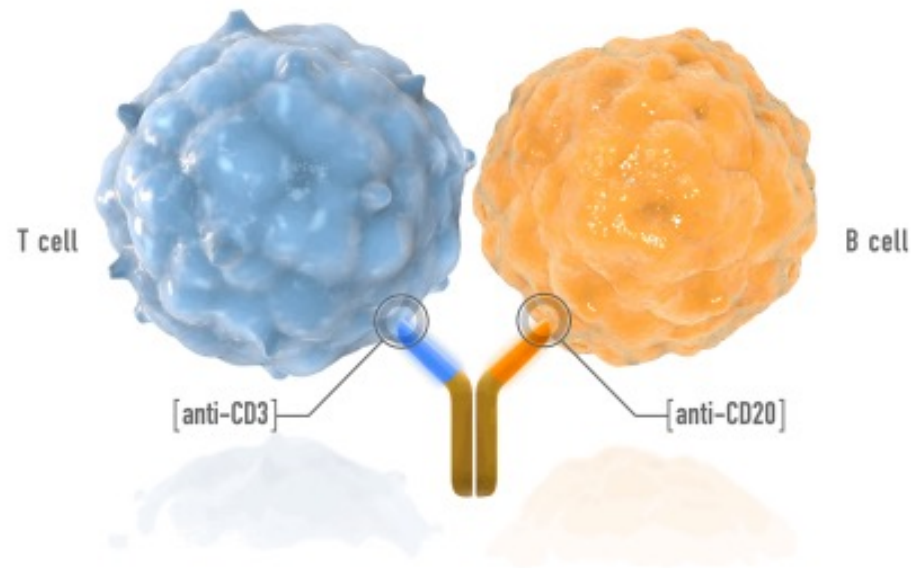
- Rapidly enlarging cervical lymphadenopathy

PET Post C2 R-ICE vs C4 R-ICE



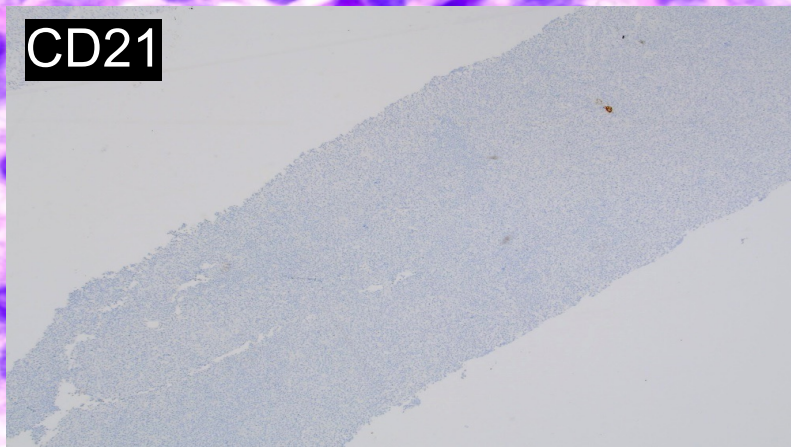
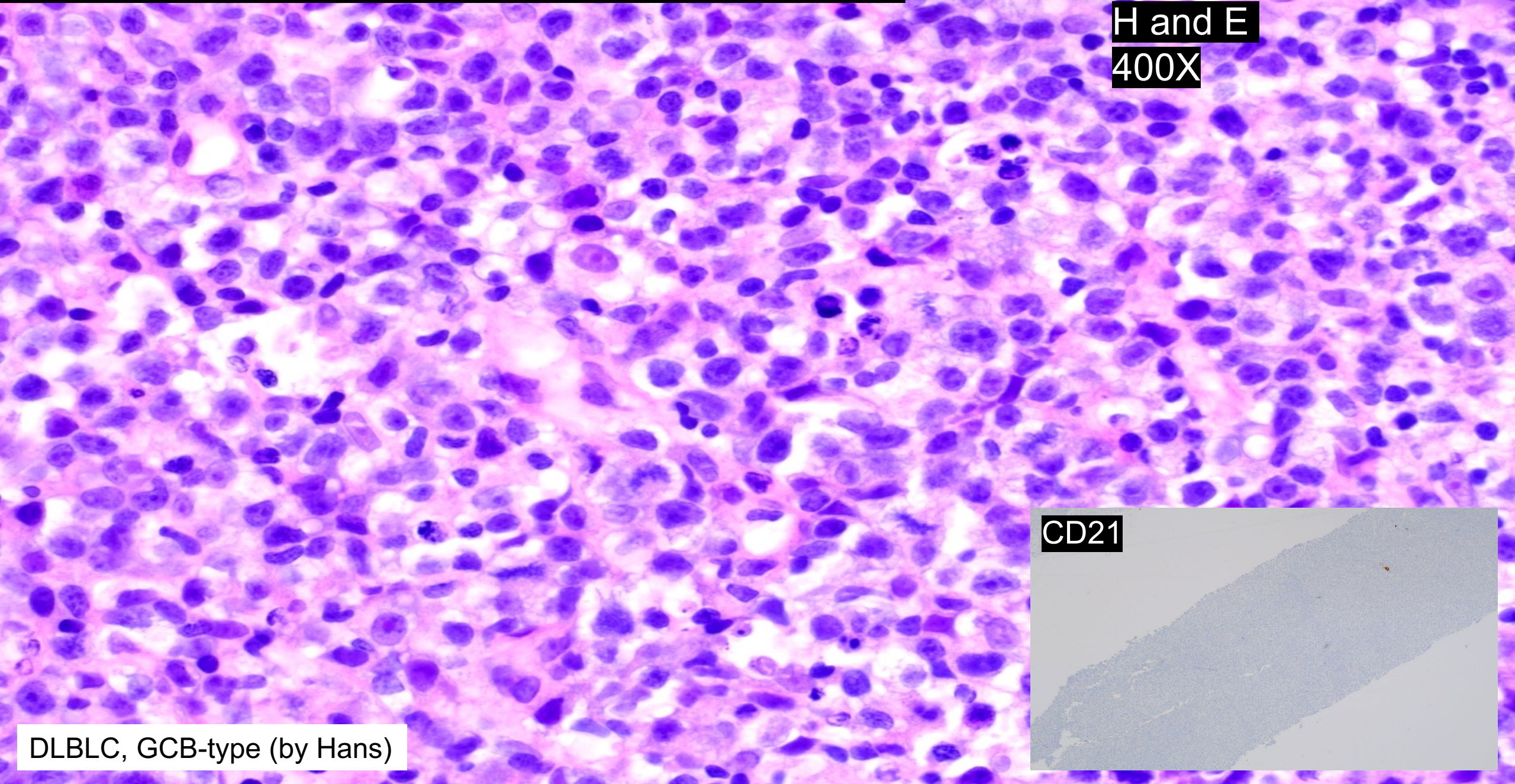
Third Line Treatment

- Rituximab and Lenalidomide
- Application for Mosunetuzumab (CD3-CD20 Bispecific antibody)
- Referral made for consideration of Cellular Therapy



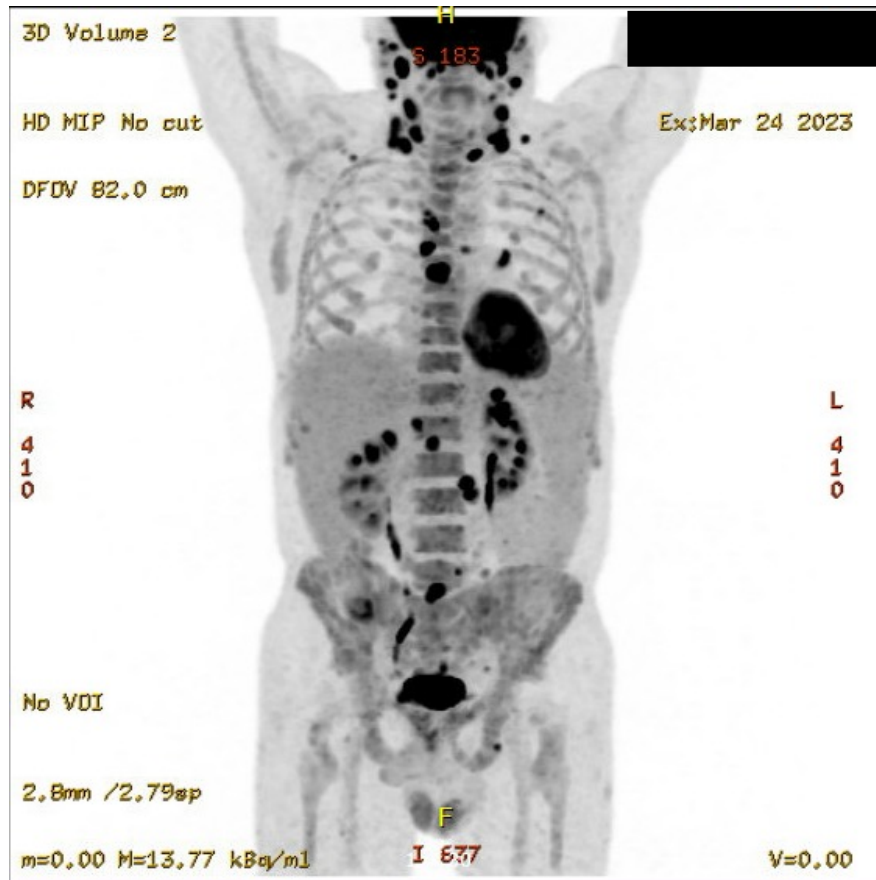
Right Cervical Lymph node Core Biopsy

H and E
400X



DLBLC, GCB-type (by Hans)

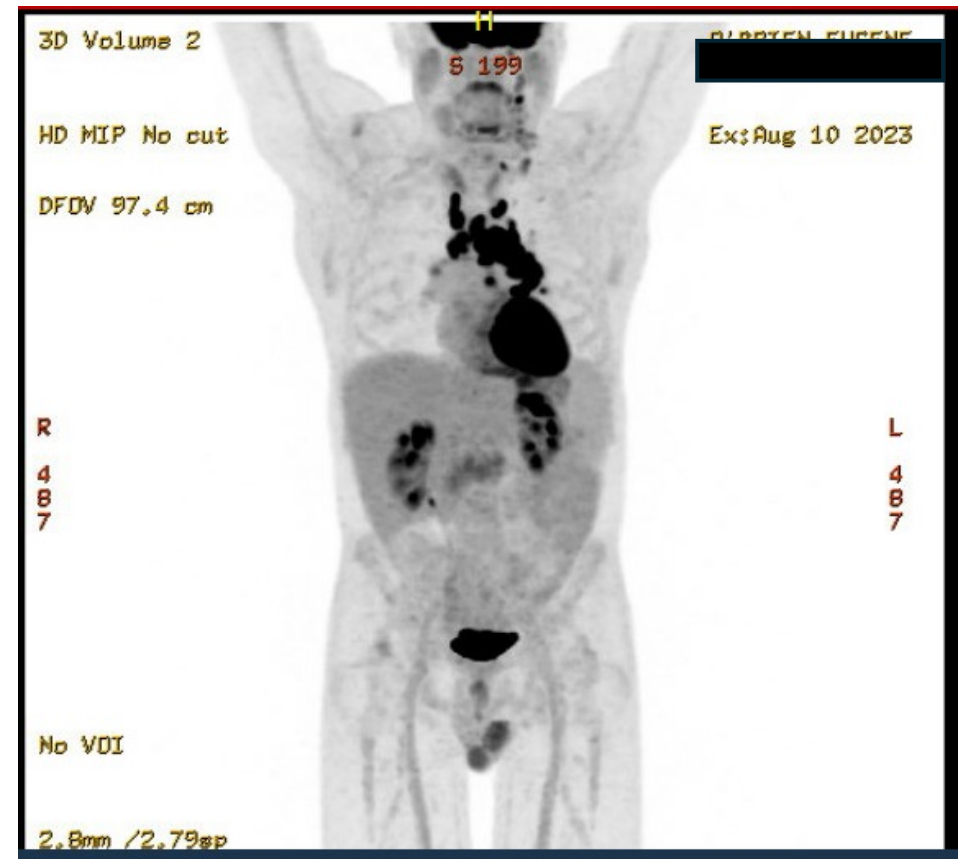
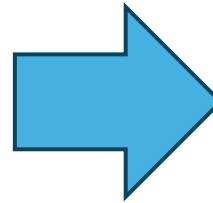
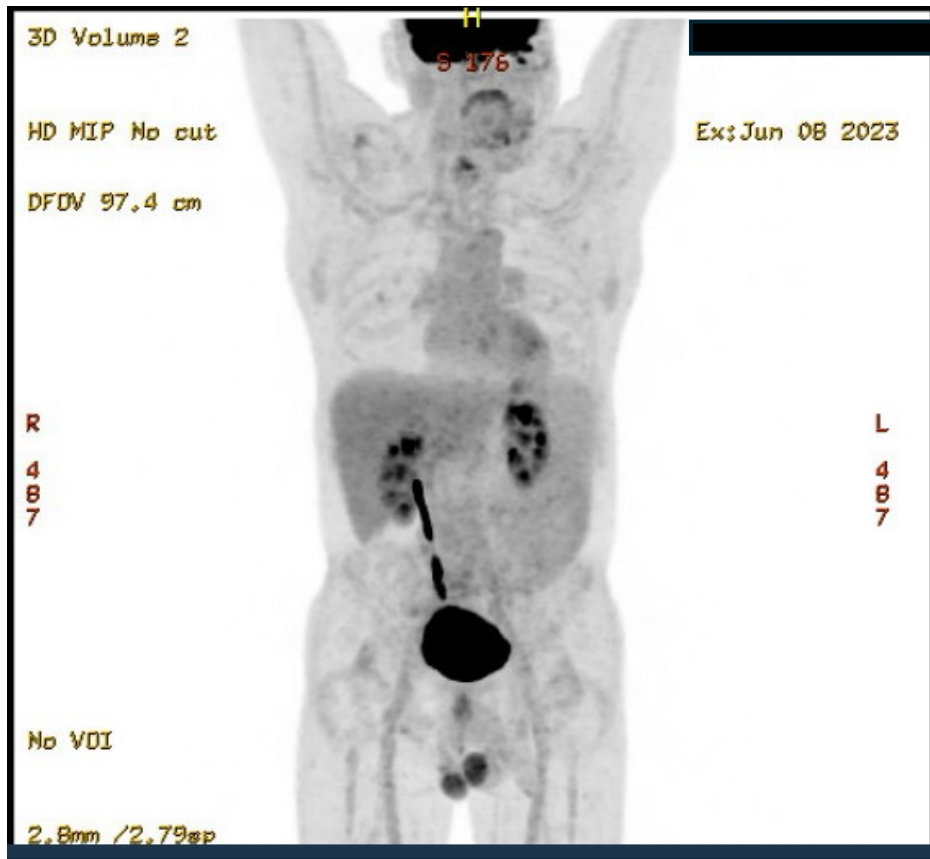
Pre Mosunetuzumab vs Post 2 Cycles



Mosunetuzamab x 4 Cycles

- Admitted to CUH for pre CAR T-cell workup

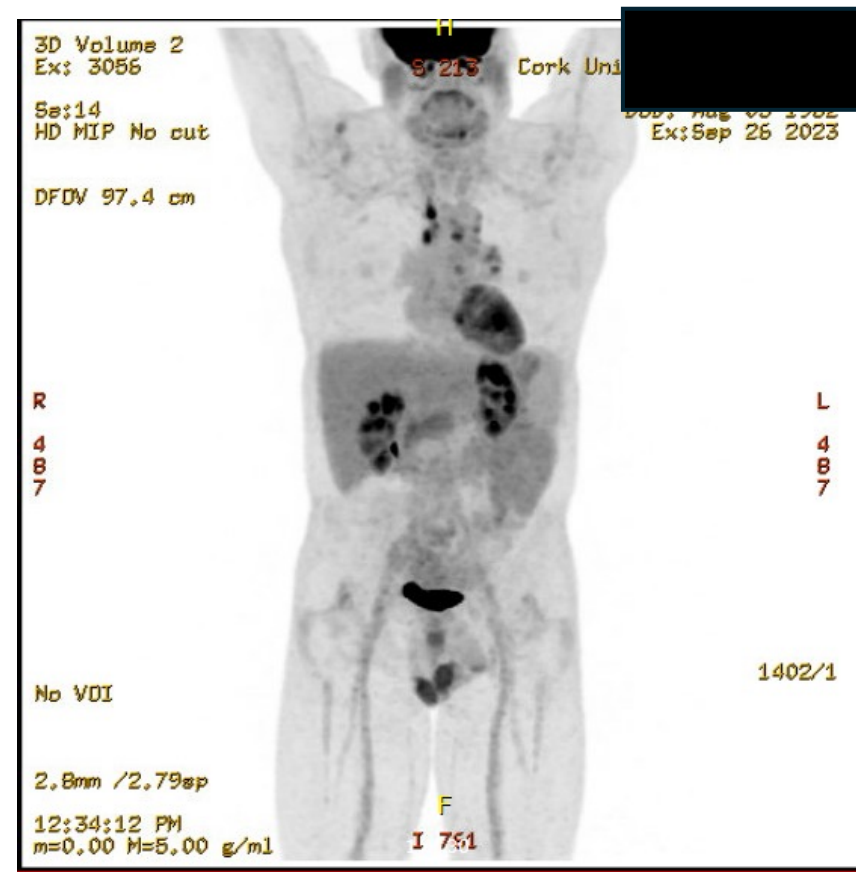
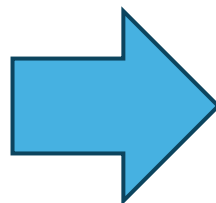
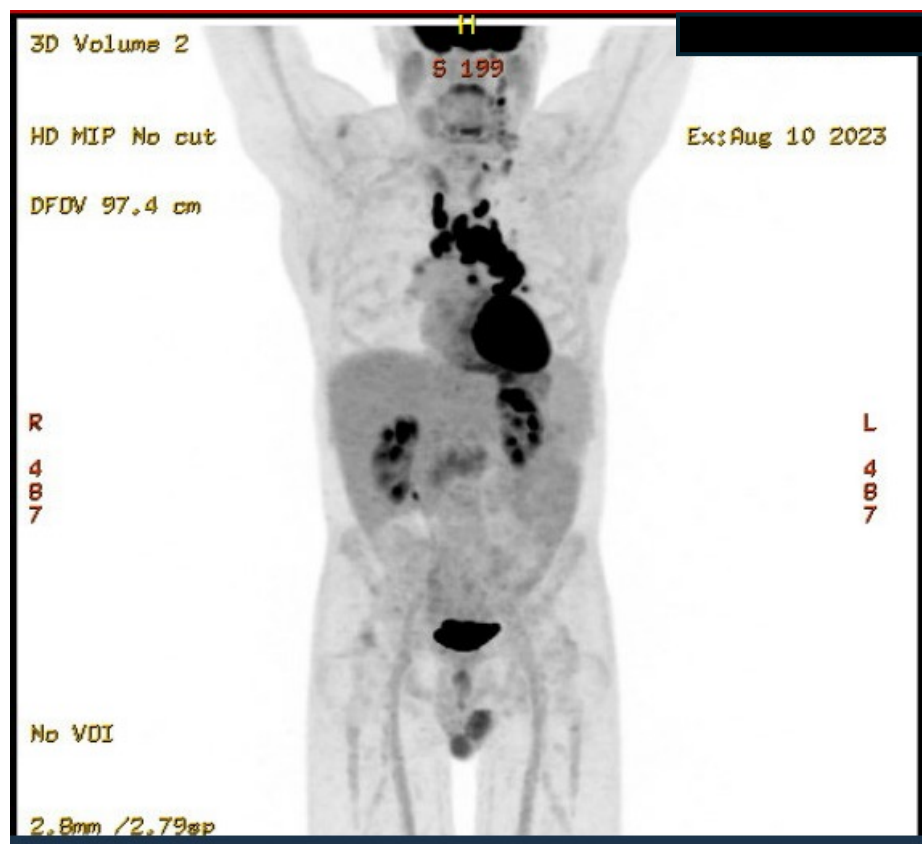
PET post C2 Mosunetuzumab vs Pre CAR T PET



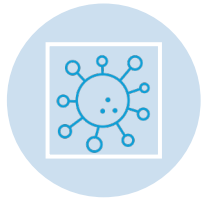
5th line Therapy

- CAR T -cell therapy postponed
- Polatuzumab, Bendamustine and Rituximab

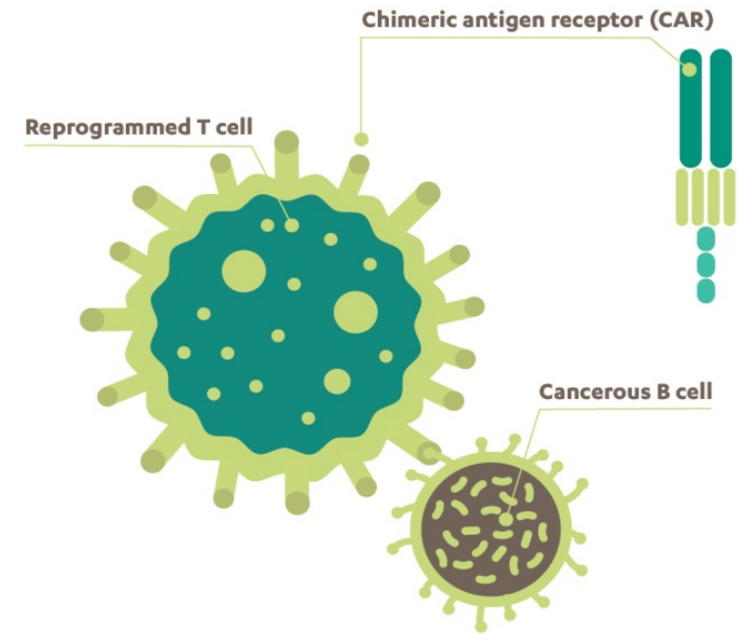
Pre and Post Pola BR



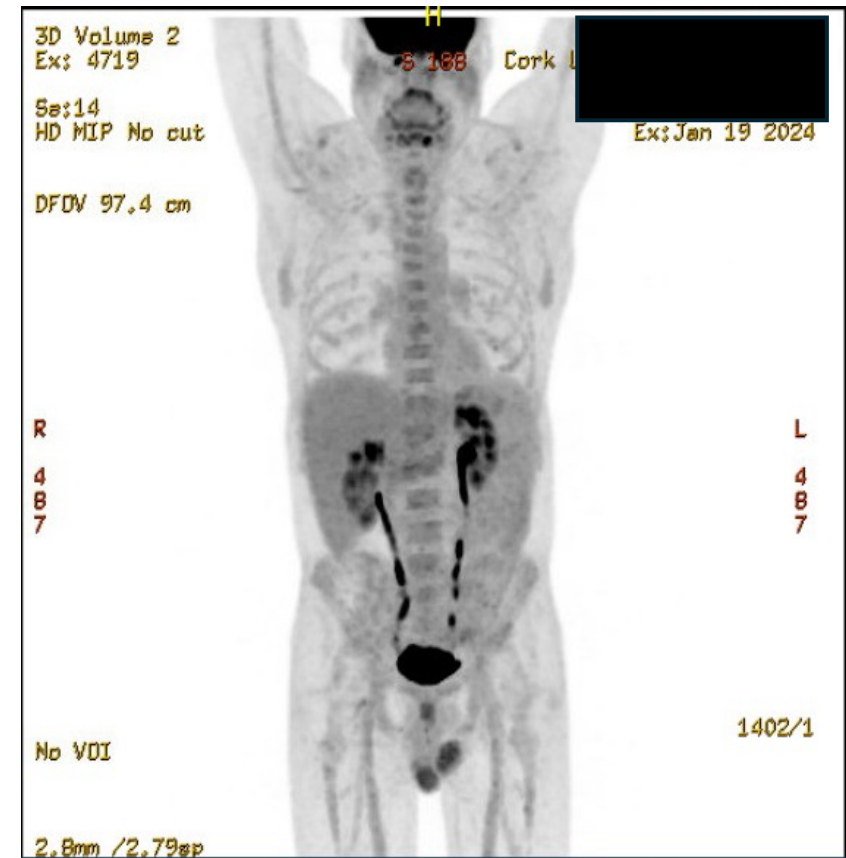
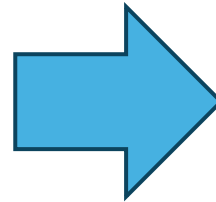
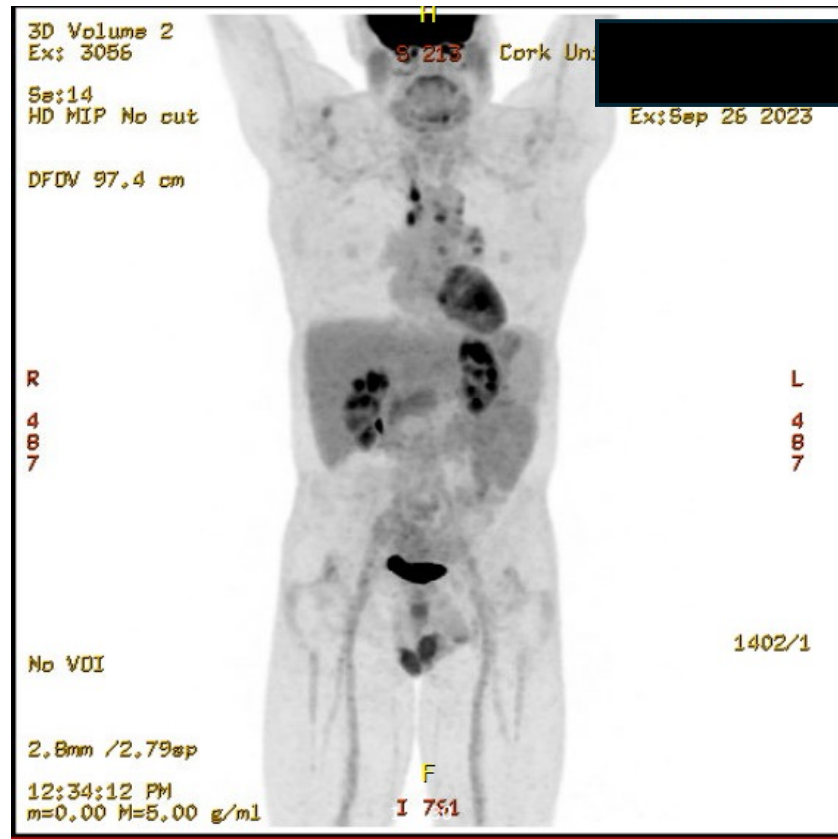
Kymriah (Tisagenlecleucel)



CD19
directed
CAR T- cell
therapy



PET Pre and Post CAR T-cell

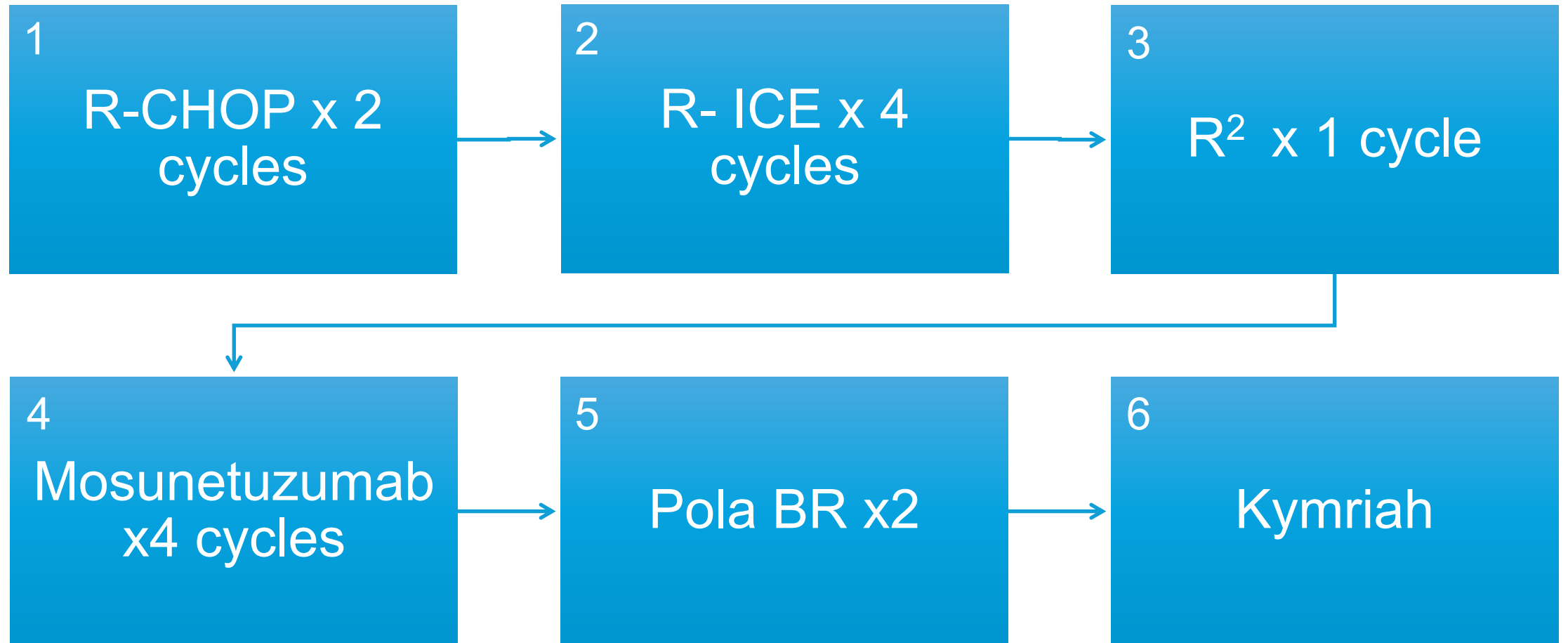




Ongoing Follow Up

- Remains in clinical remission 1 year post CAR T-cell therapy
 - Recurrent infections requiring Immunoglobulin replacement
-

Summary of treatment





Follicular Lymphoma with Unusual Cytological Features

- Cells are either medium-sized blastoid cells or large centrocytes
 - Evidence suggests a clinical course that is inferior to classic Follicular Lymphoma
 - Cases often show higher proliferation indices and/or uncommon phenotypes such as negativity for CD10 or (strong) expression of MUM1
-

Mosunetuzumab in DLBCL

CLINICAL TRIALS AND OBSERVATIONS | AUGUST 25, 2023

Mosunetuzumab monotherapy is active and tolerable in patients with relapsed/refractory diffuse large B-cell lymphoma

 Clinical Trials & Observations

Nancy L. Bartlett, Sarit Assouline, Pratyush Giri, Stephen J. Schuster, Chan Y. Cheah, Matthew Matasar, Gareth P. Gregory, Dok Hyun Yoon, Mazyar Shadman, Keith Fay, Sung-Soo Yoon, Carlos Panizo, Ian Flinn, Anna Johnston, Francesco Bosch, Laurie H. Sehn, Michael C. Wei, Shen Yin, Iris To, Chi-Chung Li, Huang Huang, Antonia Kwan, Elicia Penuel, Lihua E. Budde



Blood Adv (2023) 7 (17): 4926–4935.

<https://doi.org/10.1182/bloodadvances.2022009260>

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Mosunetuzumab with polatuzumab vedotin in relapsed or refractory aggressive large B cell lymphoma: a phase 1b/2 trial

[Lihua E. Budde](#) , [Adam J. Olszewski](#), [Sarit Assouline](#), [Izidore S. Lossos](#), [Catherine Diefenbach](#), [Manali Kamdar](#), [Nilanjan Ghosh](#), [Dipenkumar Modi](#), [Waleed Sabry](#), [Seema Naik](#), [Amitkumar Mehta](#), [Shazia K. Nakhoda](#), [Stephen D. Smith](#), [Kathleen Dorritie](#), [Ting Jia](#), [Song Pham](#), [Ling-Yuh Huw](#), [Jing Jing](#), [Hao Wu](#), [Wahib S. Ead](#), [Iris To](#), [Connie Lee Batlevi](#), [Michael C. Wei](#) & [Julio C. Chavez](#) 

Nature Medicine **30**, 229–239 (2024) | [Cite this article](#)

Real-World Outcomes in Patients with Transformed Follicular Lymphoma Treated with CD19-Targeting CAR-T Therapy

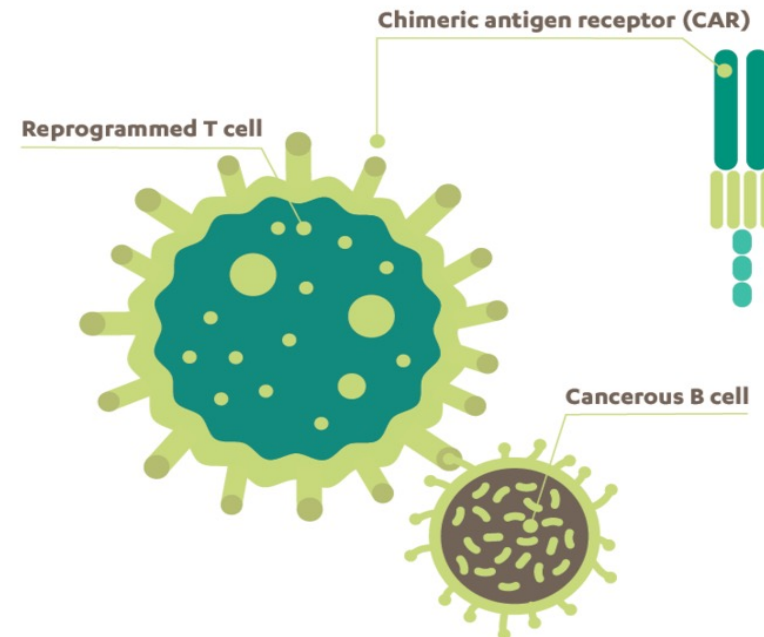
Alfredo Rivas-Delgado, Efrat Luttwak, Esther Drill, Ilan Goldstein, Ivan Landego, Ana Alarcon Tomas, Allison Parascondola, Amethyst Saldia, Philip Caron, Parastoo B. Dahi, Zachary D. Epstein-Peterson, Lorenzo Falchi, Paul A. Hamlin, William Johnson, Anita Kumar, Richard J. Lin, Jennifer Kimberly Lue, Colette Owens, Ariela Noy, Michael Scordo, Ahmet Dogan, Venkatraman Seshan, Andrew D. Zelenetz, Miguel-Angel Perales, Roni Shouval, Maria Lia Palomba, Gunjan L. Shah, Gilles Salles



Blood (2023) 142 (Supplement 1): 4888.

<https://doi.org/10.1182/blood-2023-187379>

- ORR 87%
- CR 67%





Conclusion

- Follicular lymphoma is a heterogenous disease
 - Histologic diagnosis in combination with clinical picture
 - Vigilance for high grade transformation – repeat biopsy
 - Novel therapies with Mosunetuzumab and Kymriah (Tisagenlecleucel) critical in this case achieving remission
-



Thank You

References

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