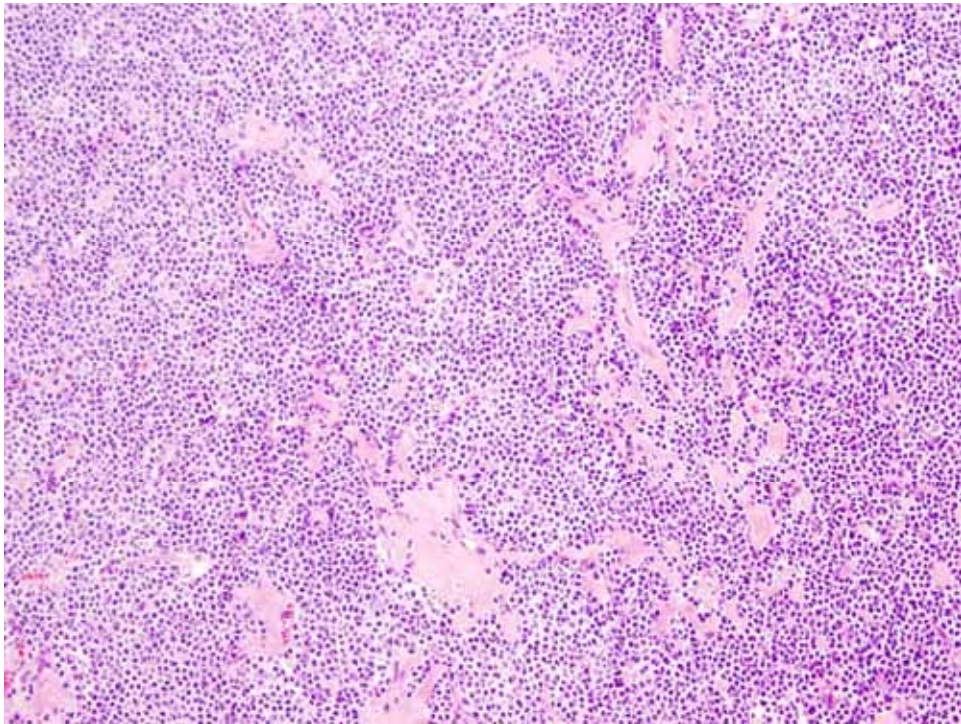
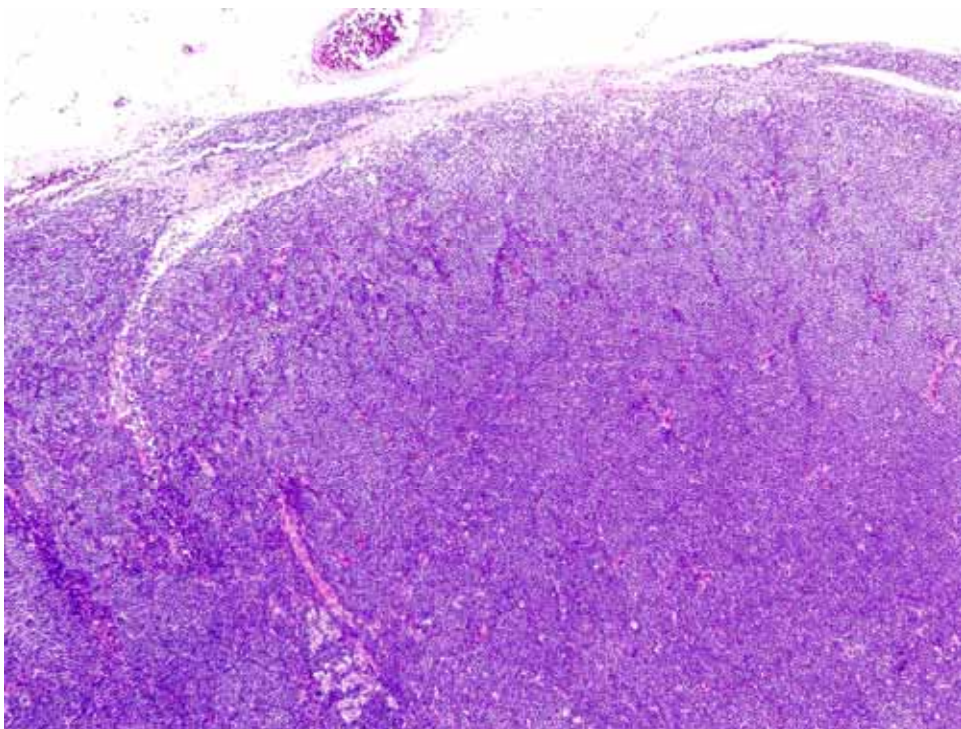


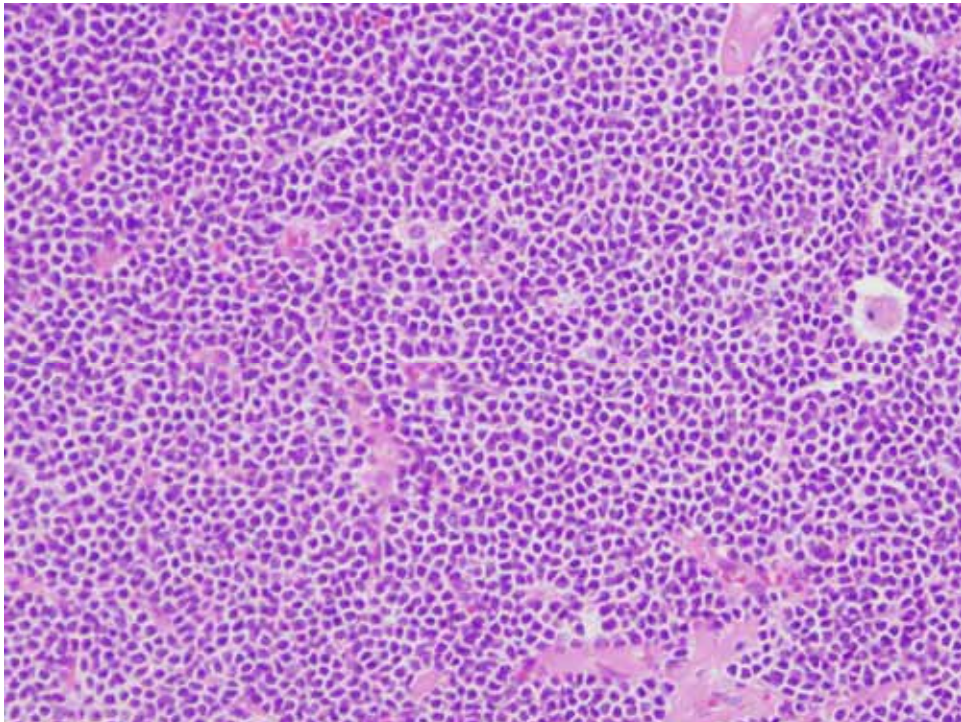
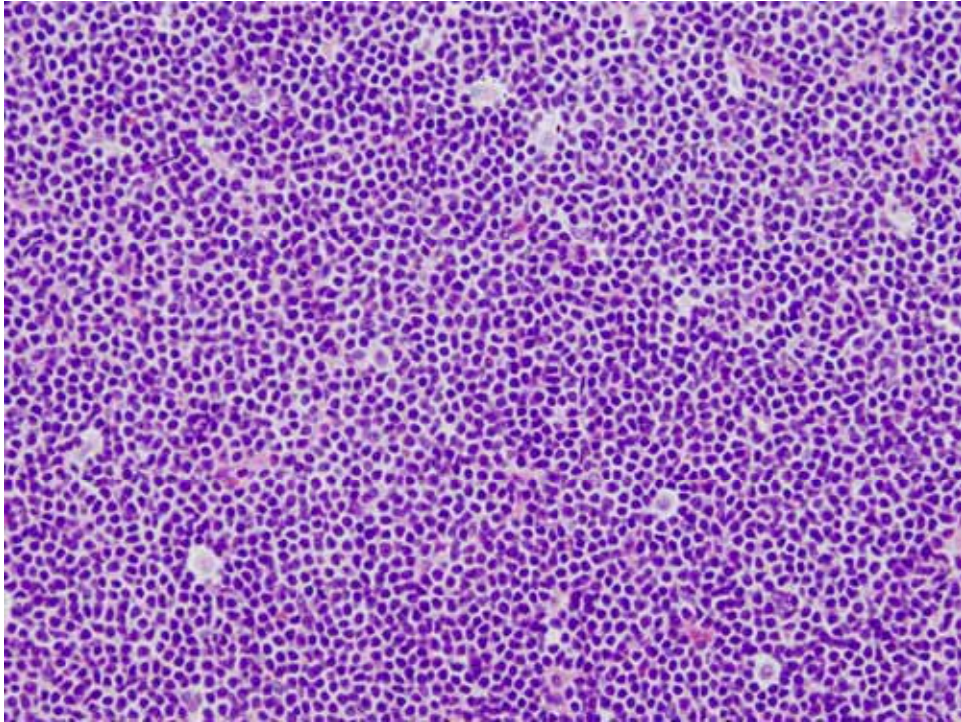
Case 1

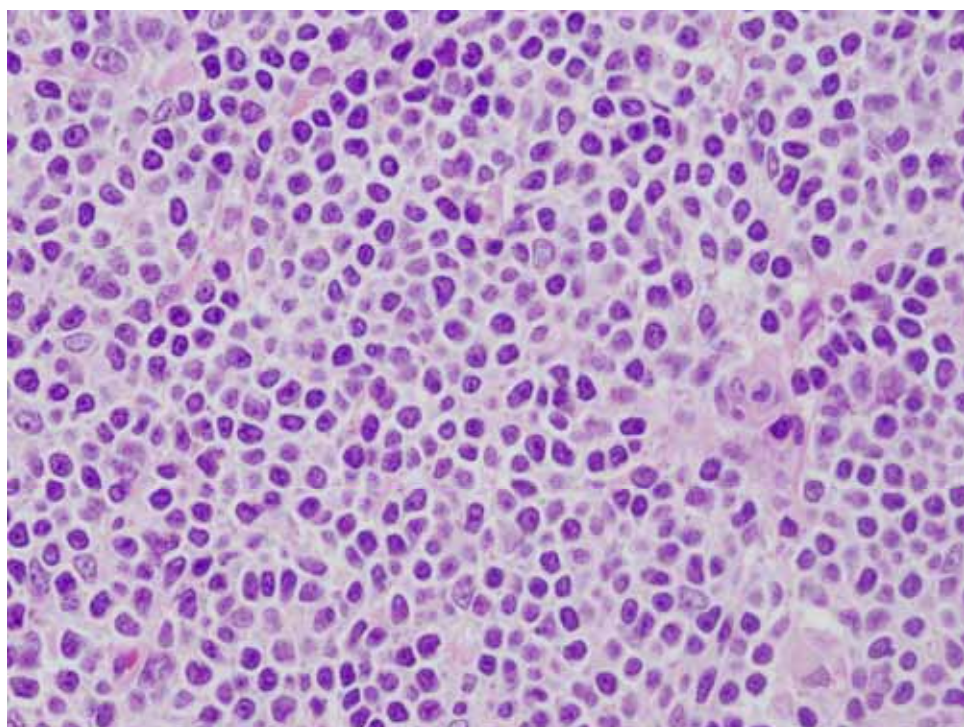
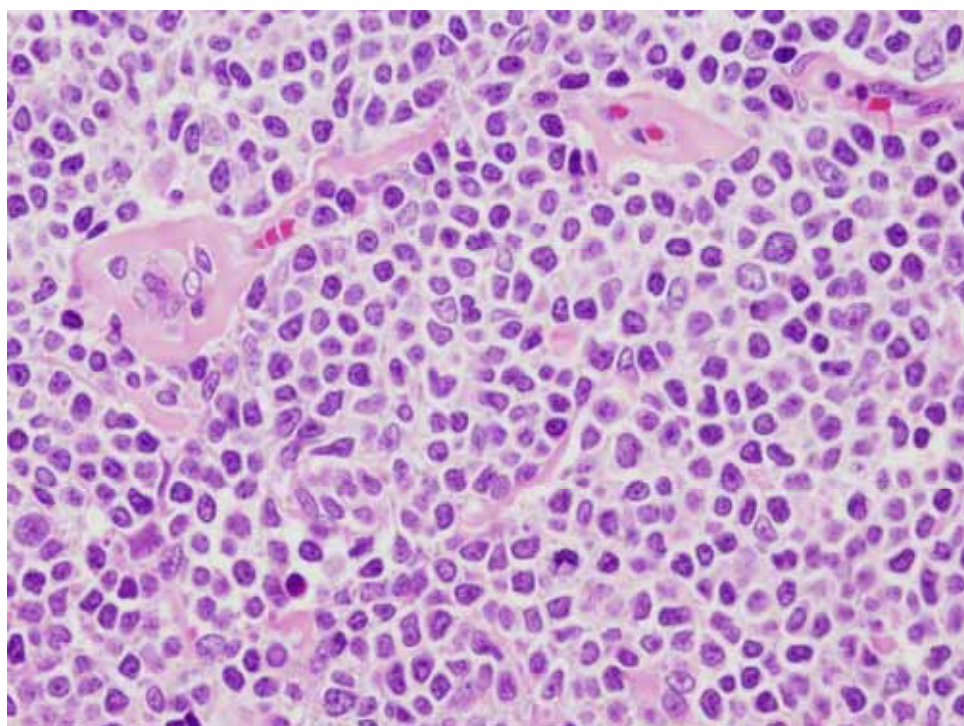
Elias Campo

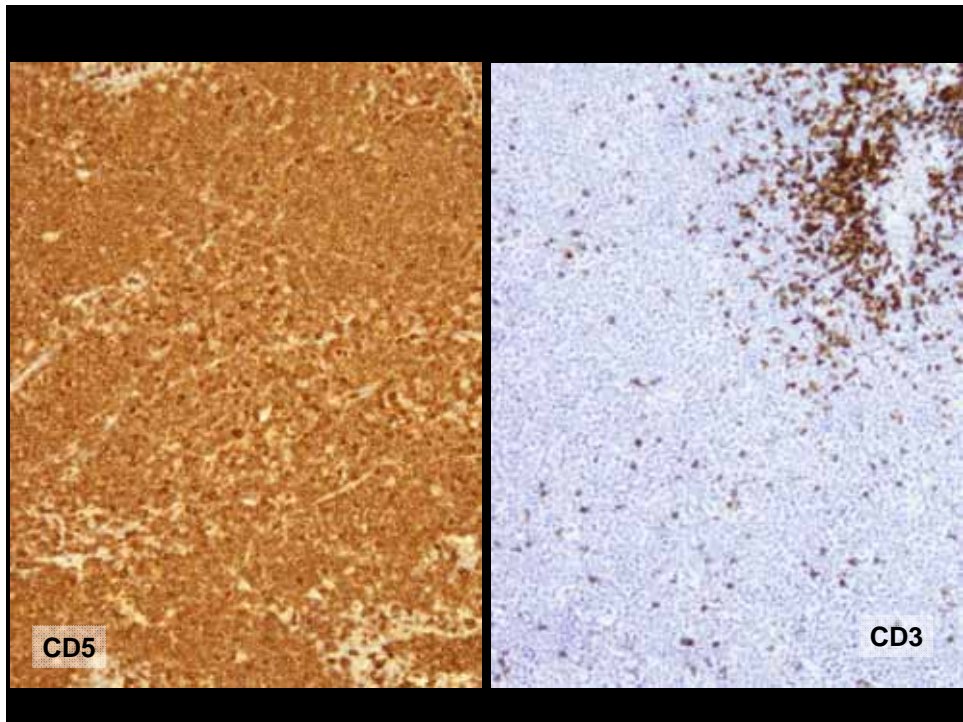
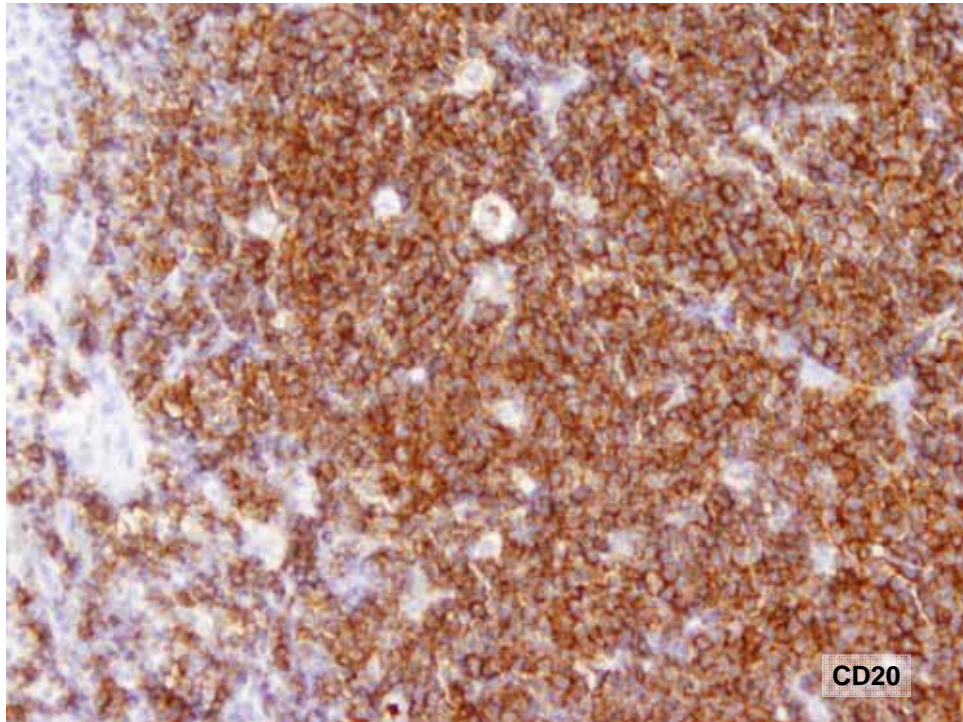
Clinical History

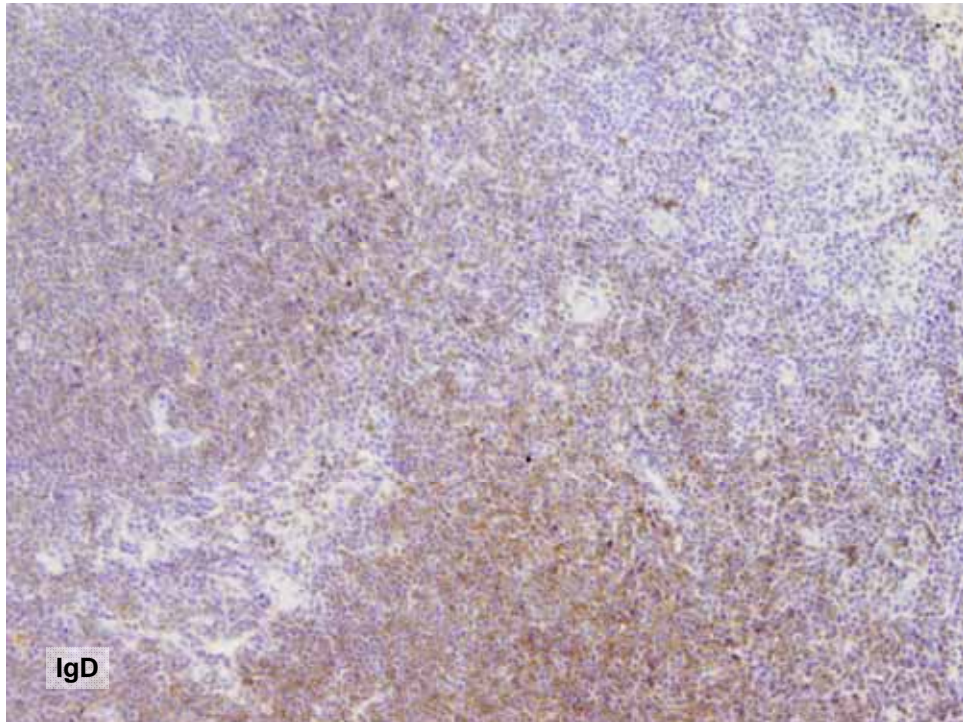
- 71-year-old Caucasian man
- Diffuse large B-cell lymphoma CD5 positive performed in 2002
- R-CHOP chemotherapy and local radiotherapy
- November 2006 inguinal lymph node enlargement. LDH normal, bone marrow biopsy normal (Submitted slide)





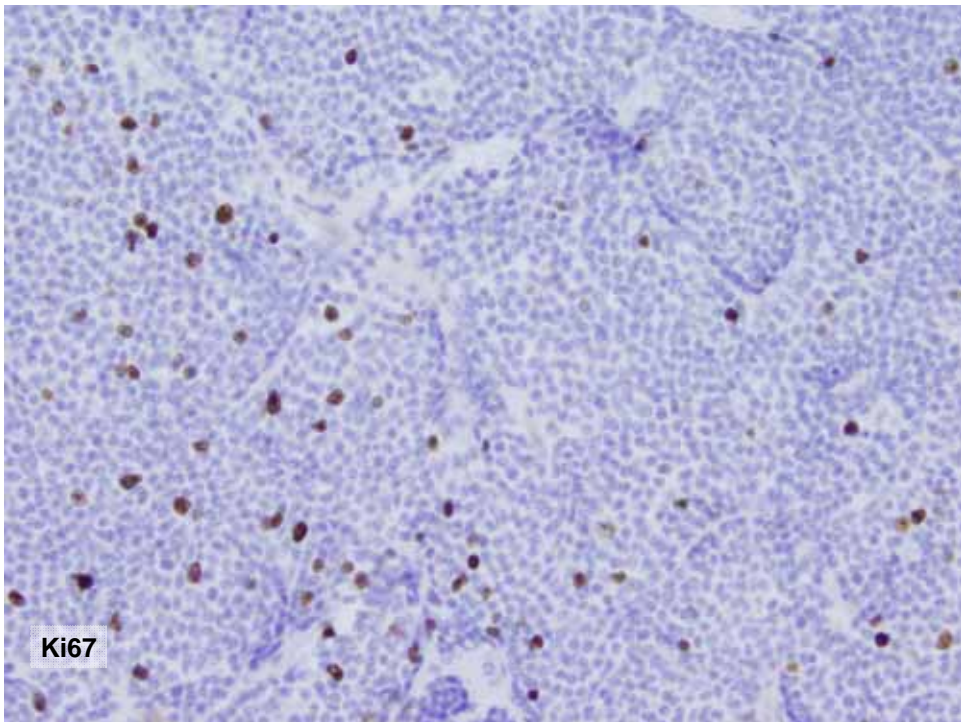
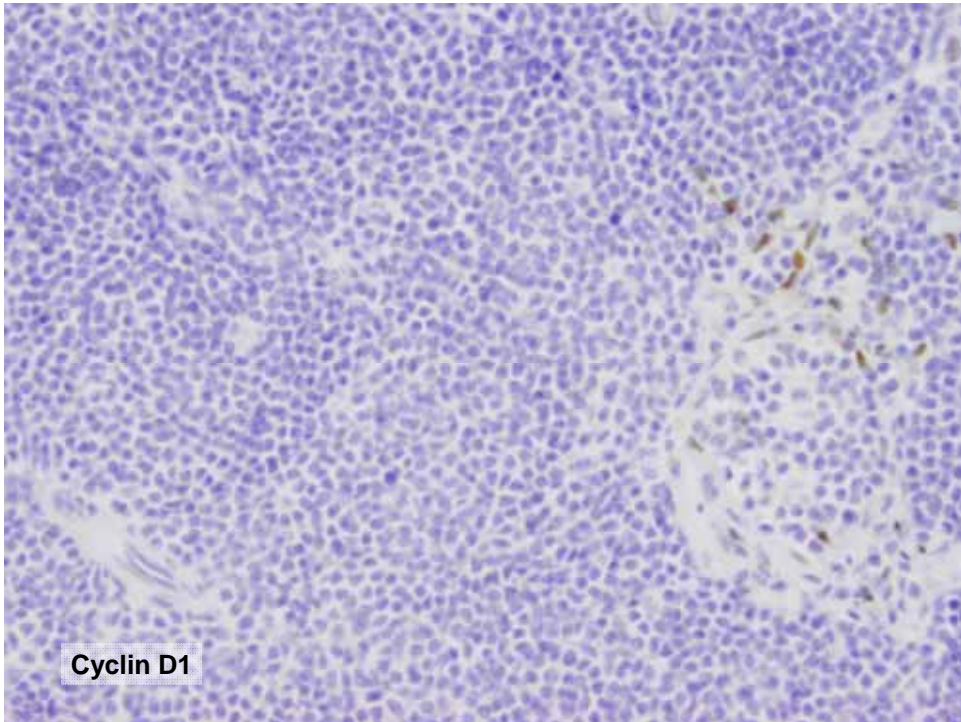






Which is your diagnosis?

1. Relapse of a diffuse large B-cell lymphoma
2. Relapse of DLBCL as a follicular lymphoma
3. Small lymphocytic lymphoma
4. Mantle cell lymphoma
5. Nodal marginal zone lymphoma

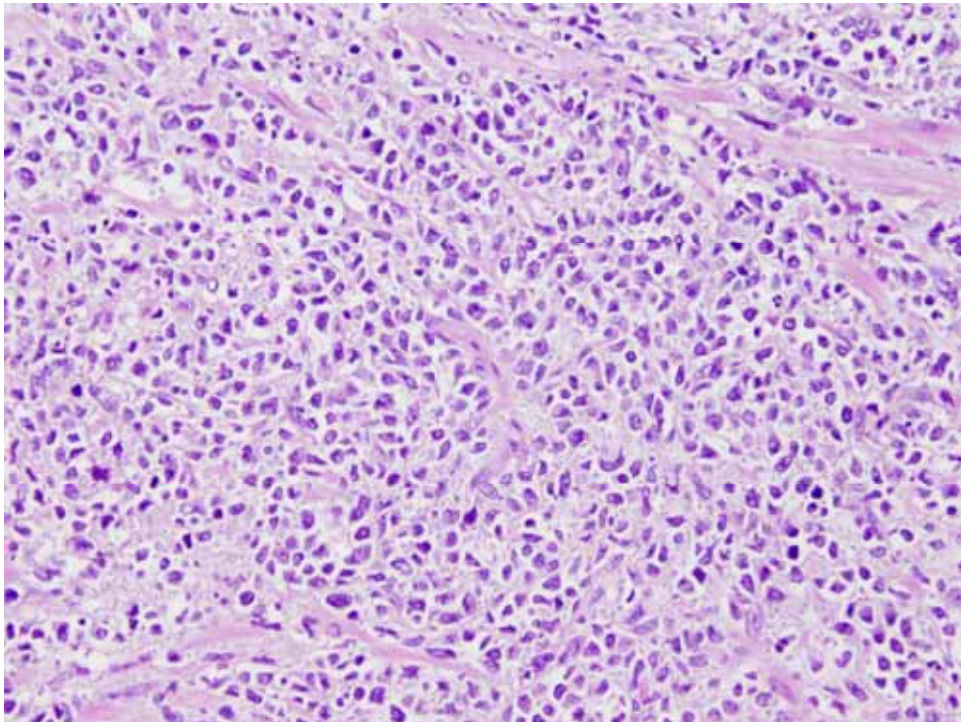
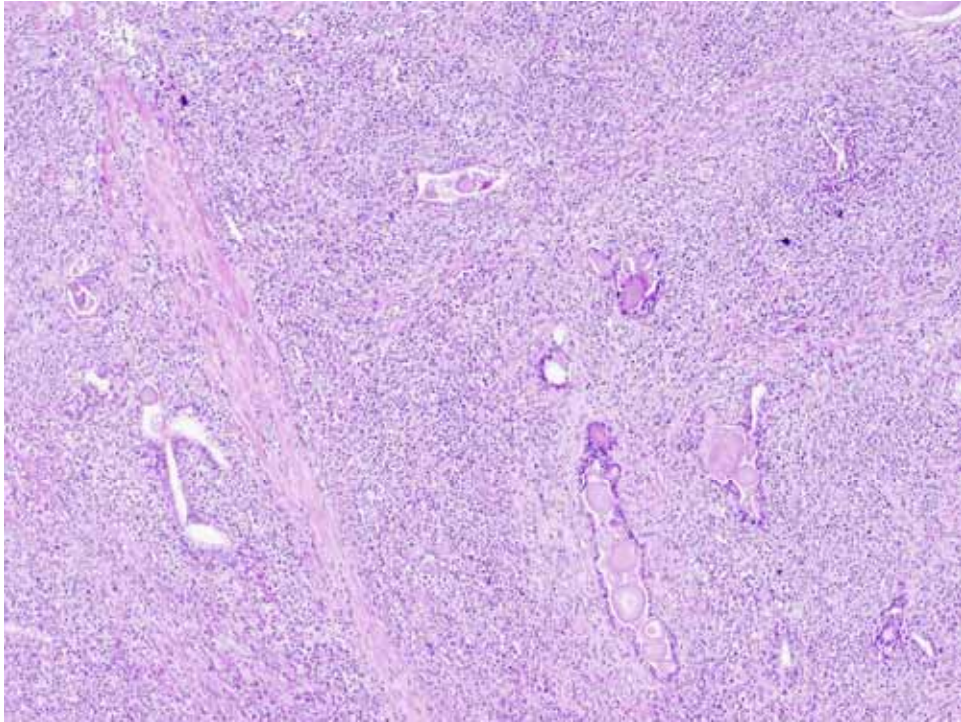


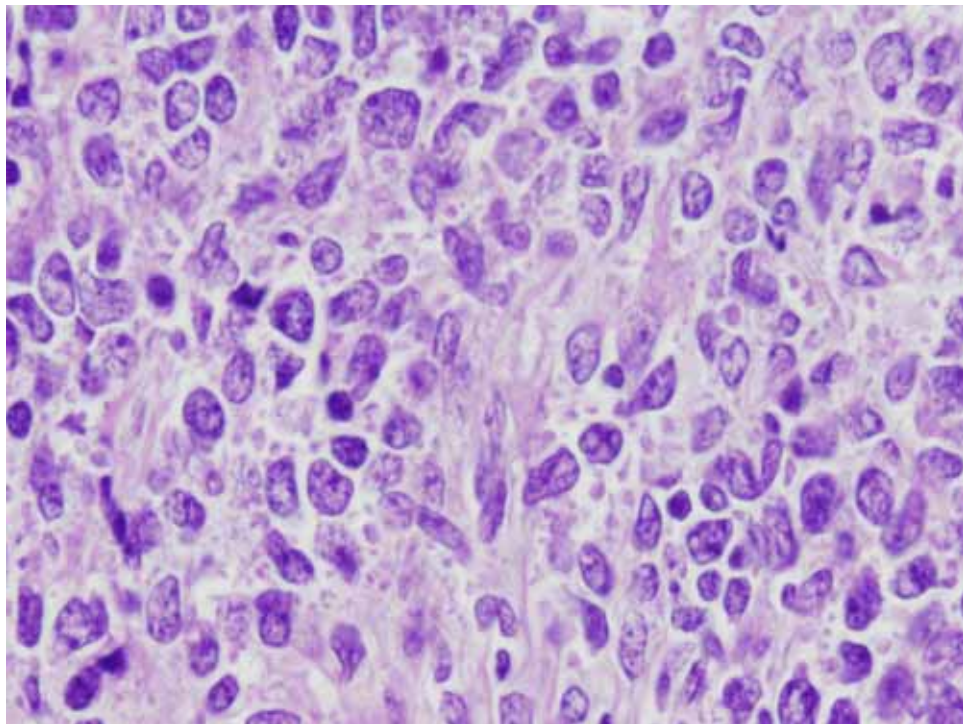
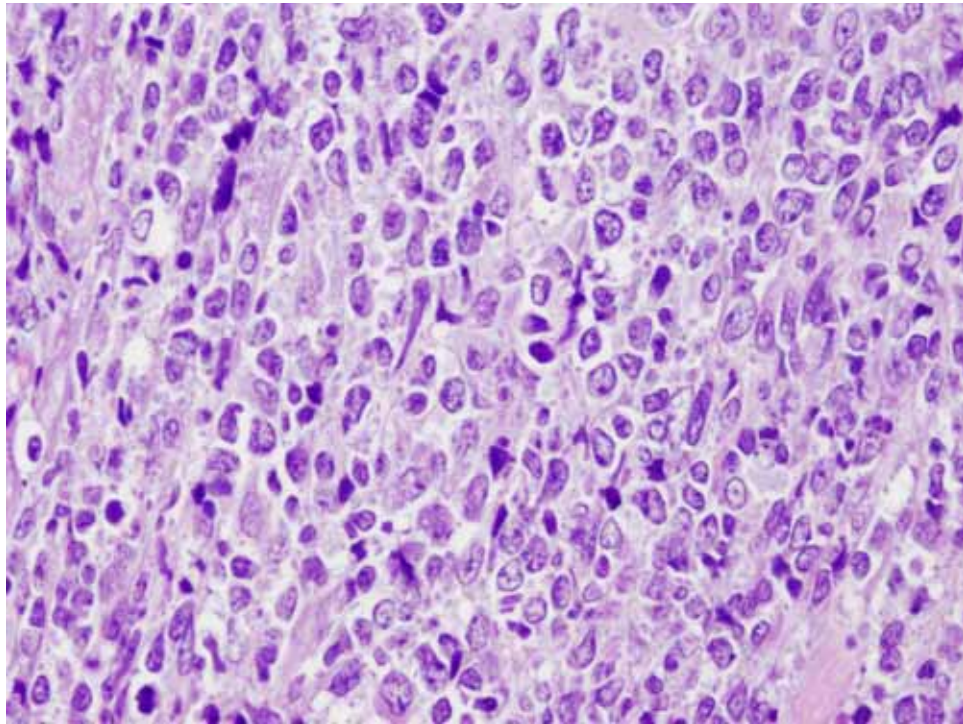
Which is your diagnosis?

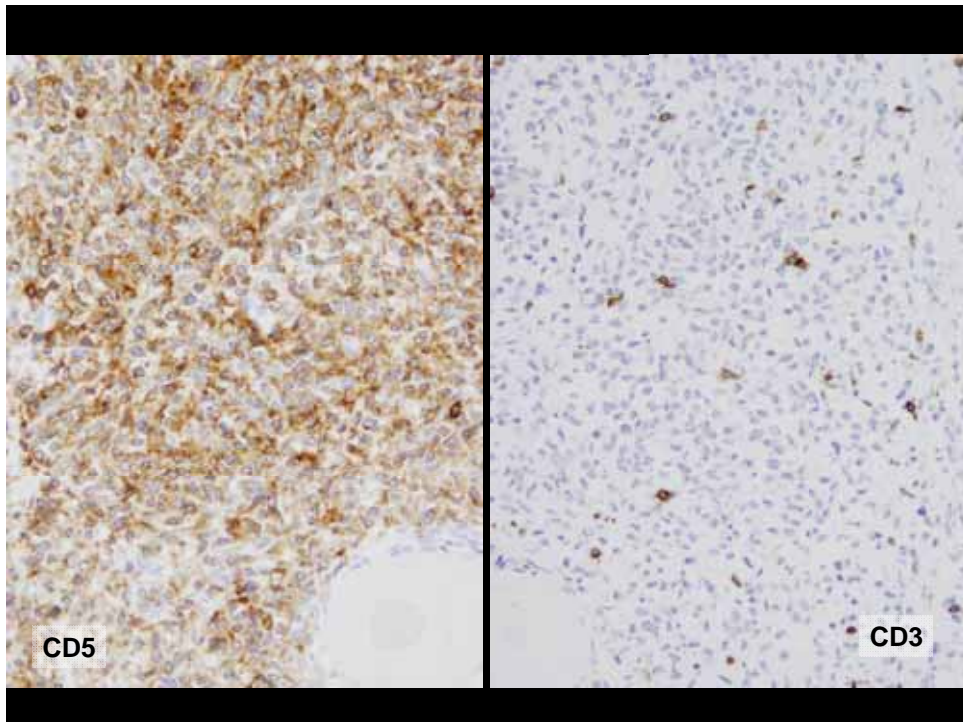
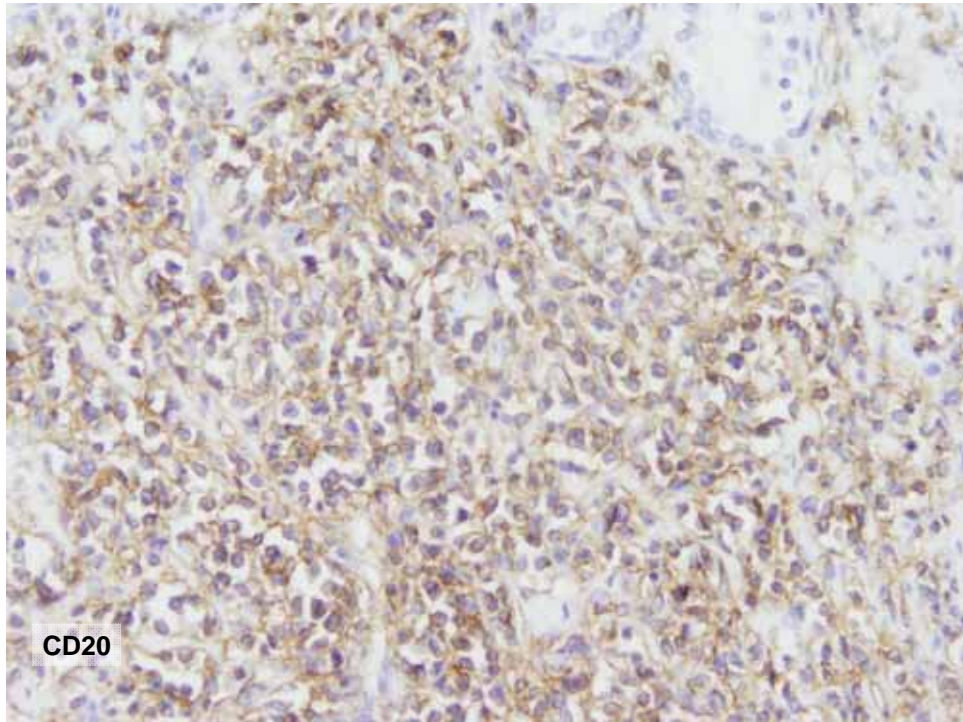
- 1. Relapse of a diffuse large B-cell lymphoma**
- 2. Relapse of DLBCL as a follicular lymphoma**
- 3. Small lymphocytic lymphoma**
- 4. Mantle cell lymphoma**
- 5. Nodal marginal zone lymphoma**

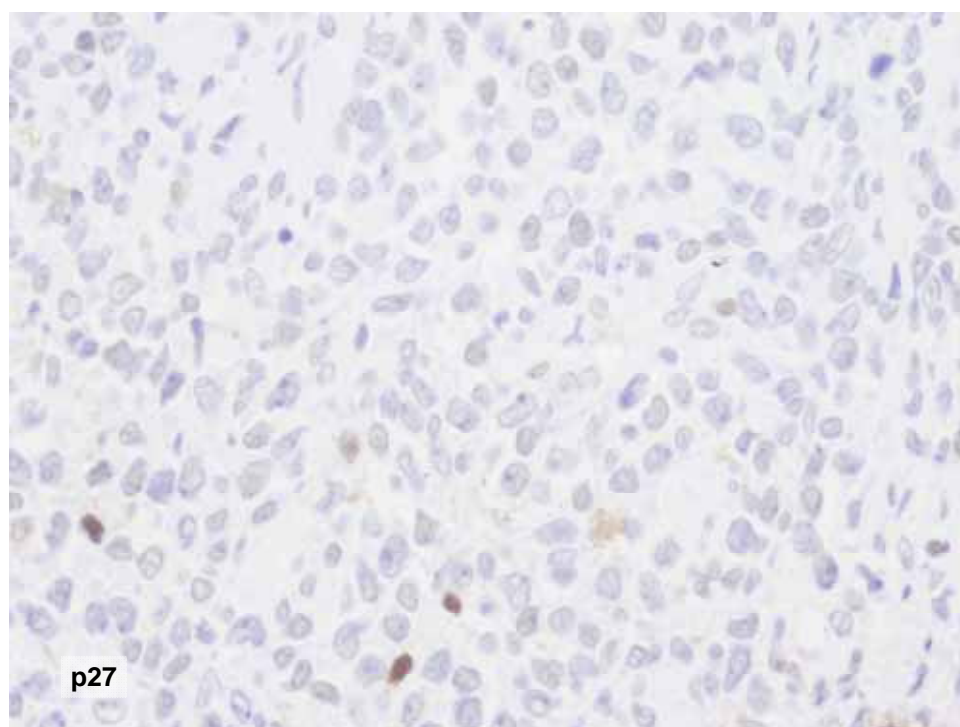
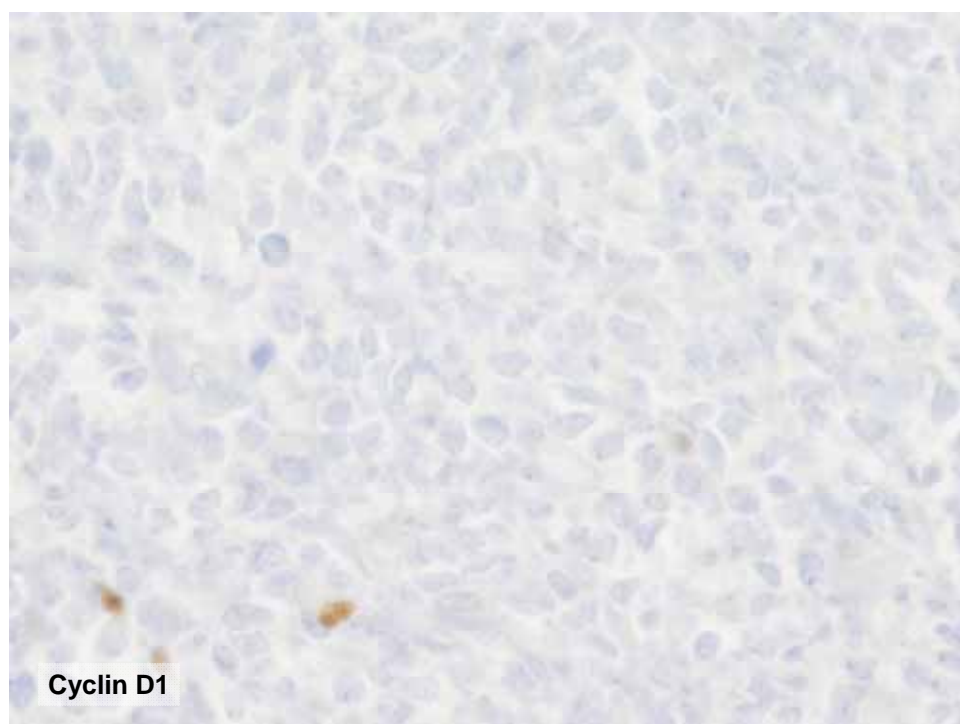
Clinical History

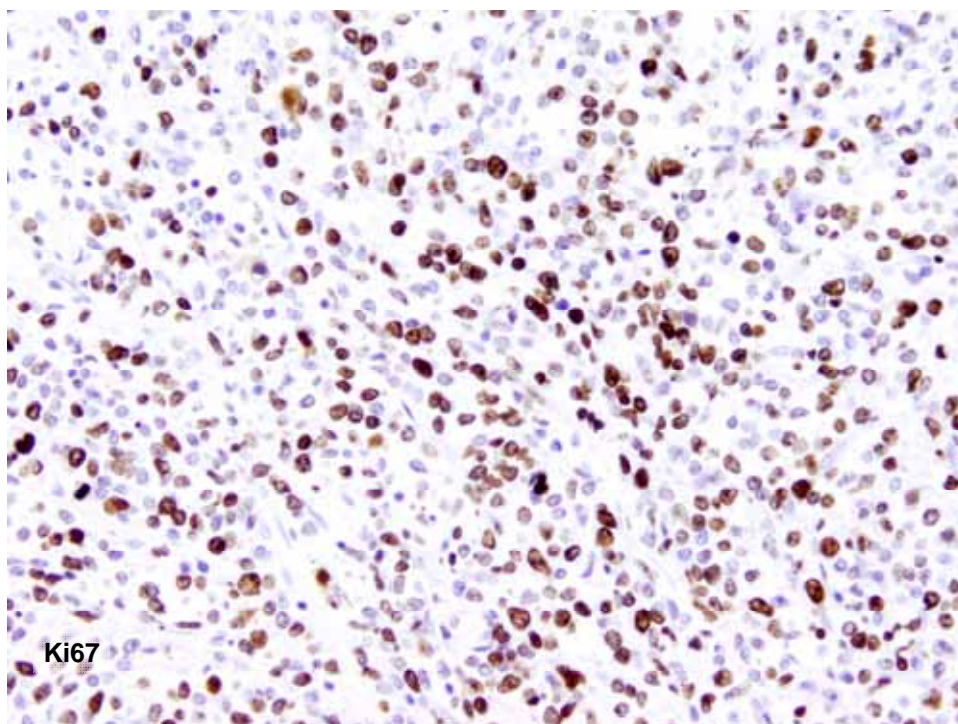
- Second line chemotherapy regime, reaching only partial response.**
- Ten months after the diagnosis, the patient presented with prostatic symptoms and partial resection of the prostate was performed.**



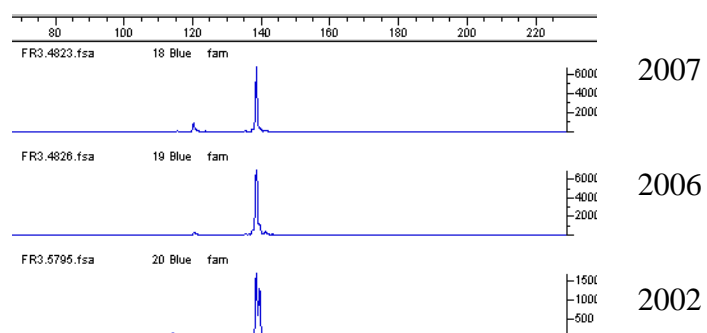






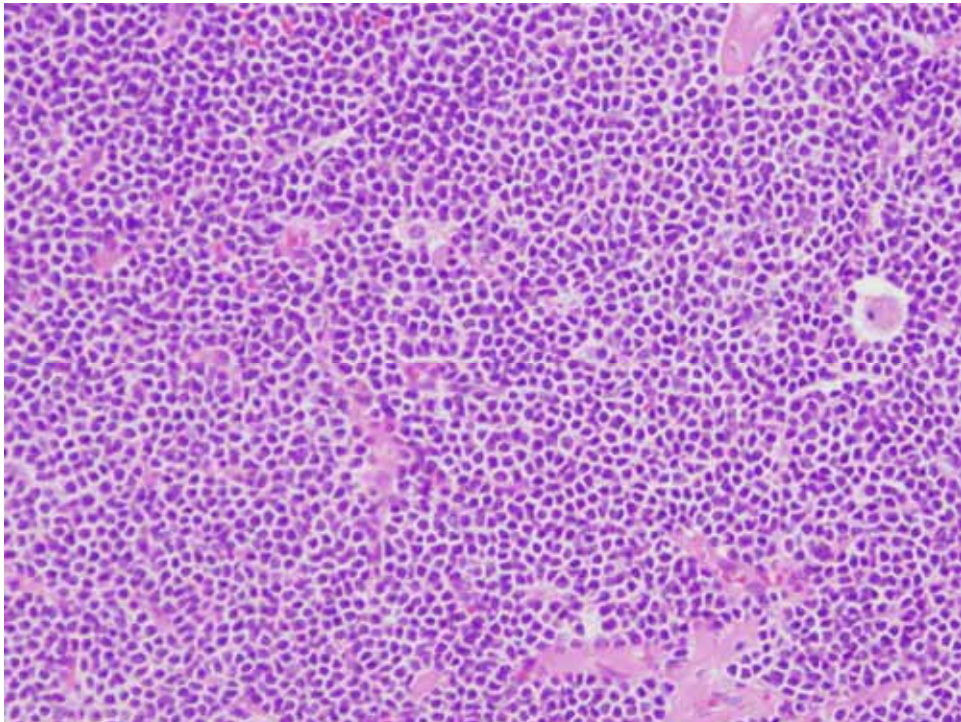


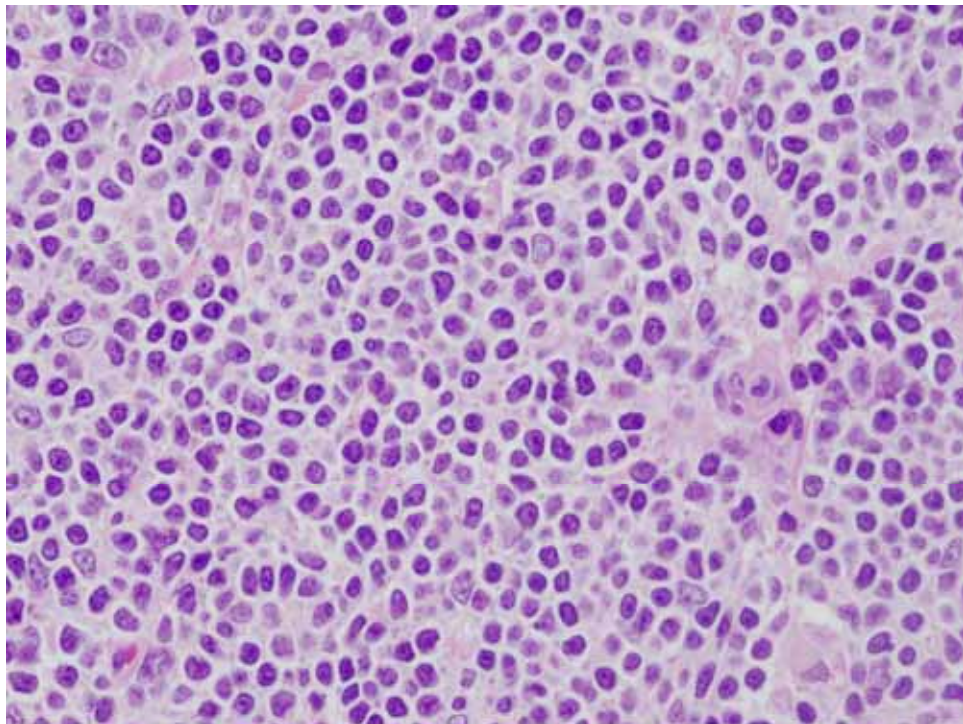
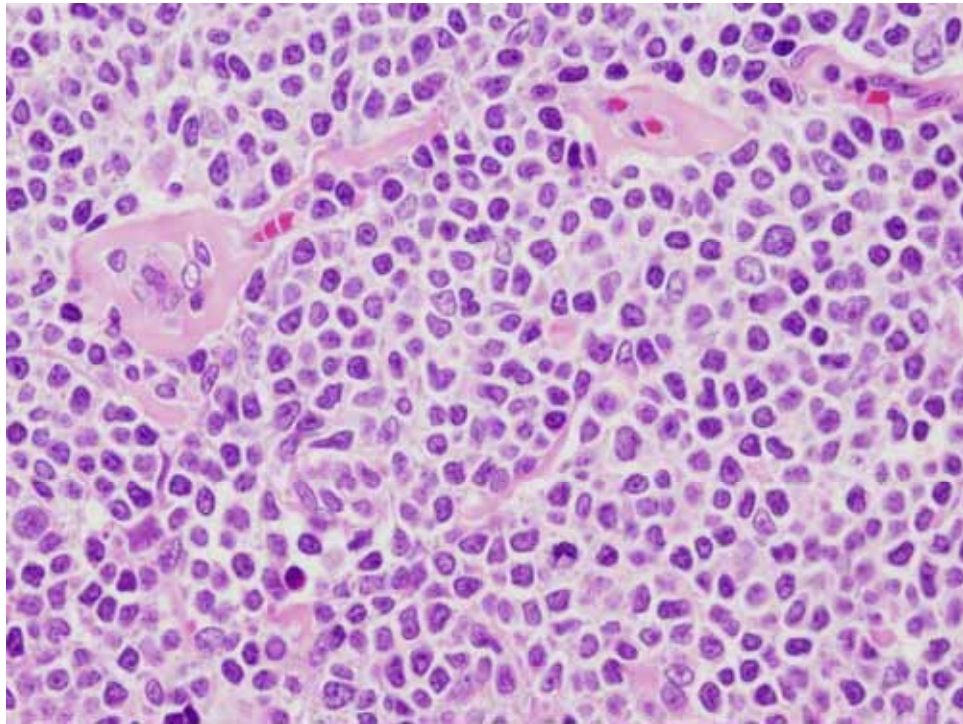
FR3 REGION IGH

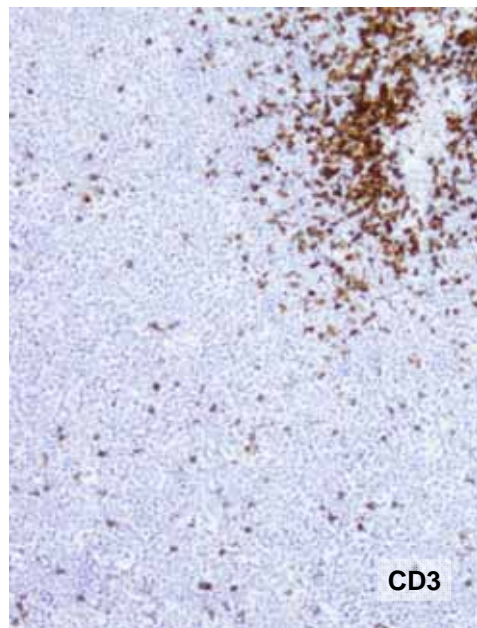
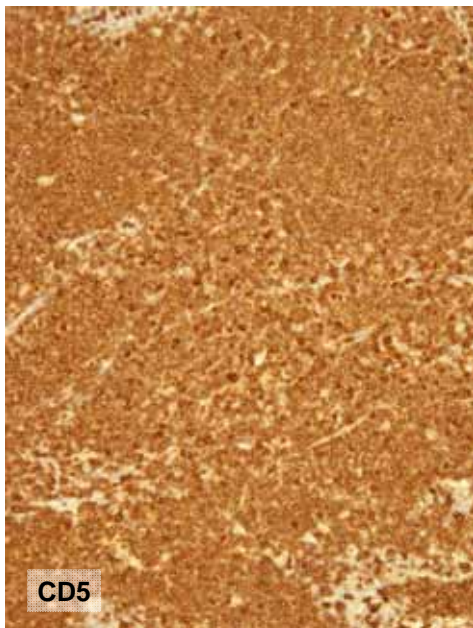
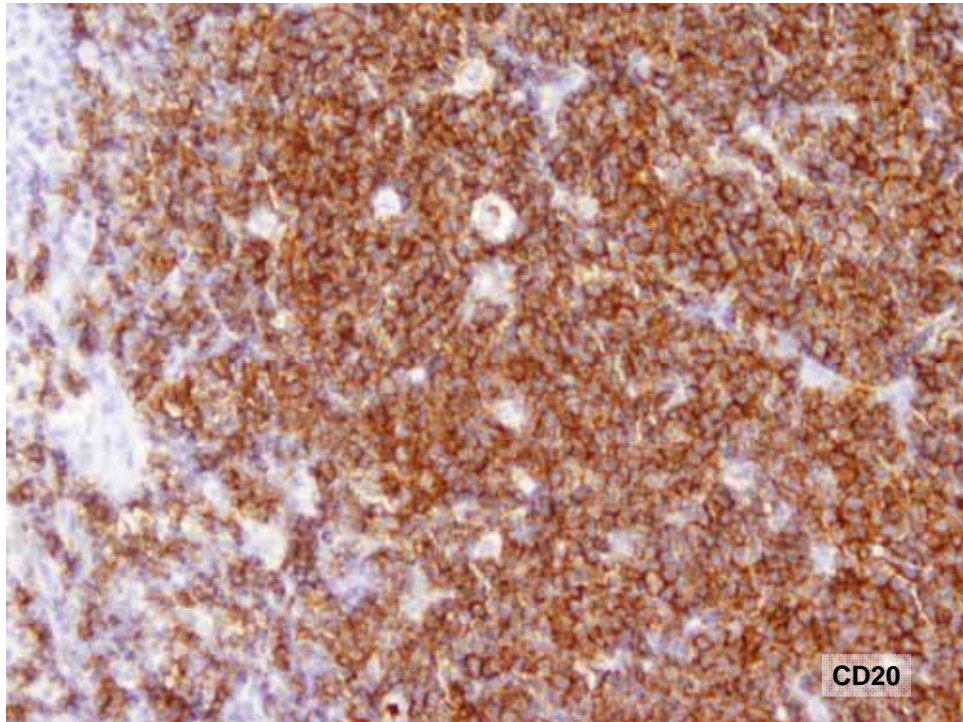


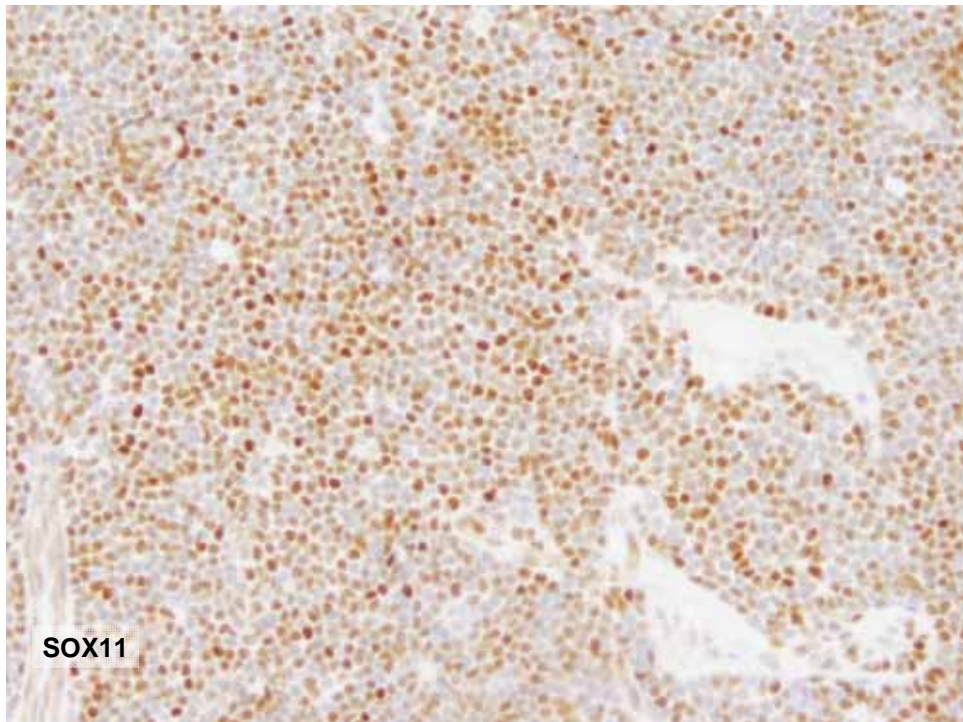
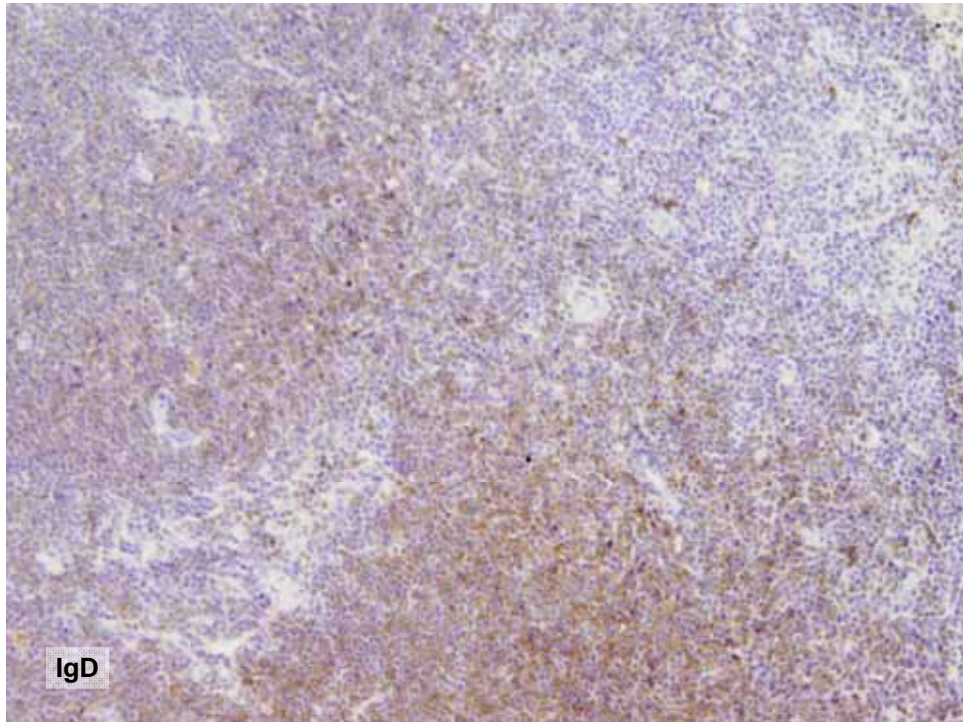
Which is your diagnosis?

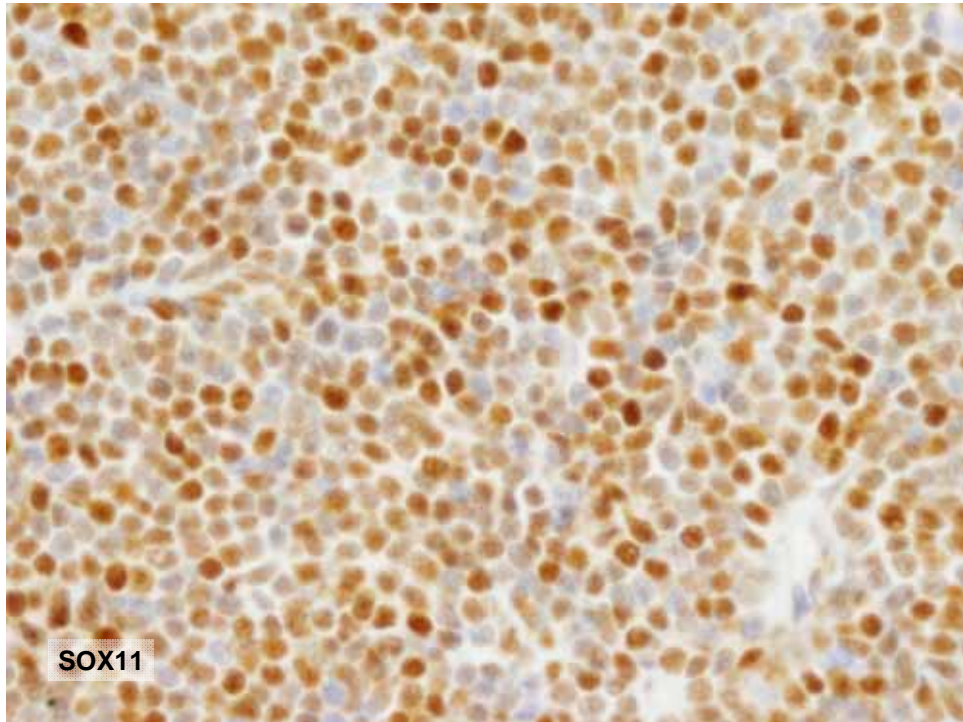
1. Relapse of a diffuse large B-cell lymphoma
2. Relapse of DLBCL as a follicular lymphoma
3. Small lymphocytic lymphoma
4. Mantle cell lymphoma
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Which is your diagnosis?

1. Relapse of a diffuse large B-cell lymphoma
2. Relapse of DLBCL as a follicular lymphoma
3. Small lymphocytic lymphoma
4. Mantle cell lymphoma
5. Nodal marginal zone lymphoma

Diagnosis

- **Mantle cell lymphoma, Cyclin D1 negative, SOX11 positivo**
- **Classical (2006) and pleomorphic variant (2002 & 2007)**

Case 2

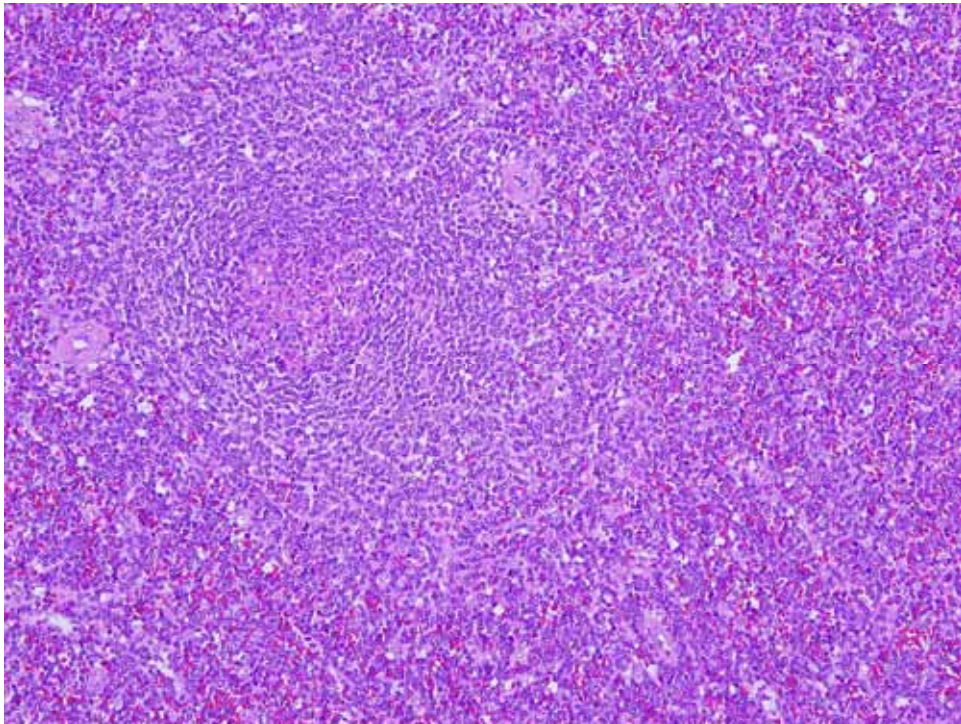
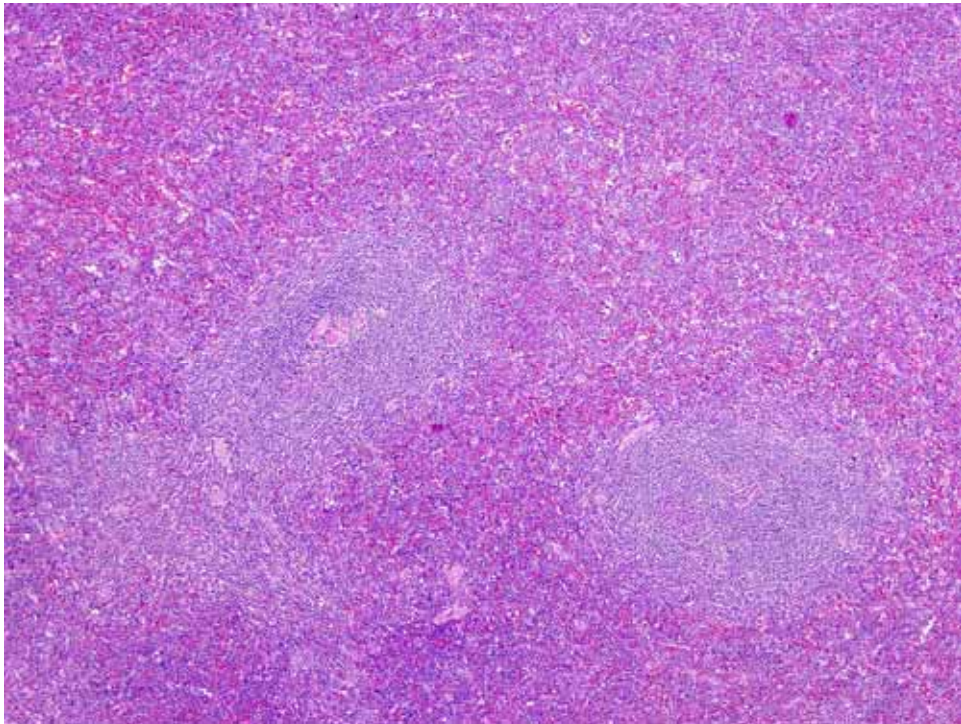
Elias Campo

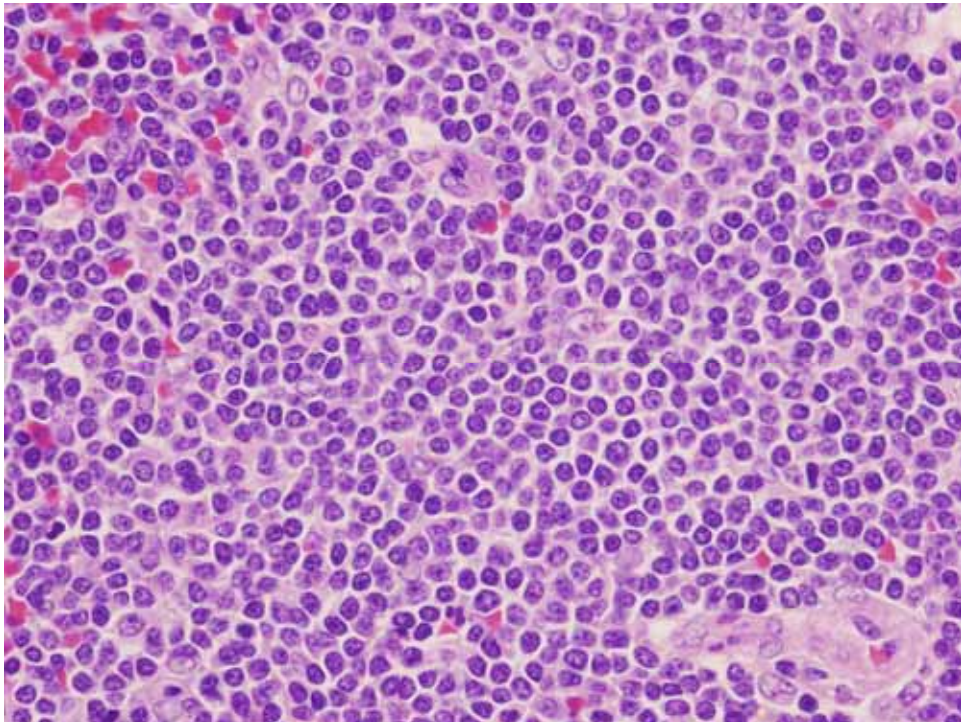
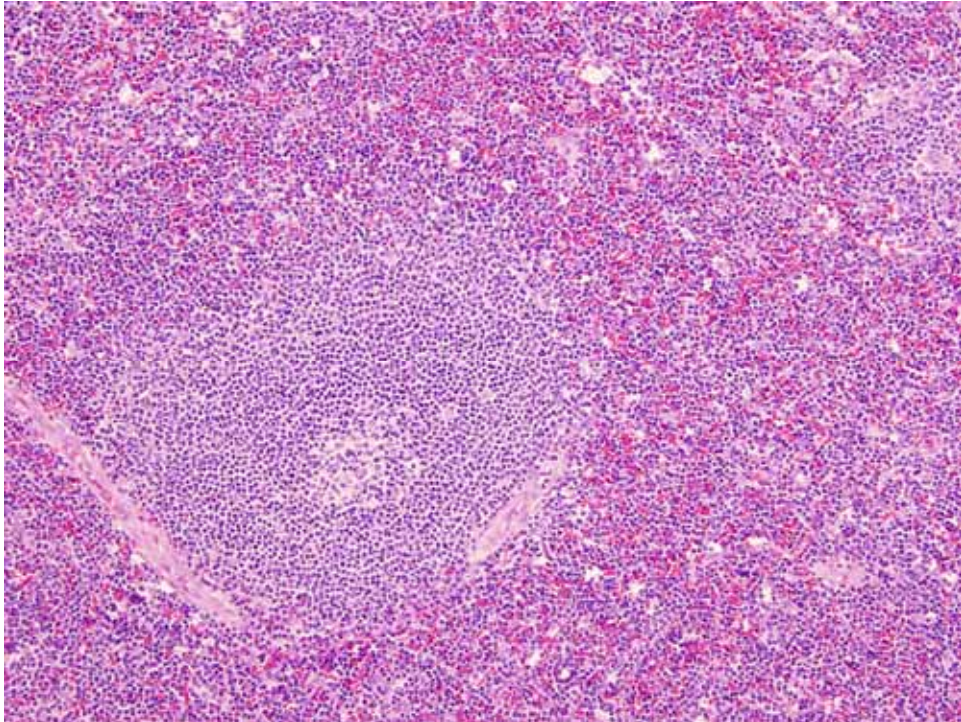
Clinical History

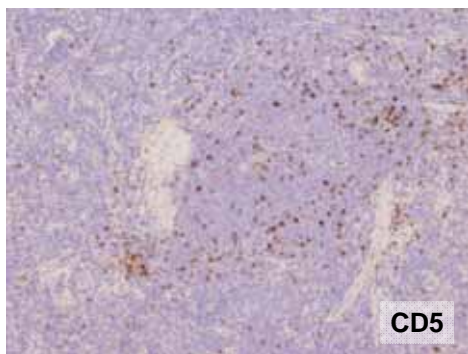
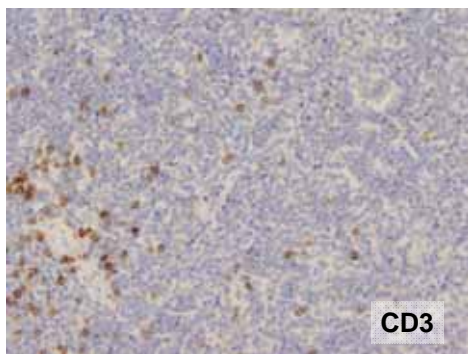
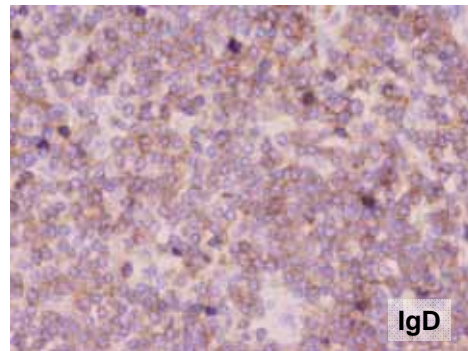
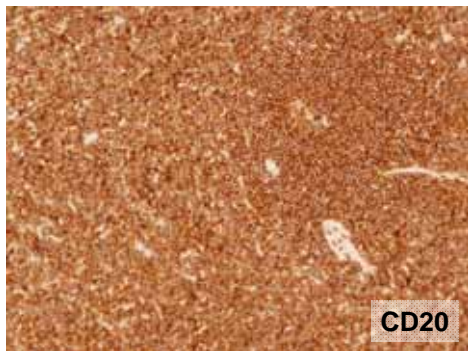
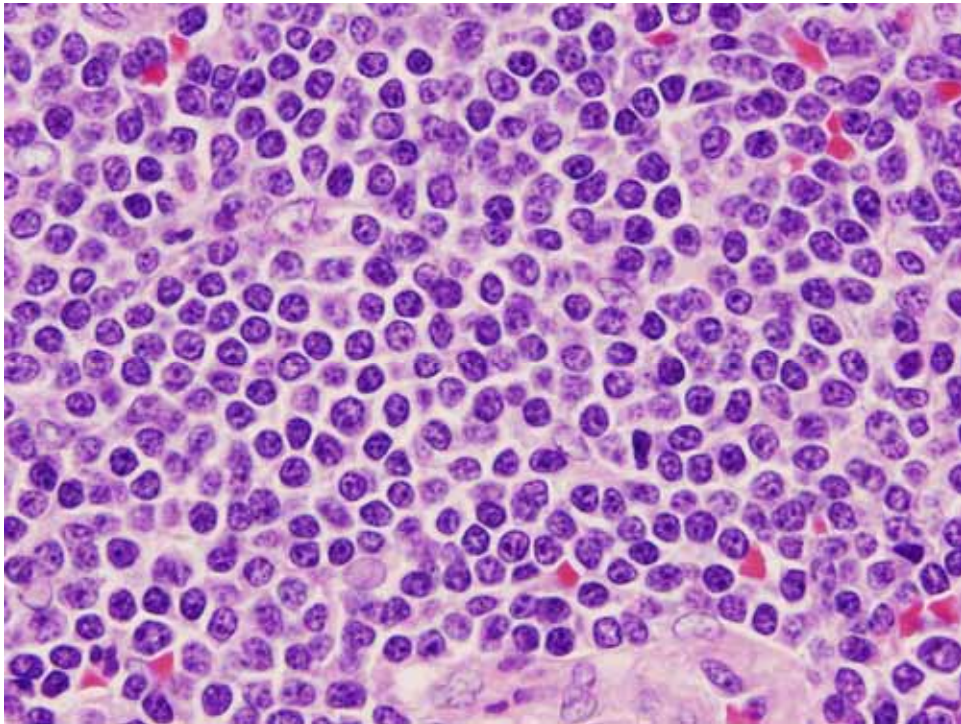
- 78 year-old female
- 10-year history of a leukemic, B-cell neoplasm, initially diagnosed as chronic lymphocytic leukemia [stage A(0)]
- December 2003, stage I renal cell adenocarcinoma
- 2004 progressive lymphocytosis, anemia, and thrombocytopenia
- Referred to our hospital for splenectomy

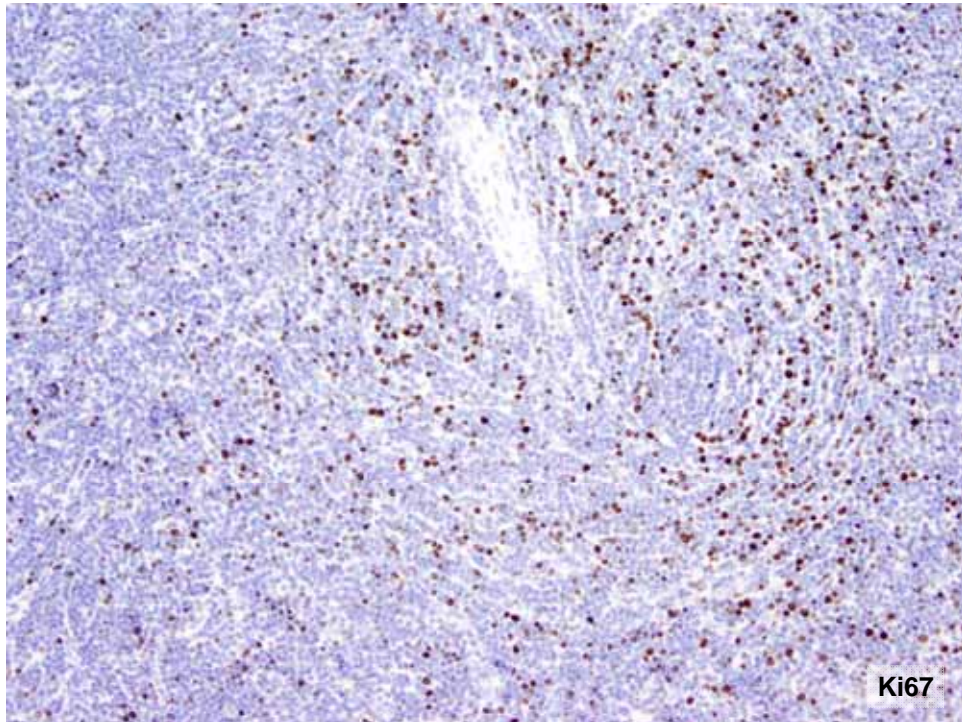
Clinical History

- Normal LDH
- High B2 microglobulin 6.2 mg/L (normal 0-2.3)
- WBC 123.40 x10³/μL (lymphocytes 85%),
- Flow cytometry peripheral blood
 - Clonal lymphoid proliferation IgM/IgD, kappa (bright)
 - Positive:
 - CD19, CD79b, CD20 (bright), FMC7, CD22
 - CD23 (66% of all B-lymphocytes)
 - Negative: CD5, CD43, CD10









Diagnosis

1. Chronic Lymphocytic Leukemia
2. Mantle Cell Lymphoma
3. Splenic Marginal Zone Lymphoma
4. Lymphoplasmacytoid lymphoma
5. Follicular lymphoma

How to treat the patient?

1. Watch and see
2. Cyclophosphamide
3. Fludarabine
4. FCM
5. R-CHOP

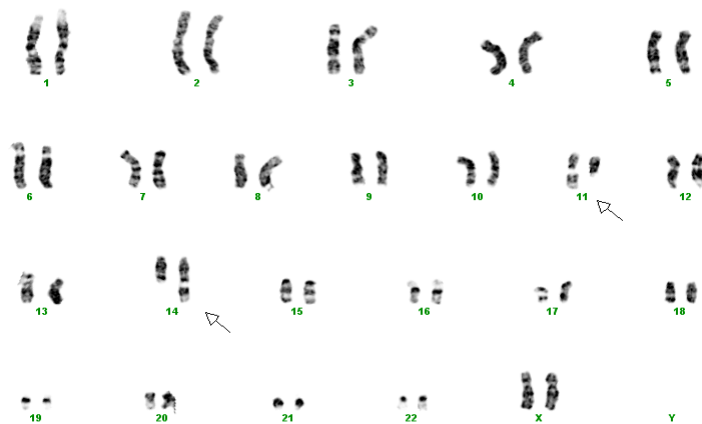
Case 3: Initial Diagnosis

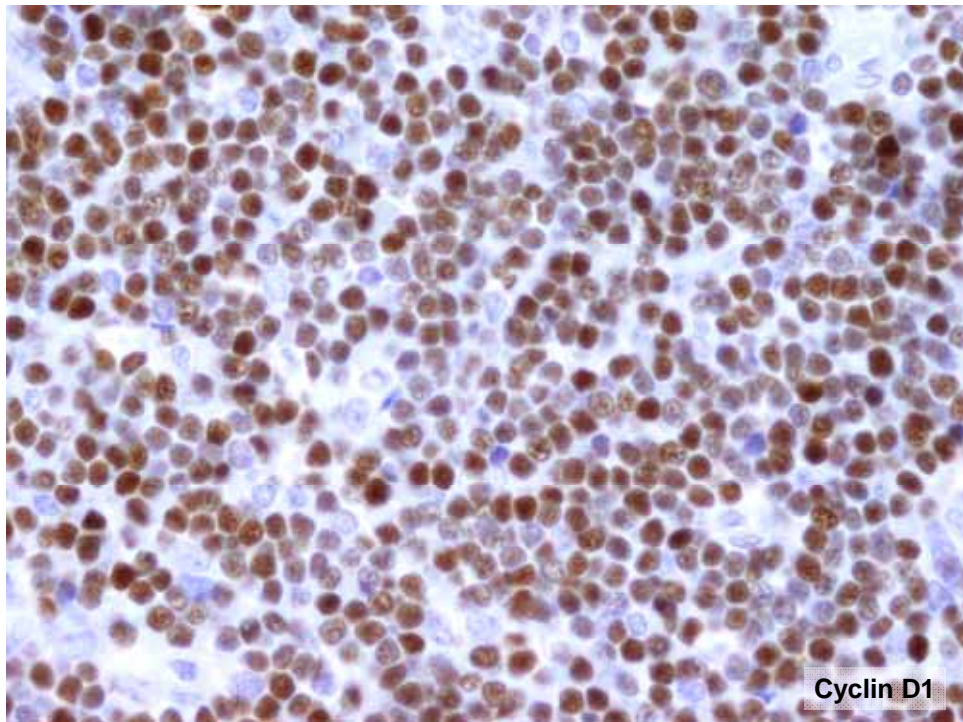
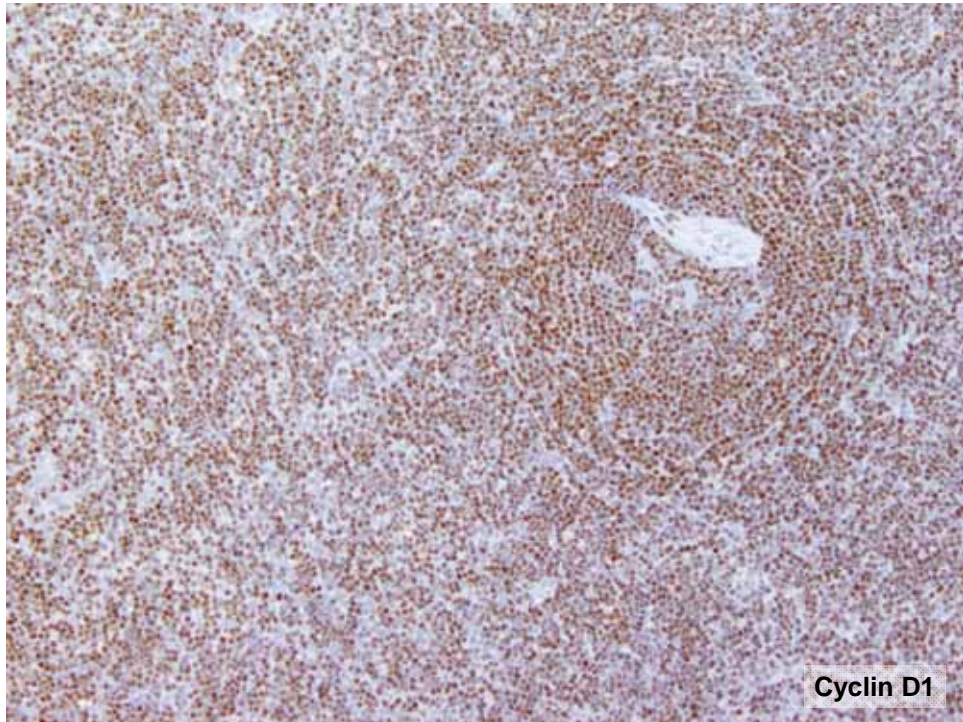
- Splenic B-cell lymphoma, unclassifiable
- Phenotype
 - Positive: CD20, CD23, IgM/IgD kappa
 - Negative: CD5, CD43, CD10, BCL-6, IRF4/MUM1, CD25, CD11c, and CD103

Evolution

- The status of the patient improved after the splenectomy, but the lymphocytosis persisted
- No additional treatment for two years
- July 2007, progressive lymphocytosis

Case 3: Conventional Cytogenetics





Diagnosis

- 1. Chronic Lymphocytic Leukemia**
- 2. Mantle Cell Lymphoma**
- 3. Splenic Marginal Zone Lymphoma**
- 4. Lymphoplasmacytoid lymphoma**
- 5. Follicular lymphoma**

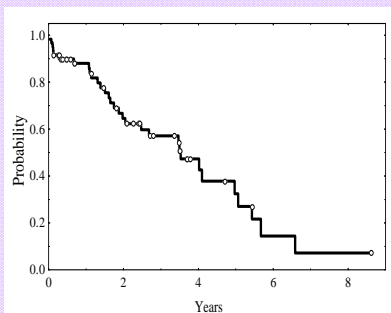
How to treat the patient?

- 1. Watch and see**
- 2. Cyclophosphamide**
- 3. Fludarabine**
- 4. FCM**
- 5. R-CHOP**

Open Questions

- 1) Is this case a real MCL? Does indolent MCL really exist?
- 2) Are indolent MCL real MCL?
- 3) If they are MCL, what are the differences between the indolent and conventional MCL with more aggressive clinical behavior?

MCL: Clinical Evolution



Complete Response 25% (6-50%)

Duration of CR 1.5 yrs (0.5-2.5 yrs)

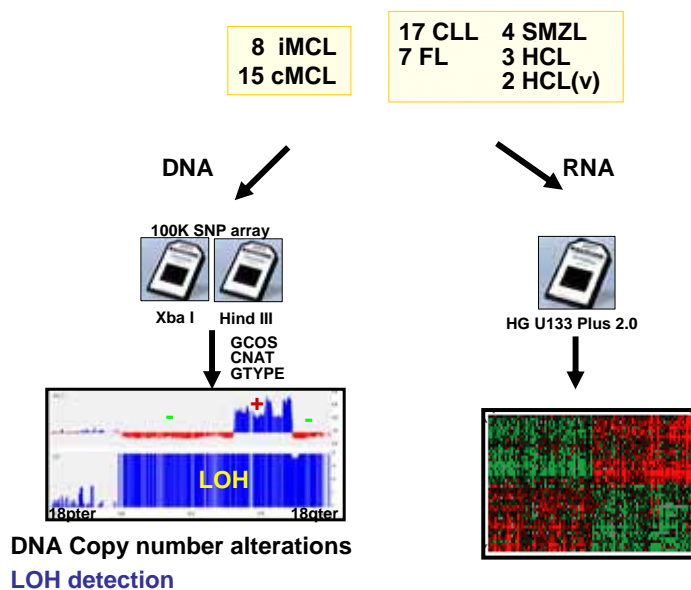
Median Survival 3-4 years

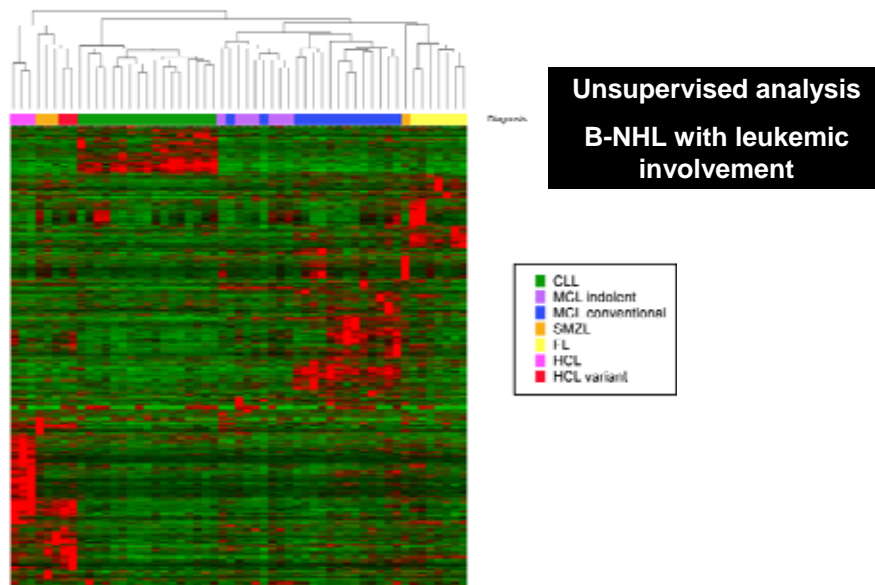
Are Indolent MCL real MCL?

- 12 patients with indolent MCL (iMCL)
- Not treated with chemotherapy and did not have evidence of clinical progression during > 2 years.
- Median follow-up 70 months, range 25-121
- Detection t(11;14) (Conventional cytogenetics, FISH)
- Overexpression CCND1

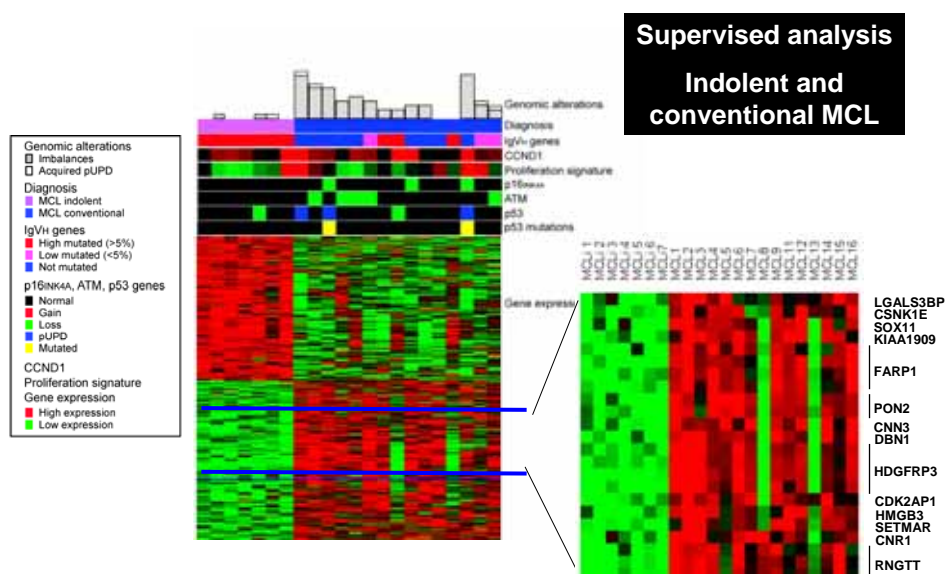
SMZL	4
CLL	2
Leukemic lymphoid neoplasm, NOS	4
"In situ" MCL	2

Are Indolent MCL real MCL?

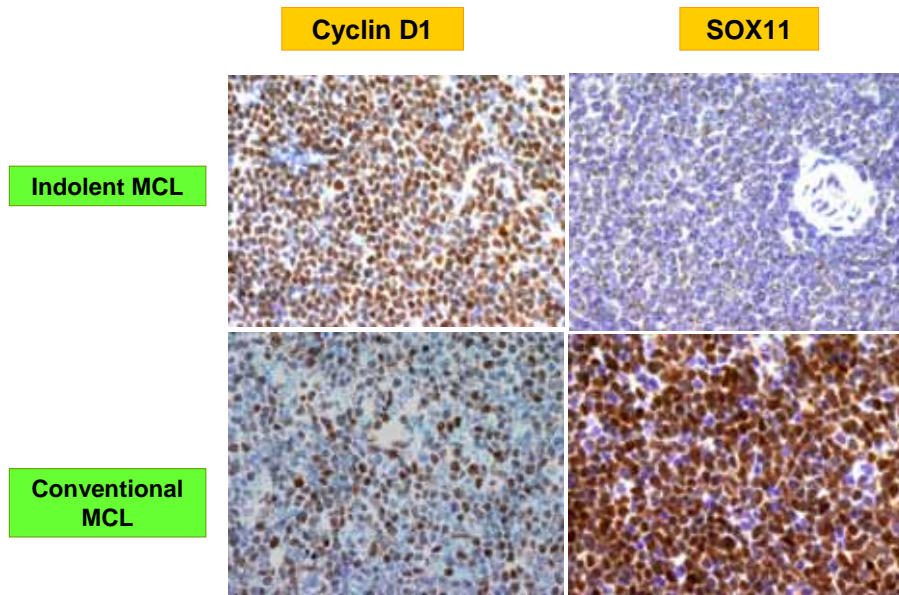




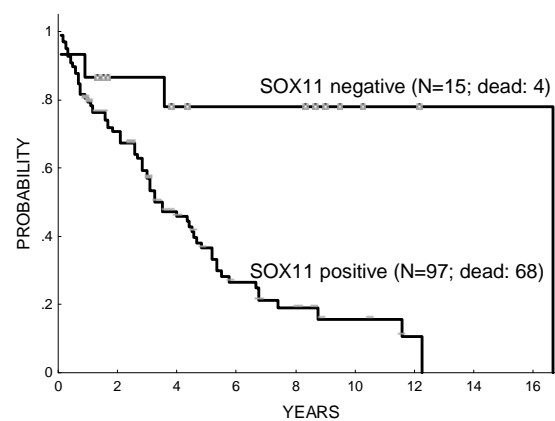
Molecular and Genetic Differences Between Indolent and Conventional MCL



SOX11 Protein Expression in MCL



Overall Survival in MCL patients according to SOX11 Expression



$P < 0.001$

Diagnosis

- 1. Chronic Lymphocytic Leukemia**
- 2. Mantle Cell Lymphoma**
- 3. Splenic Marginal Zone Lymphoma**
- 4. Lymphoplasmacytoid lymphoma**
- 5. Follicular lymphoma**

How to treat the patient?

- 1. Watch and see**
- 2. Cyclophosphamide**
- 3. Fludarabine**
- 4. FCM**
- 5. R-CHOP**

Final Diagnosis

**Mantle Cell Lymphoma, small cell variant,
with a very indolent clinical evolution**