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Turkish Society of Hematology

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# EHA-TSH Hematology Tutorial on Lymphoma

Self-assessment Case – Session [2]

*Speaker: Olivier Hermine*

İzmir, Turkey  
April 6-7, 2019



## Introduction

- 52 year-old man presented with multiple lymphadenopathy in bilaterally cervical and axillary regions.
- No past medical history; No treatment
- No Fever
- No symptomatic complaint, except few episodes of diarrhea and blood in stools.
- No splenomegaly
- No abnormalities at the neurological examination
- No skin abnormality



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## Introduction

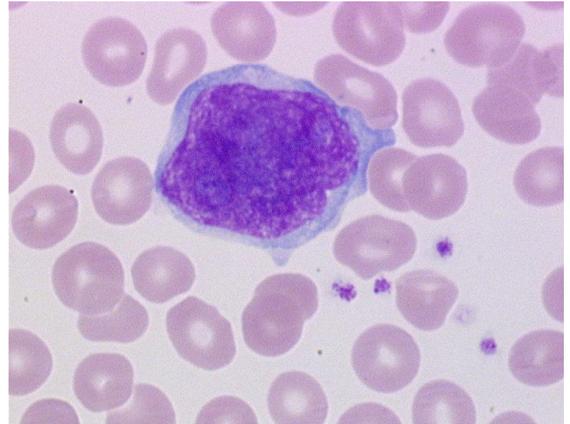
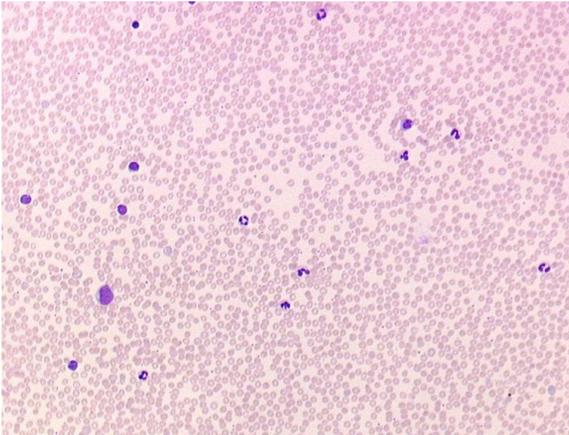
- CBC : WBC 21.8G/l PNN =10.7G/L; Mo 2.4 G/L; Ly 8.2G/l  
Hb12.8gr/dl; Platelets 231 G/L
- LDH 230 (NI<250);
- ASAT, ALAT gGT, Billuribn <1N,
- Gammaglobulins 12gr/dl



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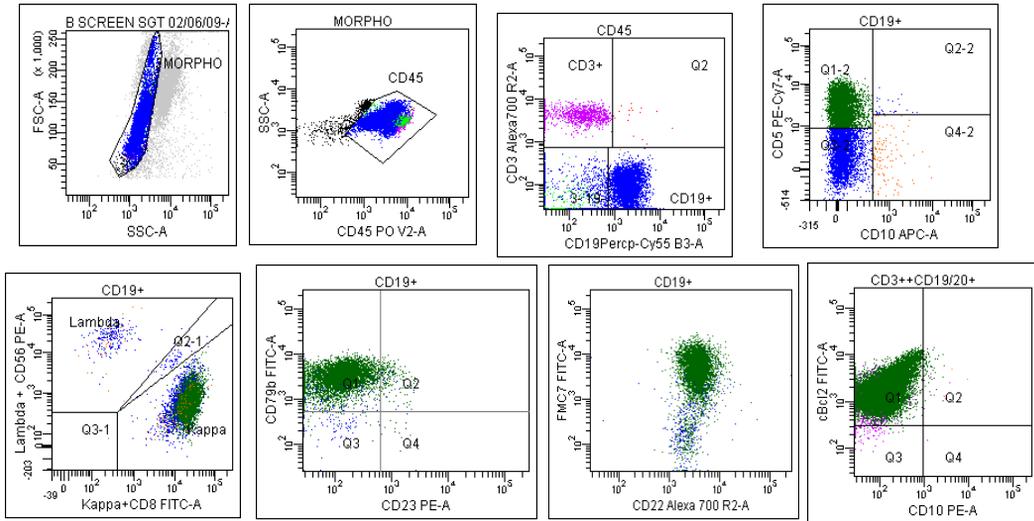


# Blood Film





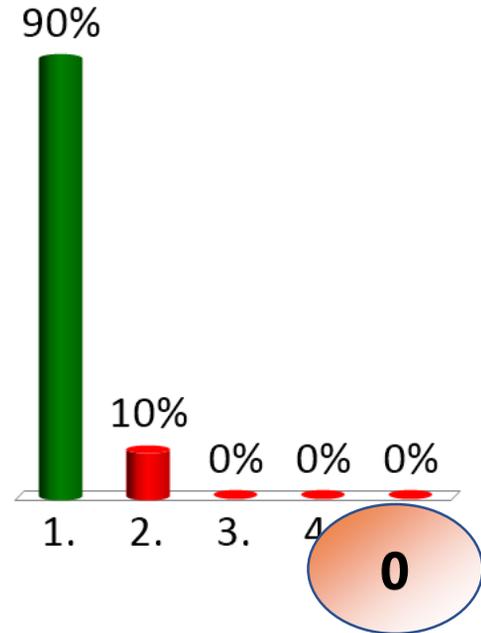
# Blood cytometry



Abnormal B Cell population CD19+ CD20+CD5+ CD11a+  
CD200+ FMC7 + CD23low

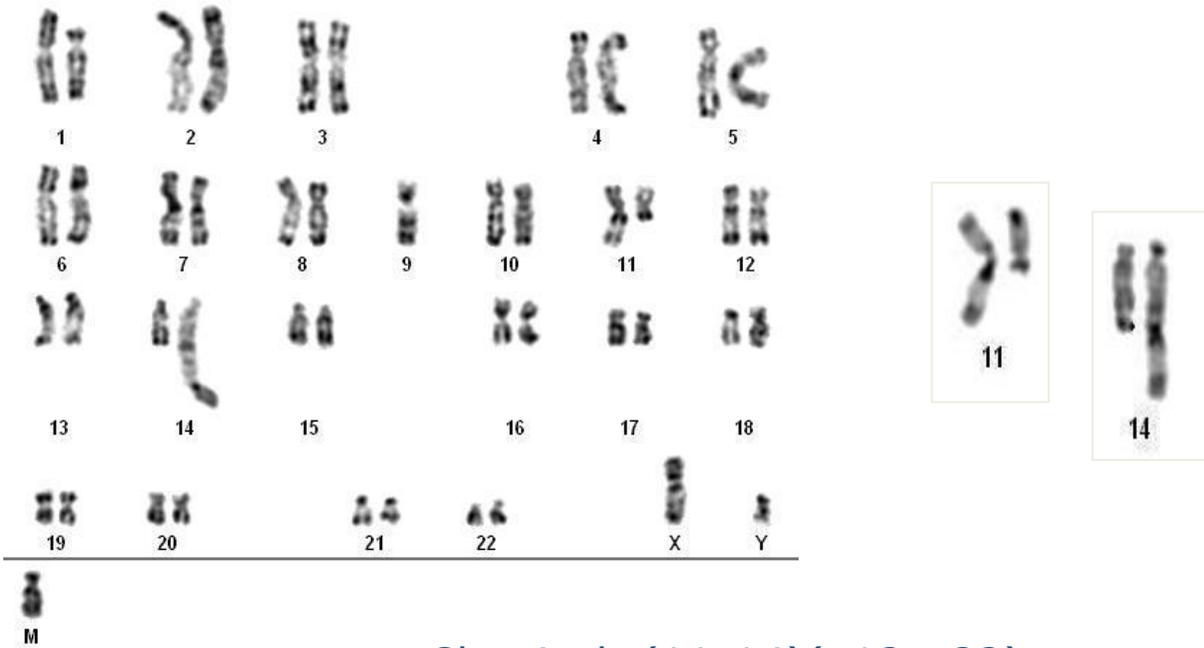
# Q1) Based on history, clinical examination what is the most likely explanation of his finding?

1. Lymphoma with Leukemic cells
2. Chronic lymphocytic leukemia
3. Primary immune deficiency
4. Chronic myelogenous monocytic leukemia
5. GI tract cancer with metastasis





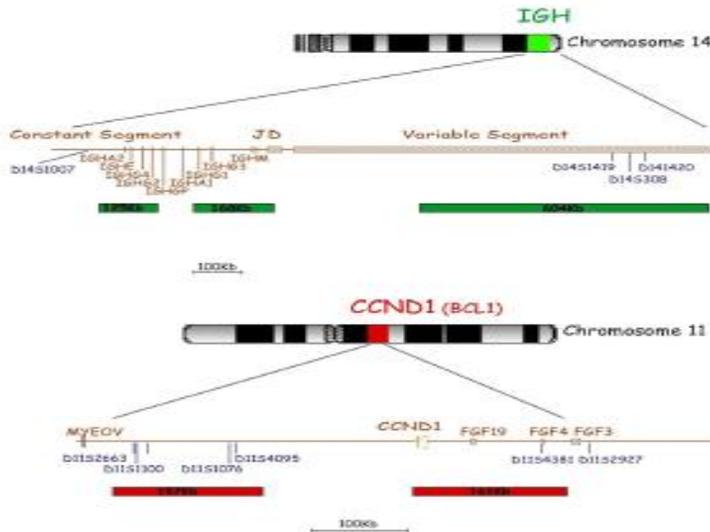
# Cytogenetic



Classical t(11;14)(q12;q32)



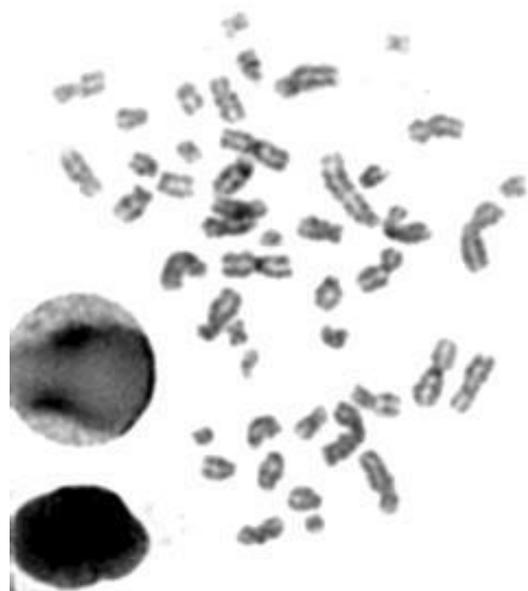
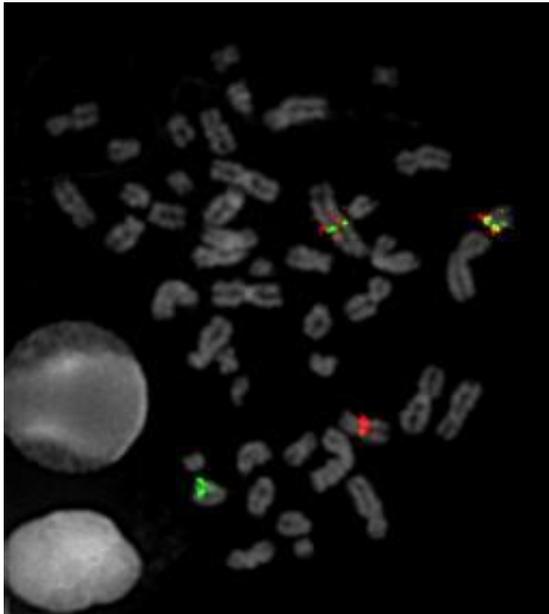
# FISH





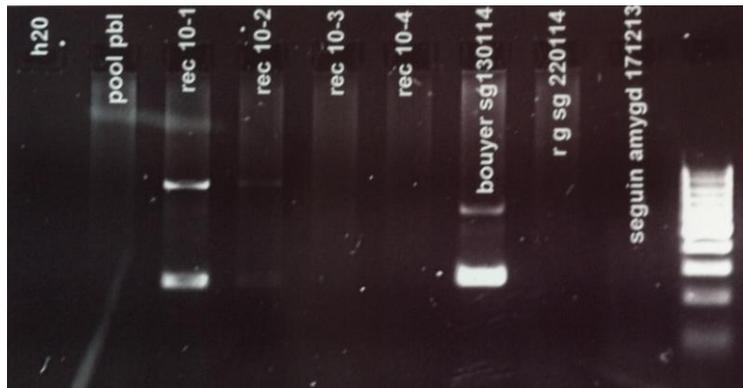
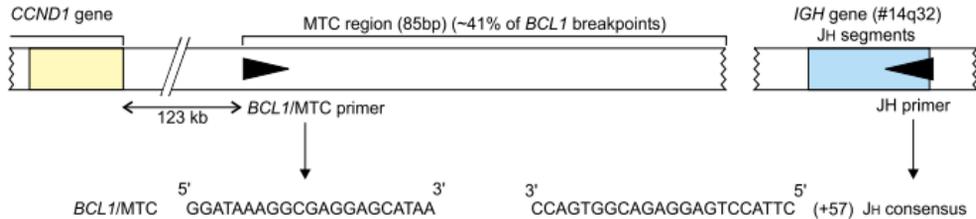
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# FISH



# Molecular Biology

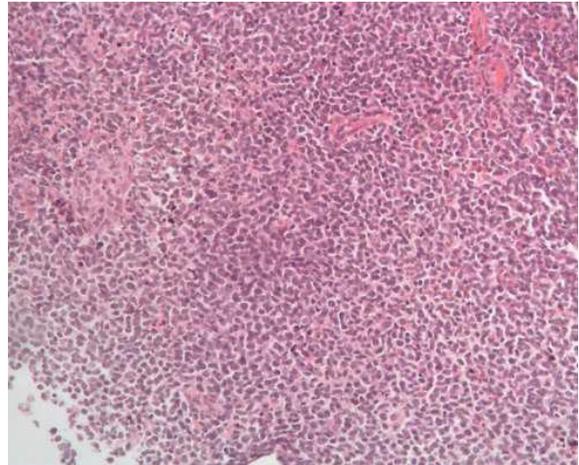
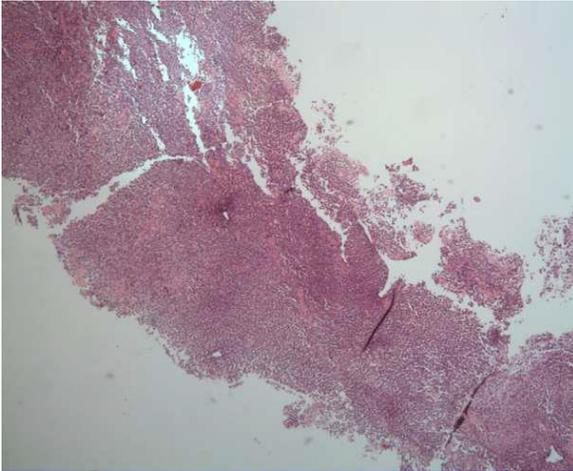
## a. *BCL1* locus (#11q13)





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## Excisional LN biopsy

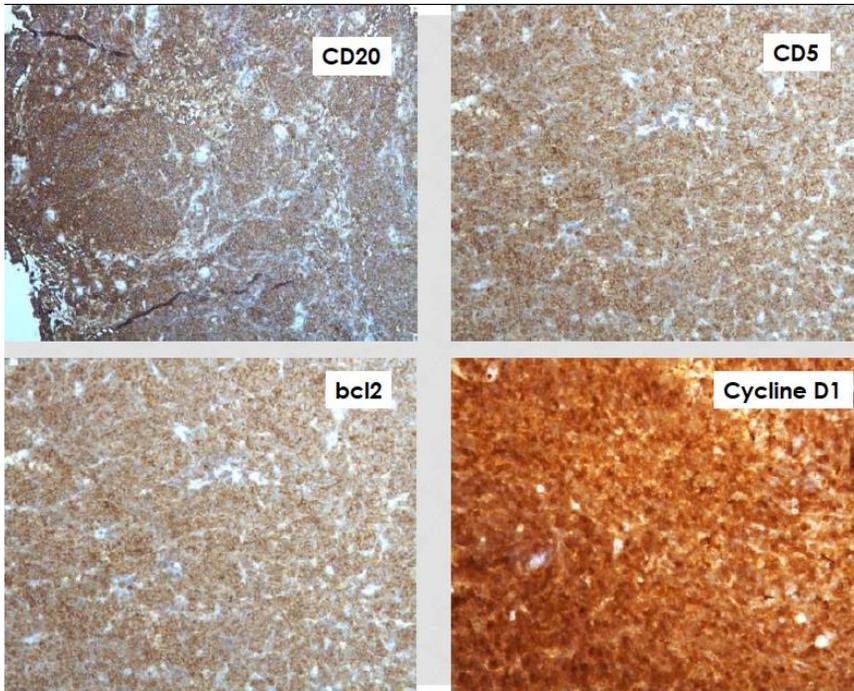




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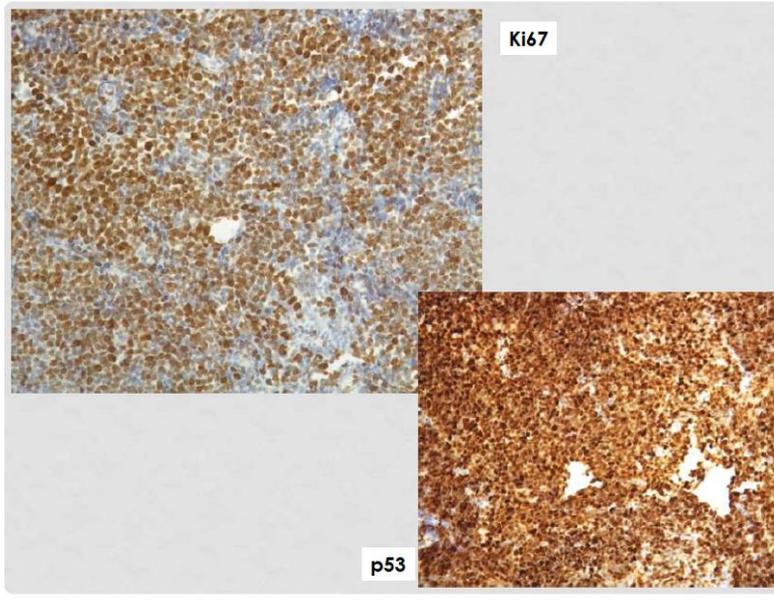


# Excisional LN biopsy



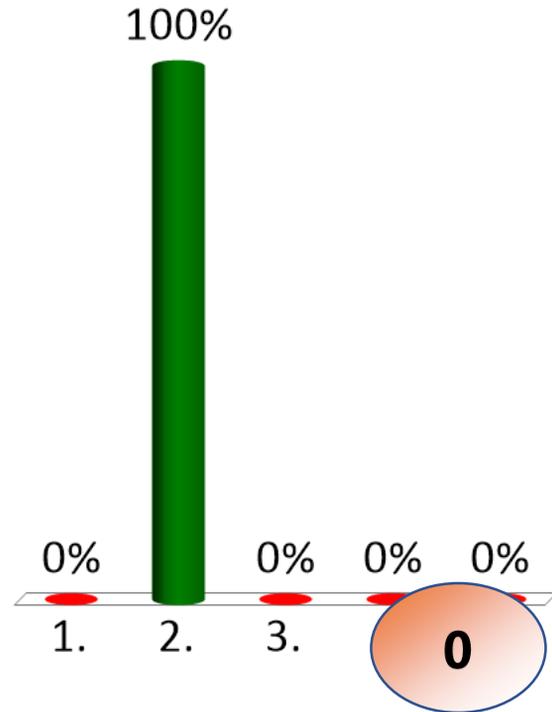


# Excisional LN biopsy



## Q2) According to the WHO classification, the diagnosis is:

1. Marginal zone lymphoma
2. Classical pleomorphic mantle cell lymphoma
3. Chronic lymphocytic leukemia
4. Acute lymphoblastic leukemia
5. CD5+ diffuse large B cell lymphoma





# Blood cytometry

**Tableau 1.** *Scoring system* selon Matutes [2]

Marqueurs	1 point	0 point
Smlg	Faible expression	Moyenne/forte expression
CD5	Positif	Négatif
CD23	Positif	Négatif
FMC7	Négatif	Positif
CD22	Faible exp/négatif	Moyenne/forte expression



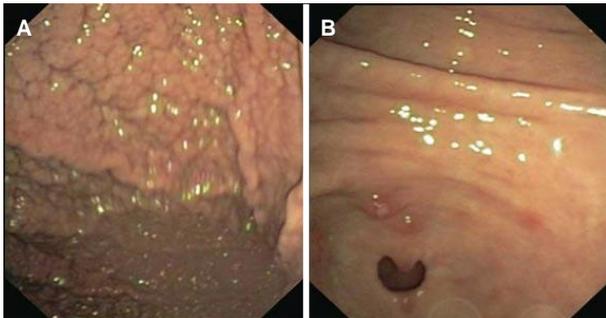
## Differential diagnosis

	CD5 <sup>?</sup>	CD10 <sup>?</sup>	CD23 <sup>?</sup>	bcl-6 <sup>?</sup>	<sup>?</sup> Chromosomal Abnormalities <sup>?</sup>
LLC <sup>?</sup> (30%) <sup>?</sup>	+ <sup>?</sup>	- <sup>?</sup>	+ <sup>?</sup>	- <sup>?</sup>	trisomy <sup>?</sup> 12 <sup>?</sup>
lympho- <sup>?</sup> plasmacytoid <sup>?</sup>	- <sup>?</sup>	- <sup>?</sup>	- <sup>?</sup>	- <sup>?</sup>	NA <sup>?</sup>
Mantle <sup>?</sup> cell <sup>?</sup>	+ <sup>?</sup>	-/+ <sup>?</sup>	- <sup>?</sup>	- <sup>?</sup>	t(11;14) <sup>?</sup>
follicular <sup>?</sup>	- <sup>?</sup>	+/- <sup>?</sup>	-/+ <sup>?</sup>	+ <sup>?</sup>	t(14;18) <sup>?</sup>
<sup>?</sup> Marginal <sup>?</sup> Zone <sup>?</sup>	<sup>?</sup> /+ <sup>?</sup>	- <sup>?</sup>	-/+ <sup>?</sup>	- <sup>?</sup>	trisomy <sup>?</sup> 3 <sup>?</sup> <sup>?</sup> <b>t(11;14)</b> <sup>?</sup>



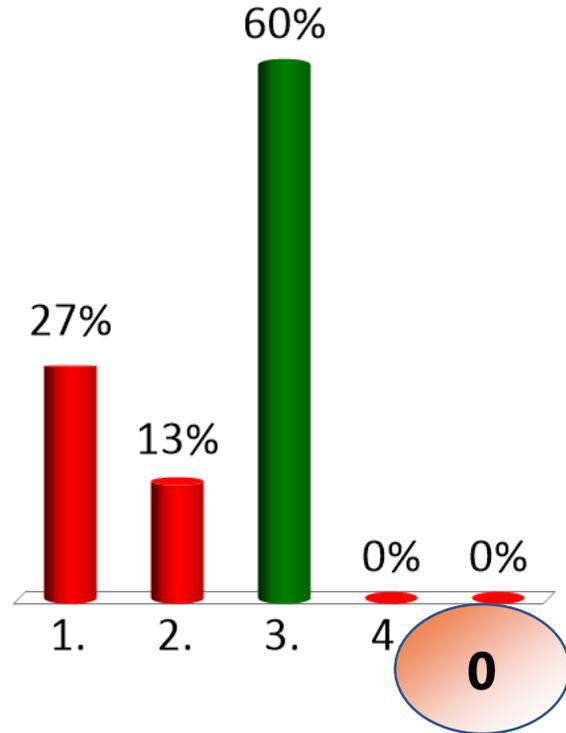
## Staging

- CT scan Lymph nodes mediastinum (small), abdominal;
- PET scan positive SUV12 (abdominal and mediastinum lymph nodes)
- GI Tract endoscopy



# Q3) According to the prognosis index of Mantle cell lymphoma it is classified as:

1. Stage IV with Low MIPI and low aggressiveness
2. Stage IV with high MIPI and low biological aggressiveness
3. Stage IV Intermediate MIPI and high biological aggressiveness
4. Lymphomatous Polyposis
5. Localized Mantle cell lymphoma





# New combined Biological MIPI MIPI-c

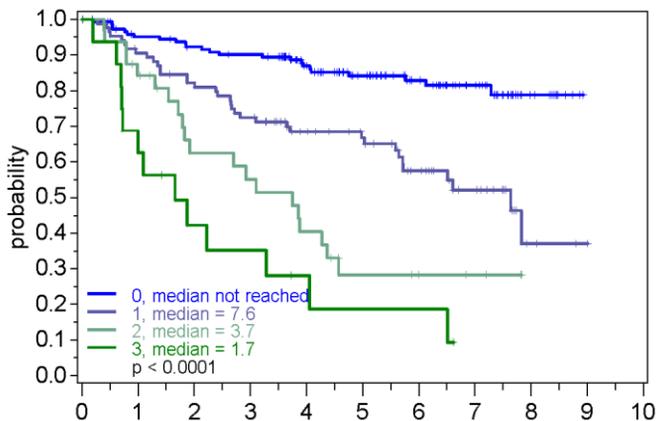
MIPI Group	Ki-67 Index	MIPI-c Group
Low Risk	<30%	Low Risk
Low Risk	≥30%	Low Intermediate Risk
Intermediate Risk	<30%	Low Intermediate Risk
Intermediate Risk	≥30%	High Intermediate Risk
High Risk	<30%	High Intermediate Risk
High Risk	≥30%	High Risk



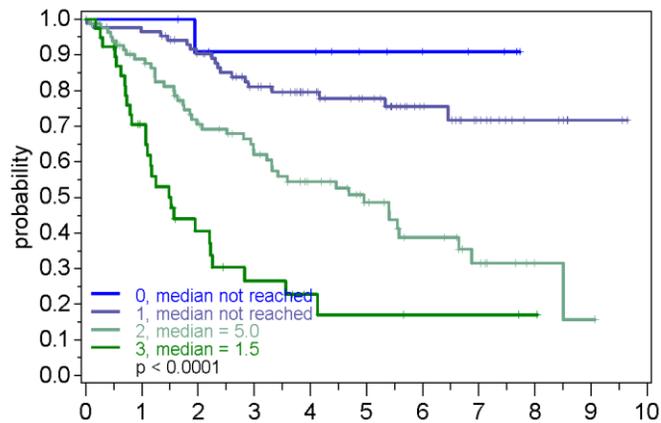
# OS according to MIPI-C In Age groups

< 65 years

>= 65 years



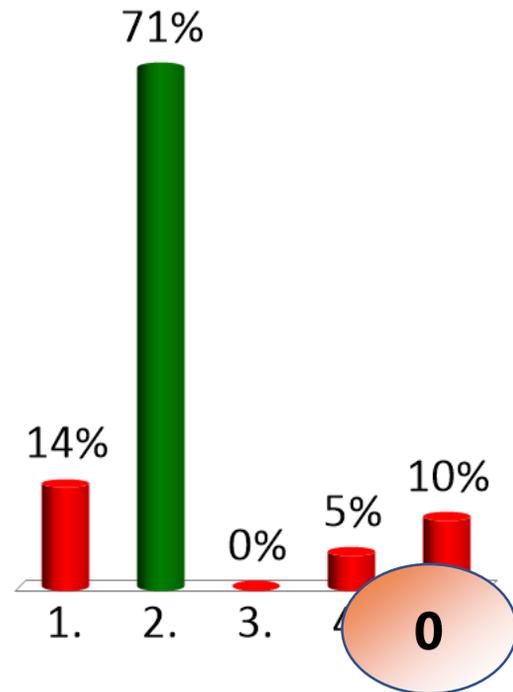
	years from registration									
Numbers At Risk	0	1	2	3	4	5	6	7	8	9
0	150	135	129	125	101	80	61	37	11	0
1	87	76	67	60	45	39	27	17	3	0
2	33	26	17	15	11	6	4	3	0	
3	16	10	6	5	3	2		0		



	years from registration									
Numbers At Risk	0	1	2	3	4	5	6	7	8	9
0	12	10	9	6	4	3	0	0	0	0
1	88	82	72	58	45	37	21	13	6	2
2	83	70	52	42	32	22	14	8	2	1
3	39	24	12	7	4	3	2	1	1	0

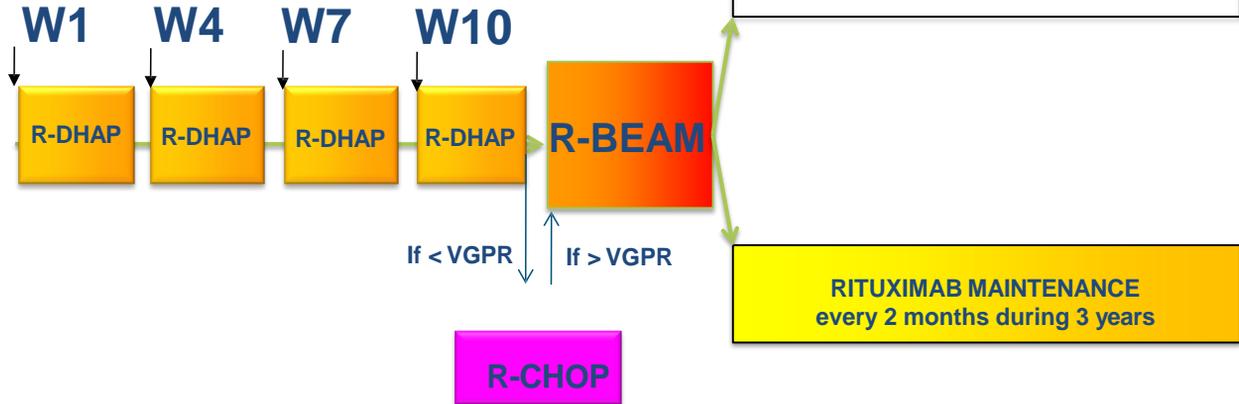
## Q4) What is the treatment approach?

1. R-CHOPX8 +R maintenance
2. 4 RDHAP/Ox +auto SCT +R maintenance
3. Revlimid+R
4. R-CHOPx6 + Allogeneous stem cell transplantation
5. R-BendamustineX6





# LyMa Trial



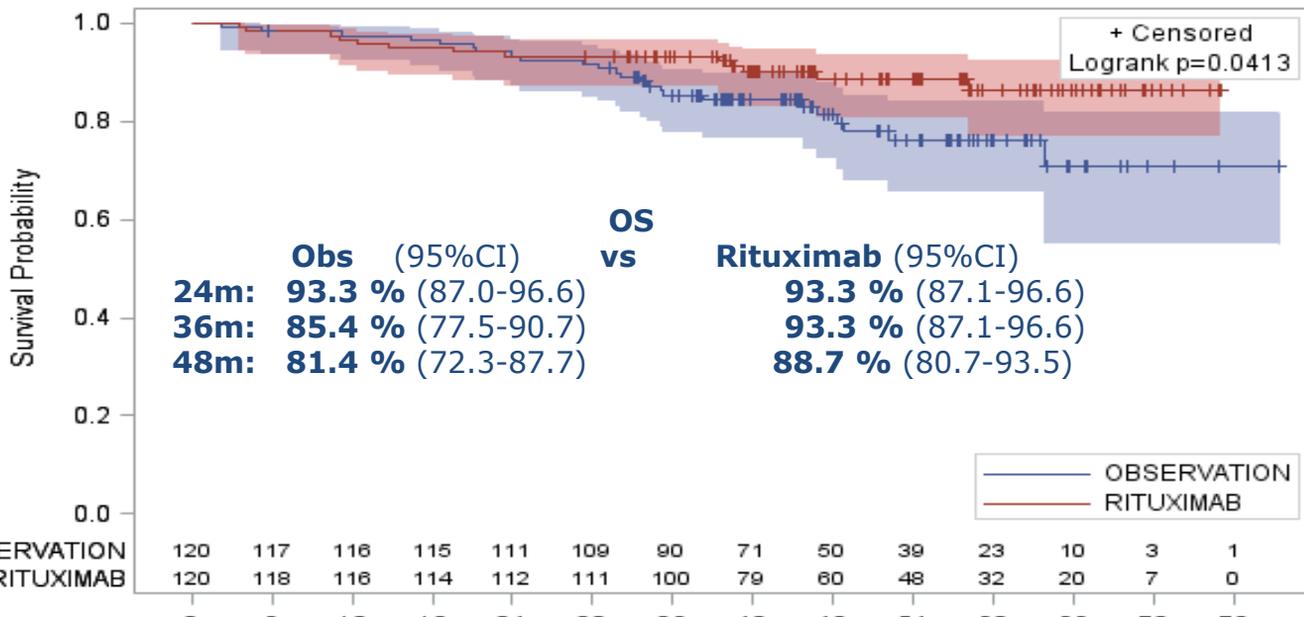
**R-DHAP:** Rituximab 375 mg/m<sup>2</sup>; cytarabine 2 g/m<sup>2</sup> x2 IV 3 hours injection 12 hours interval;  
dexamethasone 40 mg days 1-4; cisplatin 100 mg/m<sup>2</sup> day 1 (or oxaliplatin or carboplatin)

**R-BEAM:** Rituximab 500 mg/m<sup>2</sup> day 8; BCNU 300 mg/m<sup>2</sup> day 7; Etoposide 400 mg/m<sup>2</sup>/d day 6 to day 3;  
cytarabine 400 mg/m<sup>2</sup>/d day 6 to day 3;  
melphalan 140 mg/m<sup>2</sup> day 2

# OS from randomizationmFU: 50.2m (46.4-54.2)

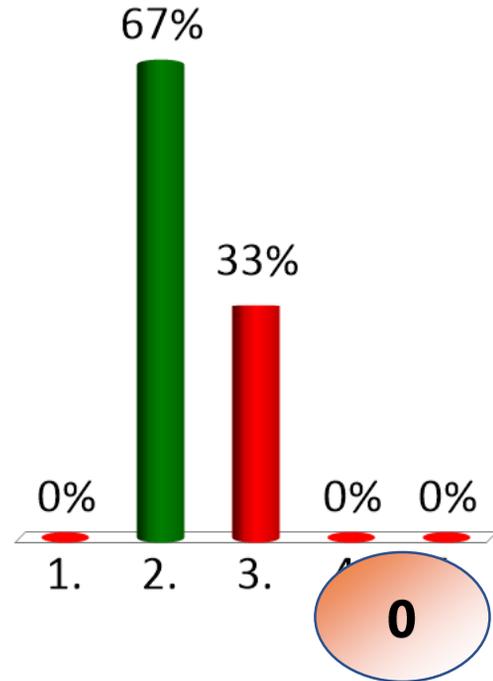
## OS from randomization according to treatment arm - ITT

With Number of Subjects at Risk and 95% Confidence Limits



# Q5) The patient relapsed within 6 years after completing first-line therapy, what is your choice in this fit patient?

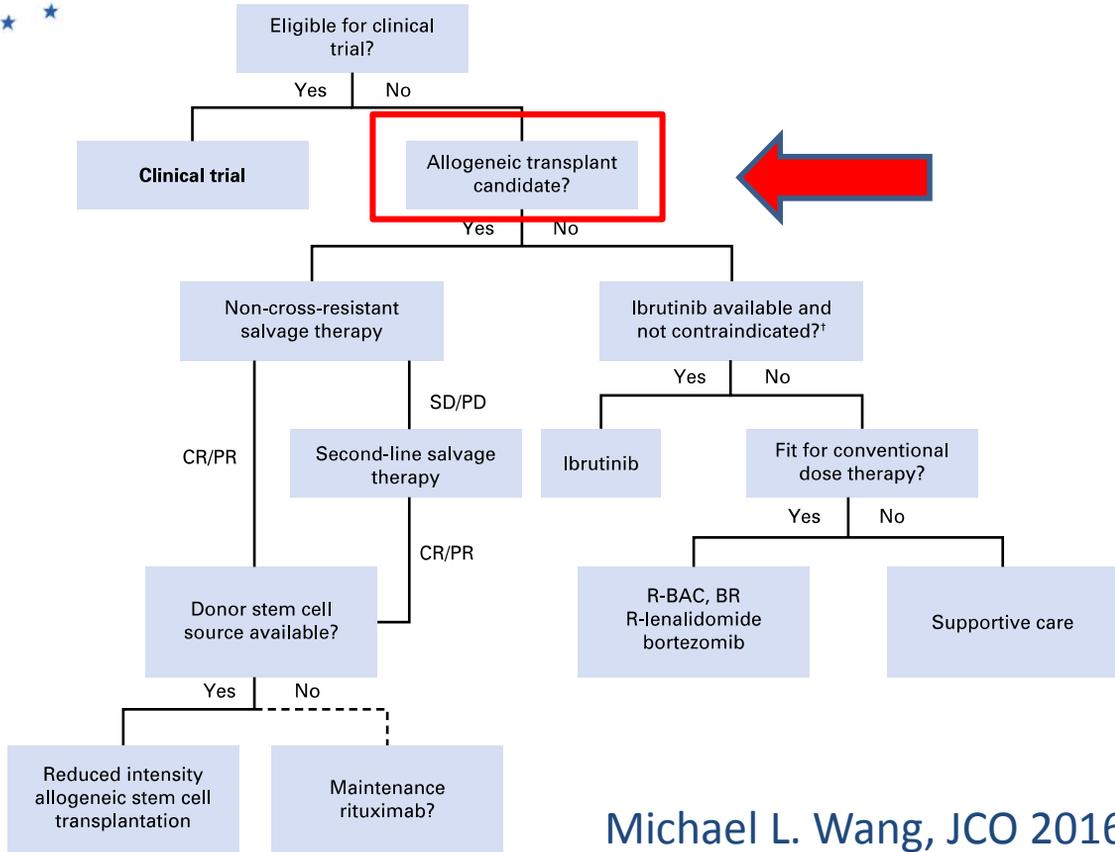
1. R-CHOP alone
2. Bendamustine containing chemotherapy or ibrutinib followed by allogeneous stem cell transplantation
3. Salvage chemotherapy followed by Autologous stem cell transplantation
4. R-BAC alone
5. Revlimide or Bortezomib alone



# Mantle Cell Lymphoma Relapse



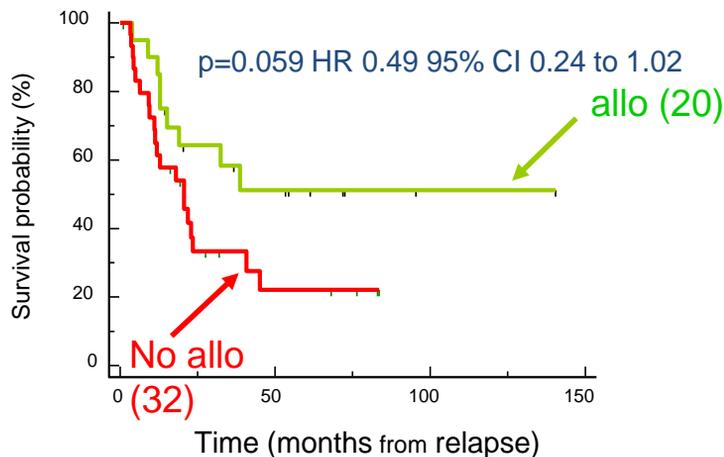
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Michael L. Wang, JCO 2016



## MCL: AlloSCT for autoSCT failure HD/KI/HH 1994-2008 (52 REL after 119 autotransplants) Overall survival





# Treatment of the patient

Patient received 4 cycles of R-BAC



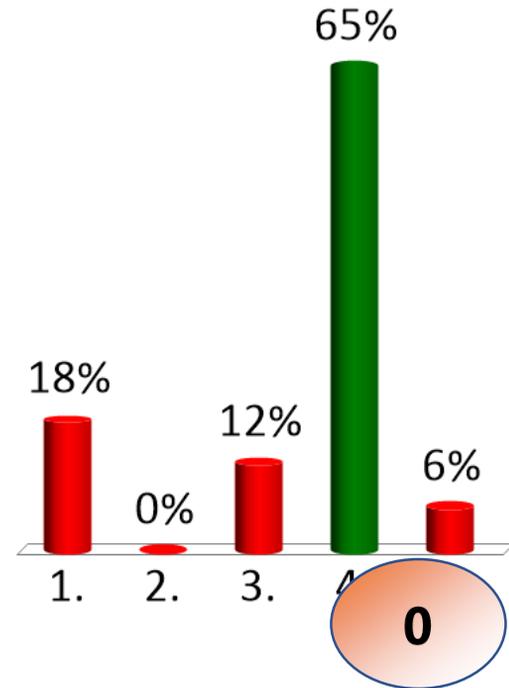
Metabolic Complete remission and MRD negative



FB2+ATG → SCT sibling donor → GVH prophylaxy by  
Ciclo

**Q6) No GVH was observed but unfortunately, he relapsed 3 months after Allo SCT at he MRD level. How is your approach?**

1. Stop immunosuppression and start DLI
2. Stop immunosuppression and start chemotherapy and DLI
3. CAR-T cells
4. Stop immunosuppression and start Ibrutinib and DLI
5. Stop immunosuppression and start revlimid+Rituximab



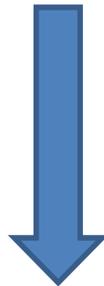


# Treatment of the patient

He received Ibrutinib and DLI



Complete remission and moderate chronic GVH (NIH score 1)



FU: 15 months

Still on Ibrutinib MRD negative