HOW IS MANTLE CELL LYMPHOMA TREATED?

Bijal Shah, MD, MS
Associate Member
Department of Malignant Hematology
Moffitt Cancer Center
Tampa, FL

LEUKEMIA & LYMPHOMA SOCIETY®

DISCLOSURES

How is Mantle Cell Lymphoma Treated?

- Celgene/Juno/BMS, Novartis, Spectrum/Acrotech, Adaptive, AstraZeneca, Precision BioSciences, Kite/Gilead, Pfizer, Amgen, BeiGene
  - Advisory Board, Honoraria
- Incyte, Jazz, Kite/Gilead
  - Research Funding
- Off-label content will be discussed

How Is Mantle Cell Lymphoma Treated?

Bijal Shah, MD, MS

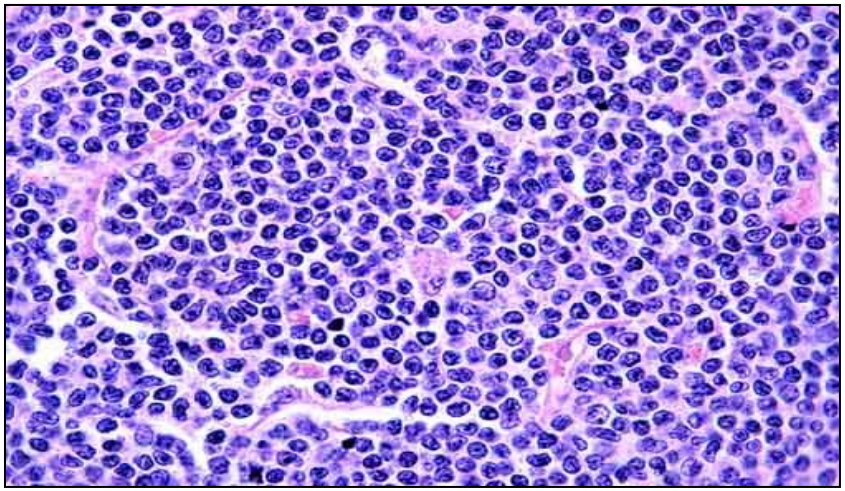
Clinical Leader for Mantle Cell Lymphoma and Acute Lymphoblastic Leukemia
Director of Translational Research Initiatives in Lymphoma & Acute Lymphoblastic Leukemia
Associate Member
H. Lee Moffitt Cancer Center

Objectives

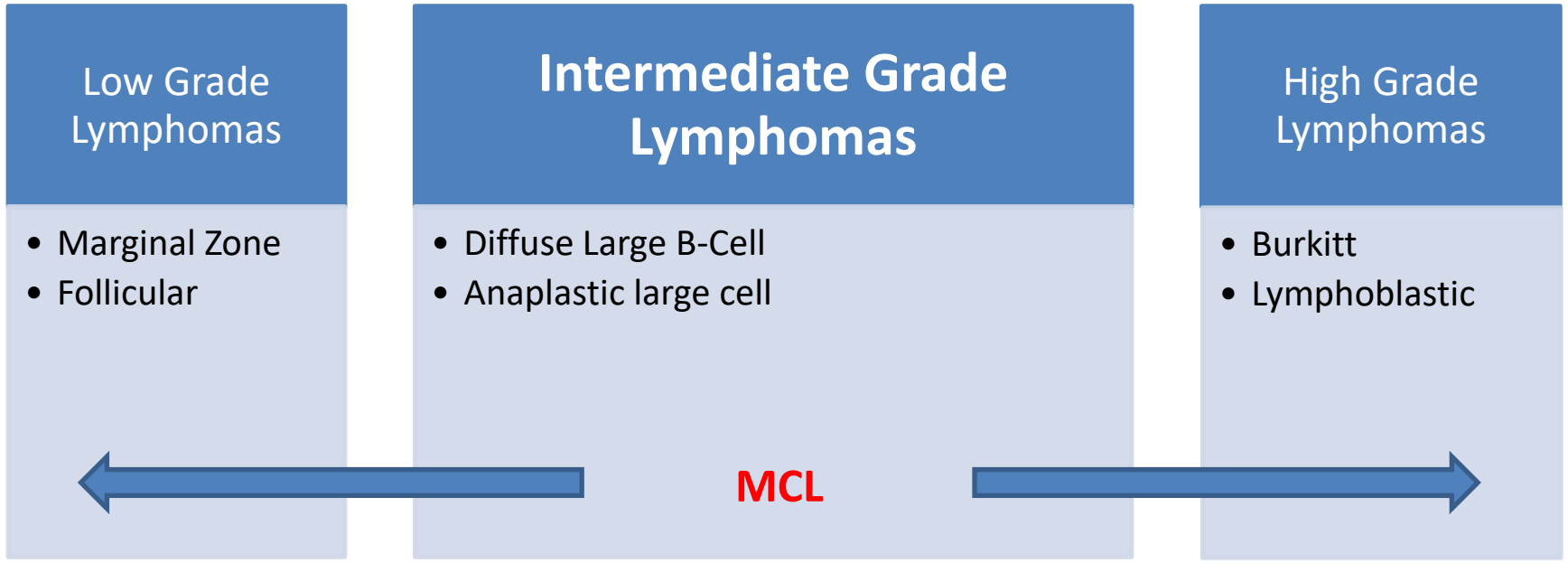
- Reconciling Heterogeneity in MCL: *The Inevitable Slope of Chemotherapy Resistance*
- Defining Treatment Objectives: *Is Intensity Still the Answer?*
- Relapsed & Refractory MCL: *Are We Getting Anywhere?*
- Roadmap for the Future: *Bringing Novel Approaches Forward*

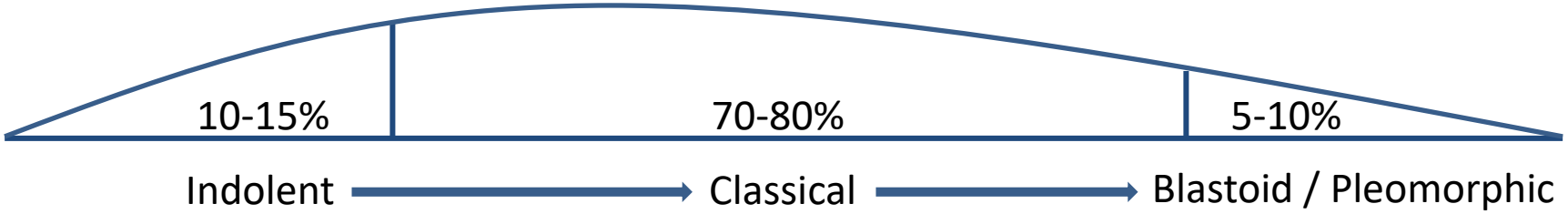
Mr. RR

- 64yo WM in excellent health presented 5/2010 with WBC of 20 in the absence of B-symptoms. Differential confirmed a lymphocyte predominance, and flow cytometry ultimately disclosed an immunophenotype compatible with MCL.
- FISH studies performed 2/2011 revealed loss of 13q [71.5%], and loss of 17p [62.5%], in addition to the expected IgH-Bcl1 translocation
- Bone marrow biopsy 5/2011 demonstrated ~2/3 involvement with MCL, with a complex cytogenetic pattern:
  - 45,XY, +7p22, t(11;14)(q13;q32),-12, der(15)t(12;15)(q12;q26), ?del(16)(q22q23), +17p11.2, +22q11.2[cp13]



How Do I "Think" About Lymphoma





Epidemiology

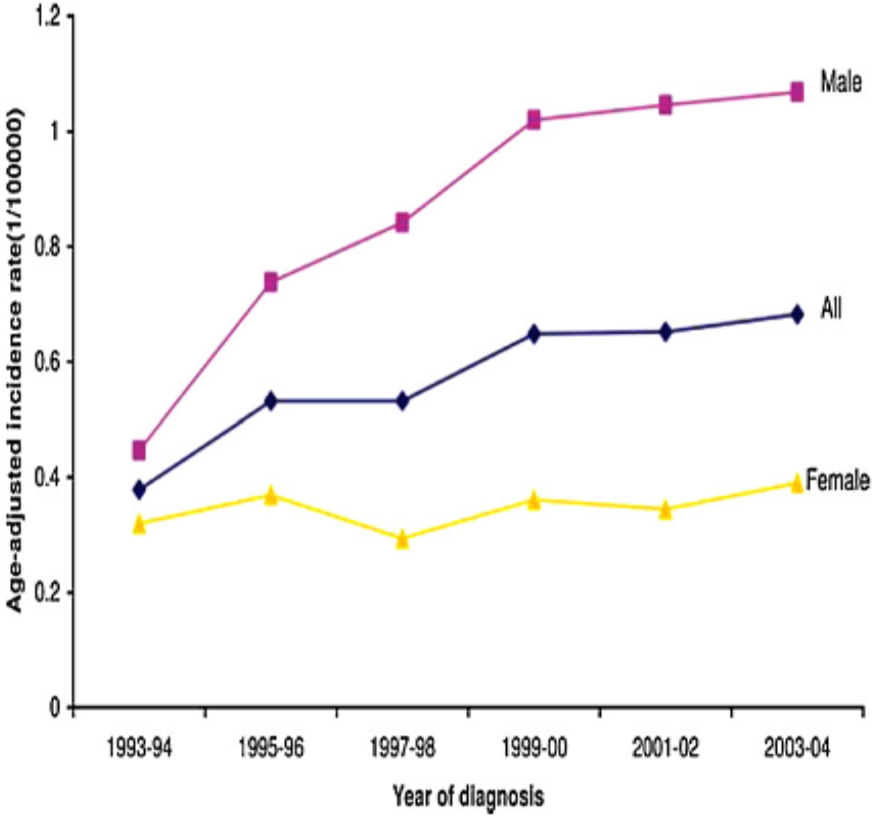
Summary of descriptive epidemiology of MCL in Europe and the US.

	Incidence rate of MCL in Europe 2000–2002 [8][a] Per 100 000 person-years	Incidence rate of MCL in the US 1992–2001/–2004 [7,9][b] Per 100 000 person-years
Overall	0.45	0.51/0.55
Sex		
Male	0.64	0.84
Female	0.27	0.34
Age (years)		
<50		0.07
50–59		0.83
60–69	NA	1.96
70–79		2.97
≥80		2.78
Race		
White		0.84/0.61
Black	NA	0.45/0.32
Asian		0.32

NA, not available.

[a] Rates were age-standardized for each included cancer register area in Europe.

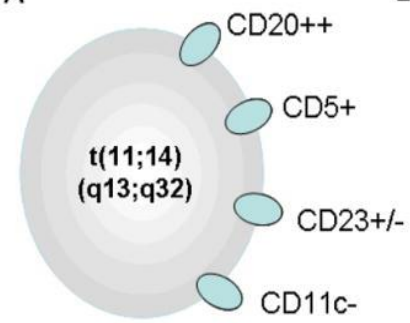
[b] Rates were age-standardized to the US population in the year 2000.



Zhou Y, et al. Cancer. 2008 Aug;113(4):791

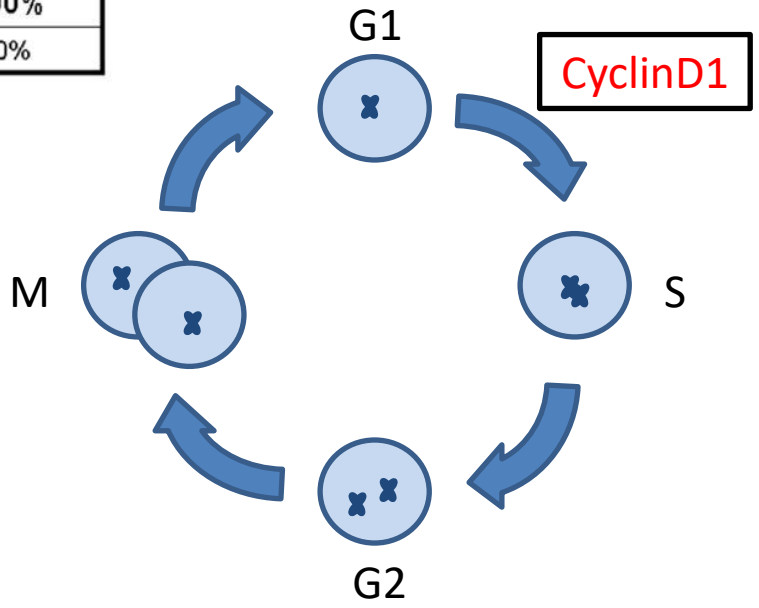
What Is MCL?

A



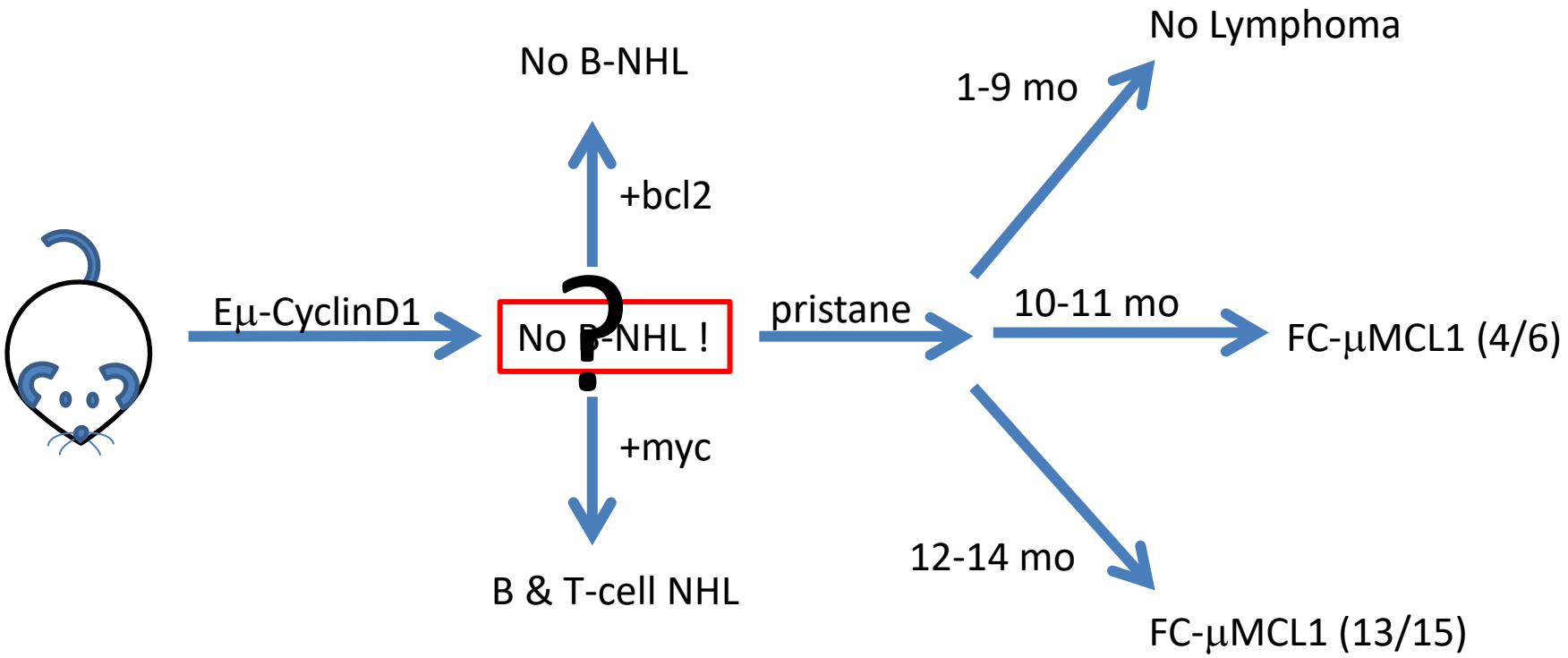
B

	Approximate Sensitivity
Cyclin D1 (Paraffin)	90%
Cyclin D1 (Frozen)	25%
Cytogenetics	50-75%
FISH for t(11;14)	**80-100%**
PCR for t(11;14)	30-40%



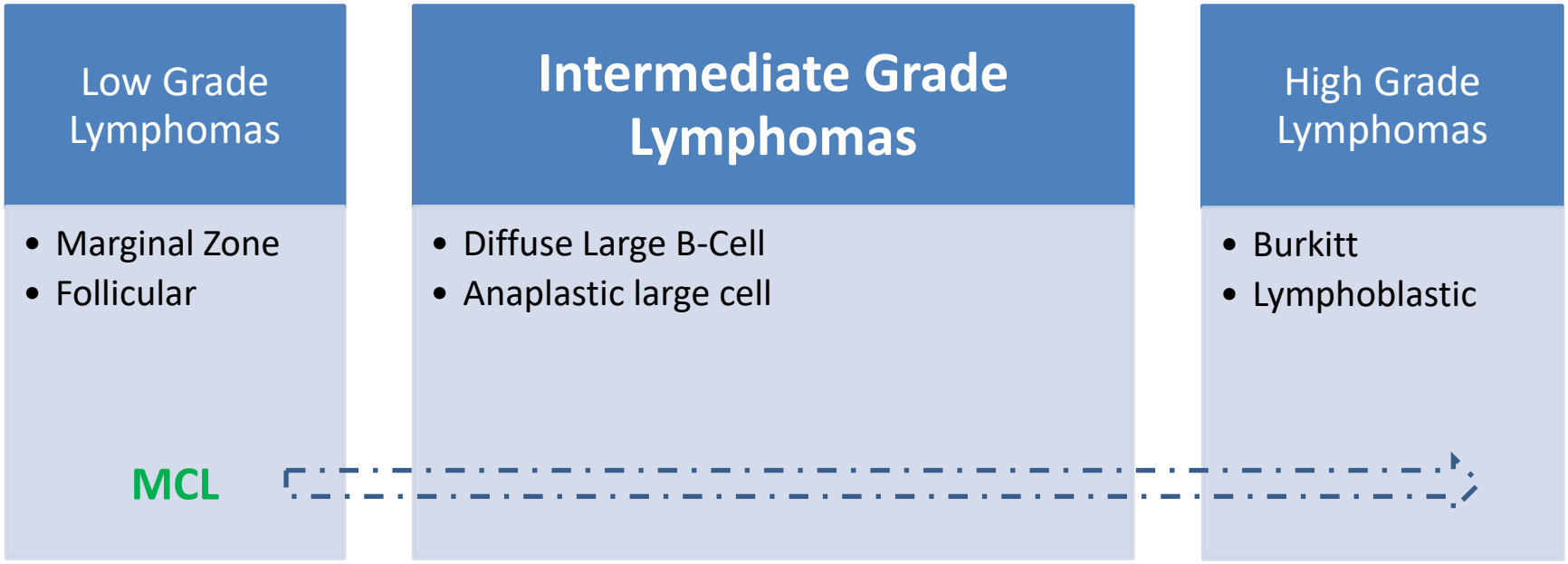
Shah B, et al. Cancer Control. 2012 Jul;19(3):227

What Is MCL?

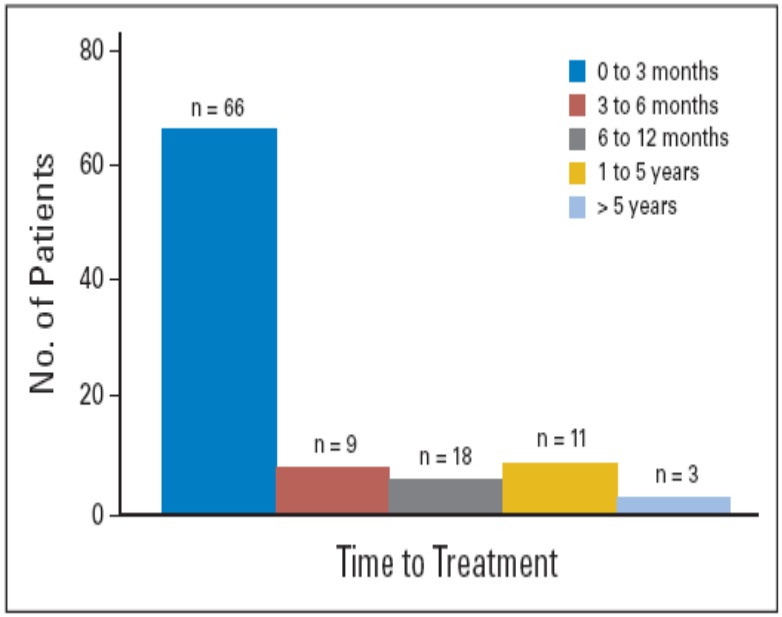


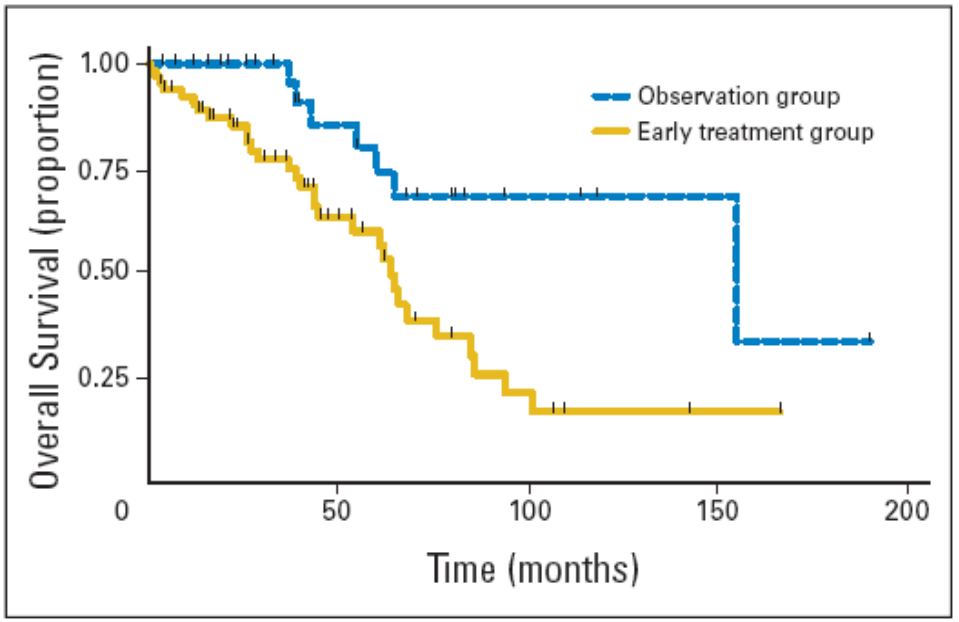
Smith MR, et al. Leukemia. 2006 May;20(5):891
Smith MR, et al. Leukemia. 2013 Jul;27(7):1592
Bodrug SE, et al. EMBO J. 1994 May;13(9):2124

“Indolent” Phase?



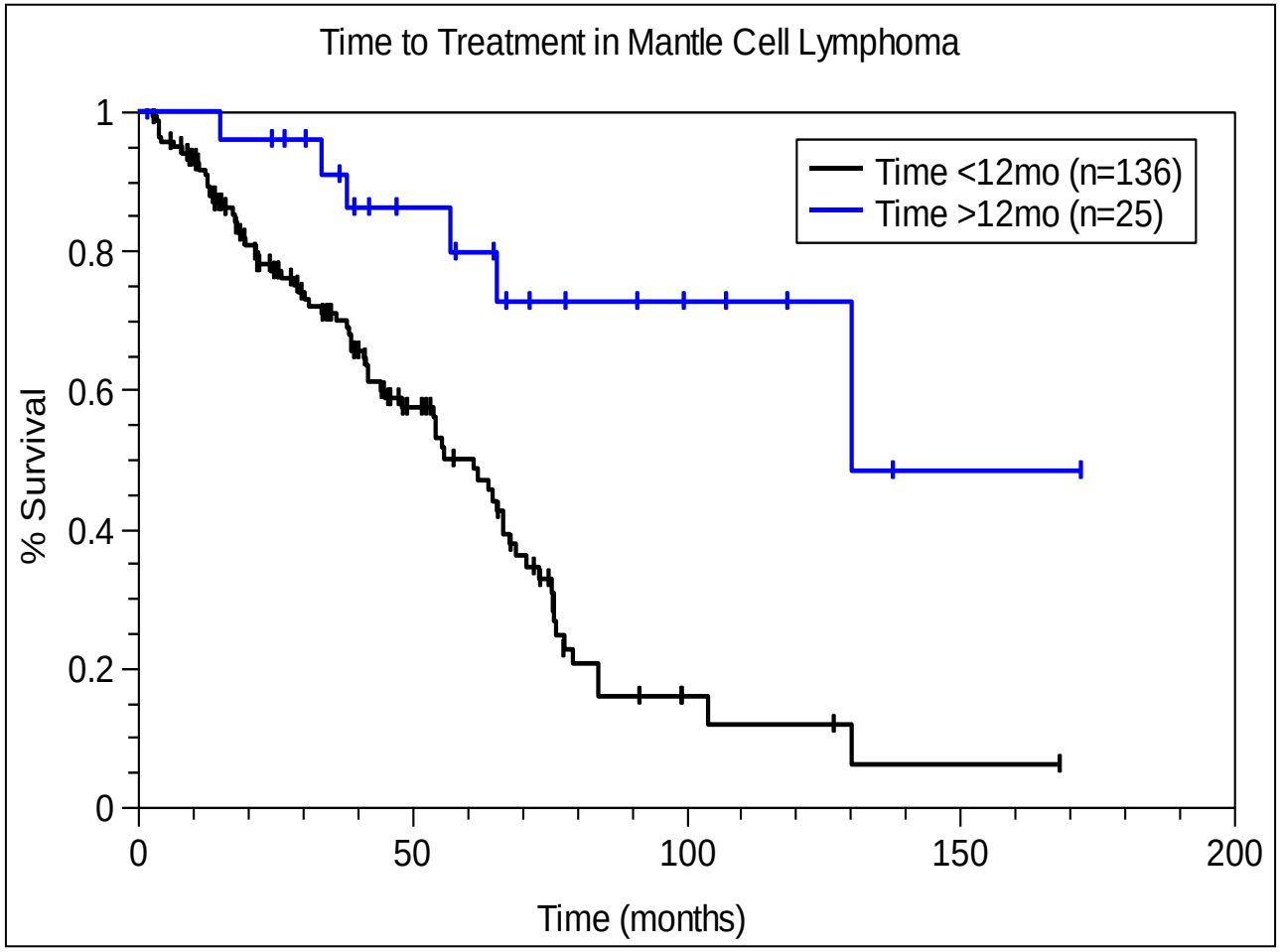
Reconciling of Indolent MCL





Martin P, et al. J Clin Oncol. 2009 Mar;27(8):1209

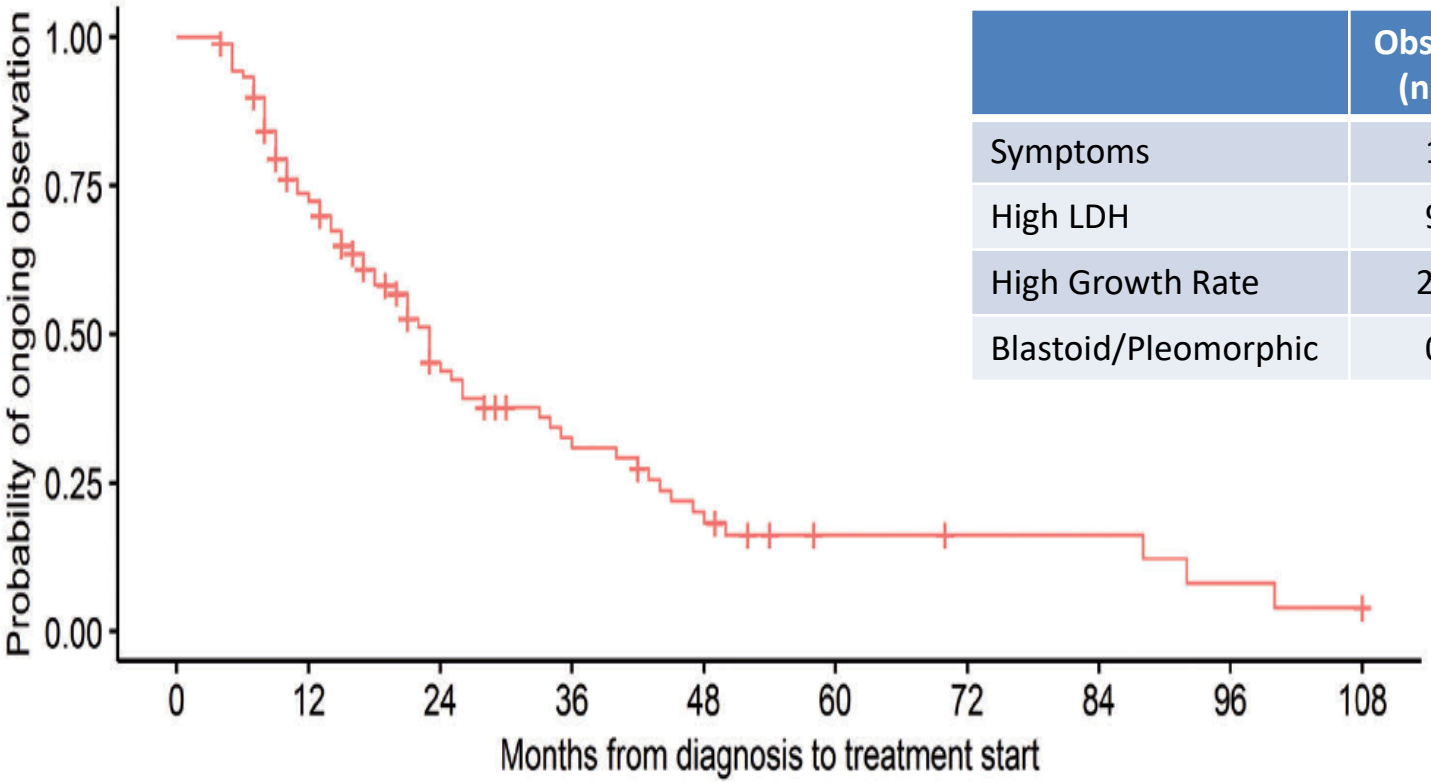
Indolent MCL: Moffitt Experience



Shah BD, et al. *Blood* (ASH Annual Meeting Abstracts) 2012 ;120: Abstract 5082

But How Do We Know Which Patients Have Indolent MCL?

Indolent MCL



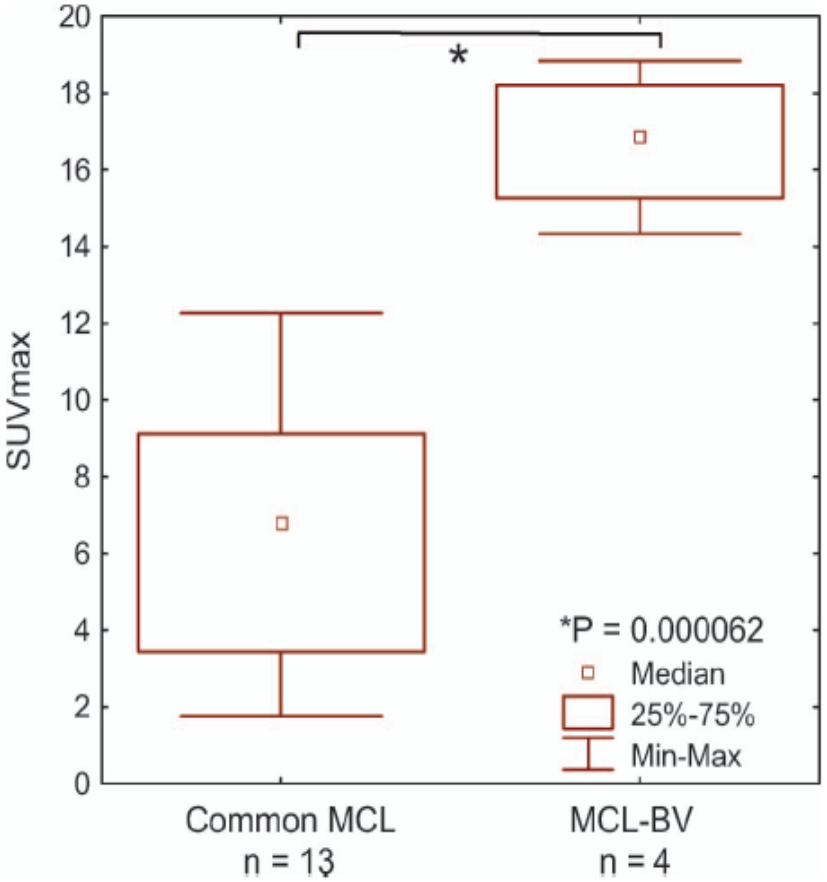
	Observed (n=90)	Treated (n=314)
Symptoms	1%	17%
High LDH	9%	35%
High Growth Rate	25%	52%
Blastoid/Pleomorphic	0%	11%

Median time to first treatment among those observed was 23 months

Kumar A, et al. Haematologica 2019; 104:e164

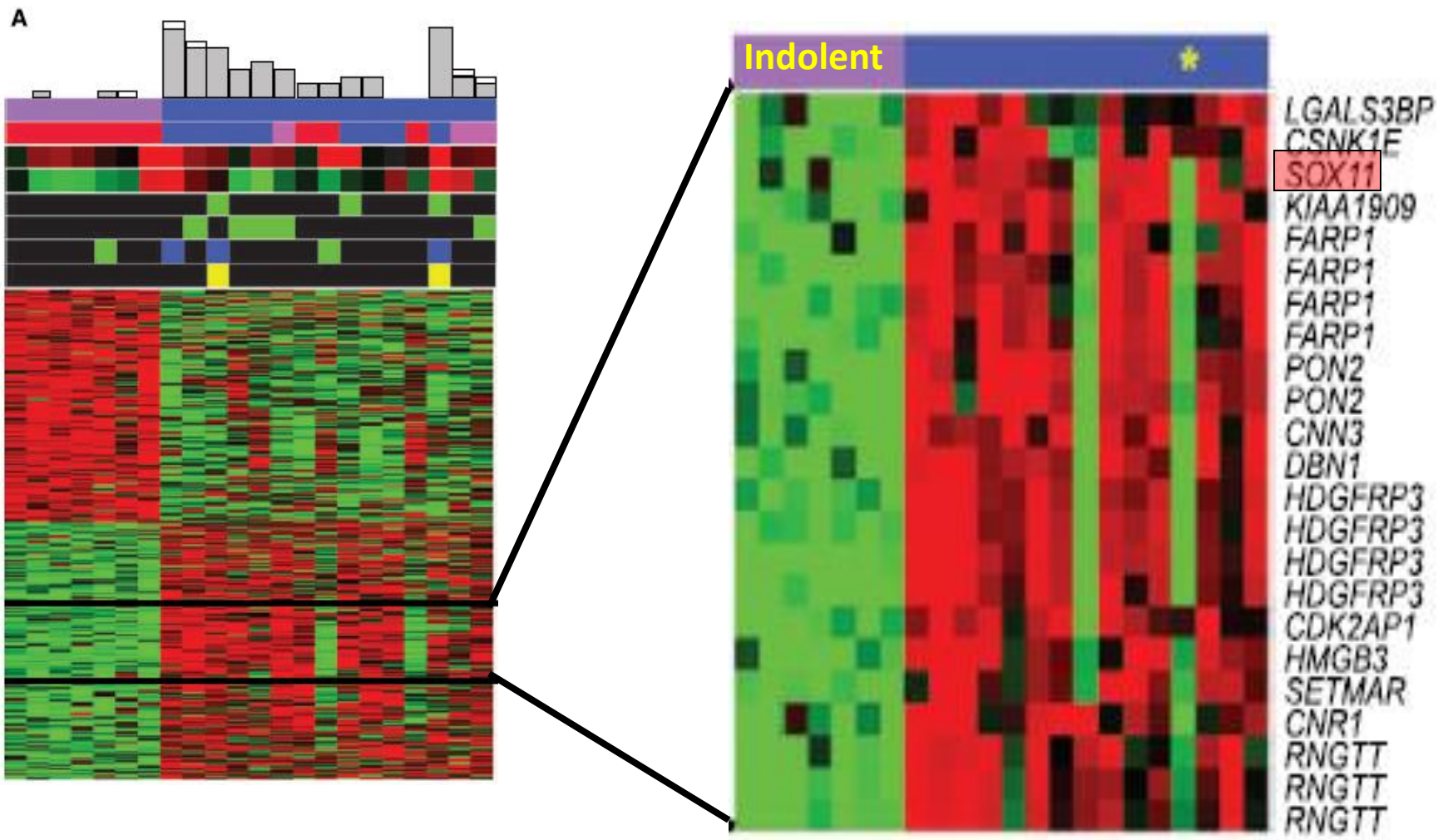
Baseline PET

- MCL-BV
  - median SUV 16.88
  - range 14.33–18.84
- MCL
  - median 6.79
  - range 2.3–12.26



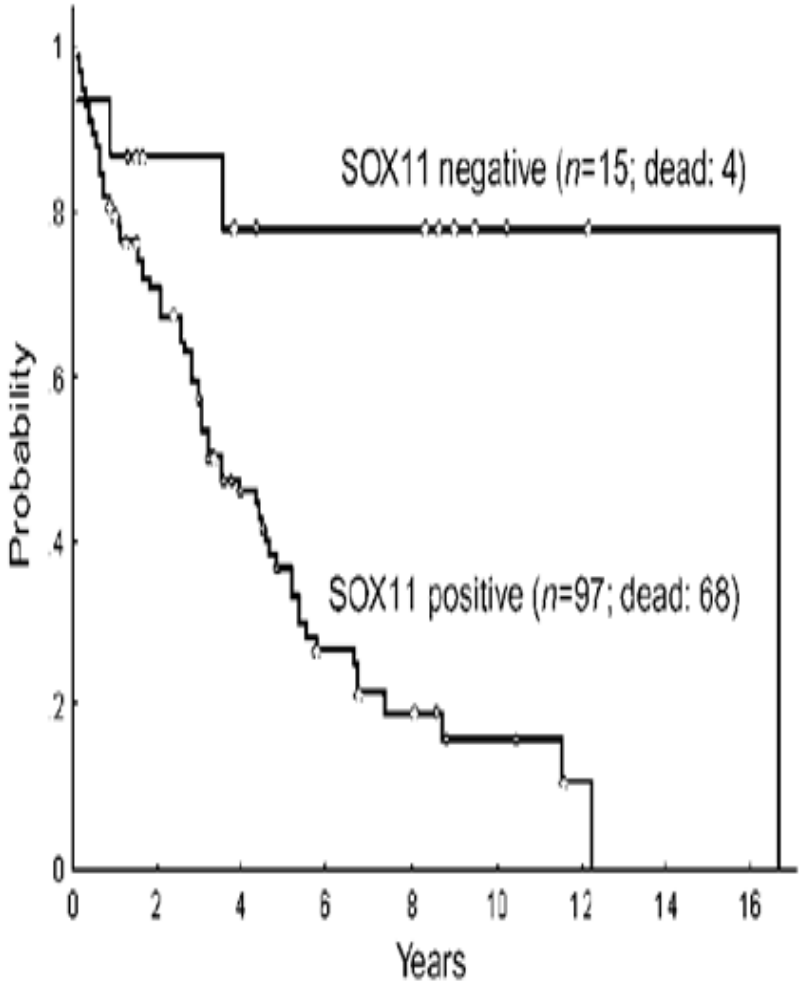
Brepoels L, et al. Leukemia & Lymphoma. 2008 Sep;49(9):1693

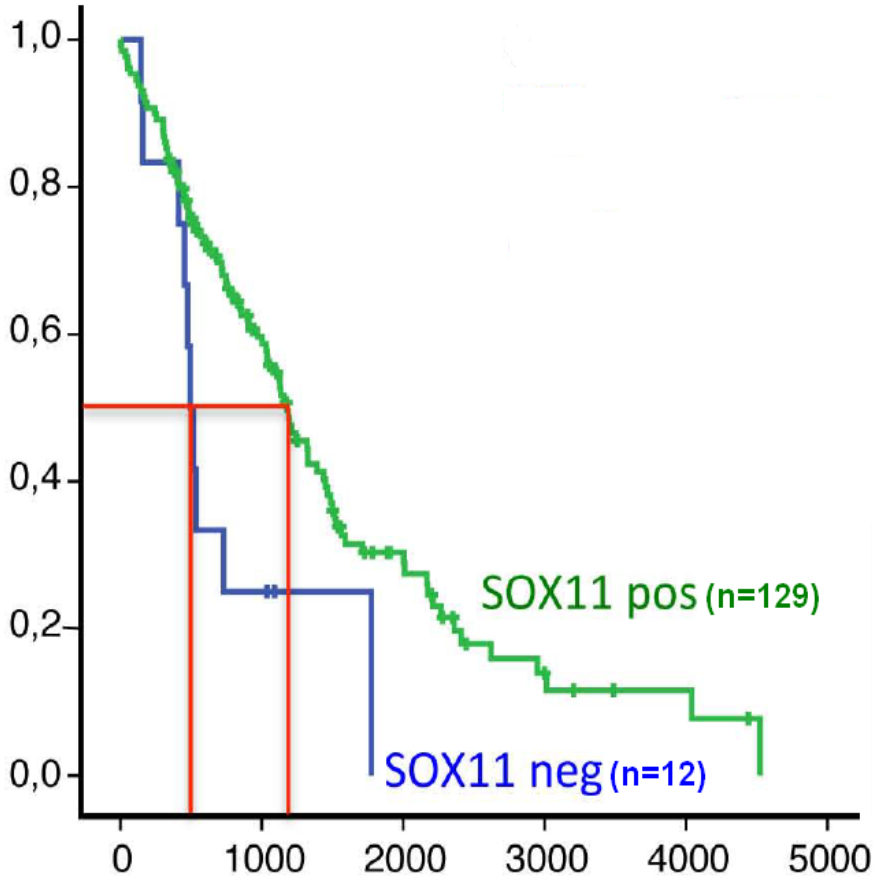
Gene Expression Profiling



Fernandez , et al. Cancer Res. 2010 Feb; 70(4): 1408

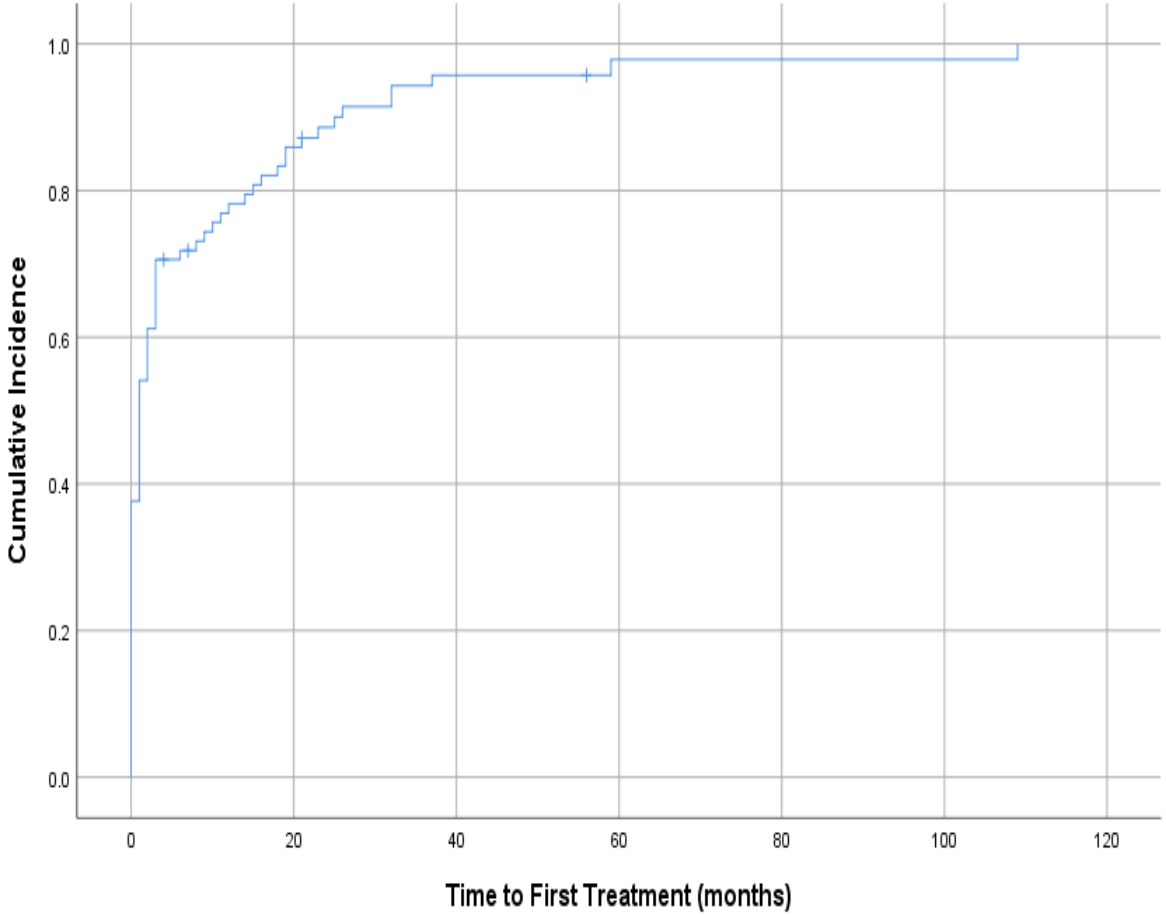
SOX11 -- Controversial





Fernandez V, et al. Cancer Res. 2010 Feb;70(4):1408
Nygren L, et al. Blood. Blood. 2012 May 3;119(18):4215-23.

High Risk Genetic Mutations May Come with Shorter Time to Treatment



Observation time among 85 patients with **TP53 mutation** in MCL

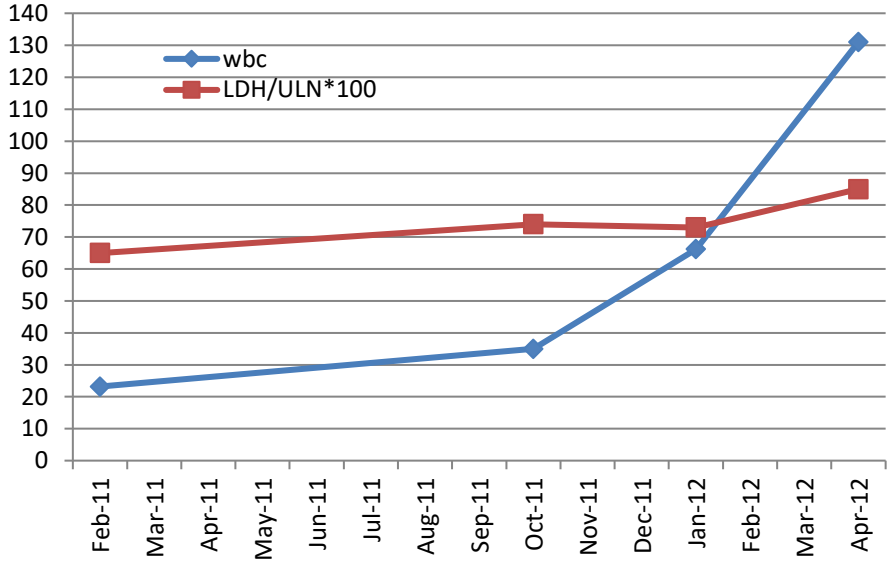
Median Time to First Treatment: **2mo**

4 patients remain under watchful waiting with a median 7mo of follow-up (**4-56 months**)

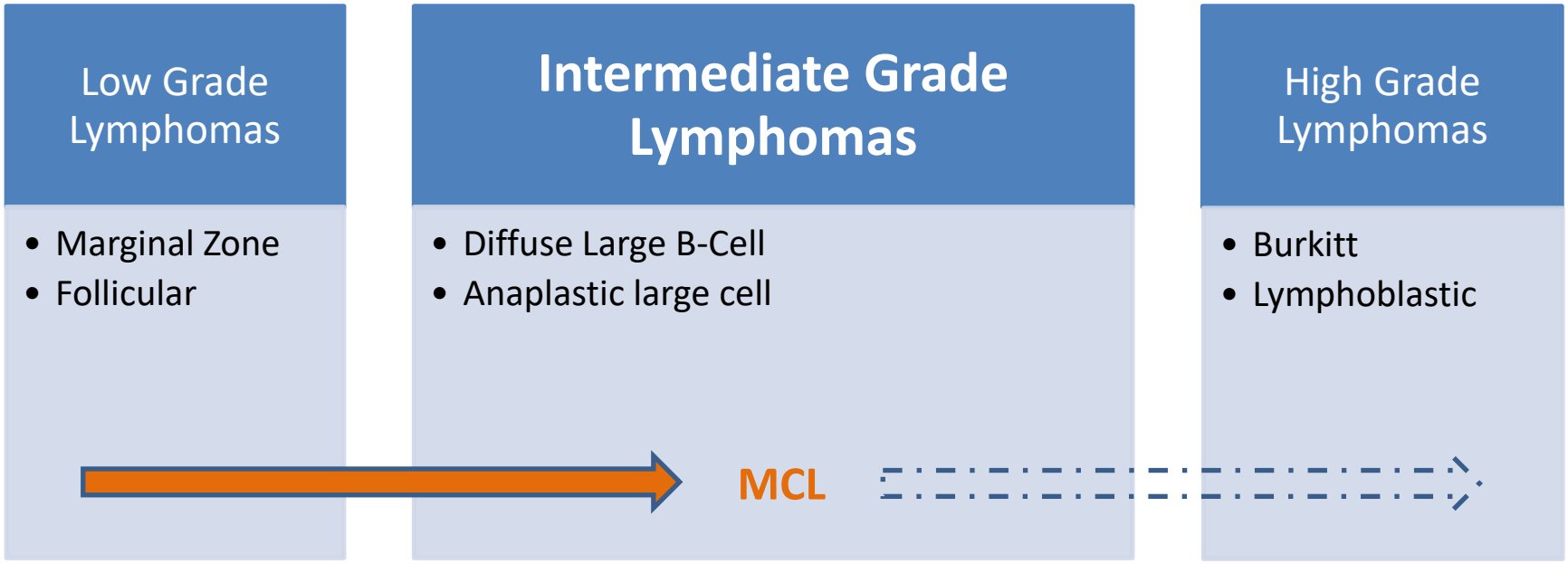
Shah N, et al. ASH 2019, Abstract 3991

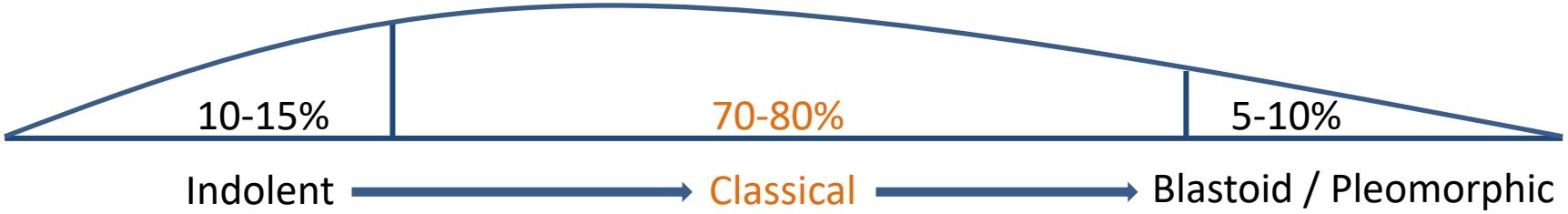
Coming Back to Mr. RR

- We decide to watch him without therapy given a lack of symptoms.
- He does well for approximately 2 years.
- In 4/2012, he was noted to have a rapidly rising WBC, with imaging showing limited lymph node enlargement (largest 2.2x1.3cm), and an enlarging spleen (16.6cm).



“Aggressive” Phase?





Predicting & Understanding Survival in MCL

The Mantle Cell Prognostic Index (MIPI)

- Evaluated 455 patients with MCL across three large German studies

- Identified four major prognostic variables
  - AGE
  - PERFORMANCE STATUS
  - LDH
  - WHITE BLOOD CELL COUNT

  AGE, PERFORMANCE STATUS: Host Tolerance

  LDH, WHITE BLOOD CELL COUNT: Disease Burden / Growth Rate

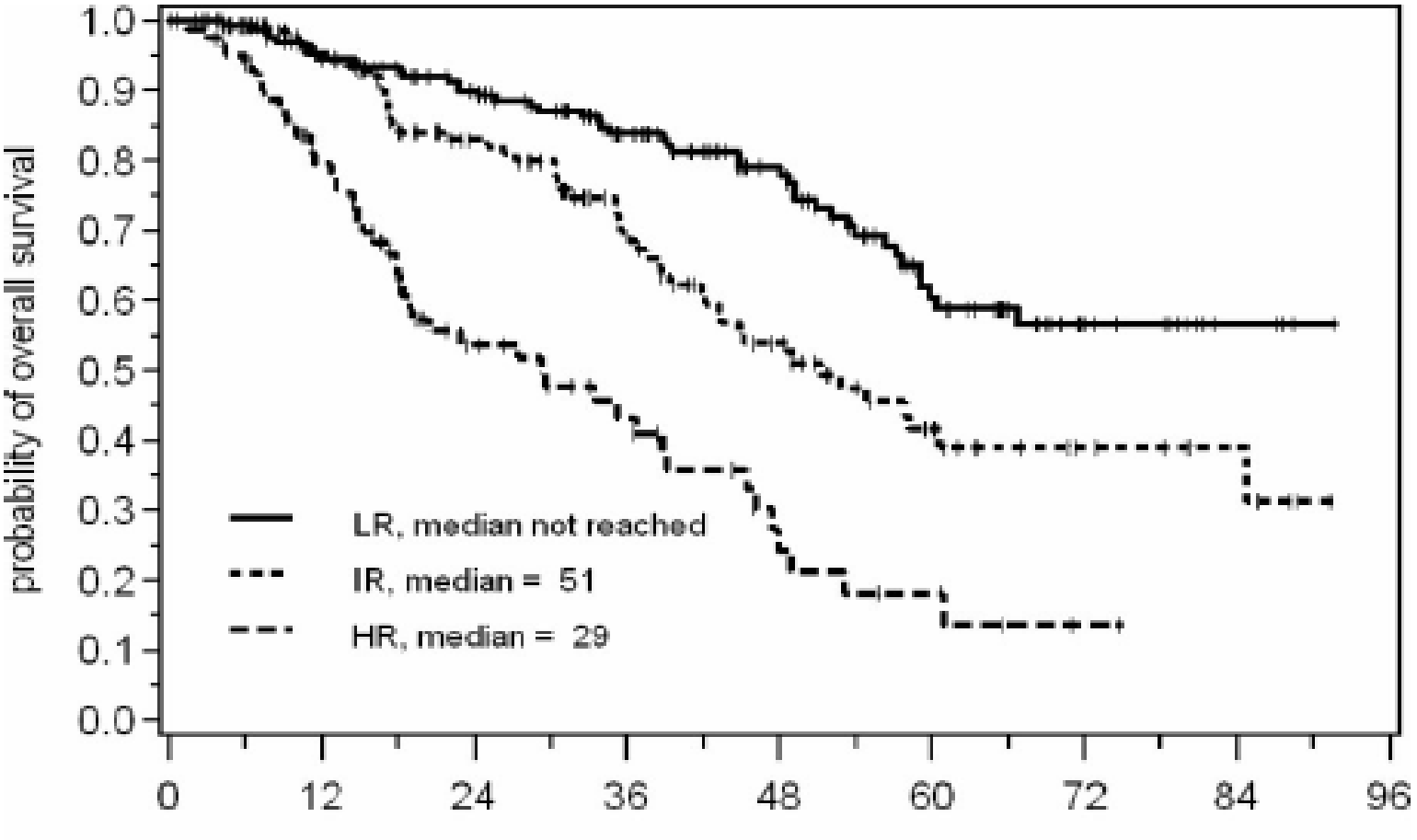
- A Complicated Formula
  - 0.03535*age (years) + 0.6978 (if ECOG performance status >1) + 1.367*log10 (LDH/ULN) + 0.9393*log10 (white blood cells k/uL)

- The Simplified MIPI:

Points	Age, y	ECOG	LDHULN	WBC, 10^9/L
0	<50	0-1	<0.67	< 6.700
1	50-59	—	0.67-0.99	6.700-9.999
2	60-69	2-4	1.000 -1.49	1.000-14.999
3	≥70	—	≥1.5000	≥15000

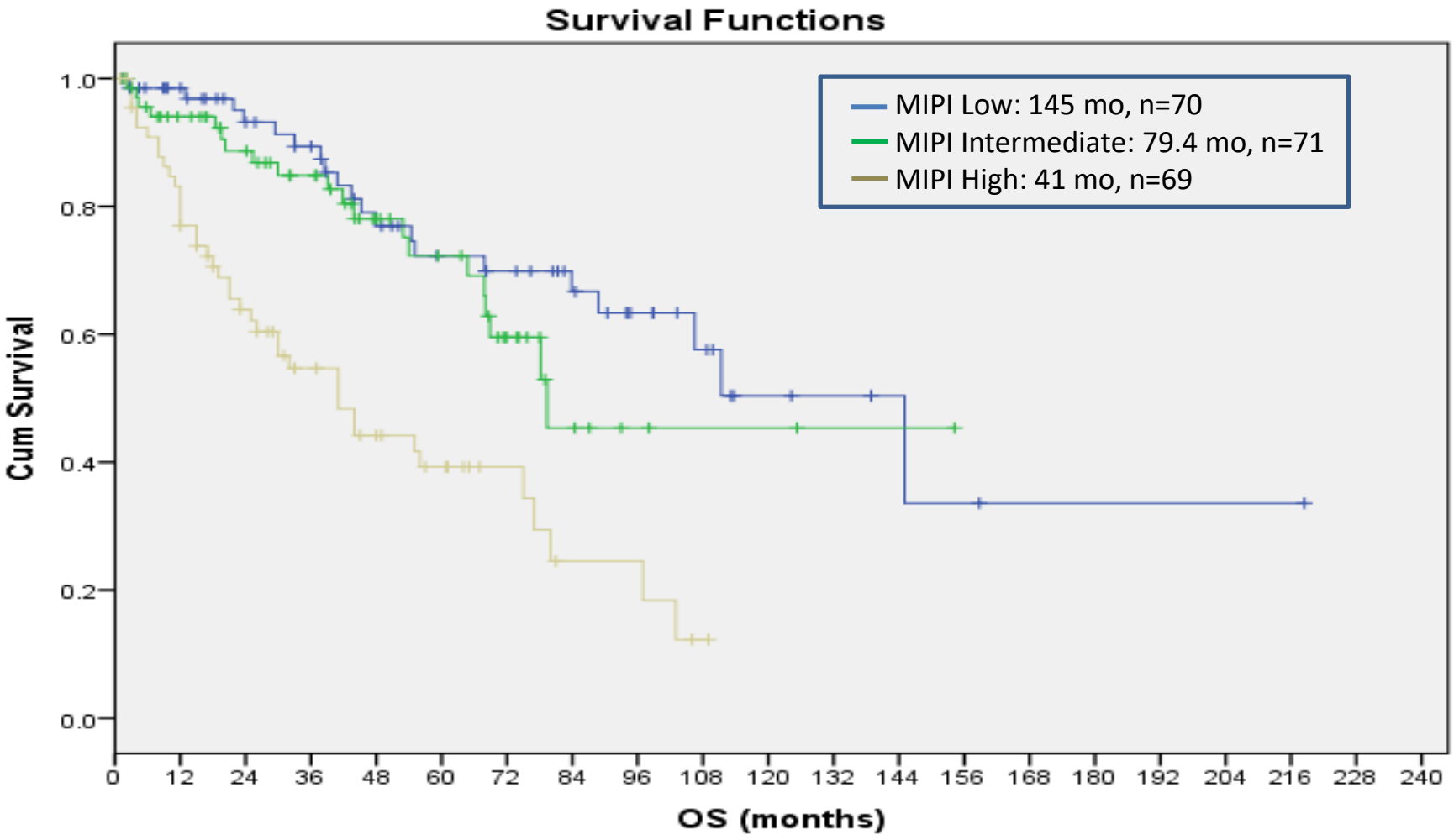
Hoster E, et al. Blood. 2008 Jan;111(2):558.

The Mantle Cell International Prognostic Index (MIPI)



Hoster E, et al. Blood. 2008 Jan;111(2):558.

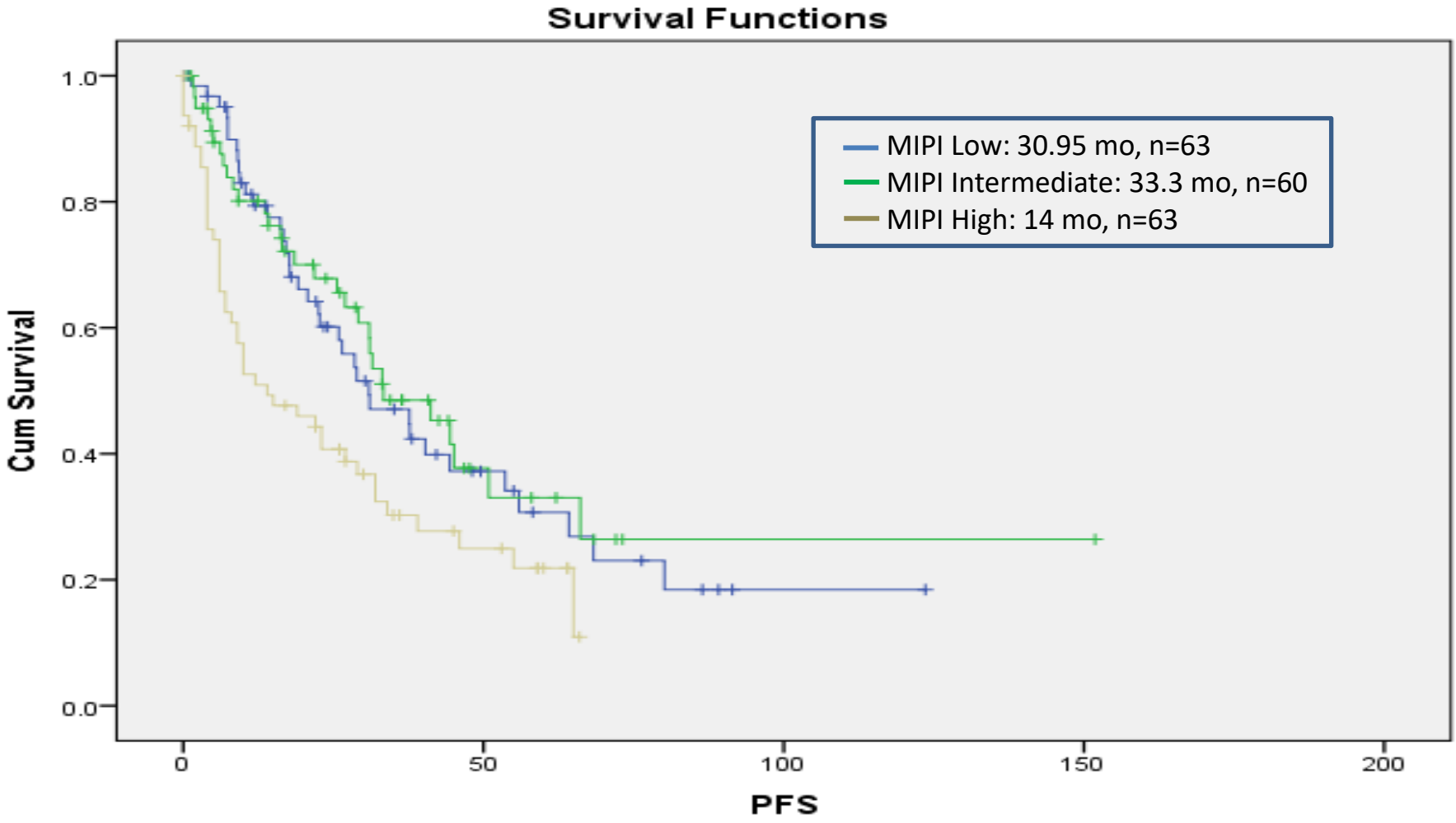
MIPI: Moffitt Experience



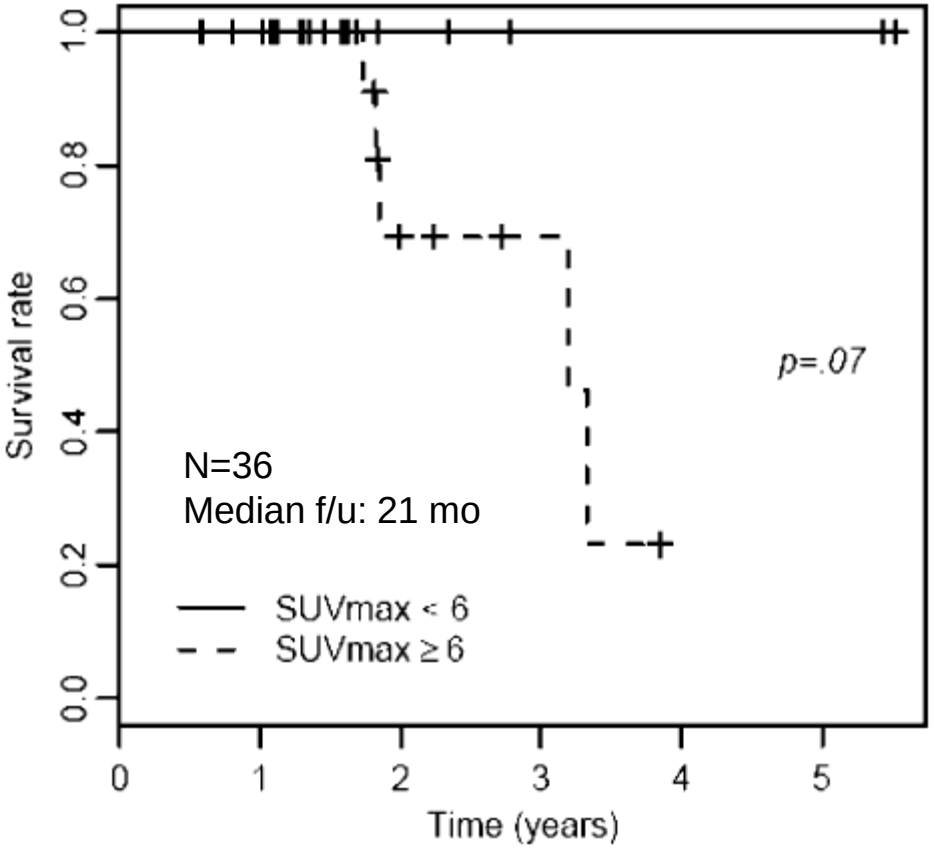
What About Length of Remission

?

“Progression-Free Survival” (PFS) According to the MIPI

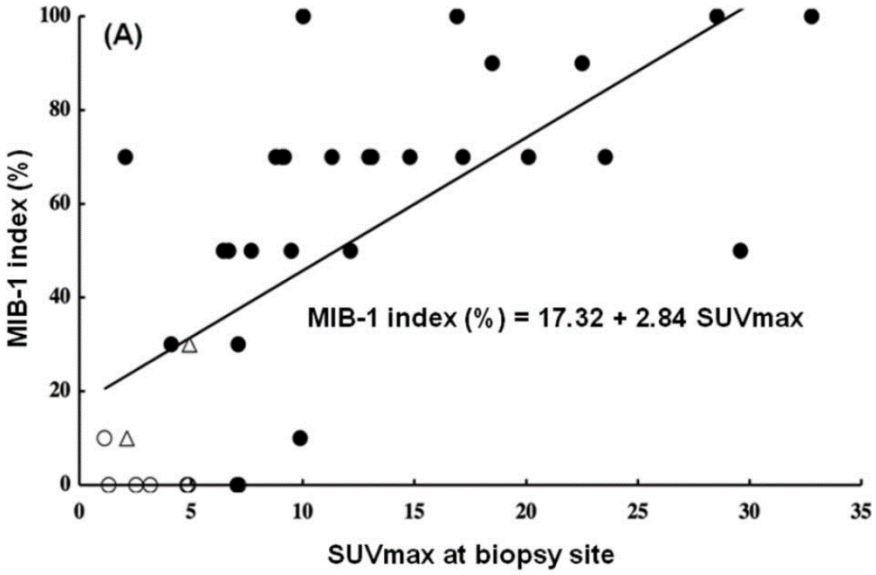


PET Signature



Bodet-Milin C, et al. Eur J Nucl Med Mol Imaging. 2010 Aug;37:1633

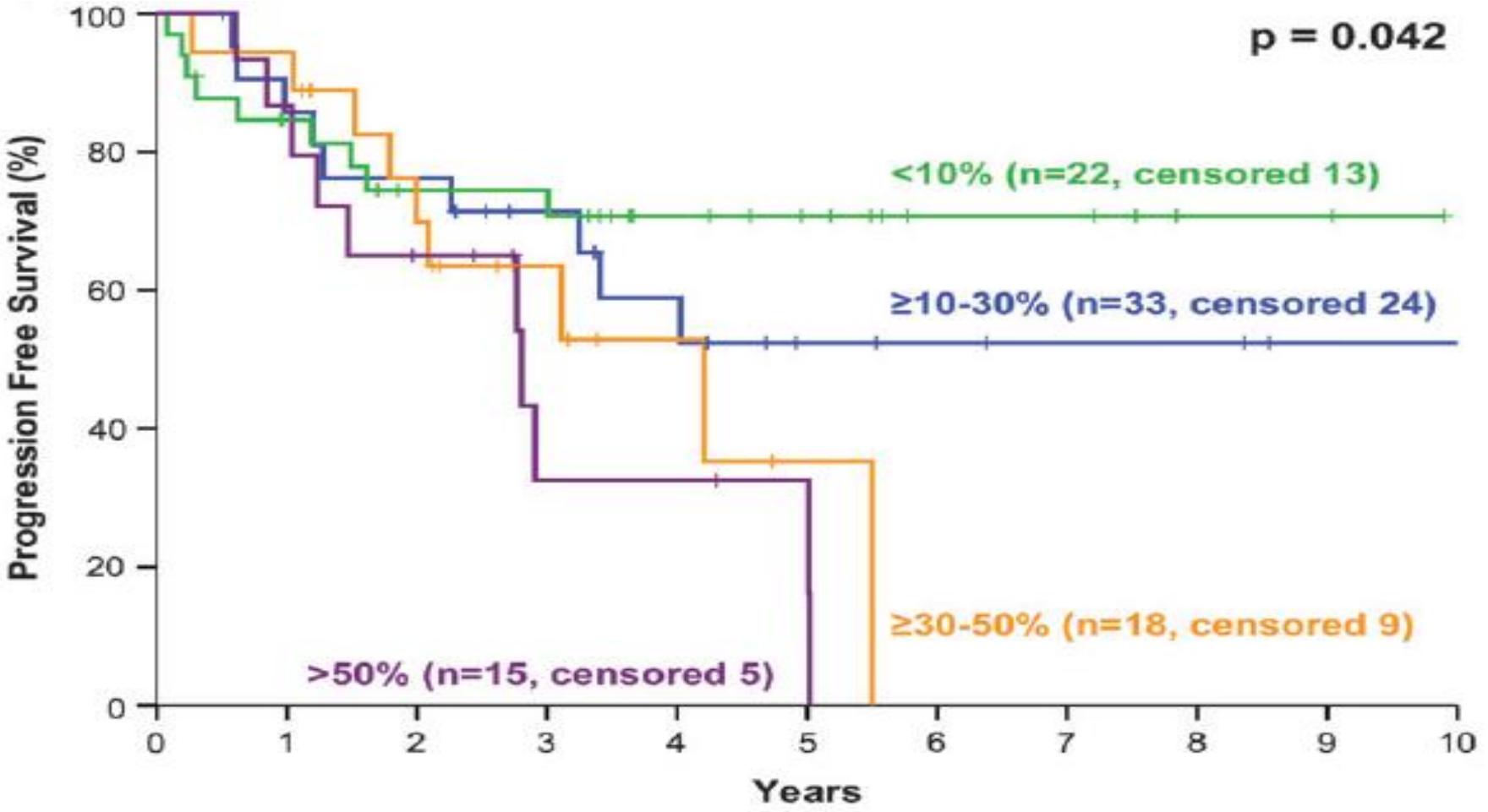
PET Uptake and Ki-67



Ki-67 (or MIB-1 index) is a marker of cells that are committed to growing to make copies of themselves

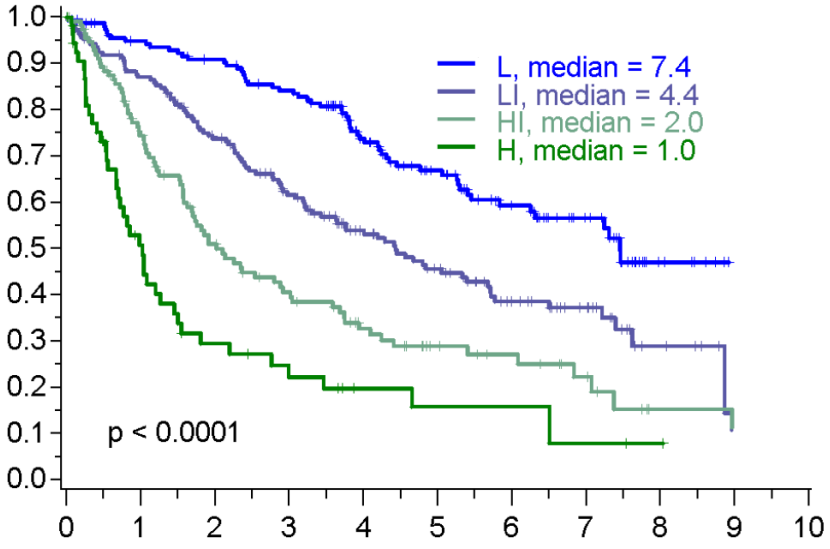
Watanabe R, et al. *Leuk Lymphoma*. 2010 Feb;51(2):279-83.

Progression-Free Survival by Ki-67

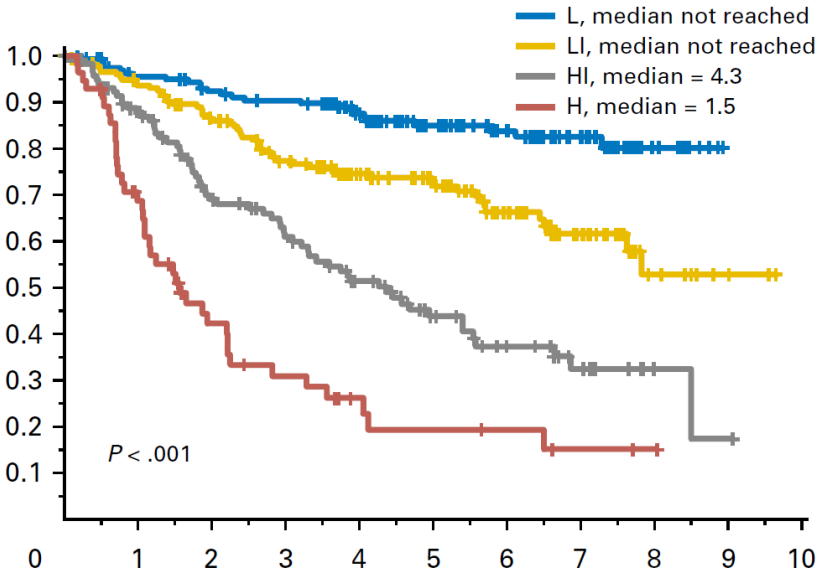


Schaffel R, et al. Annals of Oncology. 2010 Jan;21(1): 133

MIPI-C: MIPI+Ki67 (30%)



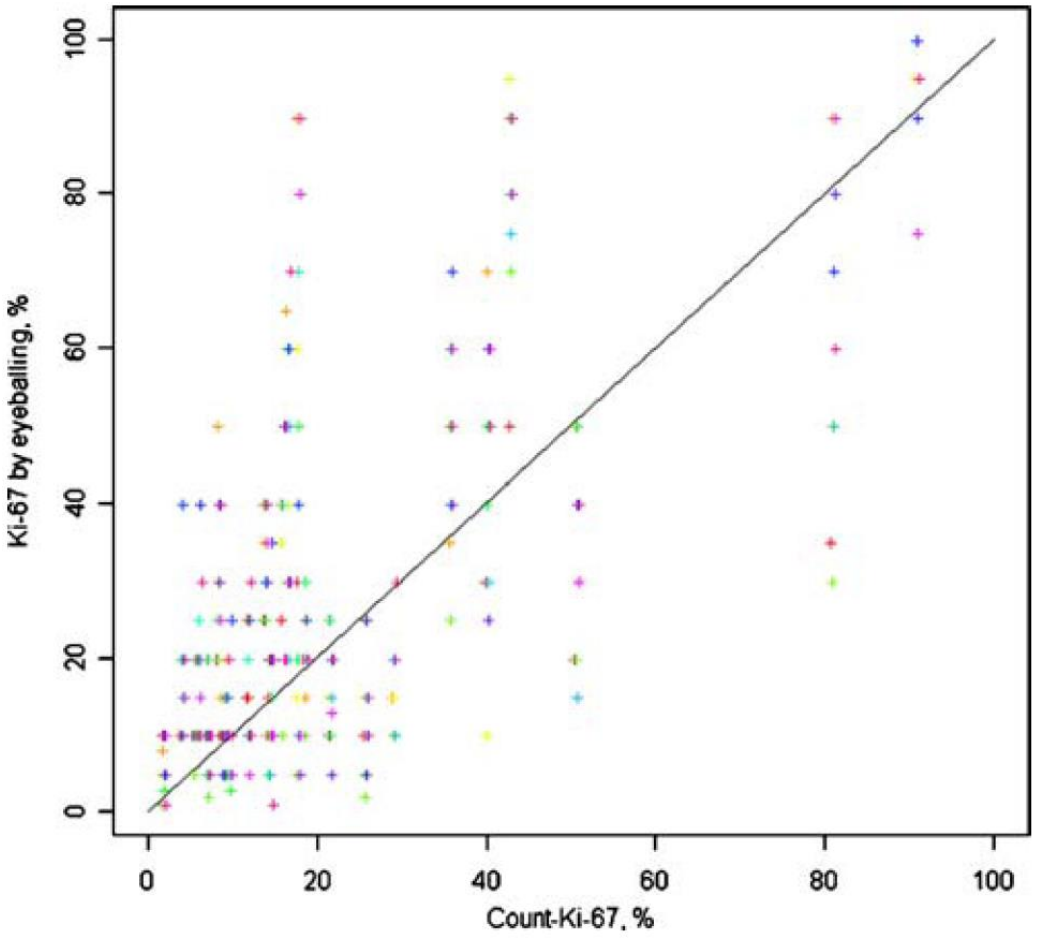
PFS



OS

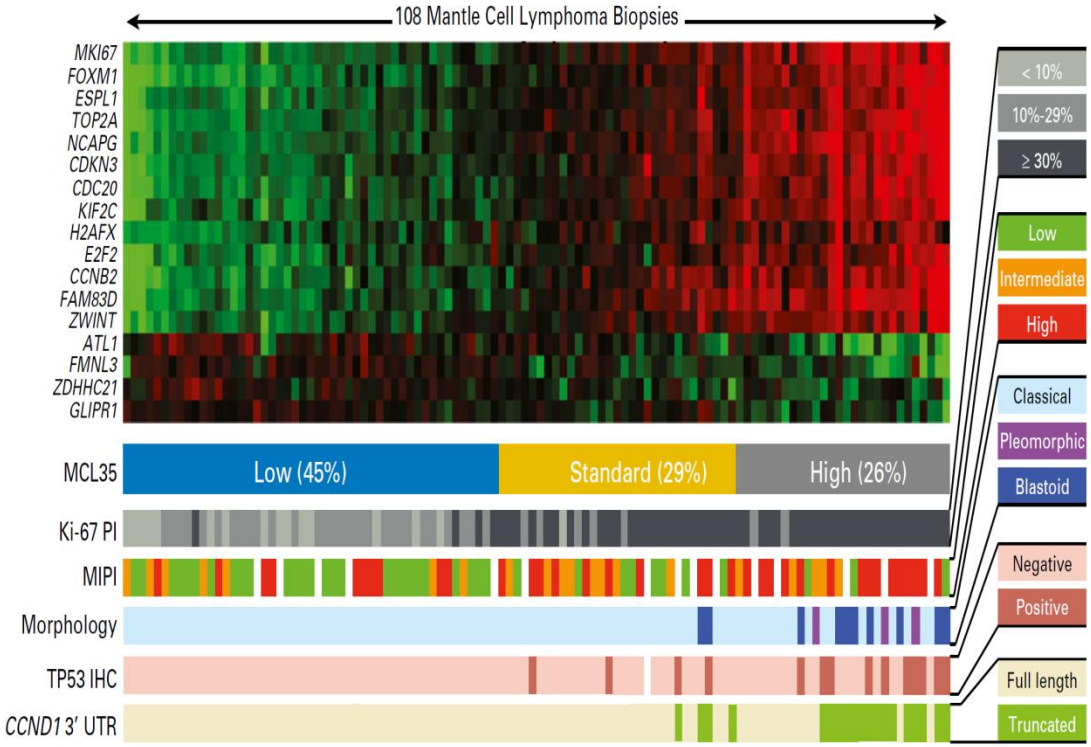
Hoster E, et al. *J Clin Oncol*. 2016 Apr 20;34(12):1386-94

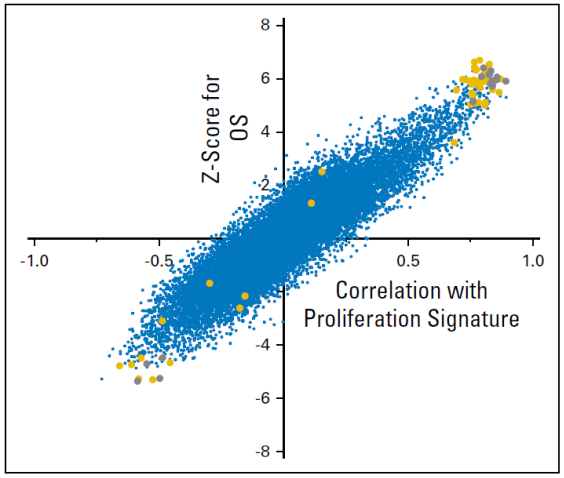
Ki-67: Inter-Observer Agreement



Klapper W, et al. J Hematopathol. 2009 July;2(2):103

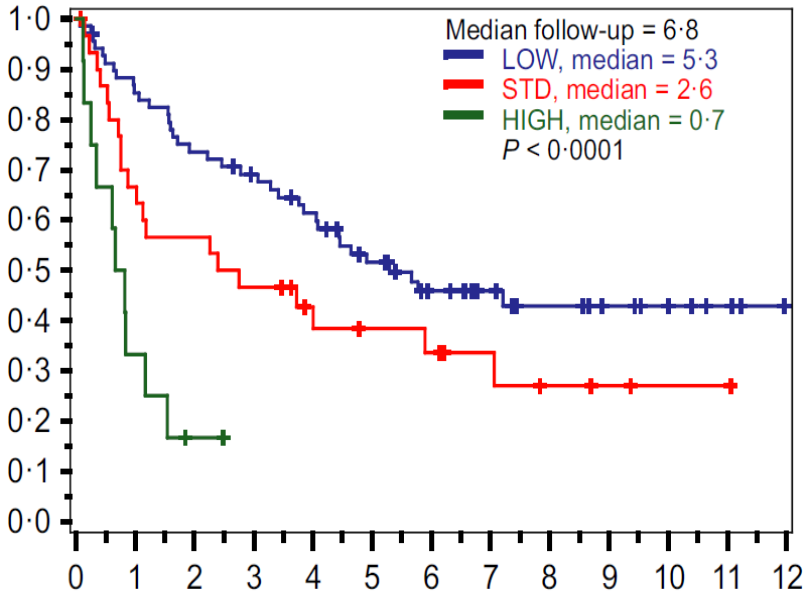
MCL35 Nanostring Signature



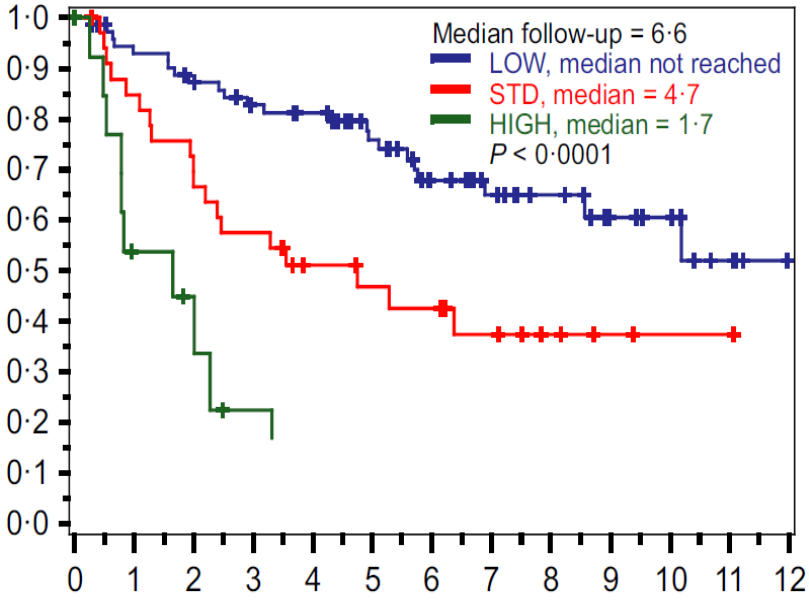


Scott DW, et al. *J Clin Oncol*. 2017 May 20;35(15):1668-1677

MCL35



FFS

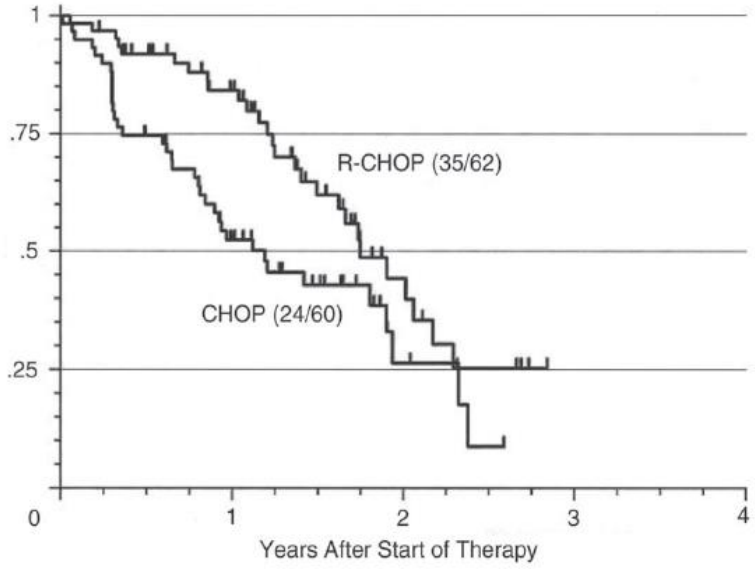


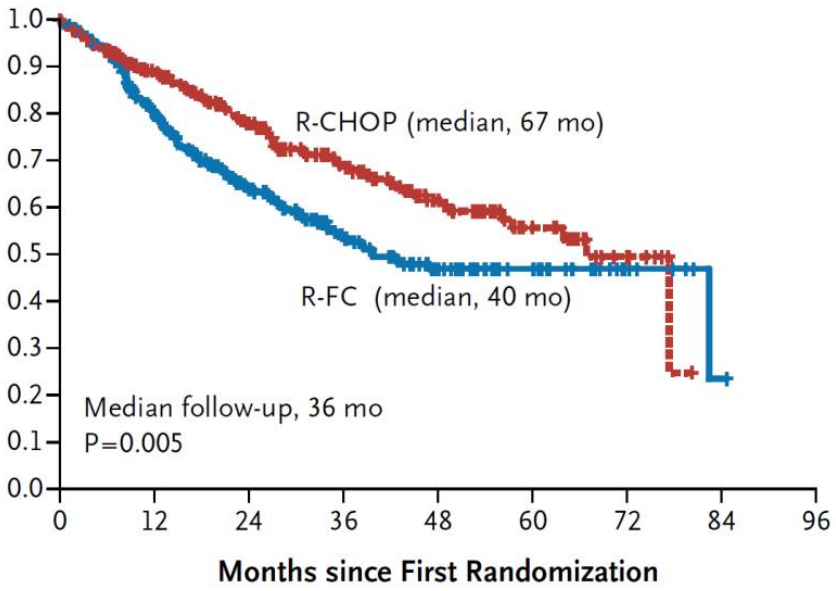
OS

Rauert-Wunderlich H, et al. Br J Haematol. 2019 Feb;184(4):616-624

Treatment Decision Making in MCL

What Have We Learned?

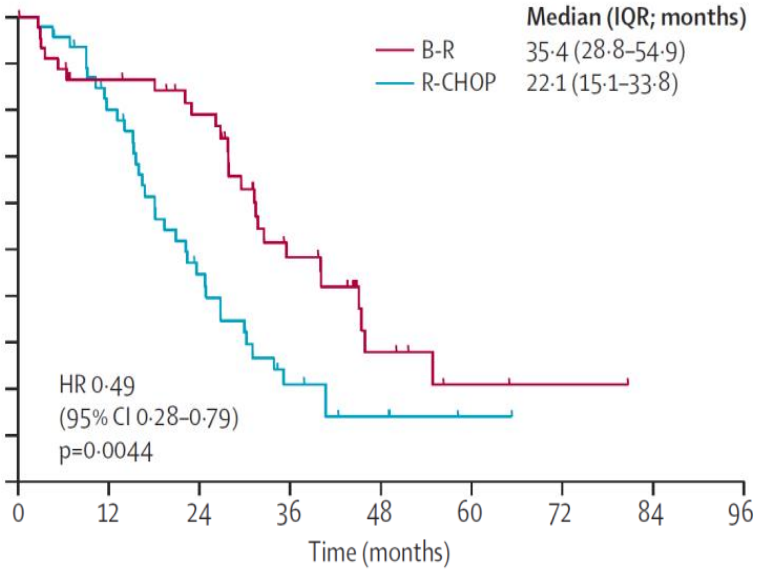


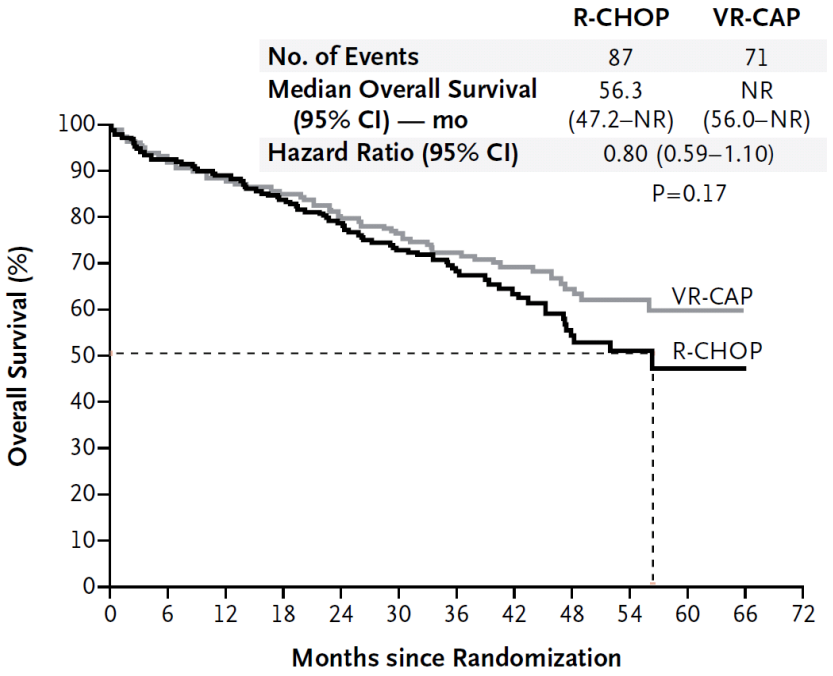


Lenz G, et al. *J Clin Oncol* 23:1984-1992

Kluin-Nelemans HC, et al. *N Engl J Med* 2012;367:520-31

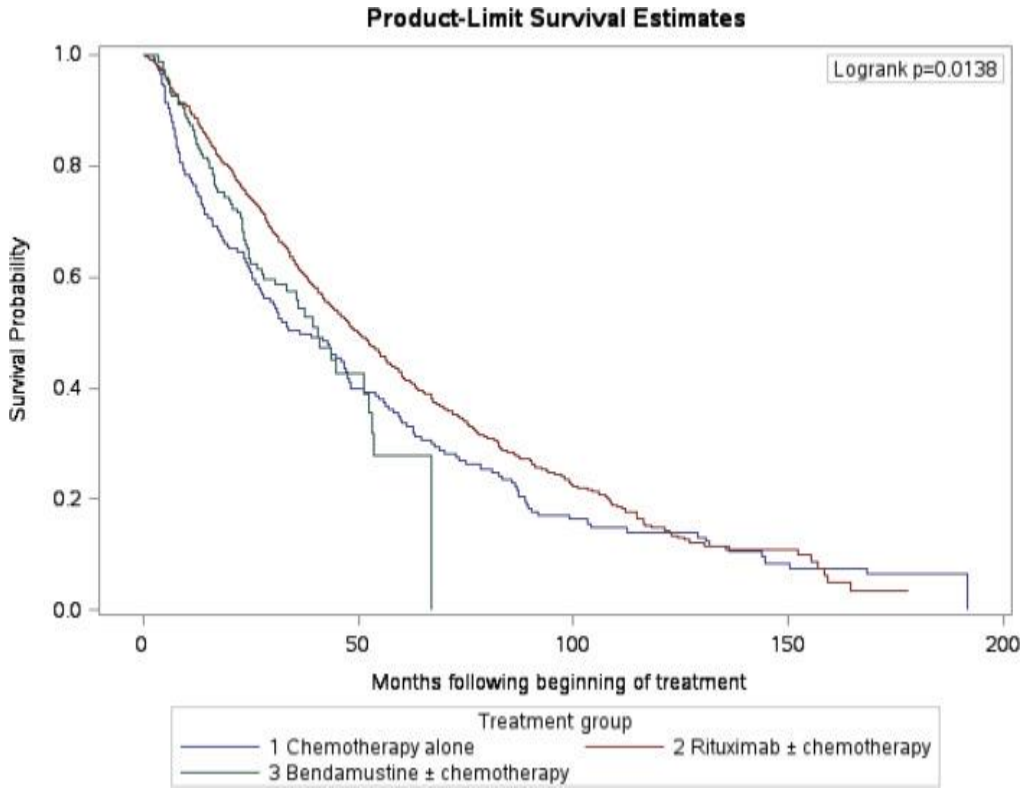
What Have We Learned?





Robak T, et al. *N Engl J Med* 2015;372:944-53
Rummel MJ, et al. *Lancet*. 2013 Apr 6;381(9873):1203-10

But Dr. Shah, You Gave Me R-CHOP??!

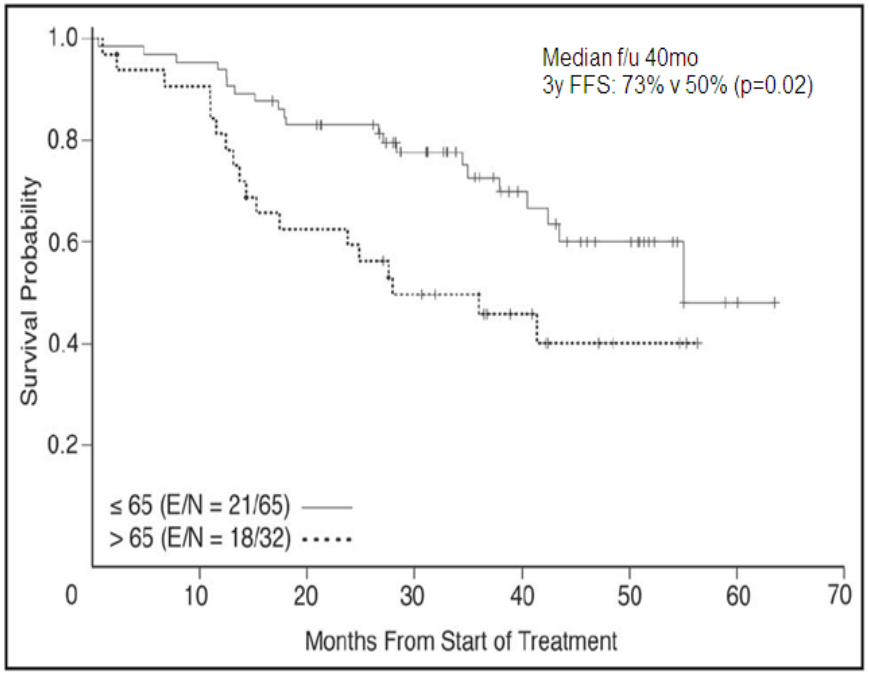


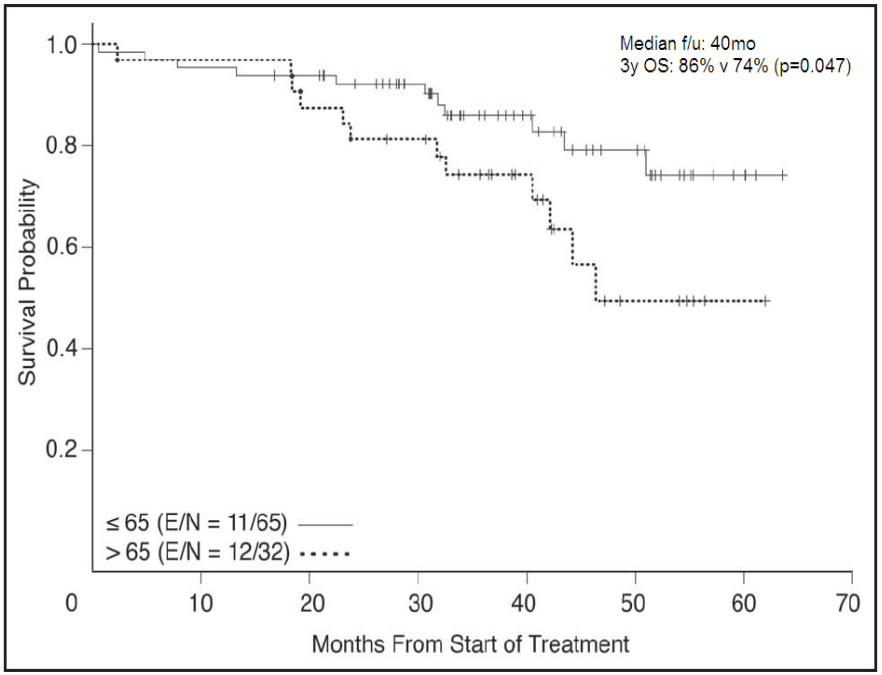
This Medicare Analysis of "Real World" patients suggests that things are not so simple!

Fu S, et al. Clin Lymphoma Myeloma Leuk. 2019 Nov;19(11):e616-e623

Defining Treatment Objectives: *How Intensively Should We Treat?*

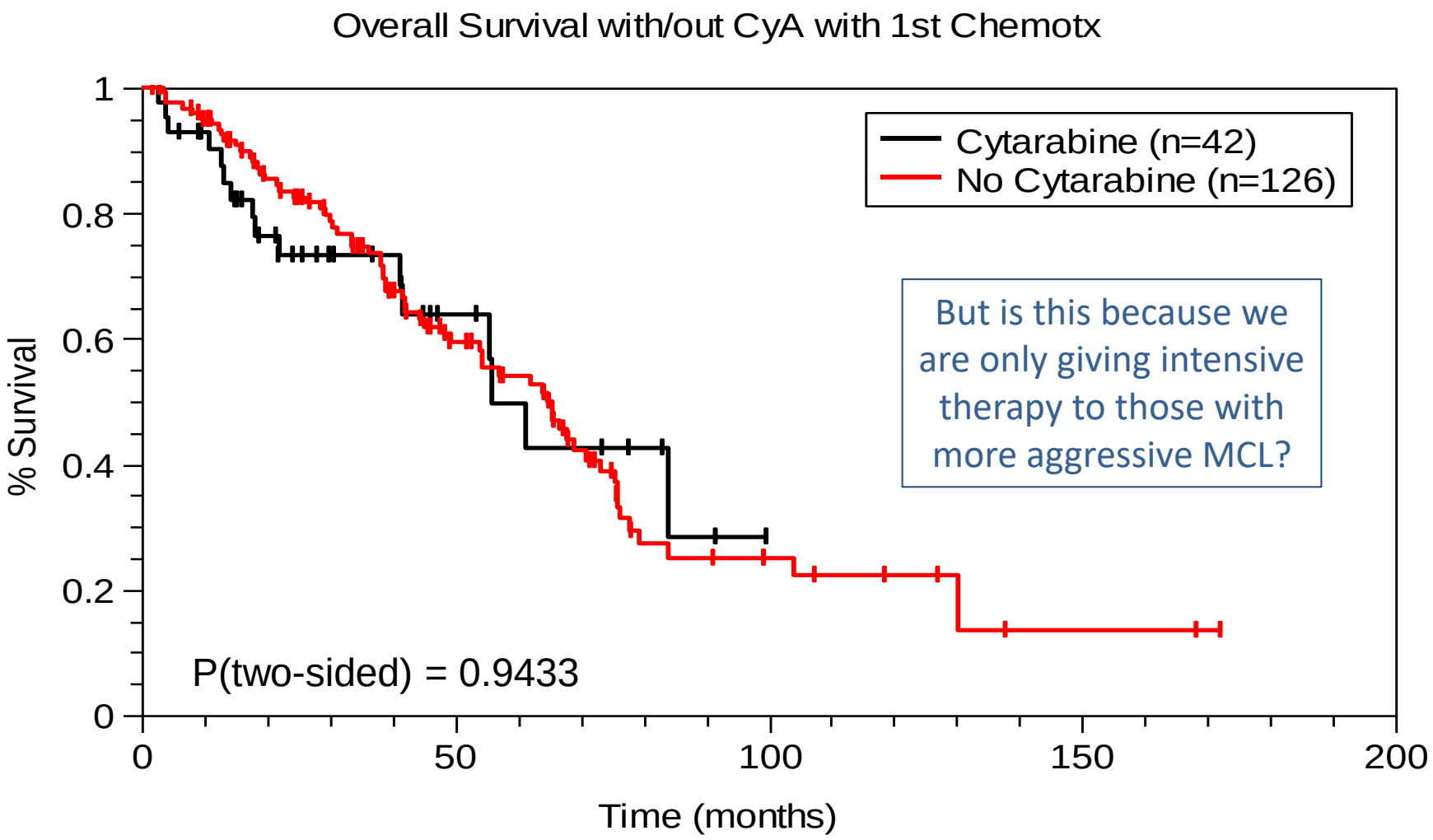
R-Hyper-CVAD



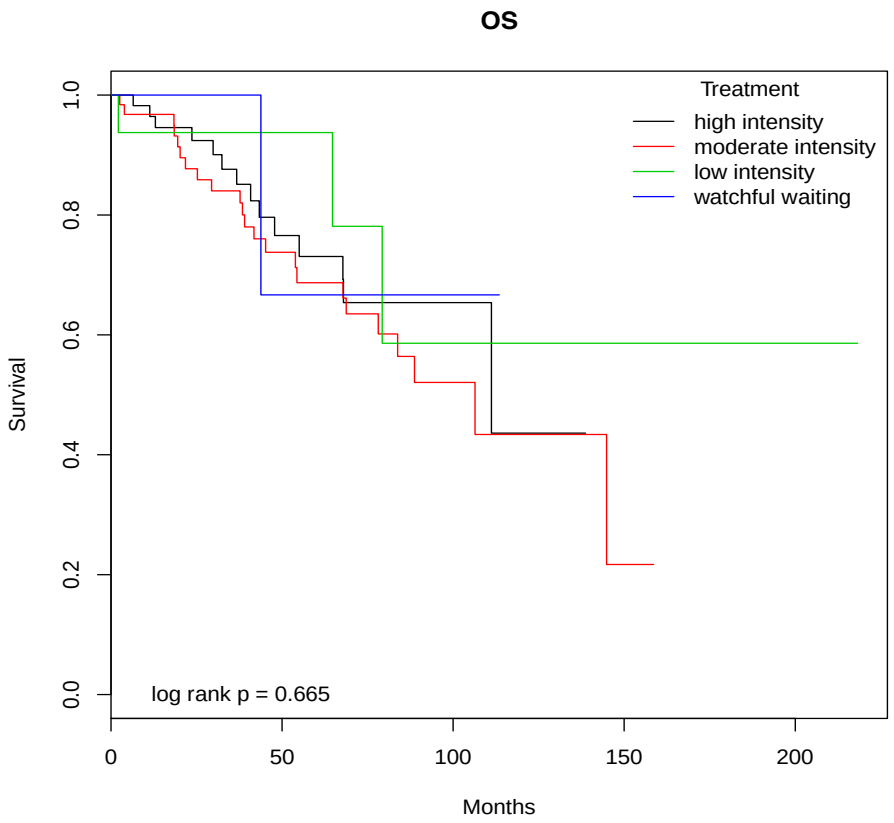


Romaguera J, et al. J Clin Oncol 2005 Oct;23(28):7013

Retrospective Evaluation of Treatment Intensification

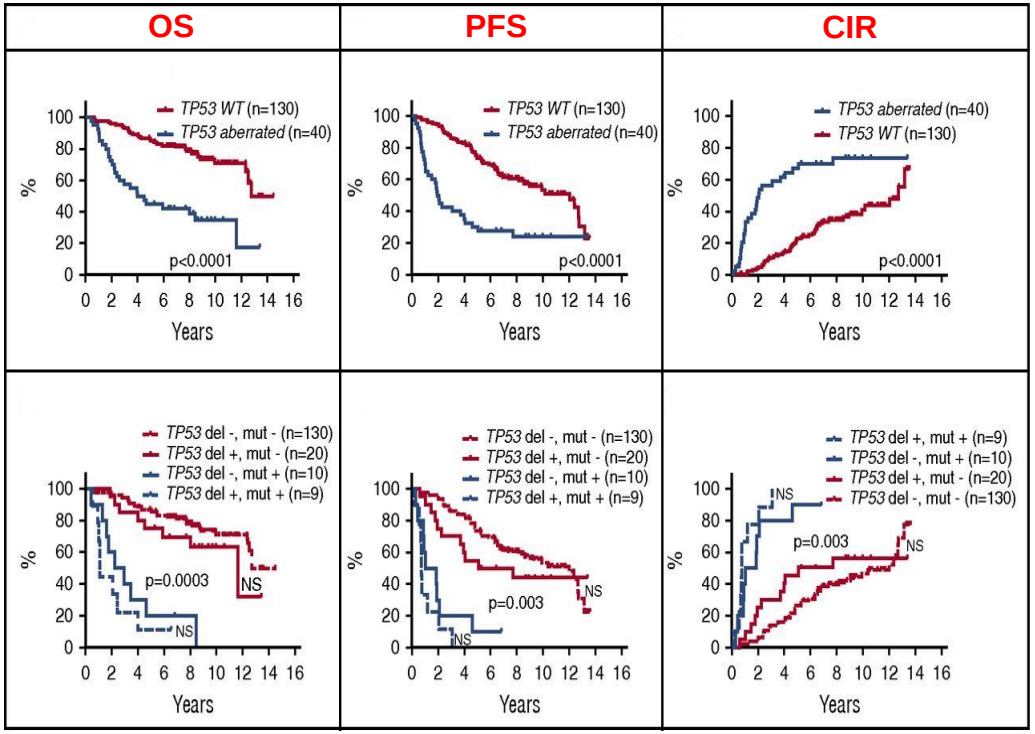


Treatment Intensity in Low & Intermediate Risk MCL



Griffin P, et al. Blood (ASH Annual Meeting Abstracts). 2014 124(21): Abstract 2981

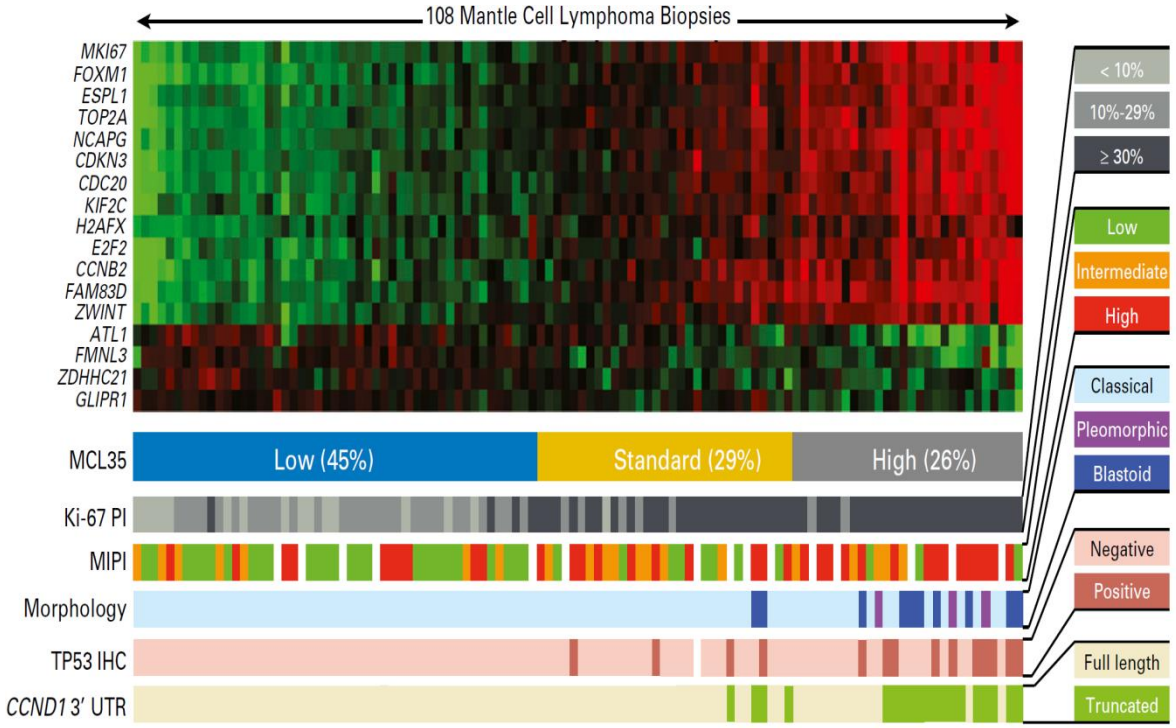
TP53 Mutation Status and Outcome with Intensive Therapy



Variables	OS		PFS		CIR	
	HR	*P*	HR	*P*	HR	*P*
mut TP53	6.2	<.0001	6.8	<.0001	6.9	<.0001
mut NOTCH1	2.7	.09	2.3	.10	2.2	.17
del TP53	1.4	.37	1.5	.15	1.7	.10
del CDKN2A	1.3	.55	1.3	.40	1.3	.43
Blastoid	1.3	.53	0.8	.62	0.9	.65
MIPI-c high-risk	1.8	.11	2.2	.01	2.6	.003
mut WHSC1	0.8	.58	—	—	—	—

Eskelund CW, et al. *Blood* 2017 130:1903-10

The Challenge…

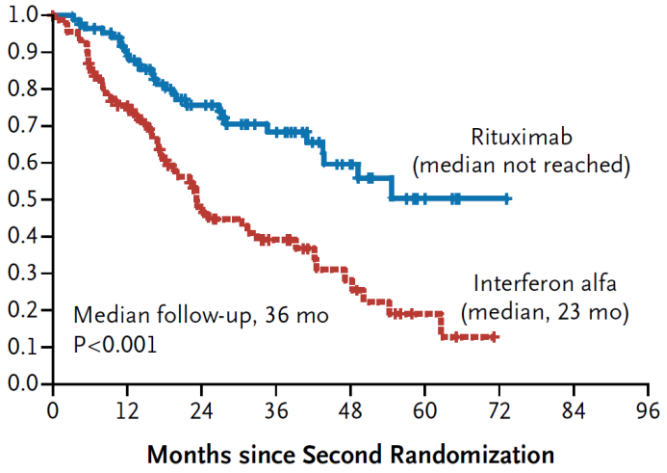


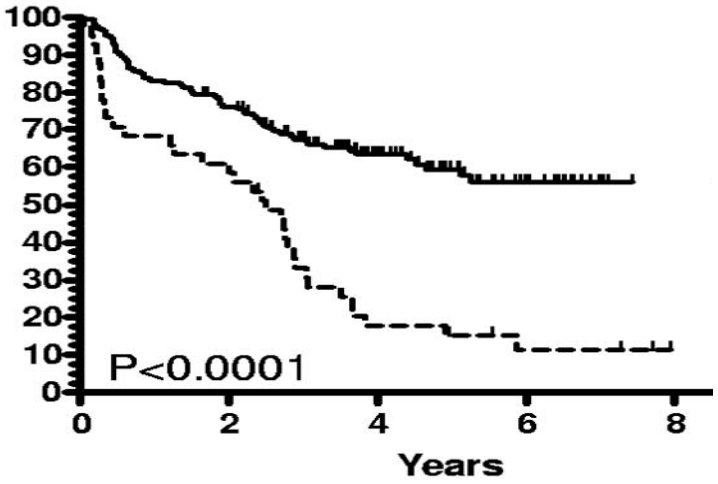
The Growth Rate of MCL is Tightly Coupled to Mutations That Impact DNA Damage Recognition and Response

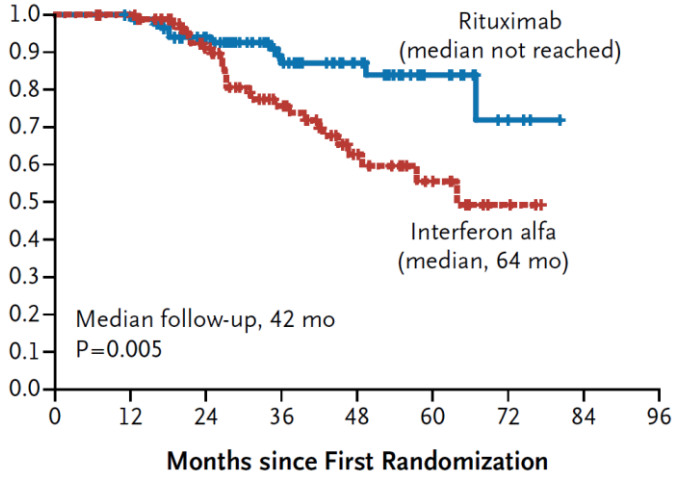
Scott DW, et al. *J Clin Oncol*. 2017 May 20;35(15):1668-1677

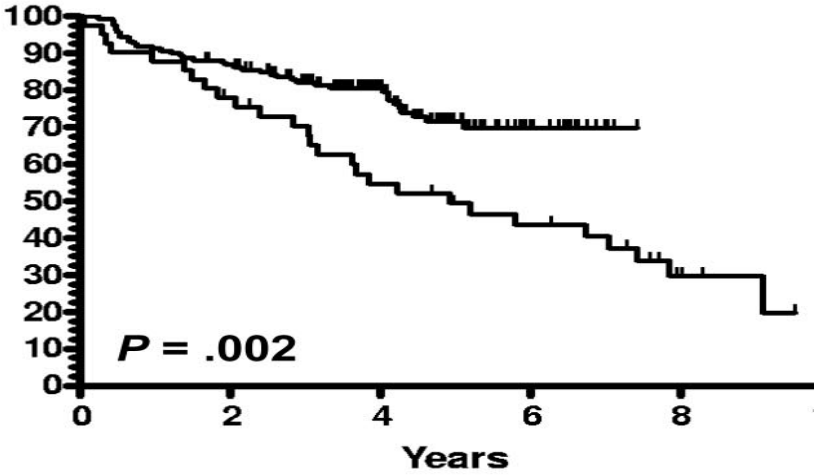
Defining Treatment Objectives: *How Intensively Should We "Consolidate"?*

Consolidation in MCL



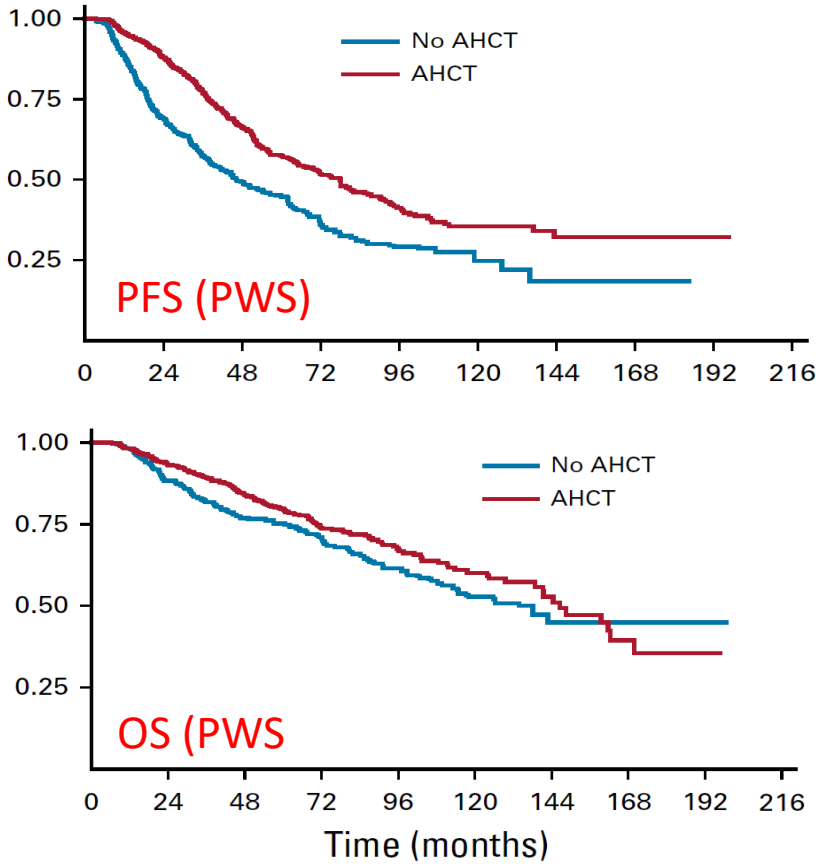


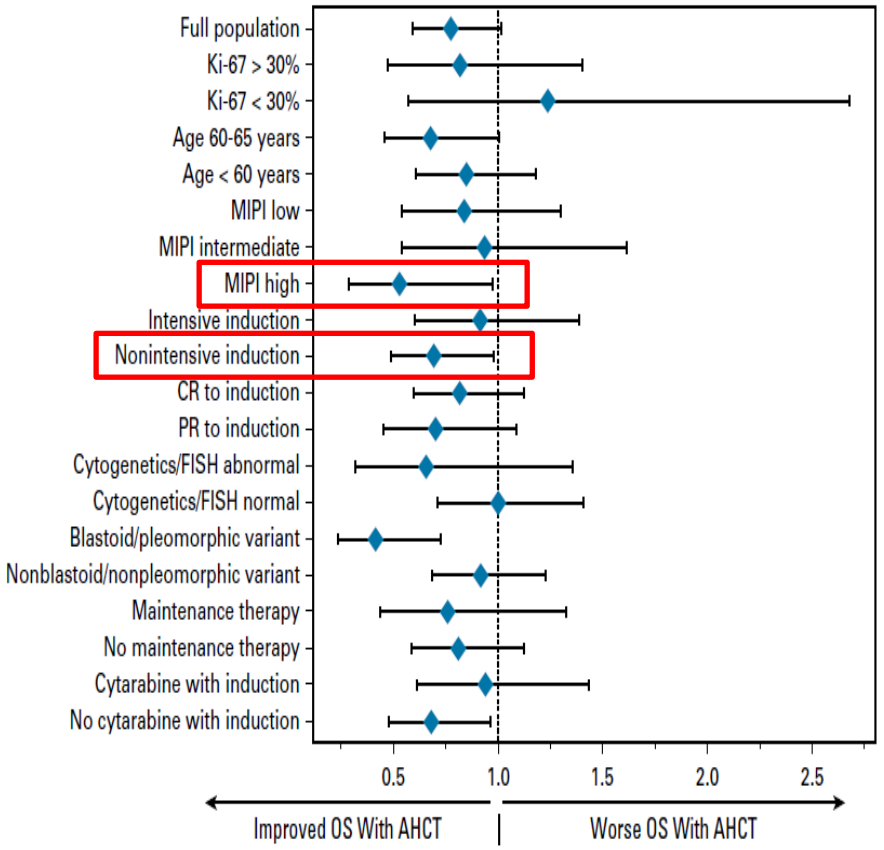




Kluin-Nelemans HC, et al. *N Engl J Med* 2012;367:520-31.
Geisler CH, et al. *Blood*. 2008;112:2687-2693

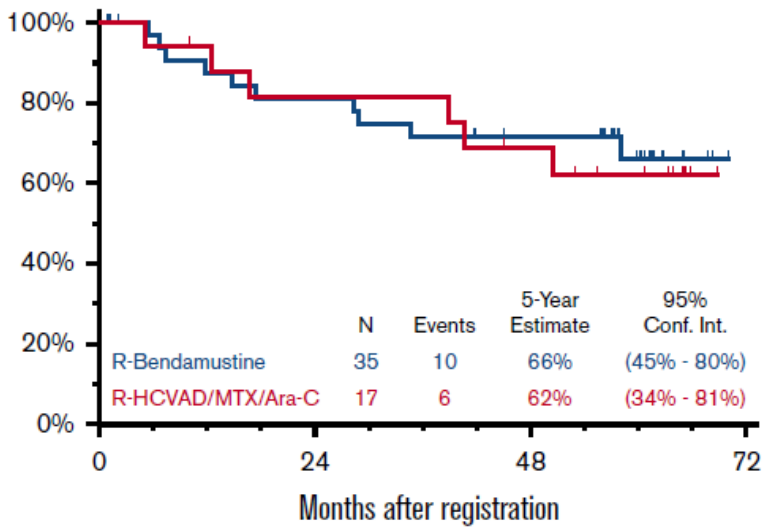
Consolidation in Younger Patients with MCL



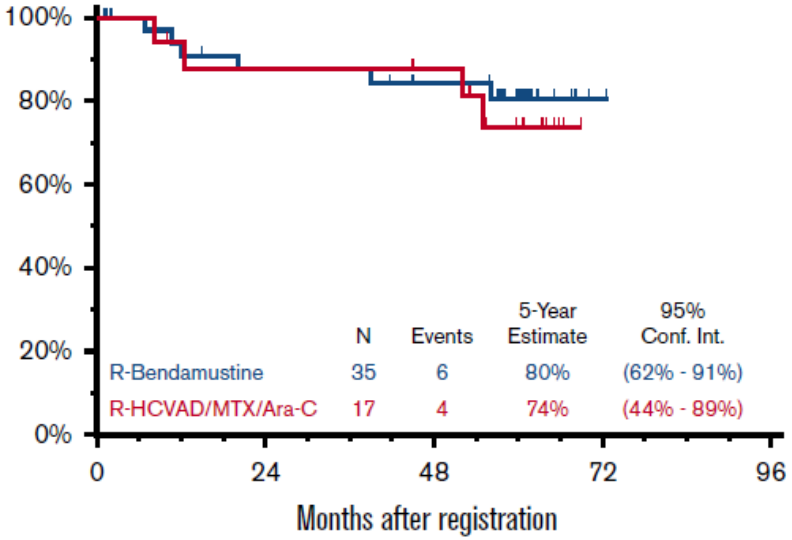


Gerson J, et al. *J Clin Oncol.* 2019 Feb 20;37(6):471-480

5-Year Outcomes with Low Intensity Therapy Followed by Autologous Transplant



PFS

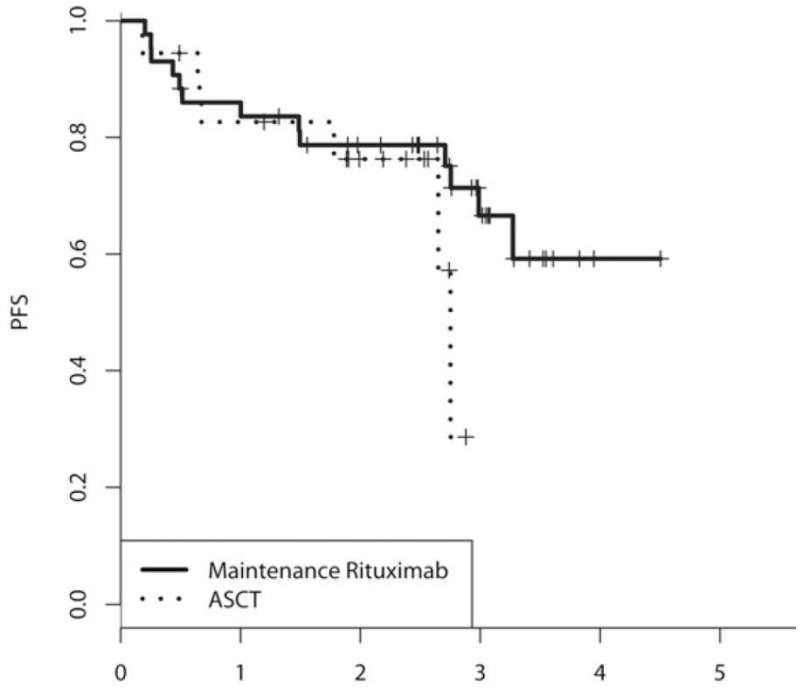


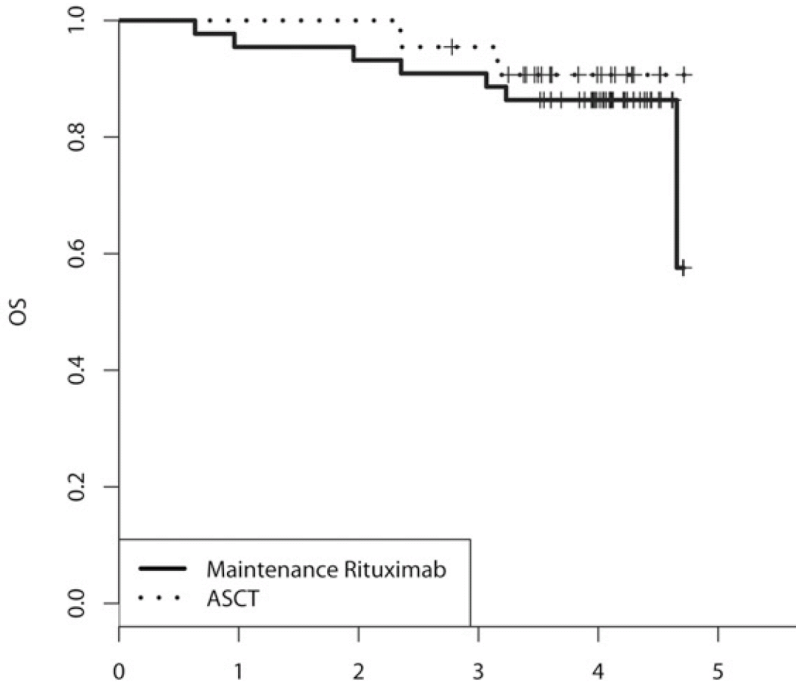
OS

A trend for improvement with transplant was only apparent in those getting lower intensity therapy (R-Bendamustine)

Kamdar M, et al. *Bld Adv.* 2019 Oct 22;20(3):3132

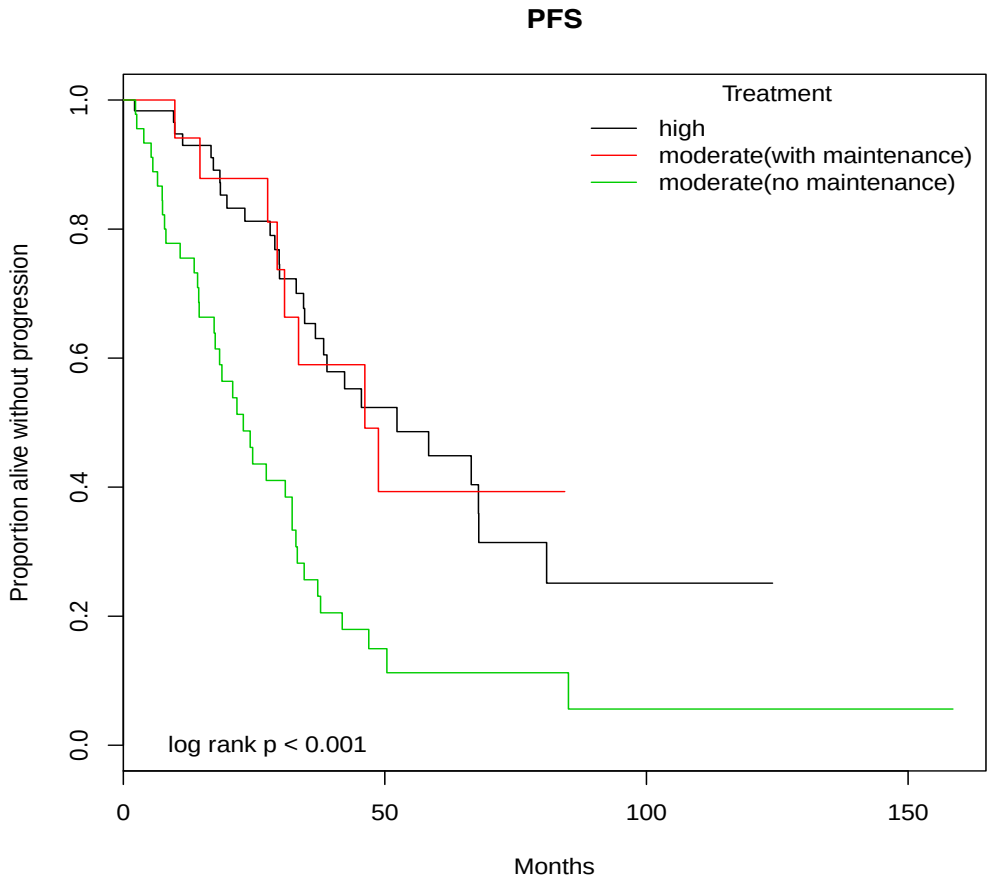
Consolidation in MCL: The VCR-CVAD Experience





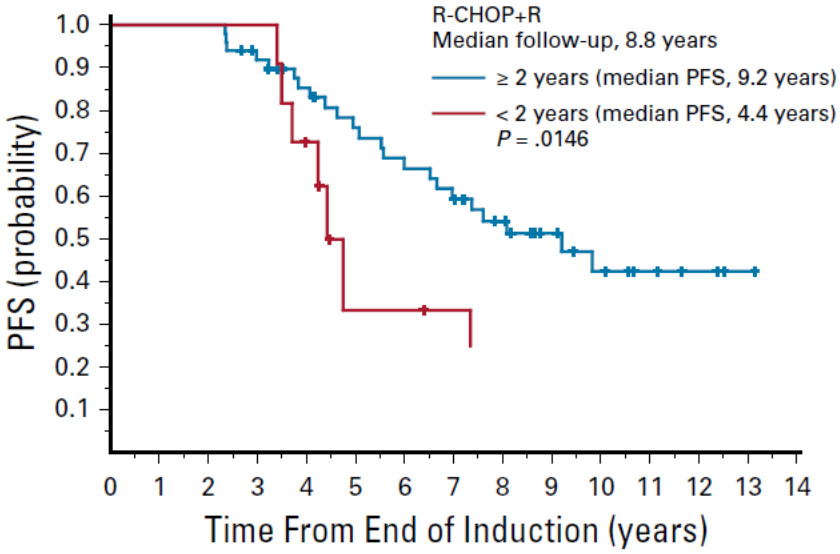
Chang JE, et al. *Blood.* 2014;123(11):1665-1673

Consolidation in Low & Intermediate Risk MCL

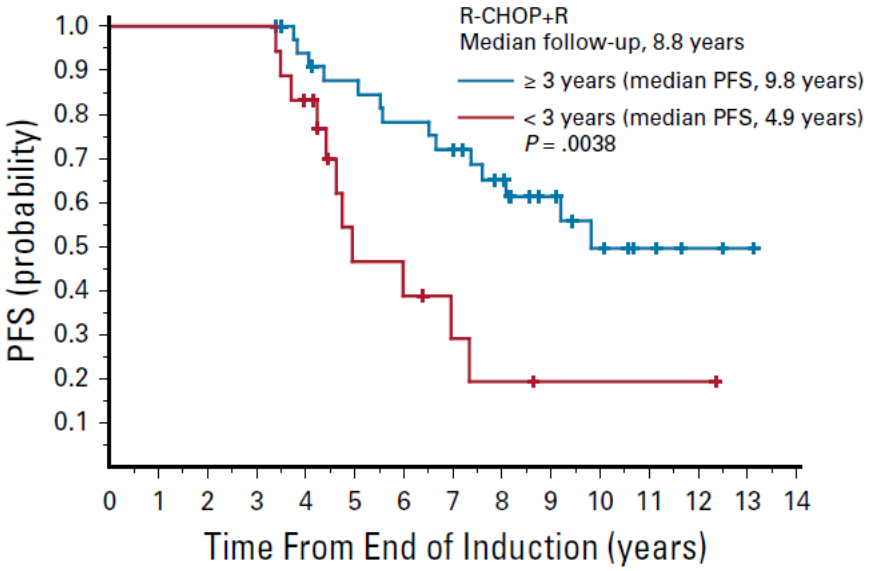


Griffin P, et al. Blood (ASH Annual Meeting Abstracts). 2014 124(21): Abstract 2981

Duration of Rituximab Maintenance



2 years

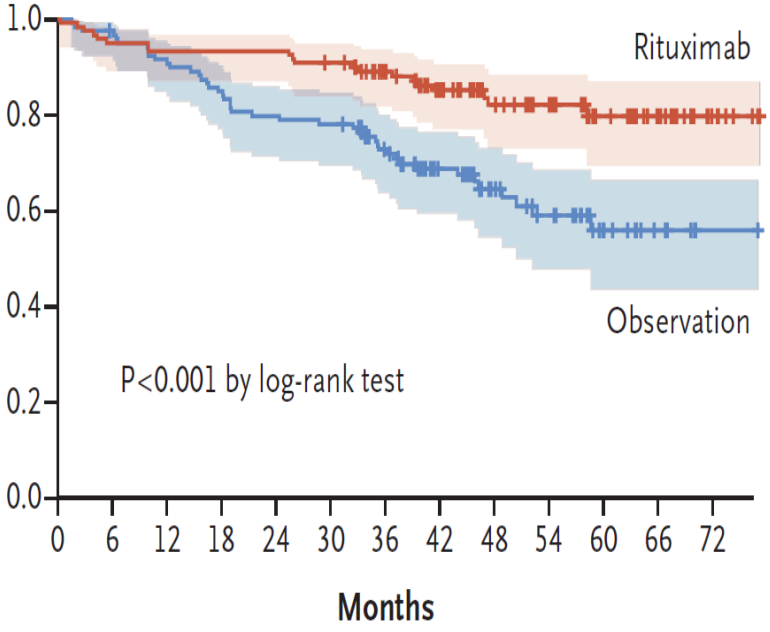


3 years

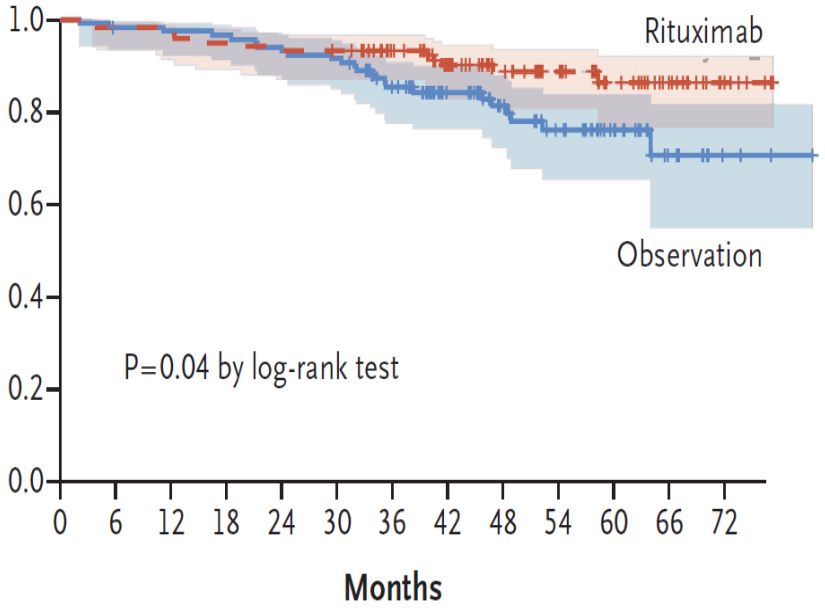
Kluin-Nelemans HC, et al. J Clin Oncol 2020 Jan 20;38:248-256

Can We Have Our Cake & Eat It Too?

PFS



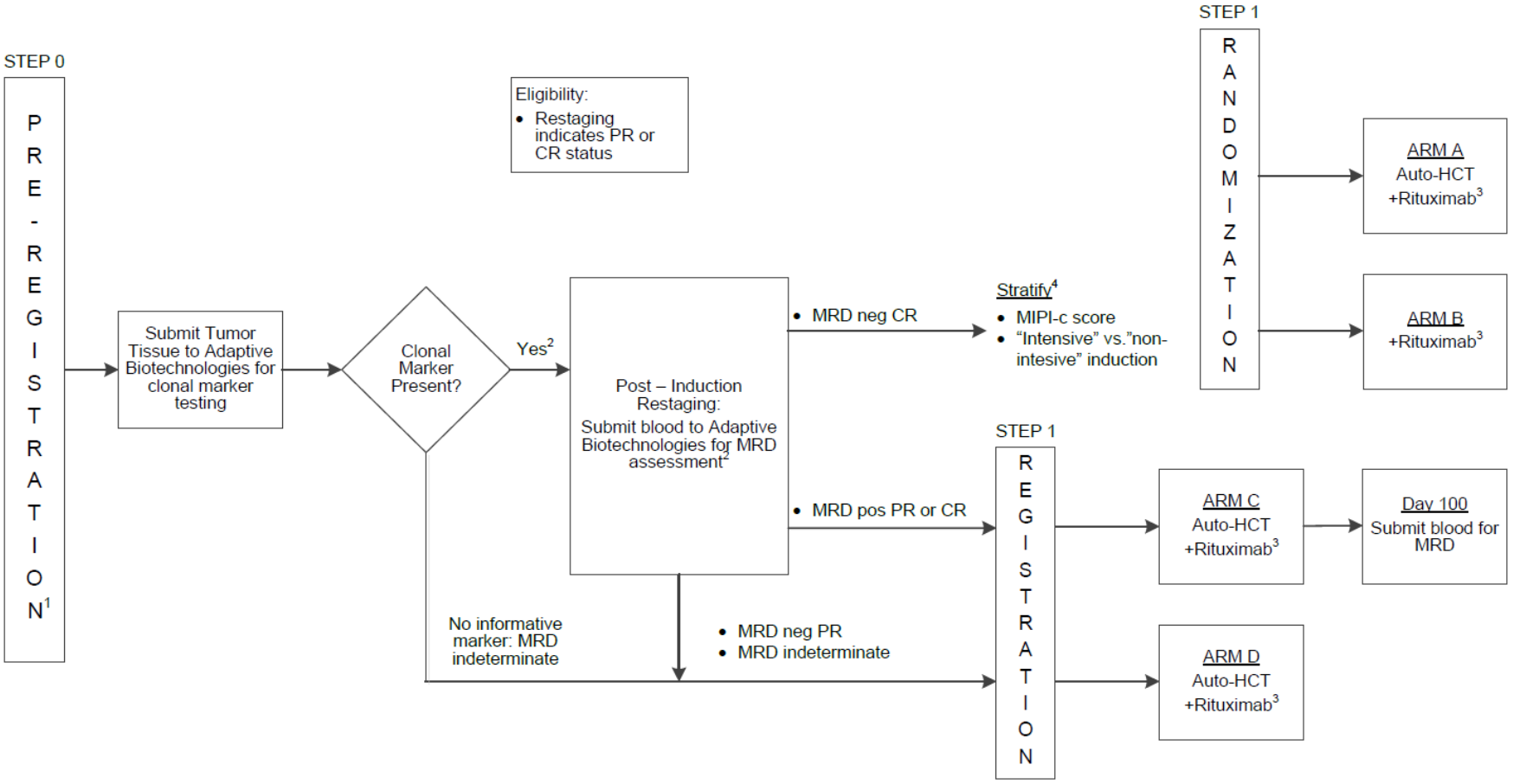
OS



R+DHAP x4 -> AutoSCT -> mR x3y

Le Gouill S, et al. *N Engl J Med*. 2017 Sep 28;377(13):1250-1260

Perhaps… But Should We?



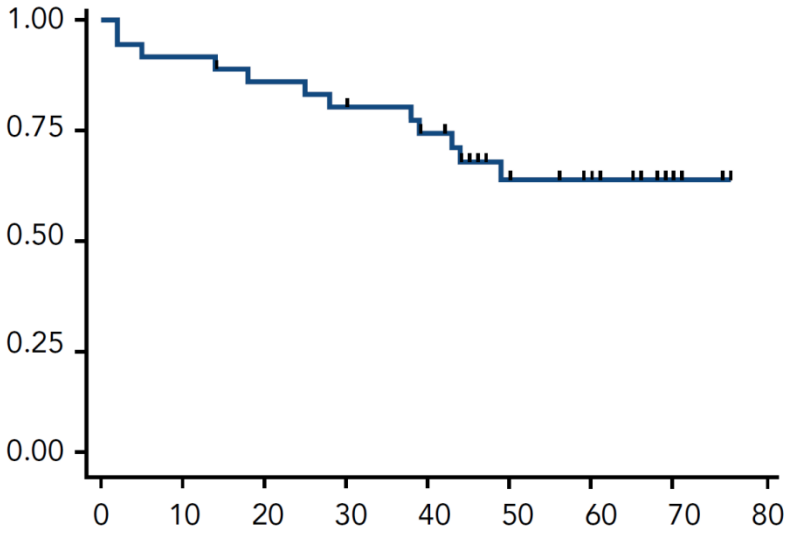
ECOG-ACRIN EA4151

Mr. RR: The Challenge

- The presence of rapidly growing disease and complex cytogenetics, including loss of TP53, suggests poor sensitivity to chemotherapy, and a bad outcome…

Mr. RR: The Outcome

PFS



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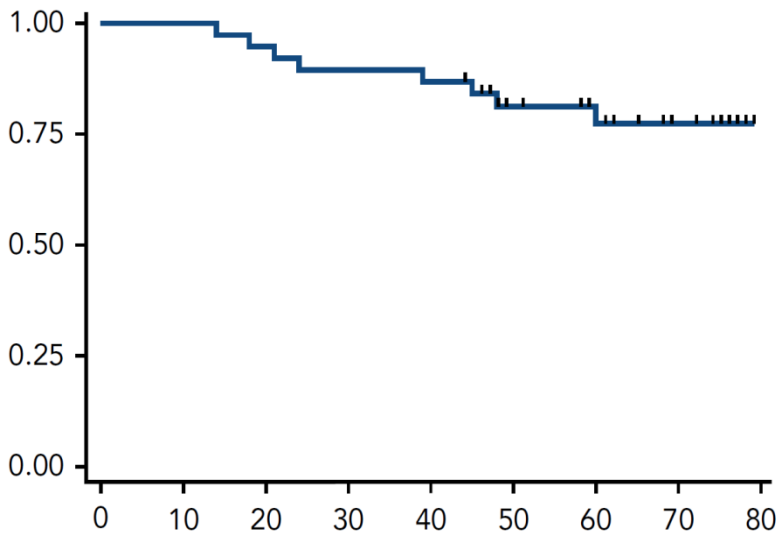


Frontline Induction: Lenalidomide + Rituximab

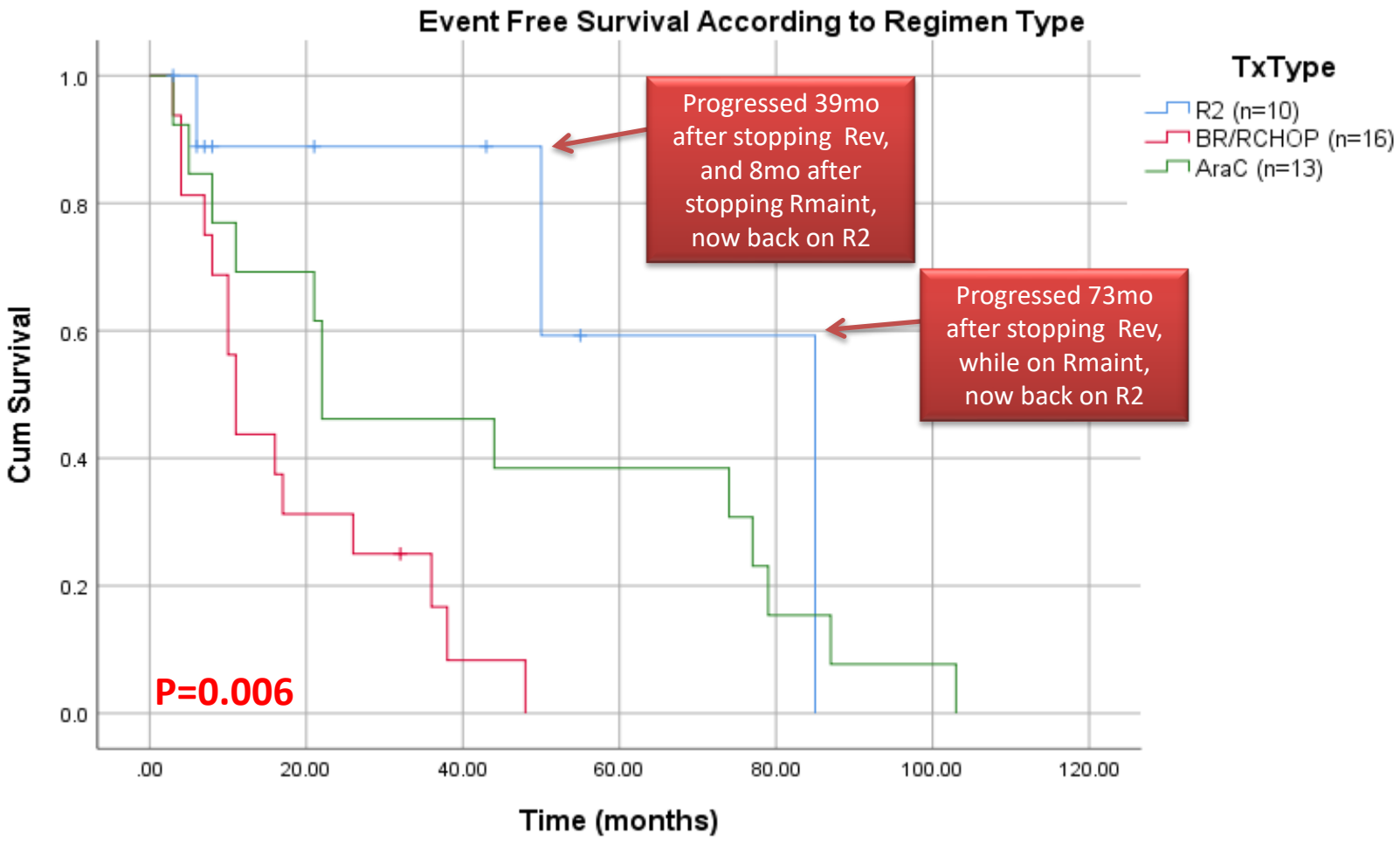
ORR: 87%

CR: 61%

Ruan J, et al. *N Engl J Med* 2015;373:1835-44.

Ruan J, et al. *Blood* Nov 8;132(19):2016-2025.

Looking Specifically Among TP53m MCL



Shah N, et al. ASH 2019, Abstract 3991

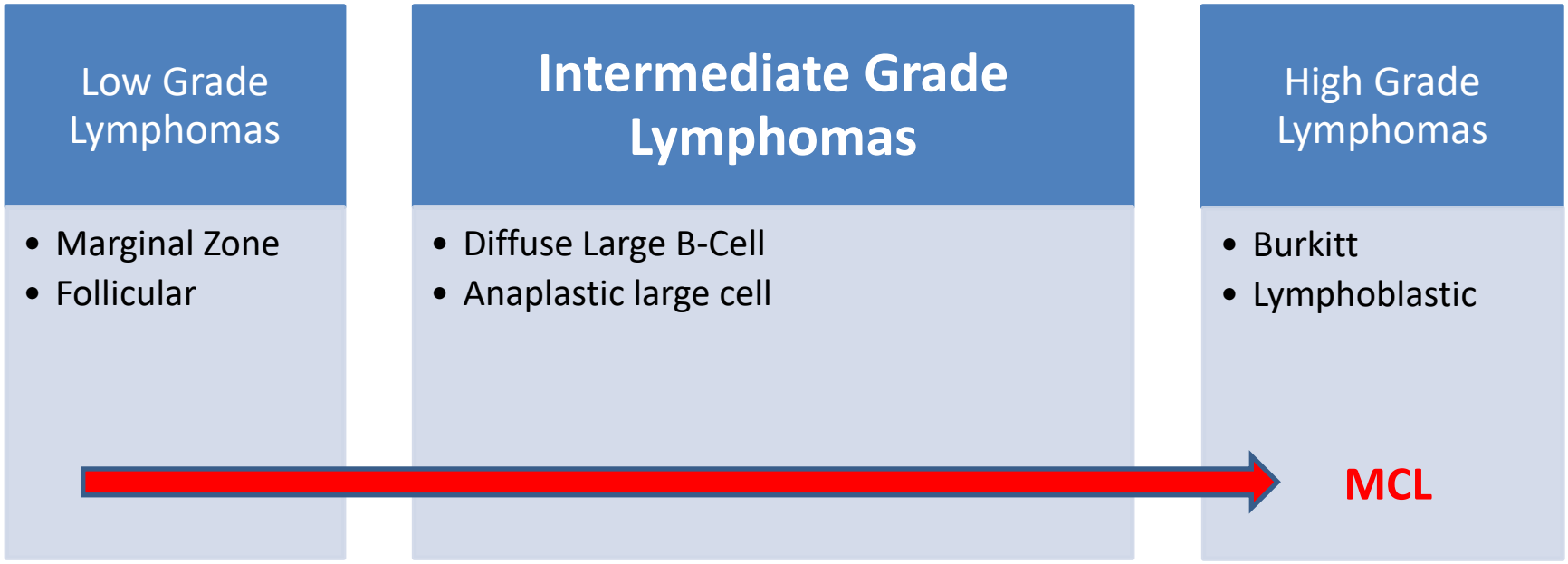
How *"I Treat MCL"*

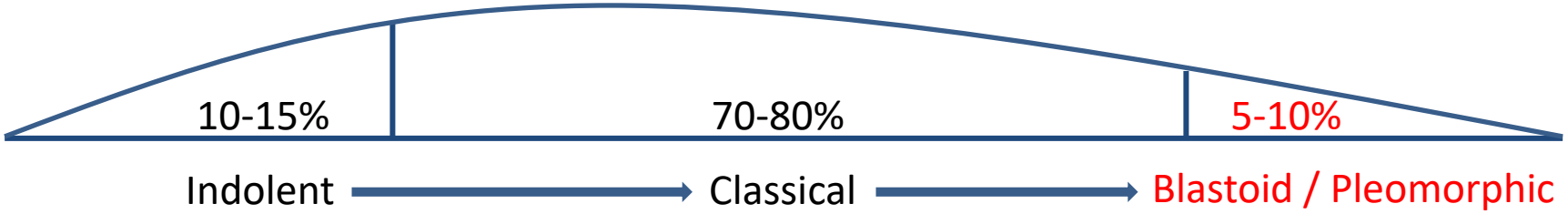
- Balance aggressiveness of disease with intensity of therapy, age/patient tolerance, and unique disease features
  - Young + Rapidly Growing = High Intensity
    - Induction: R+Hyper-CVAD, RCHOP-RDHAP, VCR-CVAD/VR-CAP, RBAC
    - Consolidation: Autologous Transplant+R, Allogeneic Transplant (p53)
  - Old + Rapidly Growing = Moderate Intensity
    - Induction: RCHOP, R+Lenalidomide
    - Consolidation: Maintenance Rituximab, Autologous Transplant+R
  - Young/Old + Slow Growing = Low Intensity
    - Induction: Watchful Waiting, R monotherapy, R+Bendamustine, R+Lenalidomide
    - Consolidation: Maintenance Rituximab

Mr. RR: 7 Years Later…

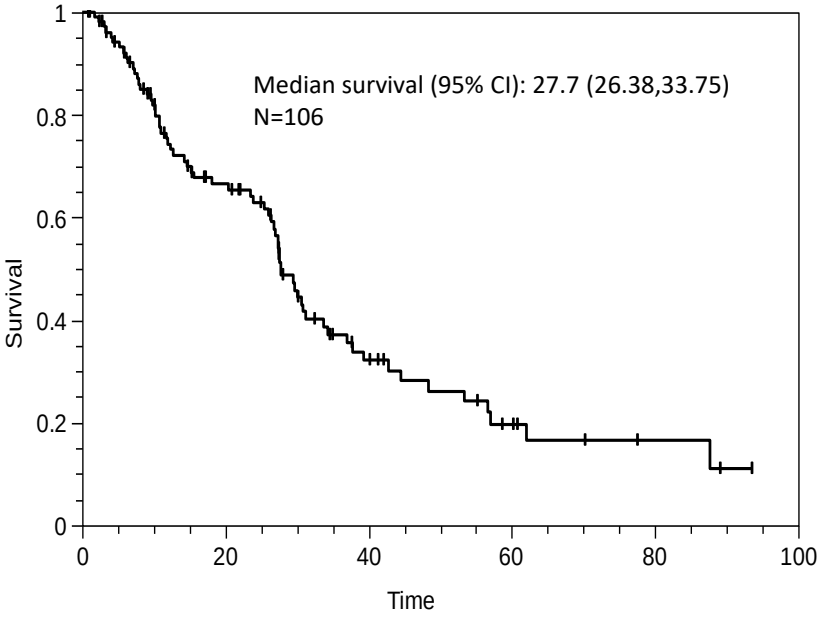
- Unfortunately, approximately 7 years later he develops a rapidly growing relapse (ki67 90%)…

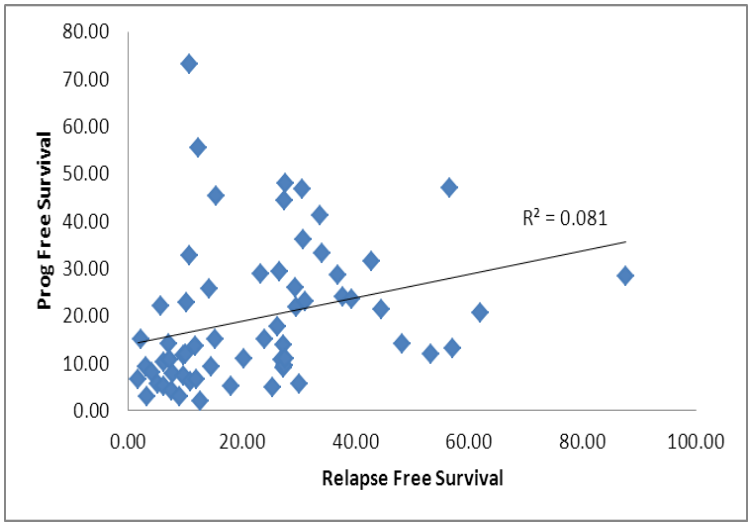
“Highly Aggressive” Phase?





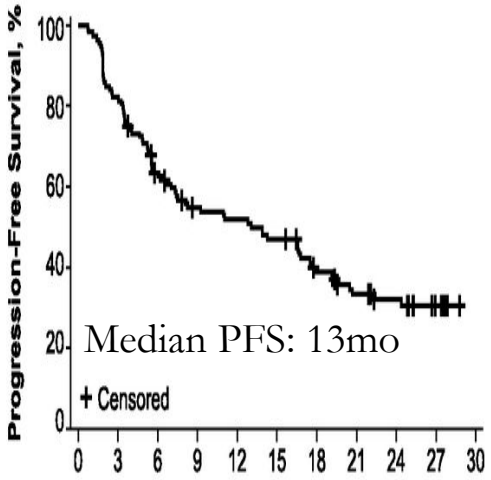
Relapsed & Refractory MCL: Can We Arrest the Descent?



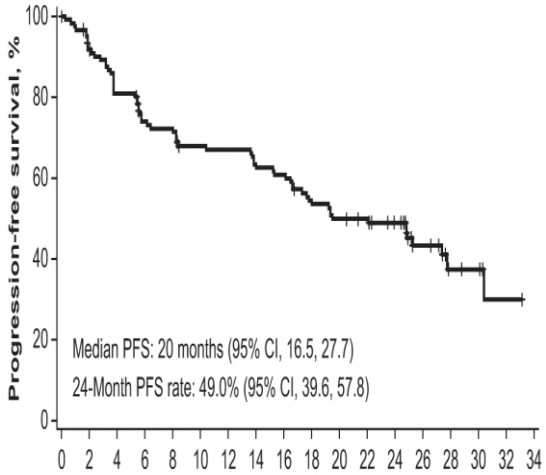


BTK Inhibitors: PFS

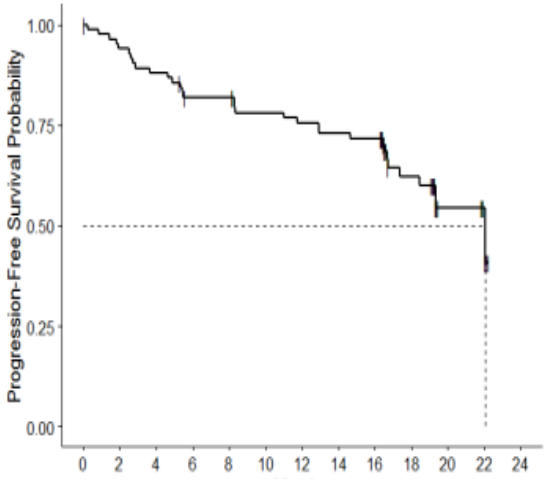
Ibrutinib



Acalabrutinib



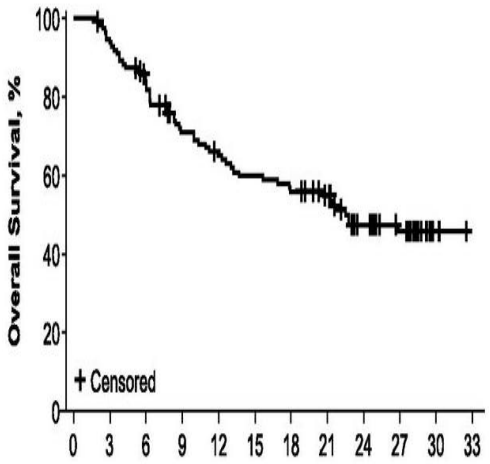
Zanubrutinib



Wang ML, et al. Blood. 2015 Aug 6; 126(6): 739
Wang ML, et al. Leukemia. 2019 Nov;33(11):2762
Song Y, et al. ASH 2018. Oral 148

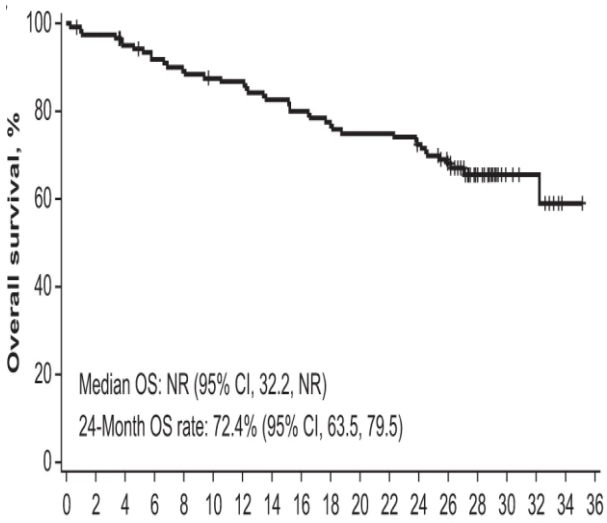
BTK Inhibitors: OS

Ibrutinib

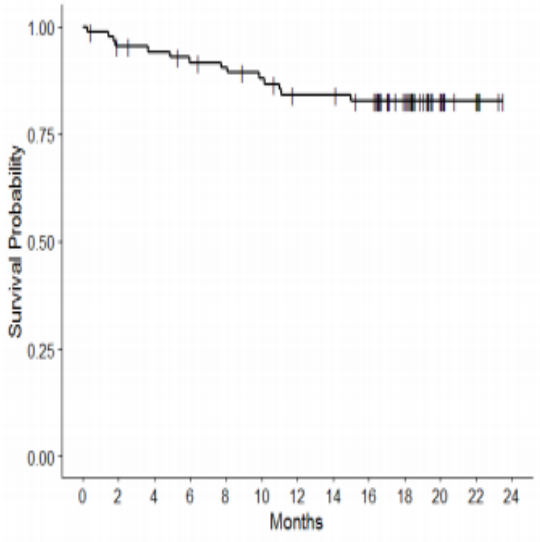


Median OS: 22.5mo

Acalabrutinib



Zanubrutinib



Wang ML, et al. Blood. 2015 Aug 6; 126(6): 739
Wang ML, et al. Leukemia. 2019 Nov;33(11):2762
Song Y, et al. ASH 2018. Oral 148

Be Careful Comparing Across Trials!

	Ibrutinib (n=111)	Acalabrutinib (n=124)	Zanubrutinib (n=86)
Median Age	68	68	61
Age ≥65y	63%	65%	**25%**
ECOG ≥2	11%	7%	**5%**
MIPI High	49%	17%	**13%**
Median Prior Tx	**3**	2	2
≥3 Prior Tx.	**55%**	23%	33%
Prior Hyper-CVAD	30%	21%	**15%**
Prior AutoSCT	11%	18%	**4%**
Prior Lenalidomide	24%	7%	14%
Refractory	45%	**24%**	52%
Median Followup	26.7 mo	15.2 mo	~16mo

Wang M, et al. NEJM 2013 ;369(6):507
Wang ML, et al. Blood. 2015 Aug 6; 126(6): 739
Wang ML, et al. Lancet 2018; 391: 659
Wang ML, et al. Leukemia. 2019 Nov;33(11):2762
Song Y, et al. ASH 2018. Abstract 148.

BTKi Non-Hematologic Toxicities

	Ibrutinib		Acalabrutinib		Zanubrutinib	
	G1-2	G3-4	G1-2	G3-4	G1-2	G3-4
General						
Headache	13%	0%	**36%**	**2%**	4.2%	
Myalgia	37%	1%	19%	2%	**11%**	**3%**
Nausea	31%	0%	18%	2%	NR	NR
Diarrhea	**46%**	**5%**	33%	3%	22%	1%
Cough	19%	0%	22%	0%	12%	0%
Rash	22%	3%	12%	2%	**36%**	**0%**
A Fib	**1%**	**6%**	0%	0%	1%	1%
HTN	7%	5%	**2%**	**1%**	9%	3%
Infection	54%	20%	**40%**	**13%**	52%	18%
PNA	6%	8%	1%	5%	5%	10%
UTI	11%	3%	2%	2%	10%	1%

Wang M, et al. NEJM 2013 ;369(6):507
Wang ML, et al. Blood. 2015 Aug 6; 126(6): 739
Wang ML, et al. Lancet 2018; 391: 659
Wang ML, et al. Leukemia. 2019 Nov;33(11):2762
Song Y, et al. ASH 2018. Abstract 148.

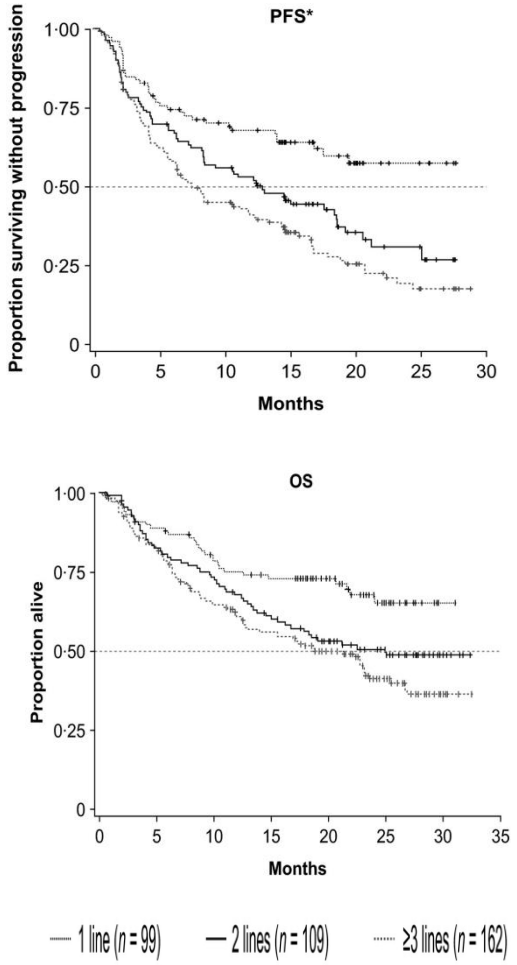
BTKi Hematologic Toxicity

	Ibrutinib		Acalabrutinib		Zanubrutinib	
	G1-2	G3-4	G1-2	G3-4	G1-2	G3-4
Heme						
Neutrophil	**18%**	**29%**	21%	15%	25%	20%
Platelet	**40%**	**17%**	32%	12%	33%	7%
Hemoglobin	32%	9%	36%	10%	**19%**	**8%**
Bleeding						
On Anticoag	55%		46%		NR	
Bruising	**41%**	**0%**	21%	0%	14%	0%
Hemorrhage	**10%**	**6%**	7%	2%	6%	5%
GI Bleed	0%	1%	2%	1%	NR	3%
CNS Bleed	2%	2%	0%	0%	0%	1%

Wang M, et al. NEJM 2013 ;369(6):507
Wang ML, et al. Blood. 2015 Aug 6; 126(6): 739
Wang ML, et al. Lancet 2018; 391: 659
Wang ML, et al. Leukemia. 2019 Nov;33(11):2762
Song Y, et al. ASH 2018. Abstract 148.

Mr. RR

- He is treated with a BTK inhibitor for 3mo without response, confirming resistance…

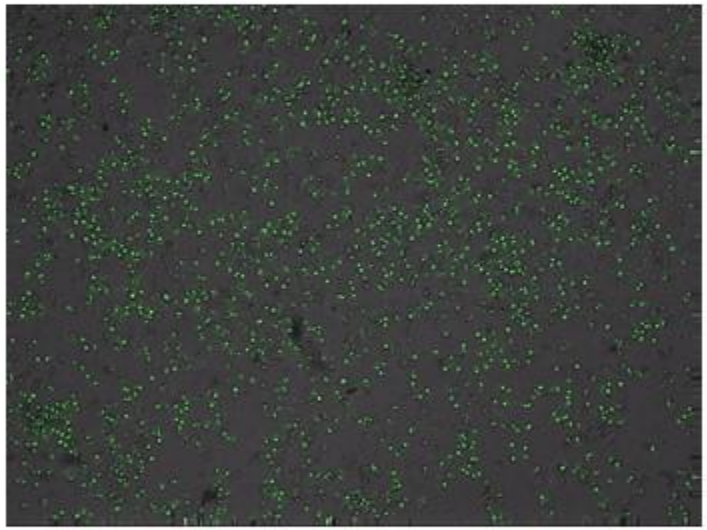


Rule S, et al. Br J Haematol. 2017 Nov;179(3):430-438

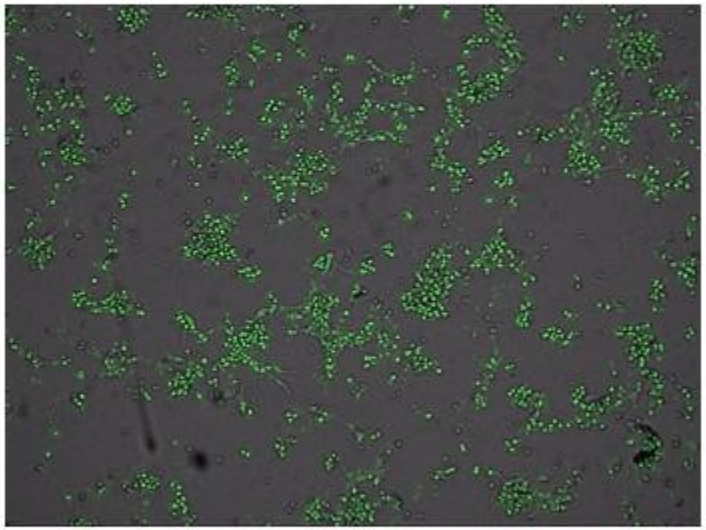
BTKi Resistance: An Emerging Problem

The Problem of BTKi Resistance

Sensitive

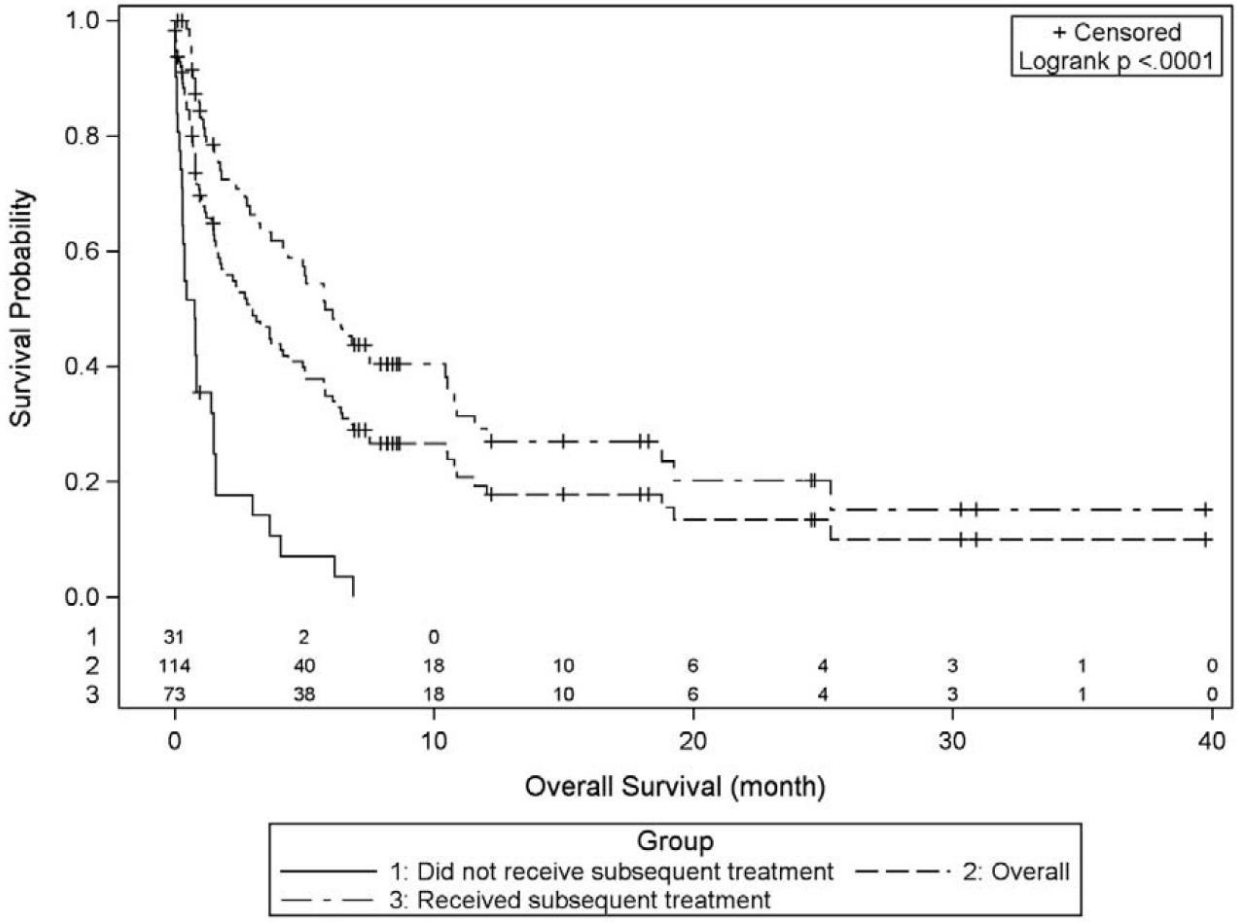


Resistant



Zhao X, et al. Nat Commun. 2017 Apr 18;8:14920

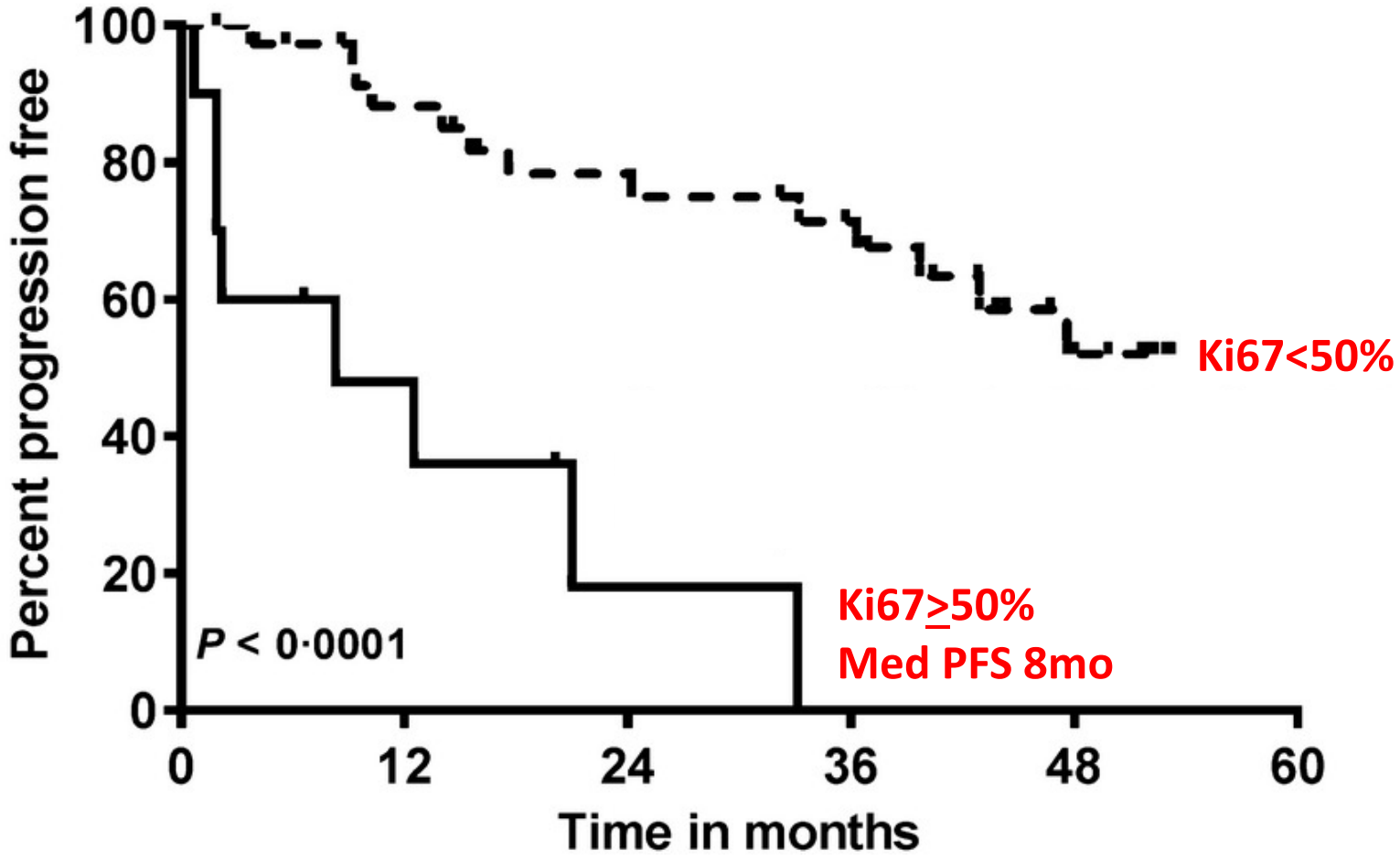
Overall Survival Post-Ibrutinib



Martin P, et al. Blood. 2016 Mar 24;127(12):1559-63

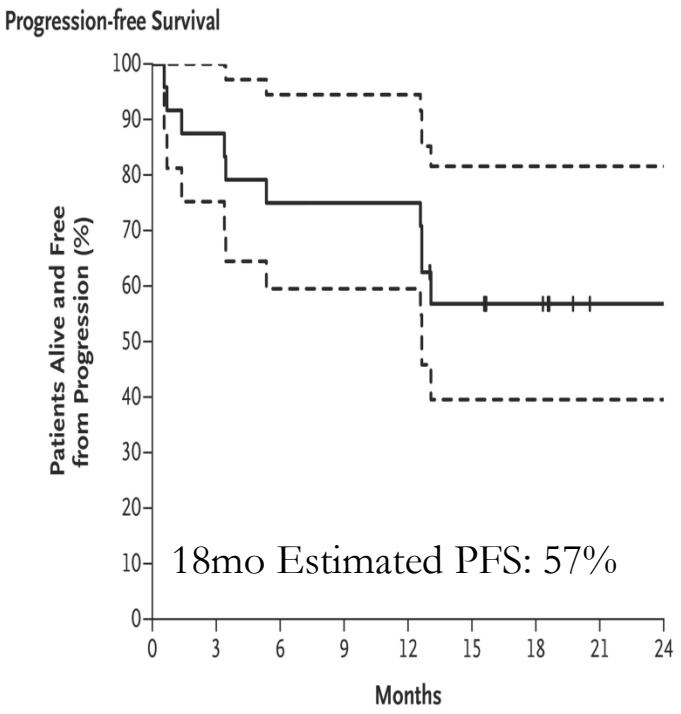
Novel Approaches?

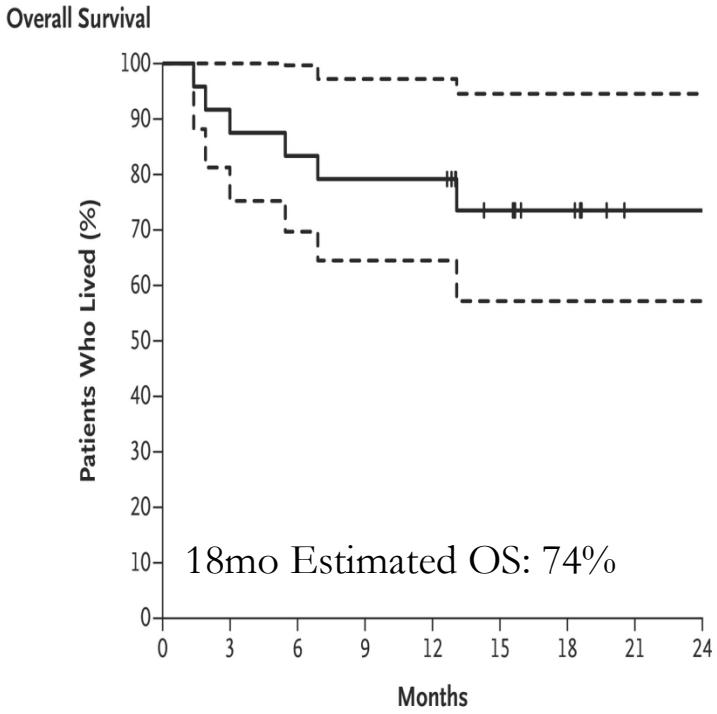
Ibrutinib + Rituximab



Jain P, et al. Br J Haematol. 2018 Aug;182(3):404-411

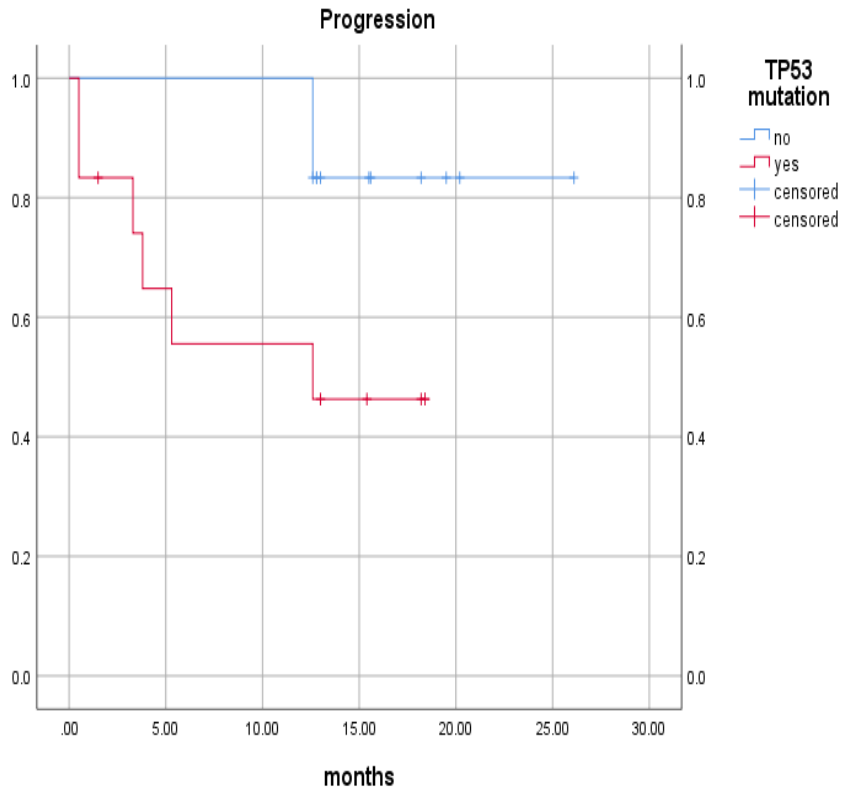
Ibrutinib + Venetoclax

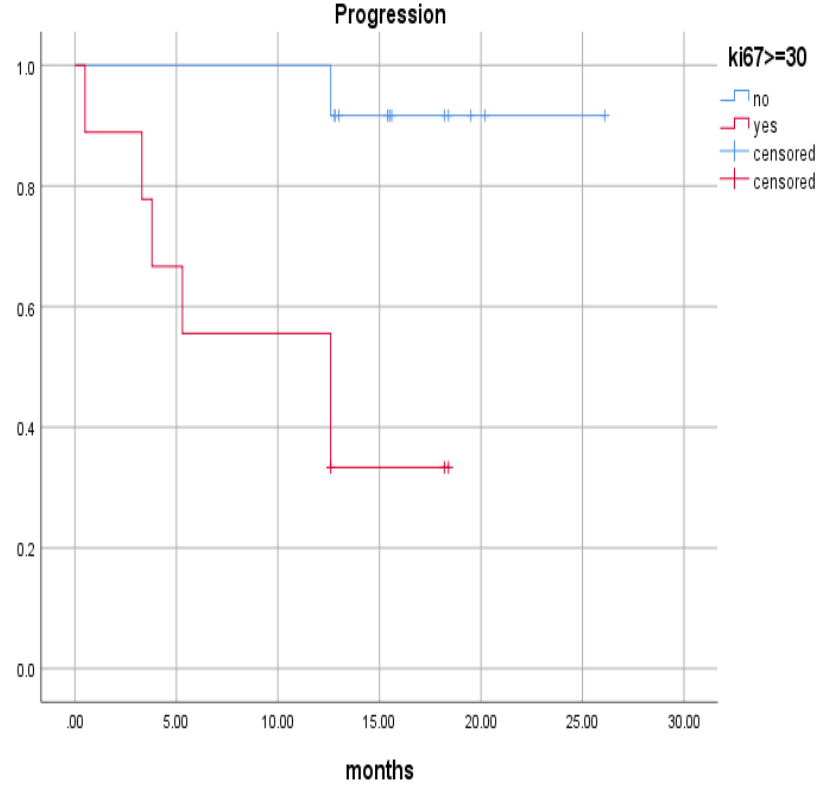




Tam CS, et al. N Engl J Med. 2018 Mar 29;378(13):1211

But We Are Still Fighting the Same Battles…



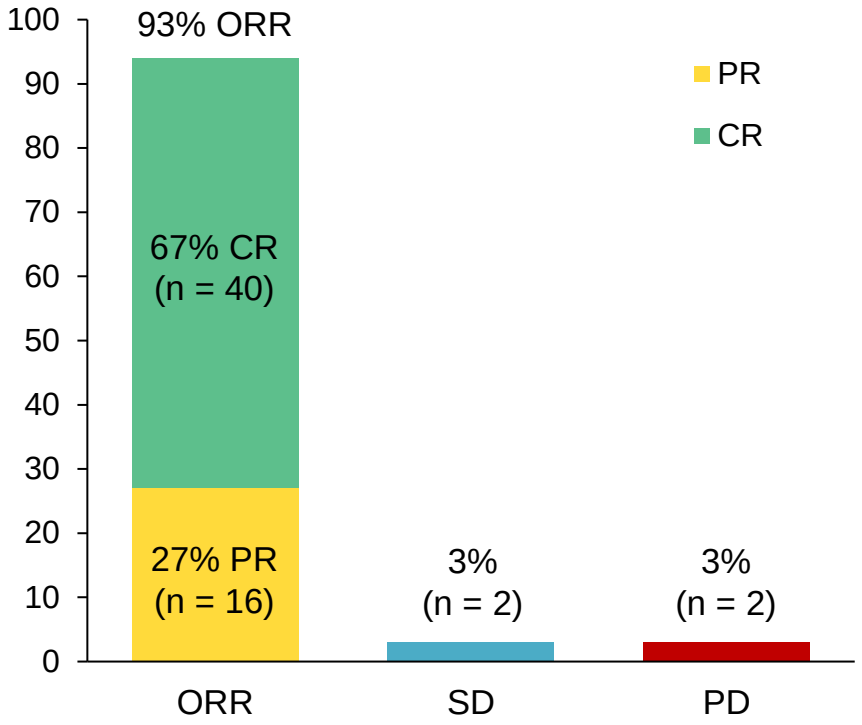


Tam CS, et al. N Engl J Med. 2018 Mar 29;378(13):1211

Can We Do Better?

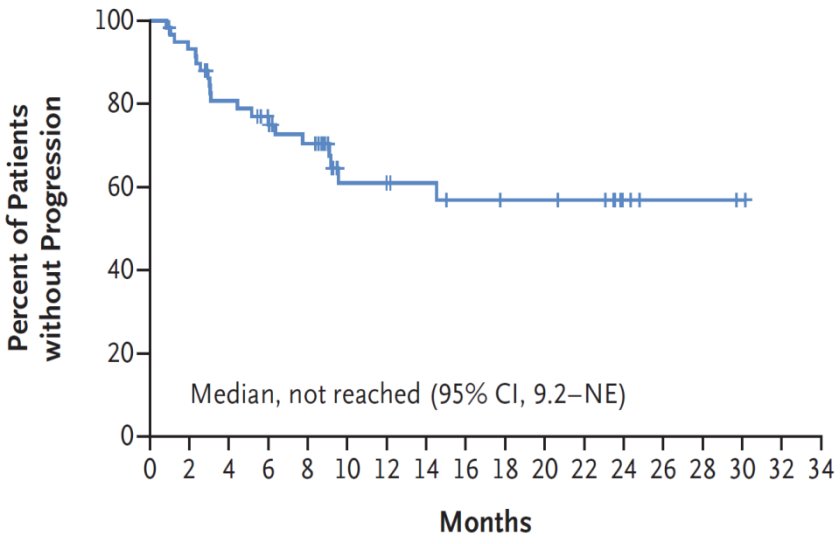
CAR T-Cell (KTE-X19) Therapy in MCL

Characteristics	Frequency
Age ≥65y	53%
Ki67≥50%	69%
TP53m	17%
≥3 prior lines	81%
BTKi R/R	96%

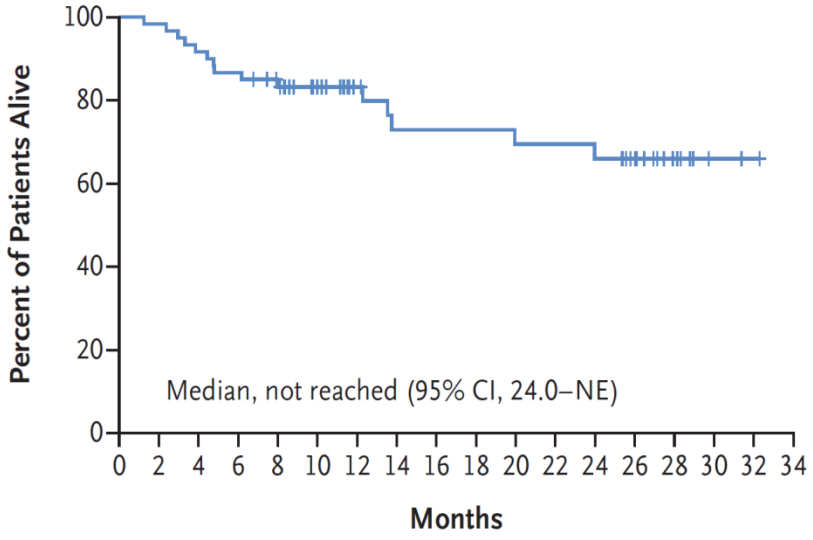


Wang M, et al. N Engl J Med. 2020 Apr 2;382(14):1331-1342

KTE-X19: Clinical Outcomes



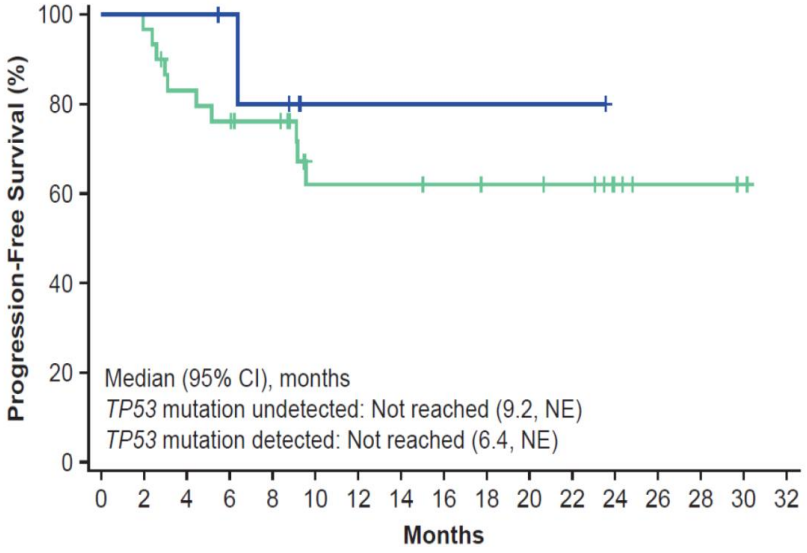
PFS

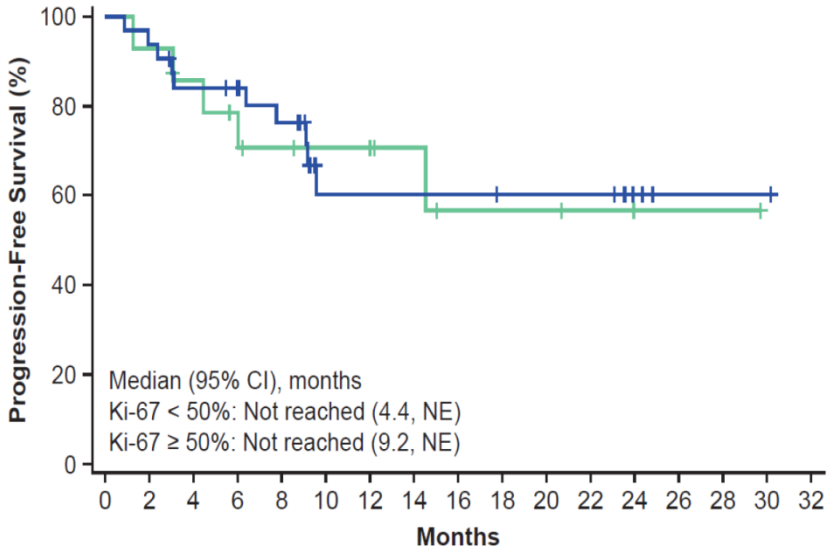


OS

Wang M, et al. N Engl J Med. 2020 Apr 2;382(14):1331-1342

KTE-X19: Outcomes in High-Risk MCL





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How *"I Treat Relapsed & Refractory MCL"*

- Balance aggressiveness of disease with intensity of therapy, age/patient tolerance, and unique disease features
  - Aggressive
    - Induction: BTKi + Rituximab +/- Venetoclax, VCR-CVAD/VRCAP, RBAC, CAR T, Clinical Trial
    - Consolidation: Allogeneic Transplant
  - Non-Aggressive
    - Induction: BTKi +/- Rituximab, Lenalidomide+Rituximab, Bendamustine+Rituximab, Clinical Trial
    - Consolidation: Maintenance Rituximab

Where Are We Going Next In MCL

- General Themes
  - Improve Tolerance
    - Low Intensity Chemotx + Novel Agent(s)
    - Replace Chemotx with Novel Agent(s)
  - Optimize the duration and intensity of maintenance
    - Rituxan *vs* Rituxan + Novel Agent(s)
    - CAR T-cell Therapy

Conclusions

- Mantle Cell Lymphoma is incurable with tendency to “evolve” to a more resistant state over time
- Intensive chemotherapy-based approaches are slowly giving way to novel therapies
- CAR T-cell therapy may finally allow us to overcome the challenge of rapidly growing and resistant MCL

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Thank You!!

Question & Answer Session

RESOURCES

- **Information Specialists**

  Master's level oncology professionals, available to help cancer survivors navigate the best route from diagnosis through treatment, clinical trials and survivorship.

  – **Email: infocenter@LLS.org**

  – **Toll-Free Phone: 1-800-955-4572**

- **Clinical Trial Support Center**

  Work one-on-one with an LLS Clinical Trial Nurse Navigator who will personally assist you throughout the entire clinical-trial process. Clinical Trial Nurse Navigators are registered nurses with expertise in blood cancers.

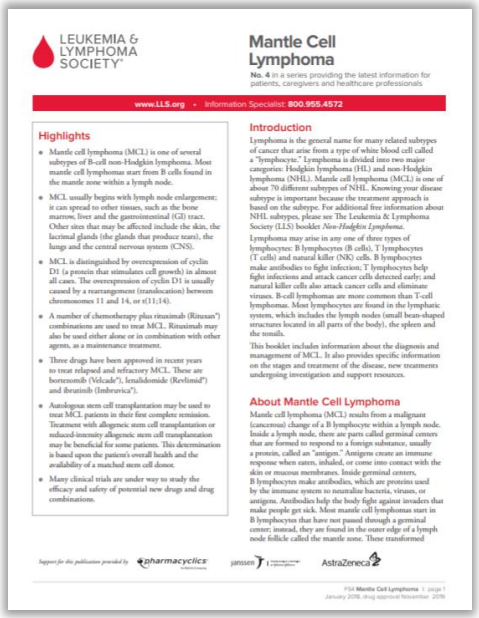
  – **Email: www.LLS.org/CTSC**

- **Additional Information about lymphoma:**

  – **www.LLS.org/Lymphoma**

FREE LLS EDUCATION & SUPPORT RESOURCES

- **Education Booklets about MCL:**
  - www.LLS.org/Booklets
- **Telephone/Web Programs:**
  - www.LLS.org/Programs



LEUKEMIA & LYMPHOMA SOCIETY®

Mantle Cell Lymphoma

No. 4 in a series providing the latest information for patients, caregivers and healthcare professionals

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Highlights

- Mantle cell lymphoma (MCL) is one of several subtypes of B-cell non-Hodgkin lymphoma. Most mantle cell lymphomas start from B cells found in the mantle zone within a lymph node.
- MCL usually begins with lymph node enlargement; it can spread to other tissues, such as the bone marrow, liver and the gastrointestinal (GI) tract. Other sites that may be affected include the skin, the lacrimal glands (the glands that produce tears), the lungs and the central nervous system (CNS).
- MCL is distinguished by overexpression of cyclin D1 (a protein that stimulates cell growth) in almost all cases. The overexpression of cyclin D1 is usually caused by a rearrangement (translocation) between chromosomes 11 and 14, or t(11;14).
- A number of chemotherapy plus rituximab (Rituxan®) combinations are used to treat MCL. Rituximab may also be used either alone or in combination with other agents, as a maintenance treatment.
- Three drugs have been approved in recent years to treat relapsed and refractory MCL. These are bortezomib (Velcade®), lenalidomide (Revlimid®) and ibrutinib (Imbruvica®).
- Autologous stem cell transplantation may be used to treat MCL patients in their first complete remission. Treatment with allogeneic stem cell transplantation or reduced-intensity allogeneic stem cell transplantation may be beneficial for some patients. This determination is based upon the patient's overall health and the availability of a matched stem cell donor.
- Many clinical trials are under way to study the efficacy and safety of potential new drugs and drug combinations.

Introduction

Lymphoma is the general name for many related subtypes of cancer that arise from a type of white blood cell called a "lymphocyte." Lymphoma is divided into two major categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Mantle cell lymphoma (MCL) is one of about 70 different subtypes of NHL. Knowing your disease subtype is important because the treatment approach is based on the subtype. For additional free information about NHL subtypes, please see The Leukemia & Lymphoma Society (LLS) booklet *Non-Hodgkin Lymphoma*.

Lymphoma may arise in any one of three types of lymphocytes: B lymphocytes (B cells), T lymphocytes (T cells) and natural killer (NK) cells. B lymphocytes make antibodies to fight infection; T lymphocytes help fight infections and attack cancer cells detected early; and natural killer cells also attack cancer cells and eliminate viruses. B-cell lymphomas are more common than T-cell lymphomas. Most lymphocytes are found in the lymphatic system, which includes the lymph nodes (small bean-shaped structures located in all parts of the body), the spleen and the tonsils.

This booklet includes information about the diagnosis and management of MCL. It also provides specific information on the stages and treatment of the disease, new treatments undergoing investigation and support resources.

About Mantle Cell Lymphoma

Mantle cell lymphoma (MCL) results from a malignant (cancerous) change of a B lymphocyte within a lymph node. Inside a lymph node, there are parts called germinal centers that are formed to respond to a foreign substance, usually a protein, called an "antigen." Antigens create an immune response when eaten, inhaled, or come into contact with the skin or mucous membranes. Inside germinal centers, B lymphocytes make antibodies, which are proteins used by the immune system to neutralize bacteria, viruses, or antigens. Antibodies help the body fight against invaders that make people get sick. Most mantle cell lymphomas start in B lymphocytes that have not passed through a germinal center; instead, they are found in the outer edge of a lymph node follicle called the mantle zone. These transformed

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January 2018, drug approval November 2018

- **Weekly Non-Hodgkin Lymphoma Chat:**
  - www.LLS.org/Chat
- **Additional LLS Information about Coronavirus:**
  - www.LLS.org/Coronavirus

BEATING CANCER IS IN OUR BLOOD.

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FREE LLS EDUCATION & SUPPORT RESOURCES

- **LLS Podcast, *The Bloodline with LLS***

  Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients: **www.thebloodline.org**

- **Education Videos**

  Free education videos about survivorship, treatment, disease updates and other topics: **www.LLS.org/EducationVideos**

- **Patti Robinson Kaufmann First Connection Program**

  Peer-to-peer program that matches newly diagnosed patients and their families: **www.LLS.org/FirstConnection**

- **Nutrition Consultations**

  Telephone and email consultations with a Registered Dietitian: **www.LLS.org/Nutrition**

- **What to Ask**

  Questions to ask your treatment team: **www.LLS.org/WhatToAsk**

- **Other Support Resources**

  LLS Community, discussion boards, blogs, support groups, financial assistance and more: **www.LLS.org/PatientSupport**

THANK YOU

We have one goal: A world without blood cancers

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