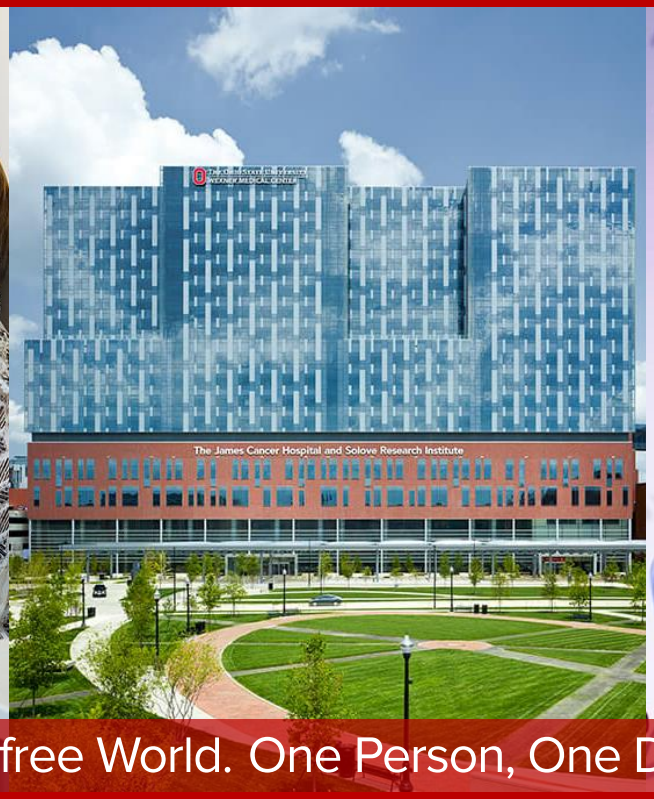

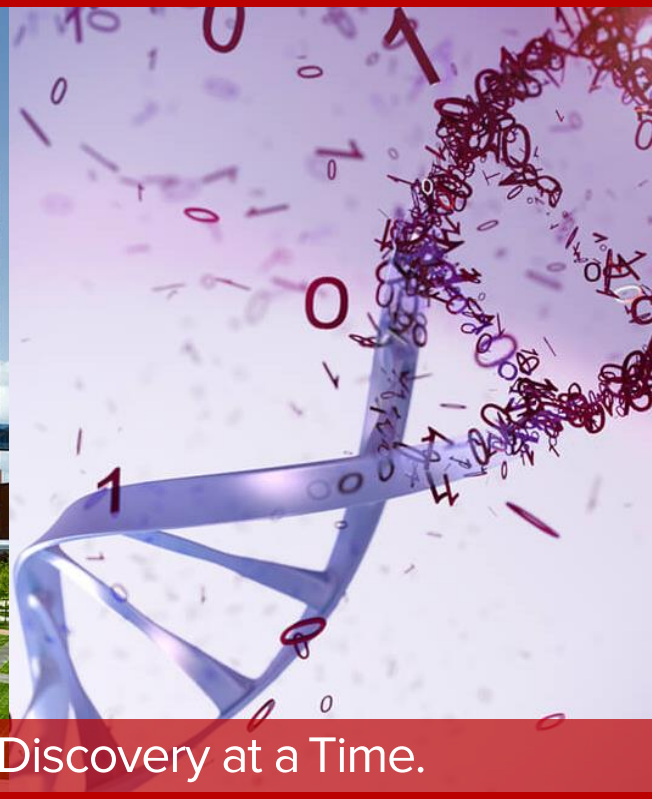

Creating a Cancer-free World. One Person, One Discovery at a Time.

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Mantle Cell Lymphoma

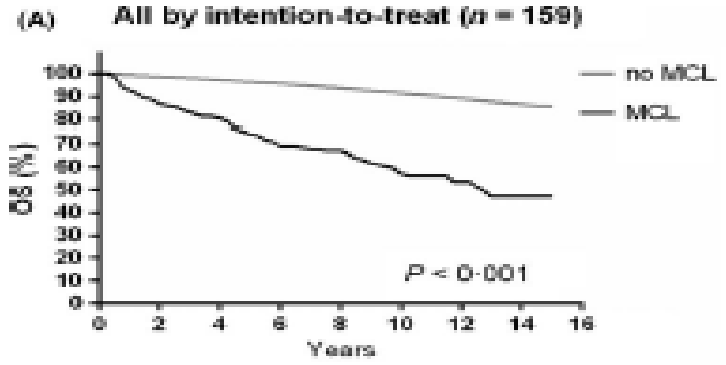
Kami Maddocks, MD
Professor
Lymphoma Program Director
The James Cancer Hospital
The Ohio State University

Disclosures

- Research Funding
  - Pharmacyclis, Novartis, Merck, BMS/Celgene
- Advisory/Honorarium
  - AstraZeneca, Acerta, Beigene, BMS, Celgene, Genmab, Genentech, Janssen, Incyte, Morphosys, Kite/Gilead, ADC Therapeutics, Epizyme, Lilly, Pharmacyclics

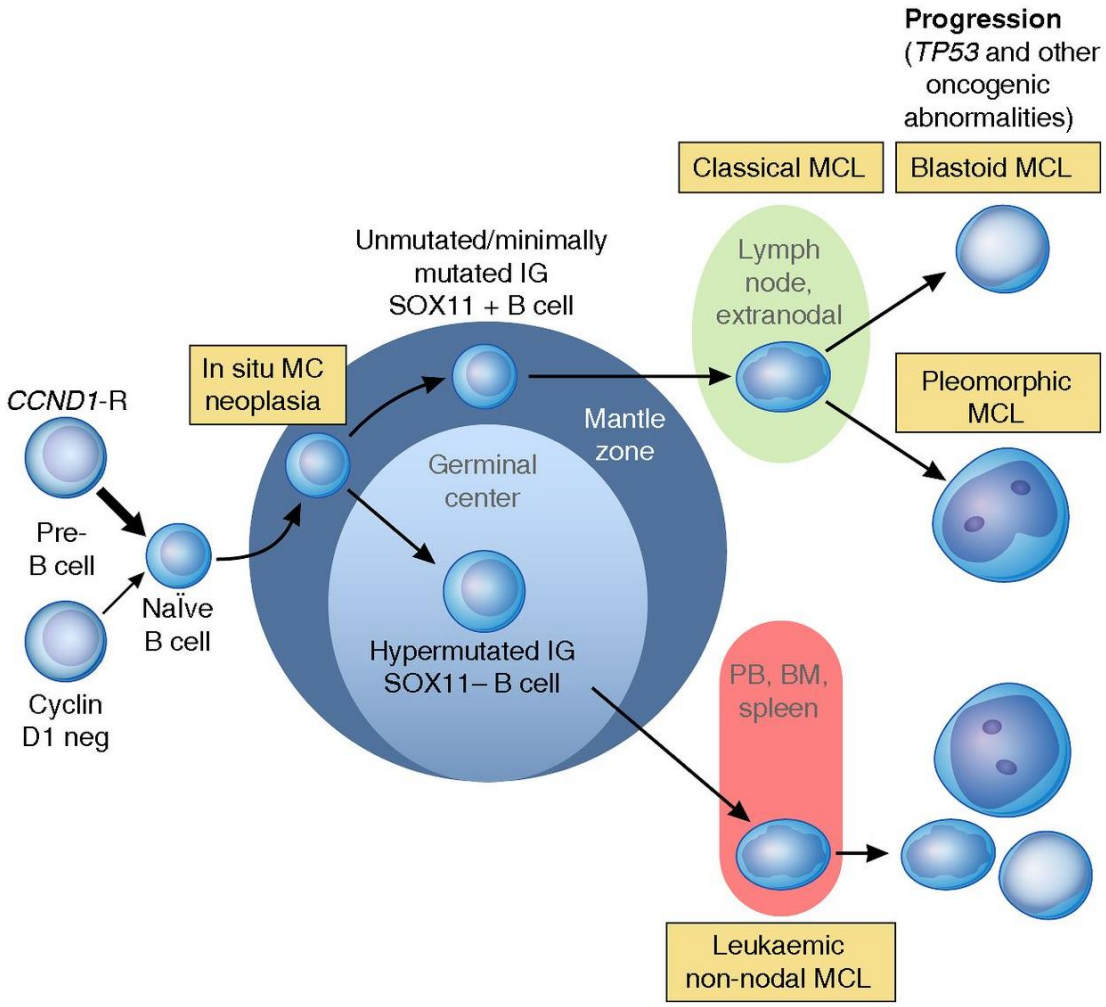
Background and Challenges

- Outcomes driven by disease biology
  - Prognostic factors defined, don't drive treatment decisions
- Survival improved (? Double) in the era of current therapies
- Rituximab, high-dose cytarabine induction, rituximab maintenance
  - Benefits of some approaches unclear
- Novel biologic/targeted therapies, cellular therapies approved at relapse
  - Resistance, access remain challenges
- Young patients still most likely to die from MCL



Eskelund et al. BJH. 2016

Proposed model of molecular pathogenesis of major subtypes of MCL



Swerdlow et al. Blood 2016

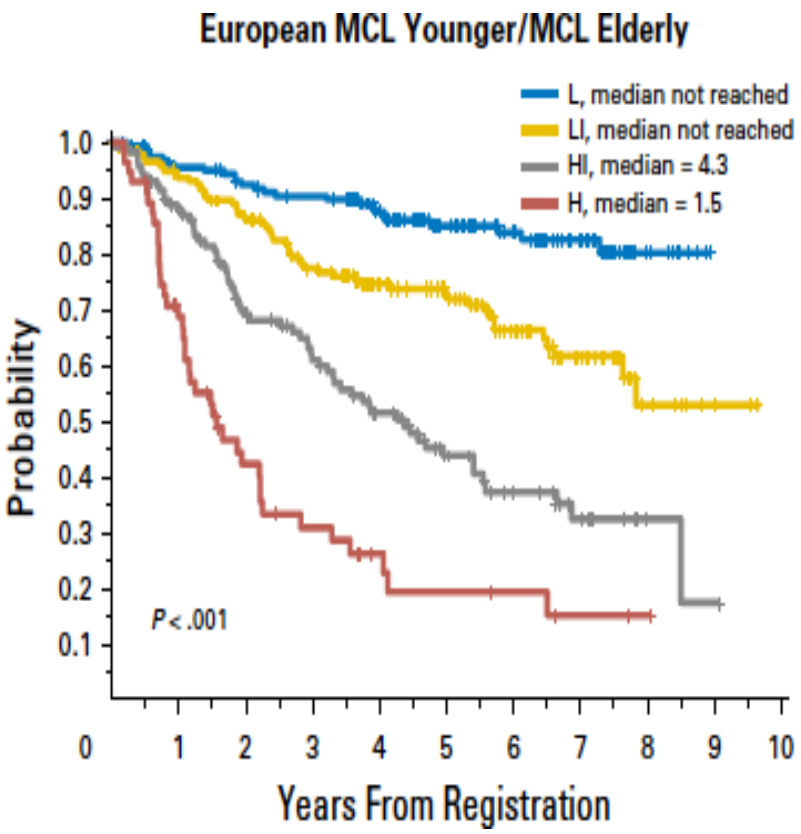
Disease biology and patient population, not treatment, is the primary driver of outcomes

Ki-67 independently prognostic

Ki-67 > 30% largely explains outcomes of blastoid and different growth patterns

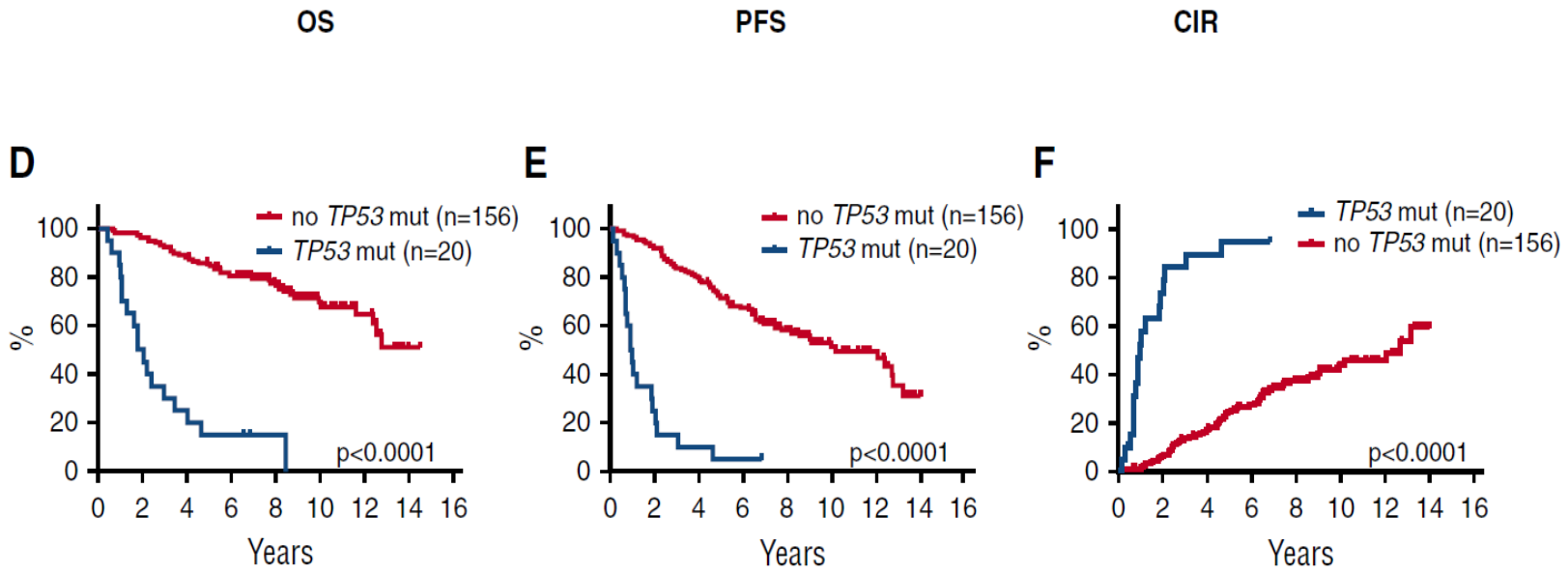
MIPI (age, PS, WBC and LDH) and Ki-67 > 30% generates 4 distinct risk groups

True in both European Younger and Older Cohorts: Independent of Treatment



Hermine et al, Lancet 2016

TP53 Predicts Poor Survival



Eskelund et al, *Blood* 2017

Frontline Treatment Approaches

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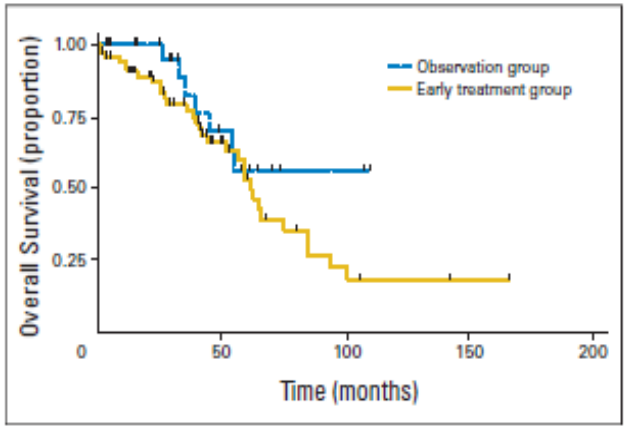
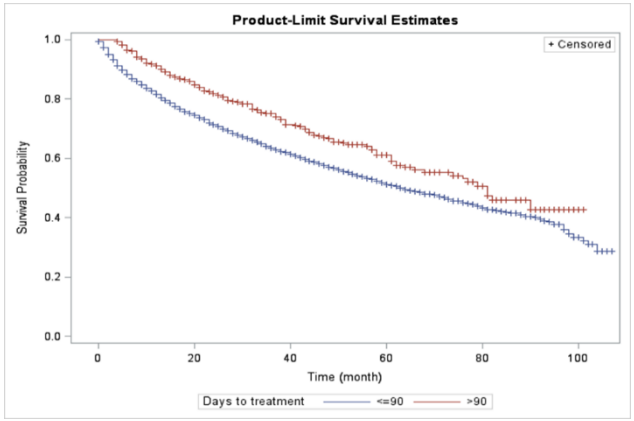
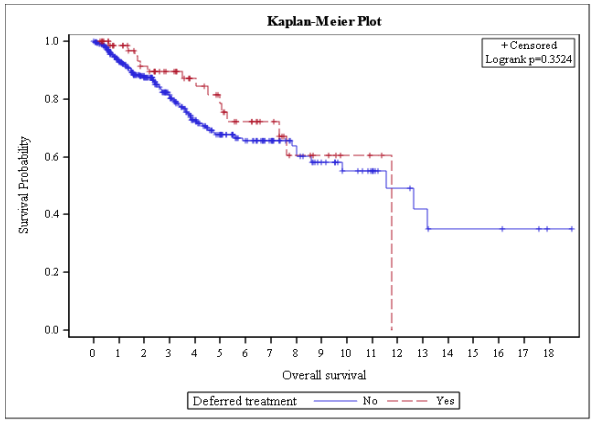
Initial Therapy

- No “standard” treatment approach
  - Prolong PFS, ? OS, toxicity considerations
- Chemoimmunotherapy
  - Role of consolidation ASCT
  - Maintenance rituximab
- Targeted therapies (BTKi, BCL-2, IMiD) incorporated into initial therapy
- Investigation of risk stratified treatment

Observation in Select Patients







Series	N Deferred (%)	TTT (Range)	OS (Deferred)	OS (Immediate)
Martin 2009	31 / 97 (32)	12 months (4-128)	Not Reached	5.3 y
Abrisqueta	74 / 439 (17)	35.5 months (5-79)	5.5 y	4.2 y
Cohen 2016	492 / 8029 (6)	4 months (3-38)*	6.6 y	-
Kumar 2015	91 / 404 (23)	23 months	10.6 y	9.4 y
Calzada 2016	72 / 395 (18)	7.8 months (3-121)*	11.8 y	11.6 y

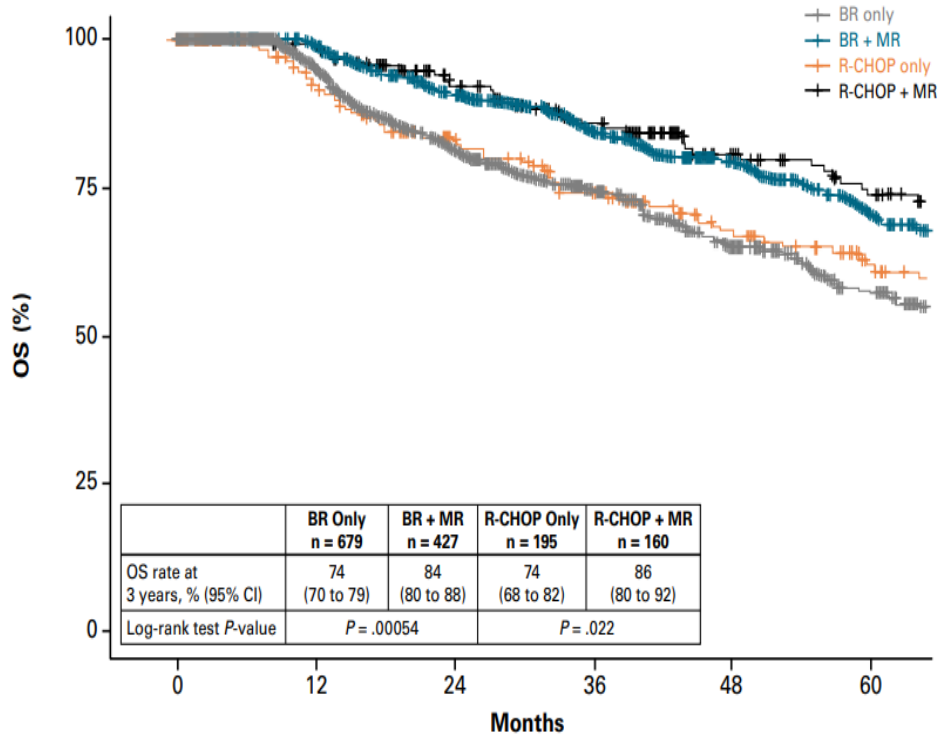
Frontline Non-transplant

Phase III	N	ORR (CR) %	FFS/PFS	Median OS	Toxicities of Interest or Significance
RCHOP vs RFC* **	455	86 vs 78 34 vs 40	TTF 28 months vs 26 months	4-year 62% vs 47% Median 6.4 years vs 4.9 years	Primary hematologic Infections (> RFC)
RCHOP vs BR	94	91 vs 93 30 vs 40	22.1 months vs. 35.4 months (median)	Median Not Reached Median Not Reached	
RCHOP vs VRCAP	487	89 vs 92 42 vs 53	14.4 months vs 24.7 months	4-year 54% vs 67%	Primary hematologic
Phase II					
RBAC 500	57	91	2-year PFS 81%	Median Not Reached	Primary hematologic

***Maintenance Included

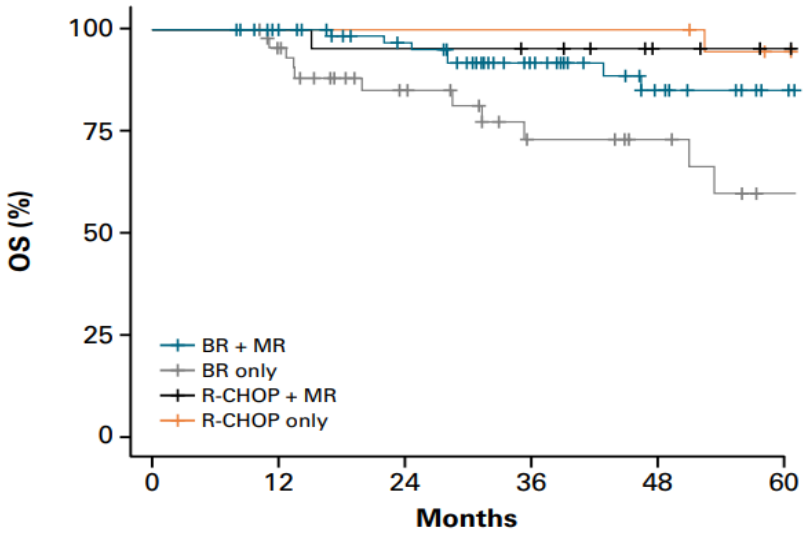
Kluin-Neleman JC Blood 2011; Rummel Lancet 2013; Robak NEJM 2015; Visco Lancet 2017

Rituximab Maintenance



	BR Only n = 679	BR + MR n = 427	R-CHOP Only n = 195	R-CHOP + MR n = 160
OS rate at 3 years, % (95% CI)	74 (70 to 79)	84 (80 to 88)	74 (68 to 82)	86 (80 to 92)
Log-rank test *P*-value	*P* = .00054		*P* = .022	

Patients at risk						
BR only	679	458	317	225	156	106
BR + MR	427	409	330	235	179	113
R-CHOP only	195	144	120	99	75	61
R-CHOP + MR	160	155	129	108	85	71



Patients at risk						
BR + MR	76	71	60	37	23	14
BR only	46	40	27	16	12	6
R-CHOP + MR	23	22	21	20	16	14
R-CHOP only	21	20	20	20	20	17

	BR Only n = 46	BR + MR n = 76	R-CHOP Only n = 21	R-CHOP + MR n = 23
OS rate at 3 years, % (95% CI)	73.2 (53.7 to 85.5)	91.9 (81.6 to 96.5)	100.0 (NR to NR)	95.5 (71.9 to 99.3)
Log-rank test *P*-value	*P* = .0004			

Martin et al JCO 2022

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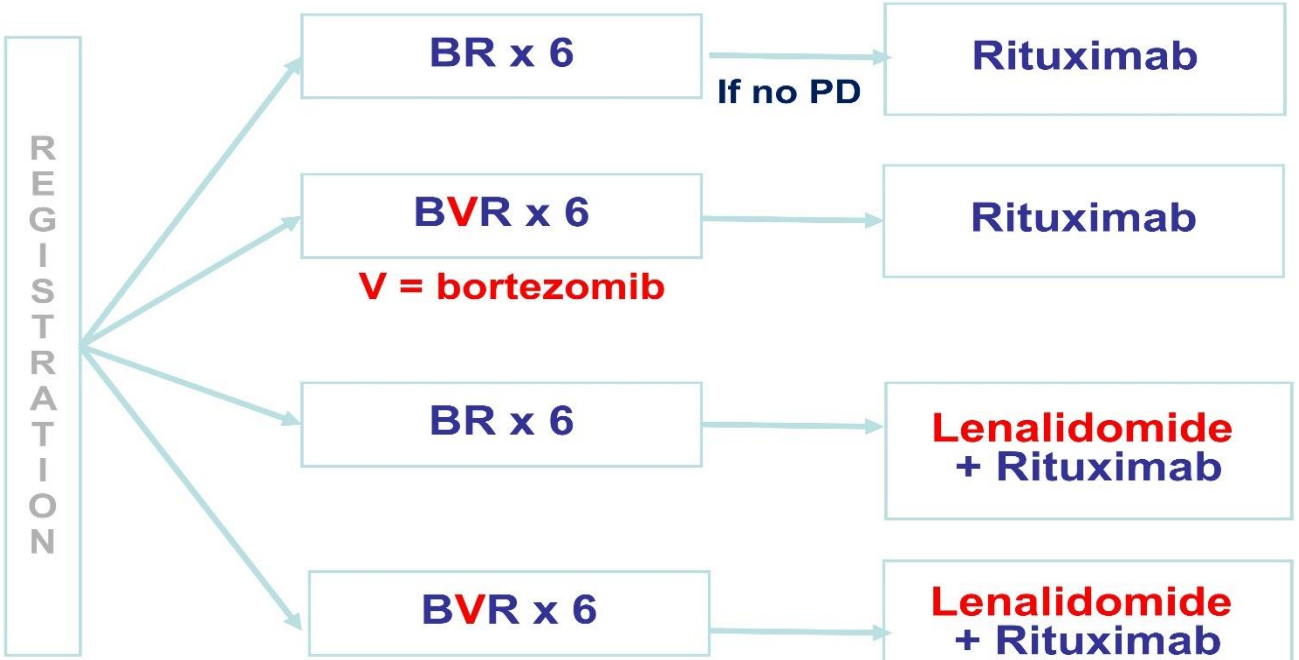
EA1411

E1411 SCHEMA



Induction:

BR = bendamustine 90 mg/m^2/d days 1, 2 + rituximab 375 mg/m^2 day 1, every 28 days x 6

BVR = BR + bortezomib 1.3 mg/m^2 days 1, 4, 8, 11 (later amended to 1.6 mg/m^2 days 1, 8), IV or SQ

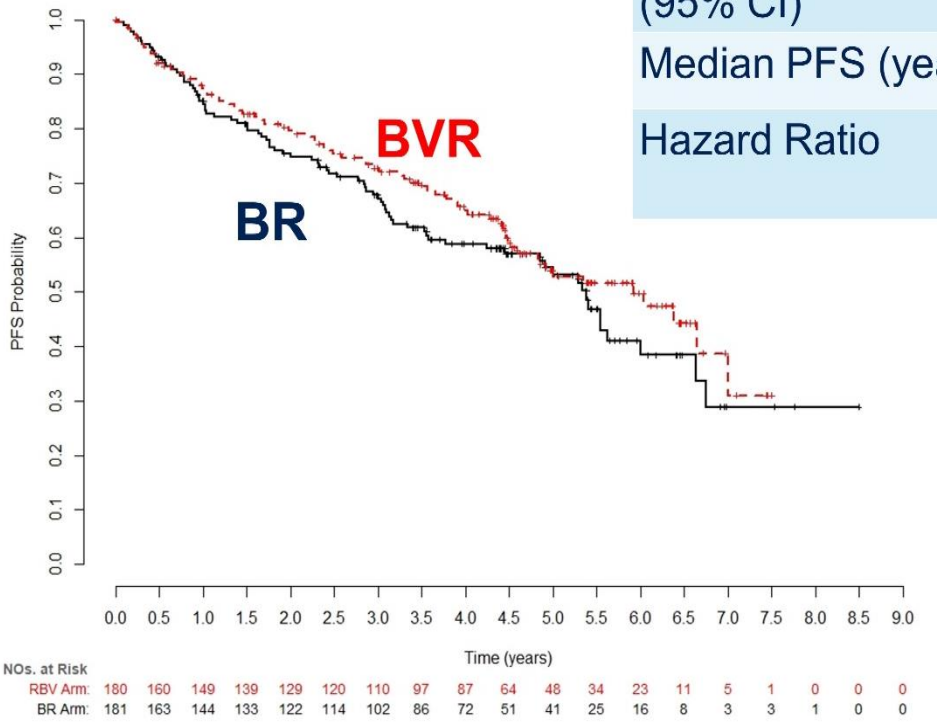
Consolidation:

Rituximab 375 mg/m^2 every 8 weeks x 12 doses ± Lenalidomide 15 mg/d 21/28 days x 24 cycles

Smith M et al, ASCO 2021

EA1411

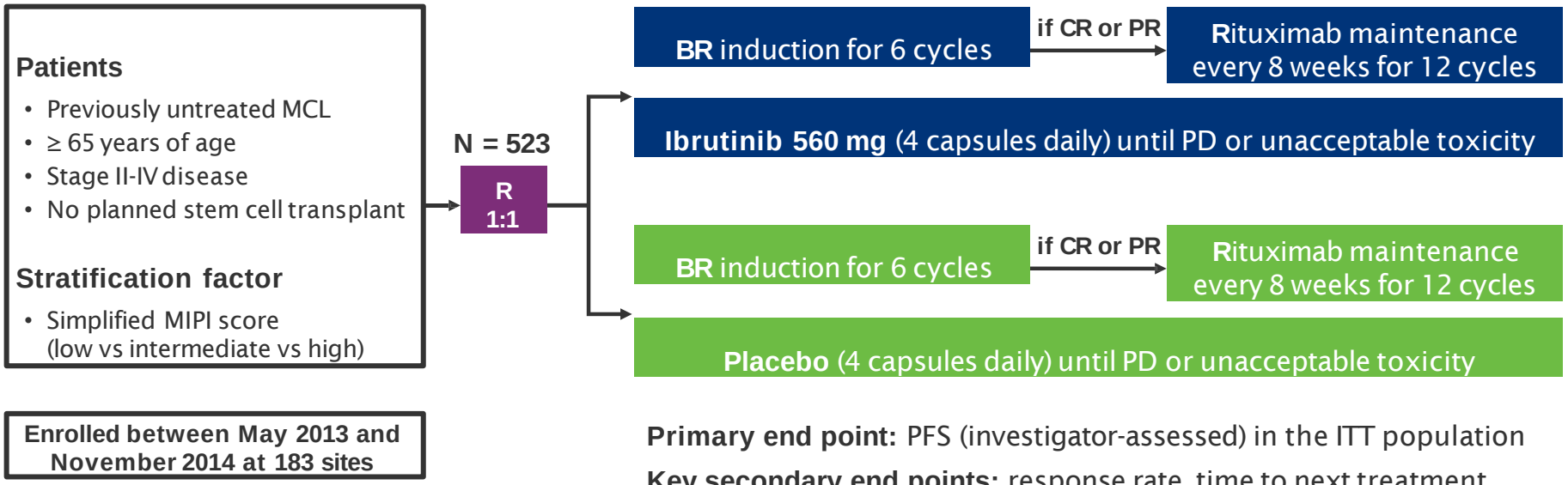
PFS: BR vs BVR



	BR	BVR
2 year PFS % (95% CI)	74.8% (68.6-81.6)	79.7% (73.9-85.9)
Median PFS (years)	5.4	5.9
Hazard Ratio	0.83 (0.60 -1.15)	

Smith M et al, ASCO 2021

SHINE: A Randomized, Double-Blind, Phase III Study



Primary end point: PFS (investigator-assessed) in the ITT population

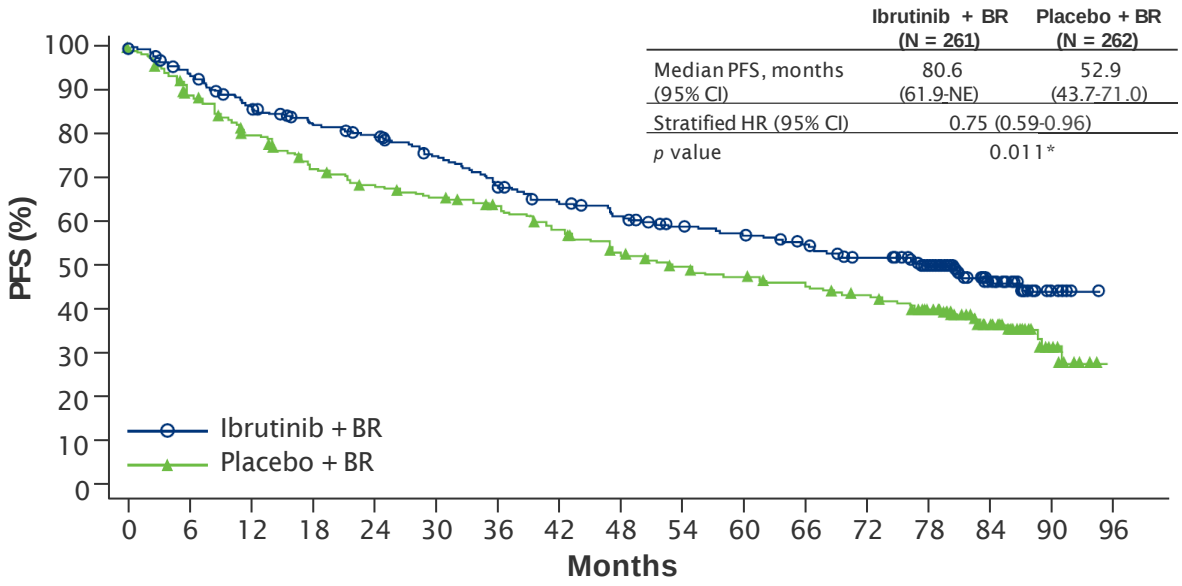
Key secondary end points: response rate, time to next treatment, overall survival, safety

Induction: Bendamustine 90 mg/m2 Days 1 and 2, Rituximab 375 mg/m2 Day 1, Q4W. A cycle is defined as 28 days.

CR, complete response; ITT, intent-to-treat; MIPI, Mantle Cell Lymphoma International Prognostic Index; PD, progressive disease; PFS, progression-free survival; PR, partial response.

Wang et al ASCO 2022, NEJM 2022

Primary End Point of Improved PFS Was Met



	Ibrutinib + BR (N = 261)	Placebo + BR (N = 262)
Median PFS, months (95% CI)	80.6 (61.9-NE)	52.9 (43.7-71.0)
Stratified HR (95% CI)	0.75 (0.59-0.96)	
p value	0.011*	

Patients at Risk																	
Ibrutinib + BR	261	228	207	191	182	167	152	139	130	120	115	106	95	78	39	11	0
Placebo + BR	262	226	199	177	166	158	148	135	119	109	103	98	90	78	41	11	0

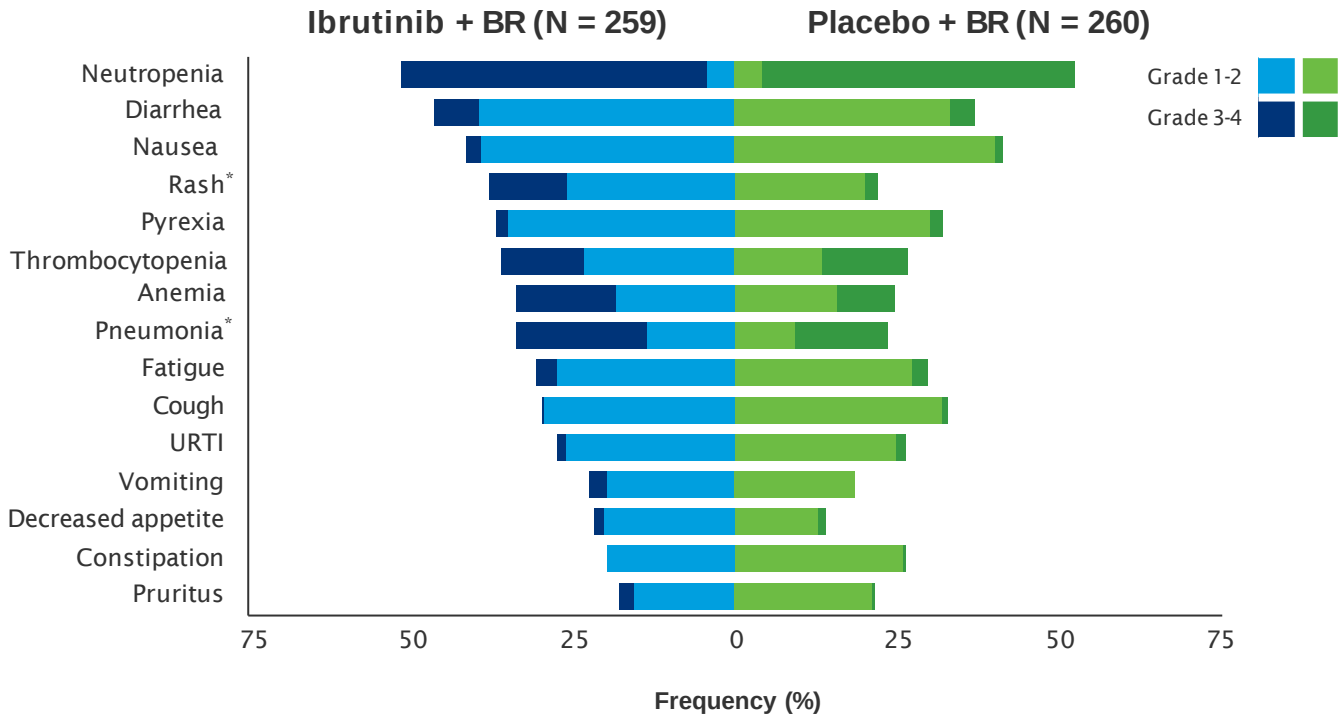
CI, confidence interval; HR, hazard ratio; NE, not evaluable.
*Significance boundary for superiority was $p < 0.023$.

- **Significant improvement in median PFS by 2.3 years** (6.7 vs 4.4 years)
- **25% reduction** in risk of PD or death

	BR+I	BR+P
ORR	89.7	88.5
CR	65.5	57.6
PR	24.1	30.9

Wang et al ASCO 2022, NEJM 2022

Common Treatment-Emergent Adverse Events (≥ 20%)



*Difference of ≥ 10% in any grade treatment-emergent adverse event (TEAE).
URTI, upper respiratory tract infection.

Wang et al ASCO 2022, NEJM 2022

TEAEs of Clinical Interest With BTKis

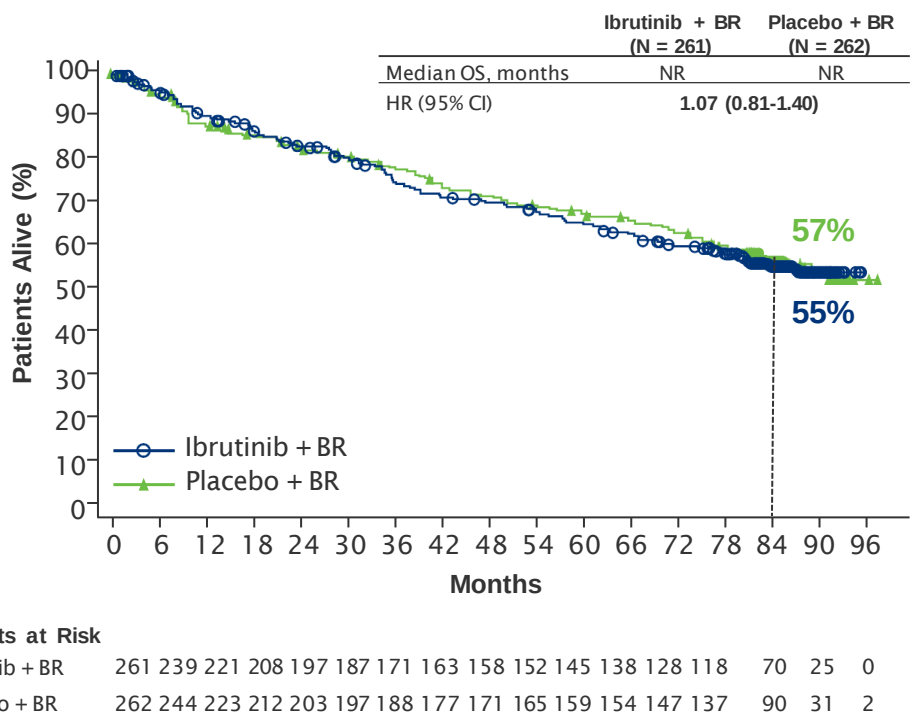
	Ibrutinib + BR (N = 259)		Placebo + BR (N = 260)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Any bleeding*	42.9%	3.5%	21.5%	1.5%
Major bleeding	5.8%	–	4.2%	–
Atrial fibrillation*	13.9%	3.9%	6.5%	0.8%
Hypertension	13.5%	8.5%	11.2%	5.8%
Arthralgia	17.4%	1.2%	16.9%	0

- These adverse events were generally not treatment limiting
- During the entire study period, second primary malignancies (including skin cancers) occurred in 21% in the ibrutinib arm and 19% in the placebo arm; MDS/AML in 2 and 3 patients, respectively

*Difference of ≥ 5% in any grade TEAE; MDS/AML, myelodysplastic syndromes/acute myeloid leukemia;
Any bleeding is based on Haemorrhage Standardized MedDRA Query (SMQ) (excluding laboratory terms). Major bleeding includes any grade 3 or higher bleeding and serious or central nervous system bleeding of any grade.

Wang et al ASCO 2022, NEJM 2022

Overall Survival



Cause of death	Ibrutinib + BR (N = 261)	Placebo + BR (N = 262)
Death due to PD and TEAE	58 (22.2%)	70 (26.7%)
Death due to PD	30 (11.5%)	54 (20.6%)
Death due to TEAEs*	28 (10.7%)	16 (6.1%)
Death during post-treatment follow-up excluding PD and TEAEs	46 (17.6%)	37 (14.1%)
Total deaths	104 (39.8%)	107 (40.8%)

- Death due to Covid-19: 3 patients in the ibrutinib arm during the TEAE period and 2 patients in the placebo arm after the TEAE period
- Exploratory analysis of cause-specific survival including only deaths due to PD or TEAEs showed an HR of 0.88

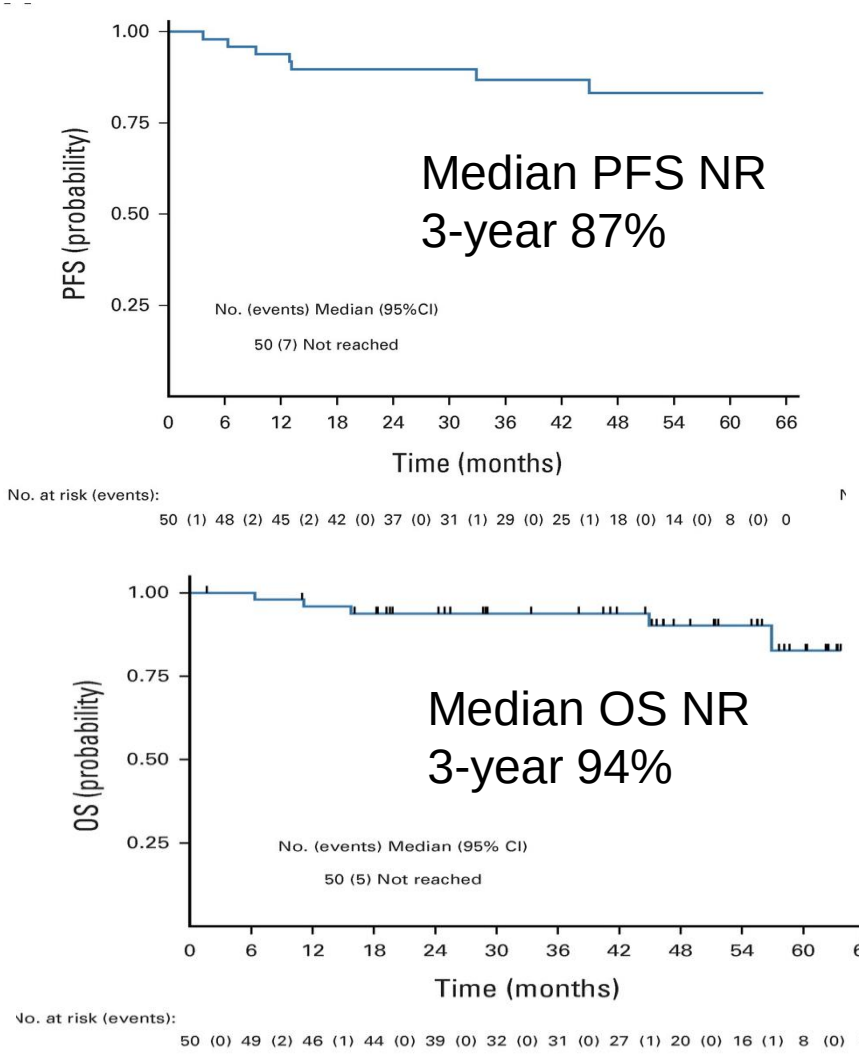
*The most common grade 5 TEAE was infections in the ibrutinib and placebo arms: 9 versus 5 patients. Grade 5 TEAE of cardiac disorders occurred in 3 versus 5 patients, respectively.
CI, confidence interval; HR, hazard ratio; NR, not reached; PD, progressive disease; TEAE, treatment-emergent adverse event.

Wang et al ASCO 2022, NEJM 2022

Rituximab + Ibrutinib Elderly MCL

Patients enrolled N=50
Patients off Study N=28
- Progression n=4
- **Intolerance n=21**
  - AF n=10
  - Bleeding n=3
  - Other n=8
- Miscellaneous n=3

ORR 96%
CRR 71%

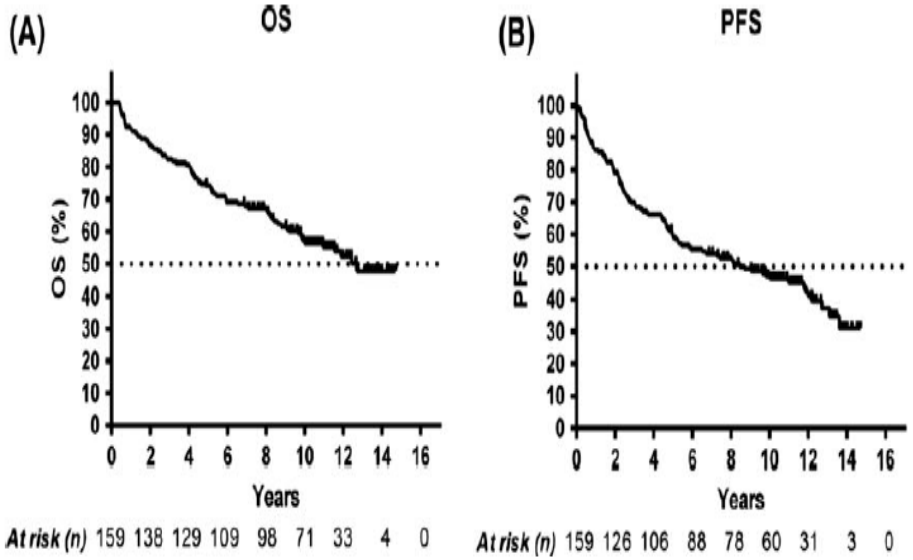


Preetesh Jain et al ; *Journal of Clinical Oncology* 2022 40202-212.

Ongoing Trials

- ACERTA 308
  - BR + MR vs BR + Acalabrutinib +MRI
- ENRICH
  - R-CHEMO (BR or RCHOP) + MR vs R-IBRUTINIB + IBRUTINIB
- MAGNOLIA
  - BR vs R-ZANUBRUTINIB
- EA1411
  - Maintenance Rituximab vs. Maintenance rituximab + Lenalidomide
- OASIS 2
  - Obinutuzumab + Ibruitnib vs Obinutuzumab + Ibrutinib +Venetoclax
- Several “non-chemo” combinations
  - R vs O; BTKi,BCL2, Imid

Nordic MCL2
R-maxiCHOP, R-HiDAC



160 patients (145 ASCT)
Median age 56
Median follow-up 11.4 years
Median OS 12.7 (NR) years
Median PFS 8.5 (11) years

European MCL
RCHOP vs RCHOP, RDHAP

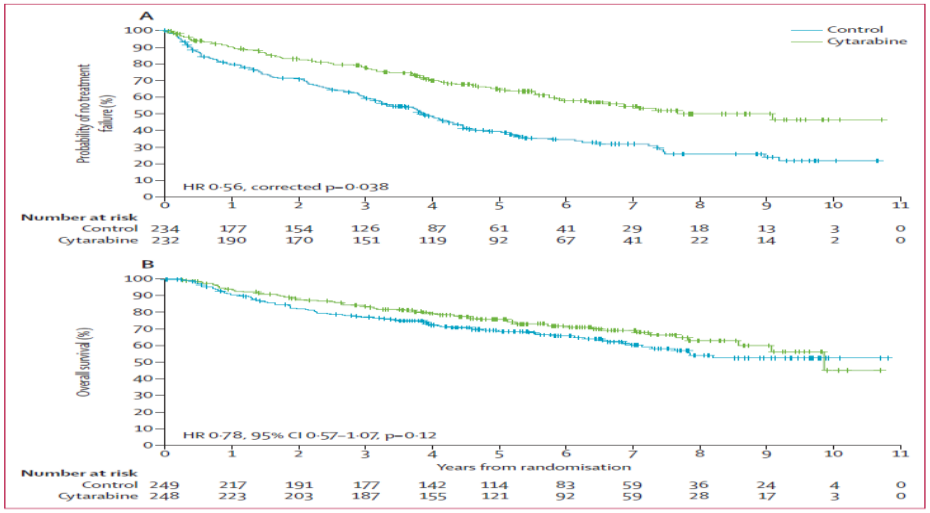


Figure 2: (A) Time to treatment failure in primary analysis and (B) overall survival
HR=hazard ratio.

497 patients
Median age 55
Median follow-up 6.1 years
Median OS 12.7 yrs NR vs 9.8 yrs (p=0.12)
Median TTF 9.1 yrs vs 3.9 yrs (p=0.038)
Median PFS 9.1 yrs vs. 4.3 yrs (p<0.0001)

Geisler et al. *Blood*. 2008, Hermine et al. *Lancet.* 2016. Eskelund et al. *BJH. 2016*.

High Risk Patients

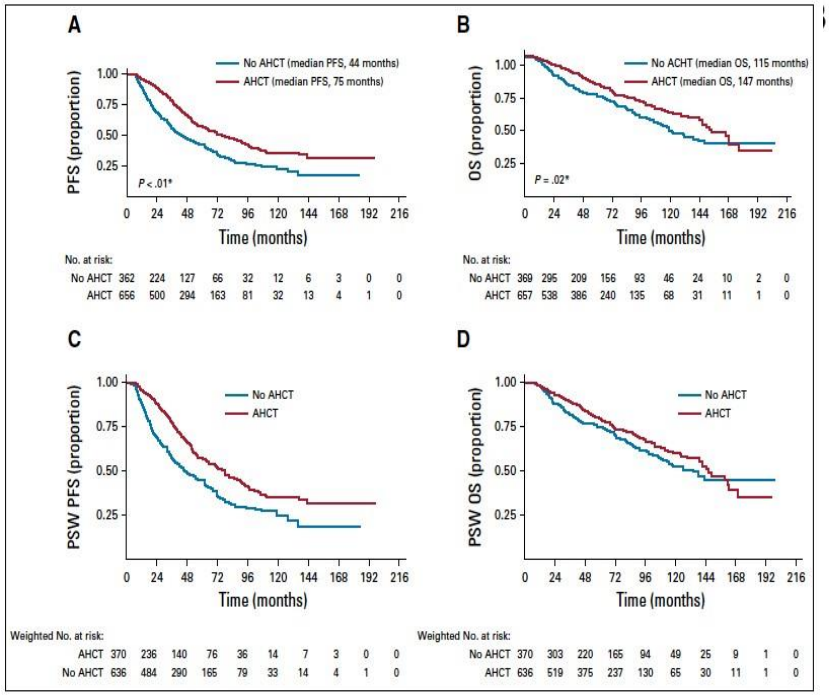
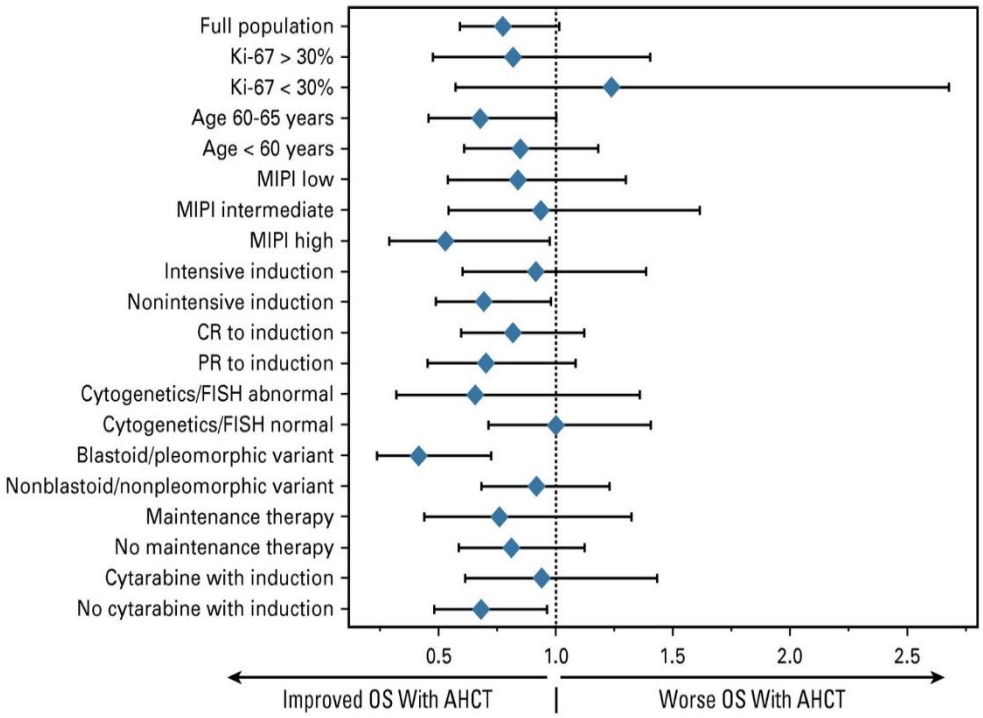
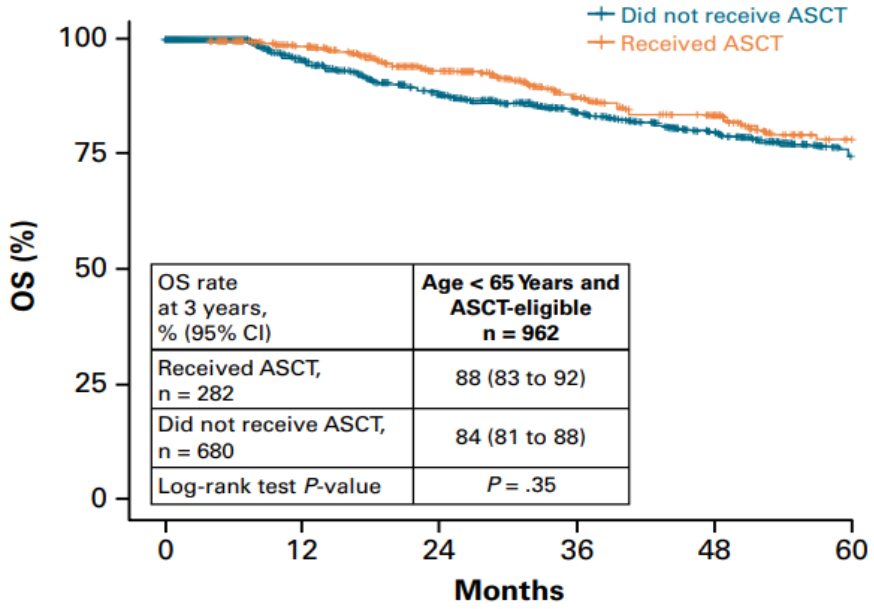


FIG 2. Kaplan-Meier curves for (A) progression-free survival (PFS) and (B) overall survival (OS) at 6 months and for (C) propensity score–weighted (PSW) PFS and (D) PSW OS at 6 months. AHCT, autologous hematopoietic cell transplantation. (*) Log-rank test.



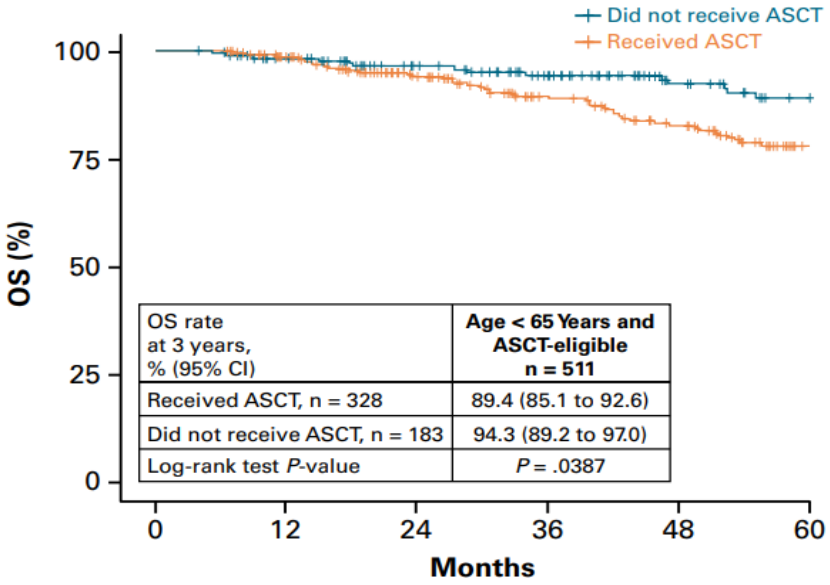
Gerson et al *J Clin Onc* 2018

Real World Outcomes



OS rate at 3 years, % (95% CI)	Age < 65 Years and ASCT-eligible n = 962
Received ASCT, n = 282	88 (83 to 92)
Did not receive ASCT, n = 680	84 (81 to 88)
Log-rank test *P*-value	*P* = .35

Patients at risk						
Did not receive ASCT	690	616	418	319	251	186
Received ASCT	282	251	194	144	112	86



OS rate at 3 years, % (95% CI)	Age < 65 Years and ASCT-eligible n = 511
Received ASCT, n = 328	89.4 (85.1 to 92.6)
Did not receive ASCT, n = 183	94.3 (89.2 to 97.0)
Log-rank test *P*-value	*P* = .0387

Patients at risk						
Did not receive ASCT	183	163	142	120	94	77
Received ASCT	328	304	249	197	170	128

Martin et al JCO 2022

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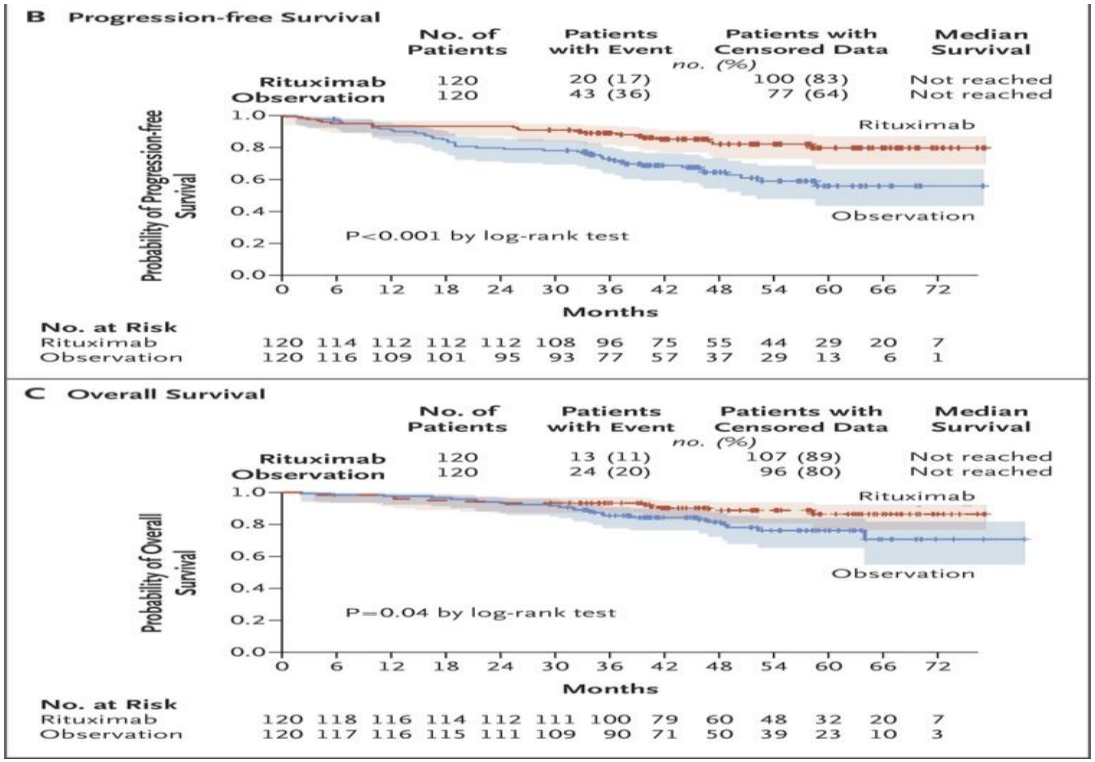
Maintenance after Transplant



299 patients enrolled
240 randomized
Median age 56

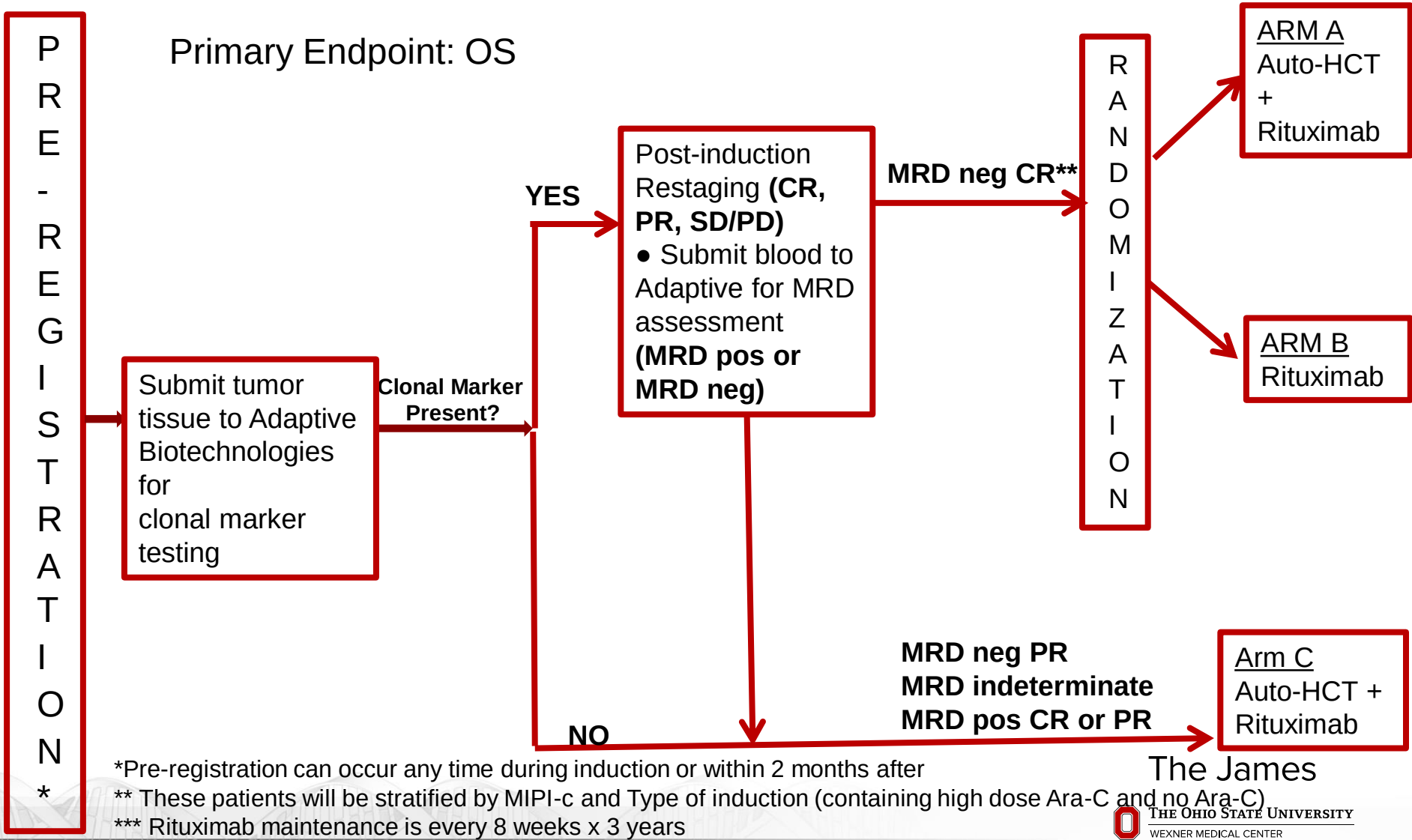
Median follow-up 50.2 mos

4-yr PFS 83% vs 64%

4-year OS 89% vs 80%

Le Gouill et al. *NEJM.* 2017.

E4151:Randomized phase 3 trial of Auto SCT +MR vs. MR alone in MRD-CR MCL



*Pre-registration can occur any time during induction or within 2 months after

** These patients will be stratified by MIPI-c and Type of induction (containing high dose Ara-C and no Ara-C)

*** Rituximab maintenance is every 8 weeks x 3 years

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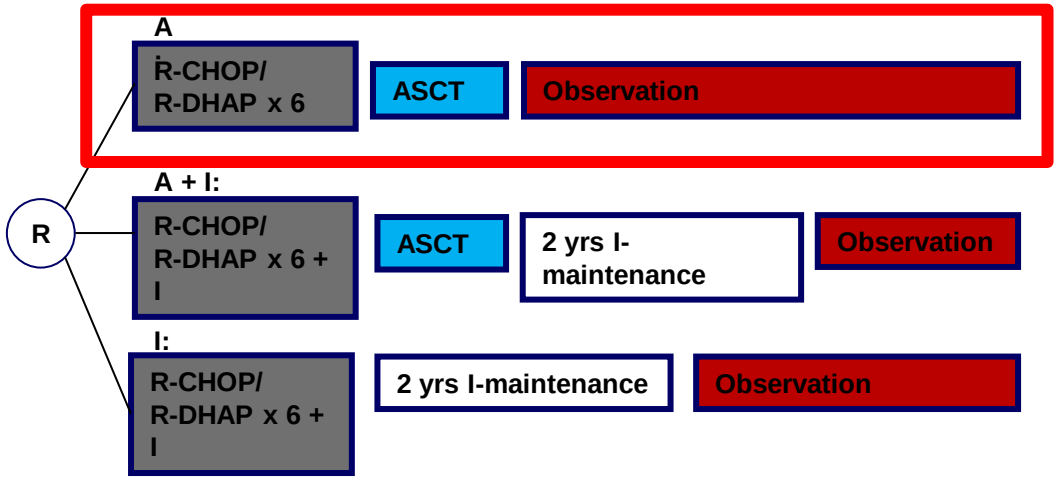
Triangle
add on vs head-to-head comparison



Age ≤ 65
PRIMARY ENDPOINT TTF

Relapsed Treatment Approaches

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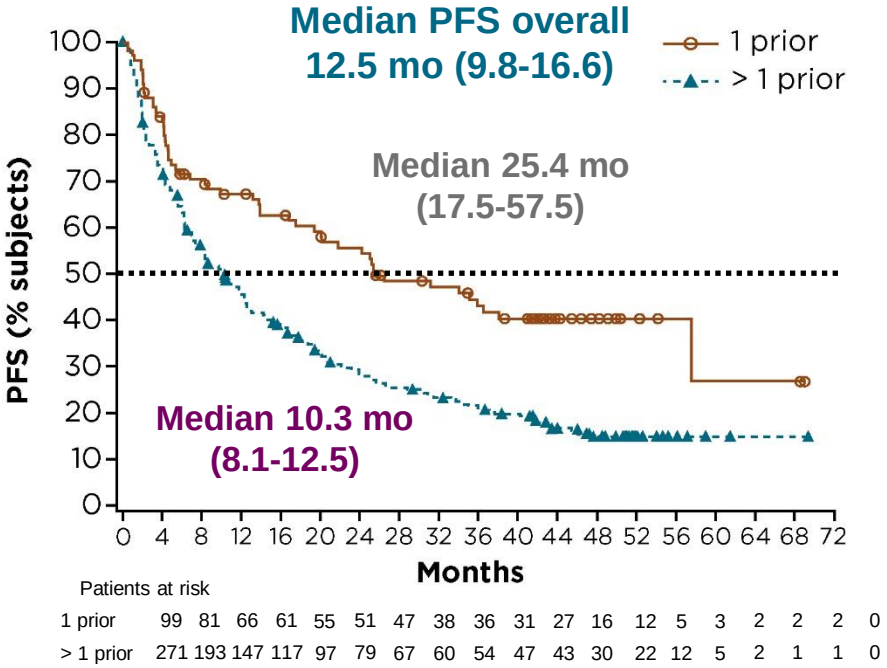
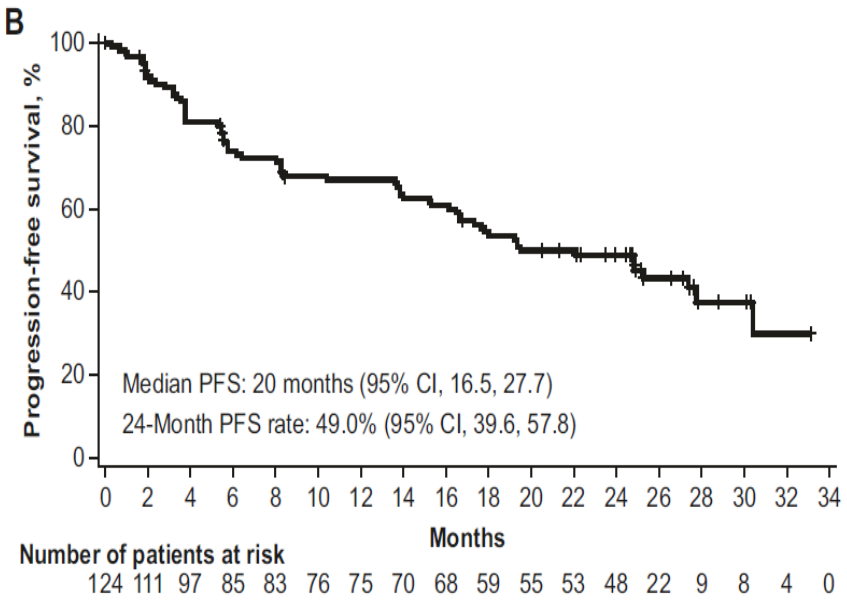
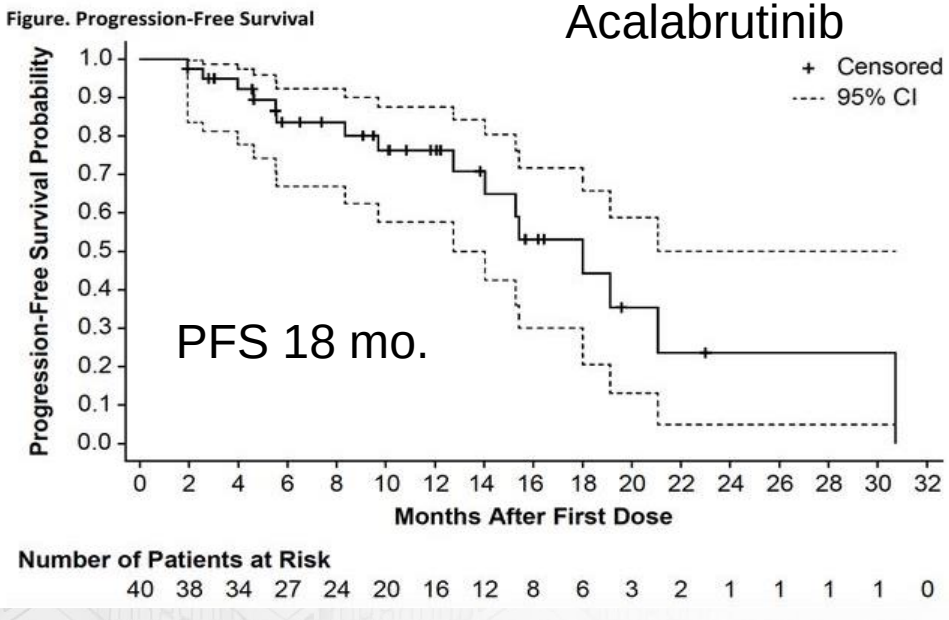


Ibrutinib



Acalabrutinib



Zanubrutinib

Rule et al *Lancet* 2018; Wang et al. Lancet Oncol 2018, Wang et al. Leukemia 2019; Tam et al. Blood 2018;132:1592

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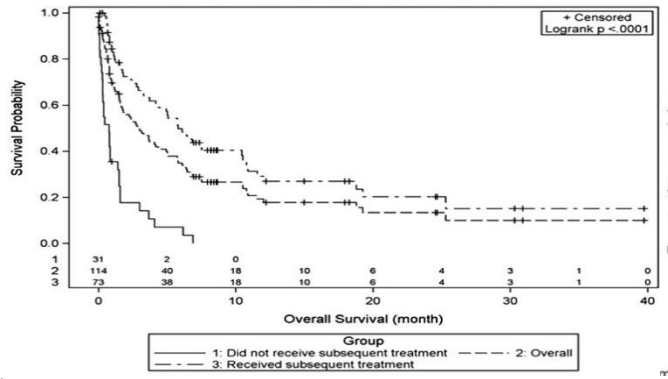
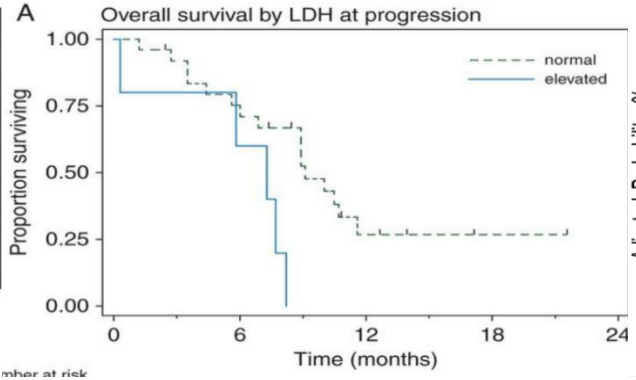
BTKi Failure

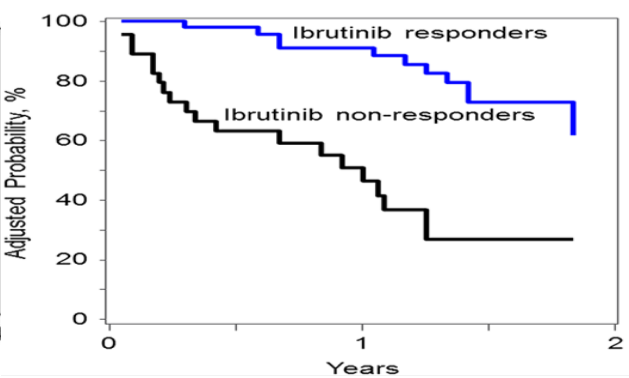
mOS 2.9 mo.
mOS^{Tx} 5.8 mo.



mOS^{Tx} 8.4 mo.



mOS 2.5 mo.
mOS^{Tx} 5 mo.



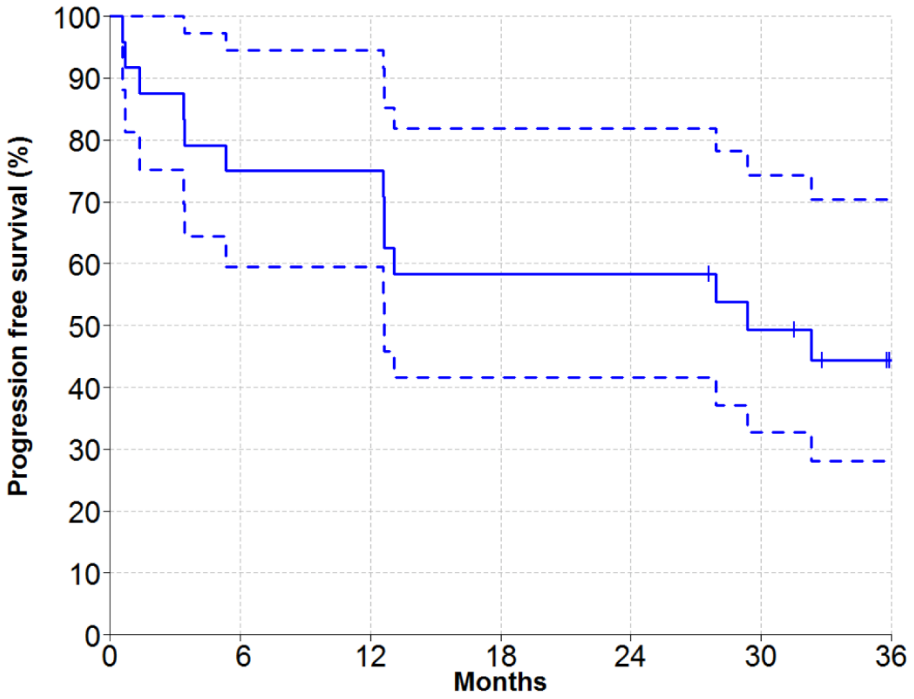
Martin et al. Blood 2016;127:1559; Cheah et al. Ann Oncol 2015;26:1175; Epperla et al. Hematological Oncol 2017;16:1099

Efforts to improve outcomes

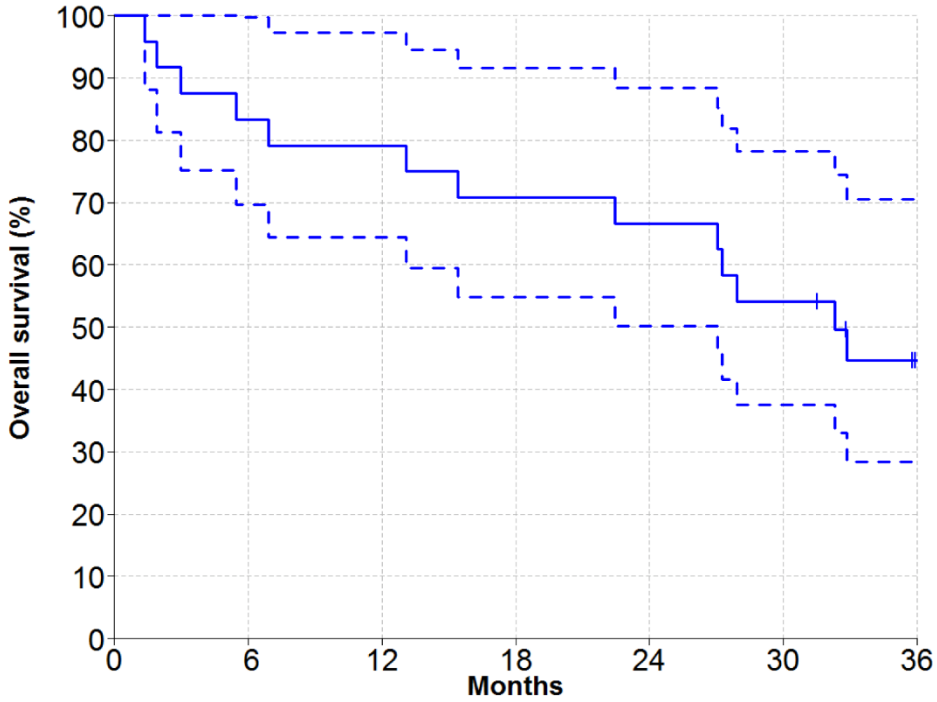
- Combination therapies
- Newer BTKi
- Novel agents

Ibrutinib plus venetoclax

Median PFS 29 months



Median OS 32 months



- 50% TP53 patients responded, all CR
- 5 off treatment in MRD negative CR after median 18.5 months treatment (range 18 – 33)
- 4 remain free of clinical or MRD progression after 6, 13, 17 and 18 months off treatment
- One patient developed radiologic progression after 7 months

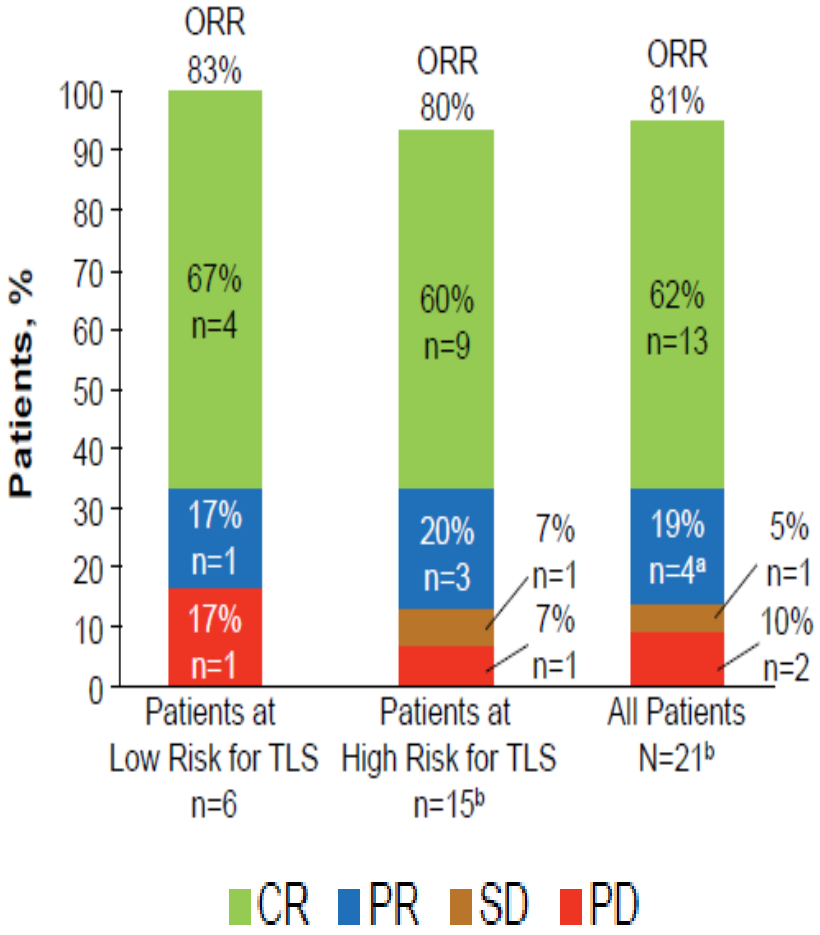
Handunetti et al ASH 2019

BTK Inhibitor + venetoclax

- AIM Trial: Ibrutinib + Venetoclax
  - 23 patients
  - CR Rate of 71%
  - Median PFS 29 months

SYMPATICO: Safety Run-In

- 21 patients
- ORR 81%, CR 62%
- Estimated 75% PFS at 18 months

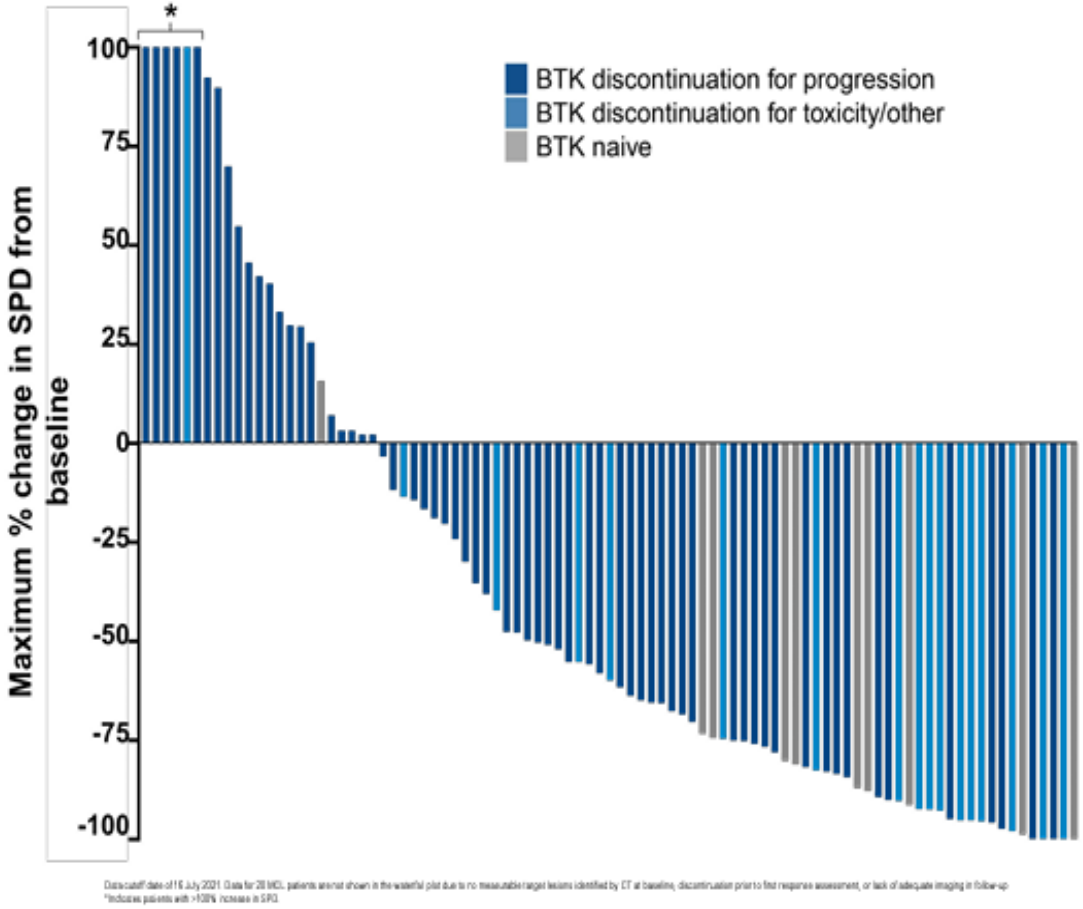


Tam et al ASH 2020

Combinations

- BTKi + anti-CD20
- BTKi + Ven + anti-CD20
  - Higher ORR, higher CR, ?improved PFS but follow up short
- BTKi + Len + R
  - Similar ORR, higher CR, ? Similar PFS, higher toxicity, benefit is some higher risk subgroups
- BTKi + NFkB
  - Similar ORR, similar CR, ? Similar PFS, higher toxicity, benefit in some high-risk subgroups
- BTKi + CDKi
  - Similar ORR, higher CR, ? PFS
- BTKi + PI3Ki
  - Similar ORR, CR
- Len + Ven + anti-CD20

Pirtobrutinib (LOXO-305)



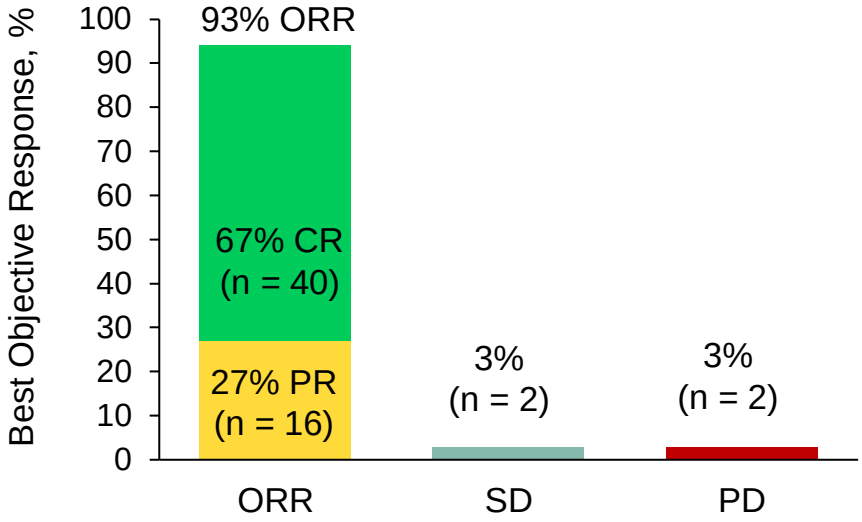
BTK Pre-Treated MCL Patients[a]	n=100
Overall Response Rate[b], % (95% CI)	**51% (41-61)**
Best Response	
CR, n (%)	25 (25)
PR, n (%)	26 (26)
SD, n (%)	16 (16)
BTK Naive MCL Patients[a]	**n=11**
Overall Response Rate[b], % (95% CI)	**82% (48-98)**
Best Response	
CR, n (%)	2 (18)
PR, n (%)	7 (64)
SD, n (%)	1 (9)

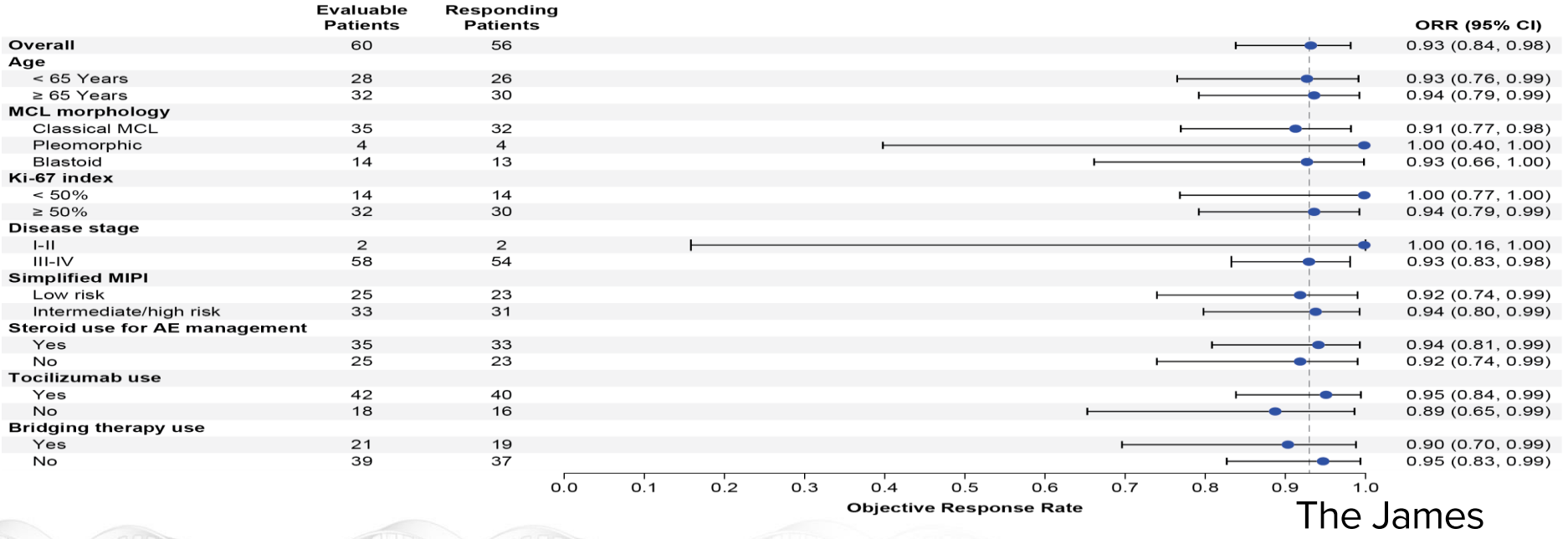
- Efficacy also seen in patients with prior:
  - Stem cell transplant (n=28): ORR 64% (95% CI: 44-81)
  - CAR-T therapy (n=6): ORR 50% (95% CI: 12-88)

Eyre et al, EHA 2022

ZUMA-2, KTE-X19 Responses

CRS, n (%)[a]	
Any grade	62 (91)
Grade ≥ 3	10 (15)
Neurologic events, n (%)[a]	
Any grade	43 (63)
Grade ≥ 3	21 (31)





Wang et al ASH 2019

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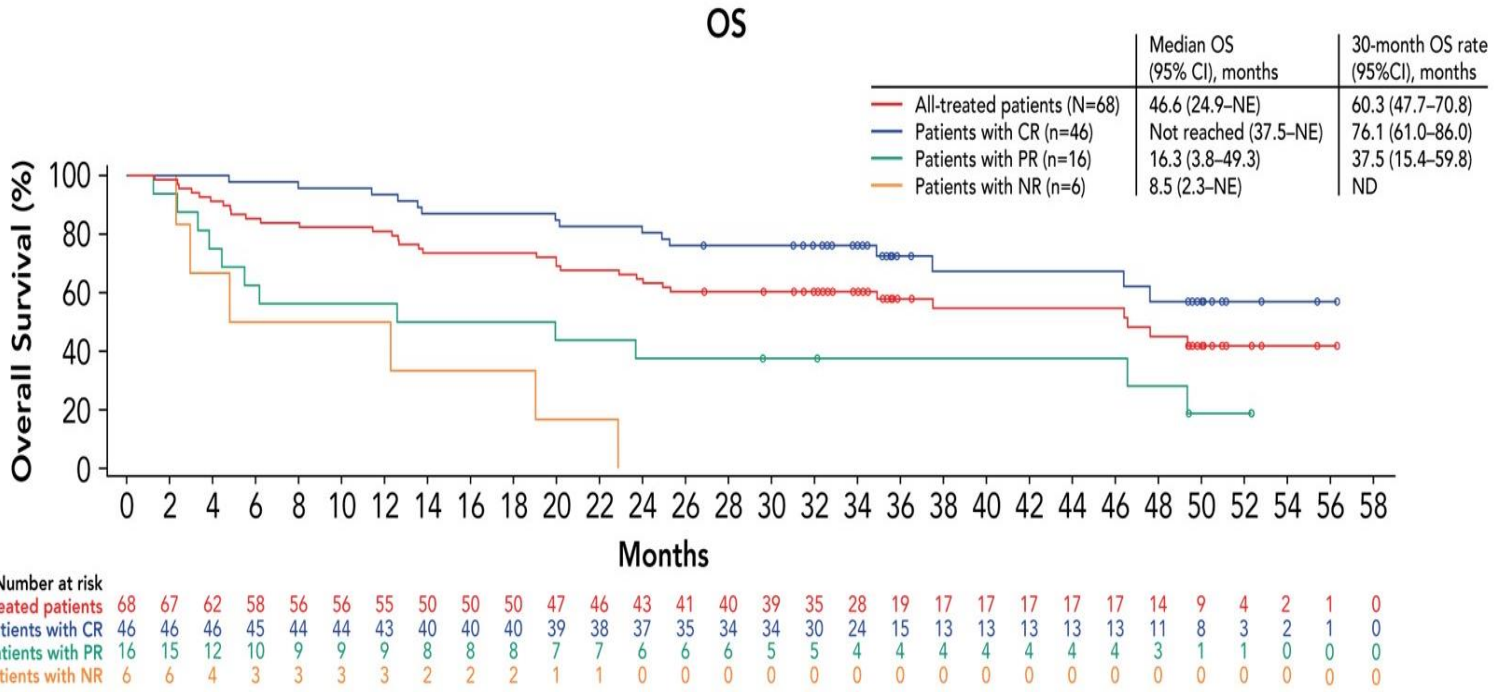
Toxicities of Brexu-cel

- Cytopenias
  - Grade 3 or higher – 94%
  - Persistent grade 3 – 26% beyond 90 days of treatment
- Infections – 32%
- Grade 5 Toxicities
  - 2 patients (3%) – likely from lymphodepletion
  - 1 organizing pneumonia
  - 1 septicemia (Staph bacteremia)

- Wang et al, NEJM 382:1331-42, 2020

ZUMA-2, 3-Year Follow Up

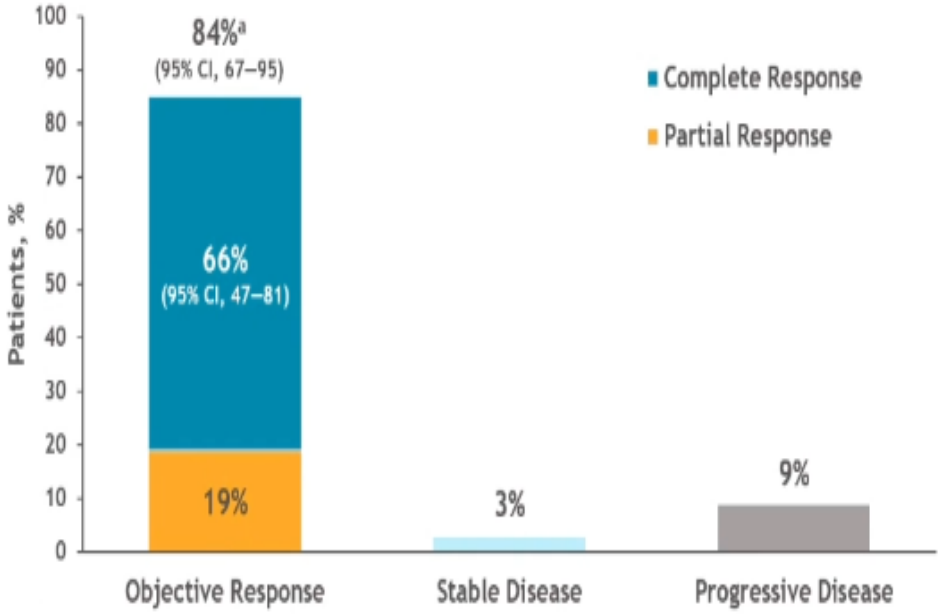


- The median progression-free survival (PFS) was 25.8 months, as shown in the full poster
- In the ITT population (data not shown), the median PFS was 24.0 months and the median OS was 47.4 months

Median OS among treated patients was 46.6 months and was not reached among those who achieved CR.

Wang et al ASH 2022

TRANSCEND, Liso-cel



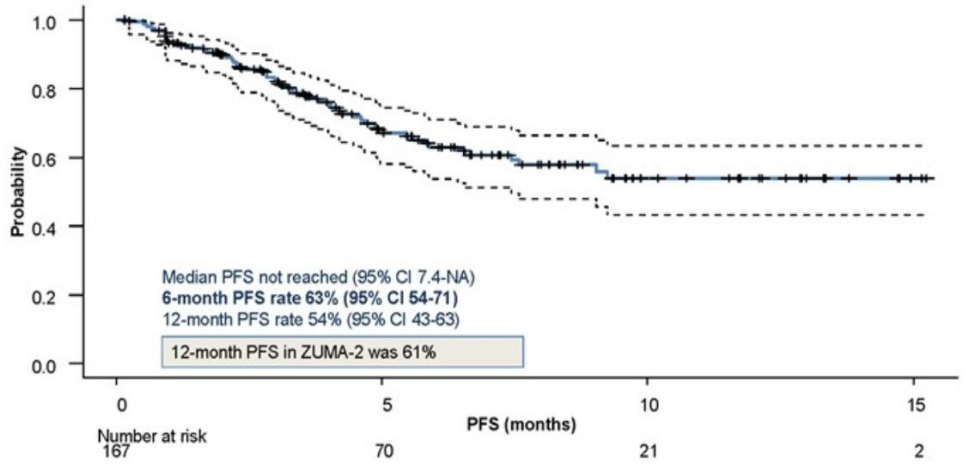
- ORR and CR rate, respectively, for patients with high-risk features:
  - Ki67 ≥30% (n = 23): 83% and 65%
  - Blastoid morphology (n = 13): 77% and 54%
  - *TP53* mutations (n = 7): 100% and 57%

	All liso-cel–Treated Patients (N = 32)
CRS or NE, n (%)	
Any grade	19 (59)
Grade ≥3	5 (16)
CRS	
Any grade, n (%)	16 (50)
Grade ≥3, n (%)	1 (3)
Time to onset, median (range), days	6 (2–10)
Time to resolution, median (range), days	4 (2–9)
NE	
Any grade, n (%)	11 (34)
Grade ≥3, n (%)	4 (12.5)
Time to onset, median (range), days	8 (2–25)
Time to resolution, median (range), days	4 (1–27)
ICU admissions, n (%)	3 (9)
CRS and/or NE	3 (9)
Other reasons	0

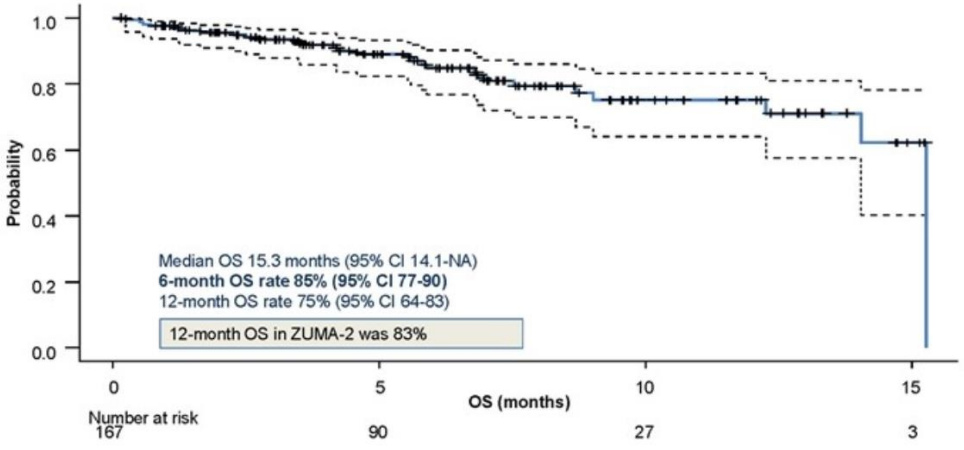
Palomba et al ASH 2020

US CART Cell Consortium

PROGRESSION-FREE SURVIVAL



OVERALL SURVIVAL



	CRS, n (%)	ICANS, n (%)	ZUMA-2 CRS (%)	ZUMA-2 NE (%)
Total	147 (90%)	100 (61%)	91%	63%
Max Grade*				
1-2	135 (82%)	48 (29%)	76%	32%
3-4	11 (7%)	52 (32%)	15%	31%
5	1 (1%)			
Days to onset	4 (0-13)	6 (1-18)	2 (1-13)	7
Days to max Grade	5 (0-30)	7 (1-18)	-	-
Duration	5 (1-33)	6 (1-144+)	11	12

*CRS grading: ASTCT (n=13), Lee (n=2), CARTOX (n=1);
ICANS grading: ASTCT (n=14), CTCAE (n=1), CARTOX (n=1).
CRS = cytokine release syndrome;
ICANS = immune effector cell-associated neurotoxicity syndrome;
NE = neurological events.

Incidence of CRS and ICANS similar

Wang et al ASCO 2022

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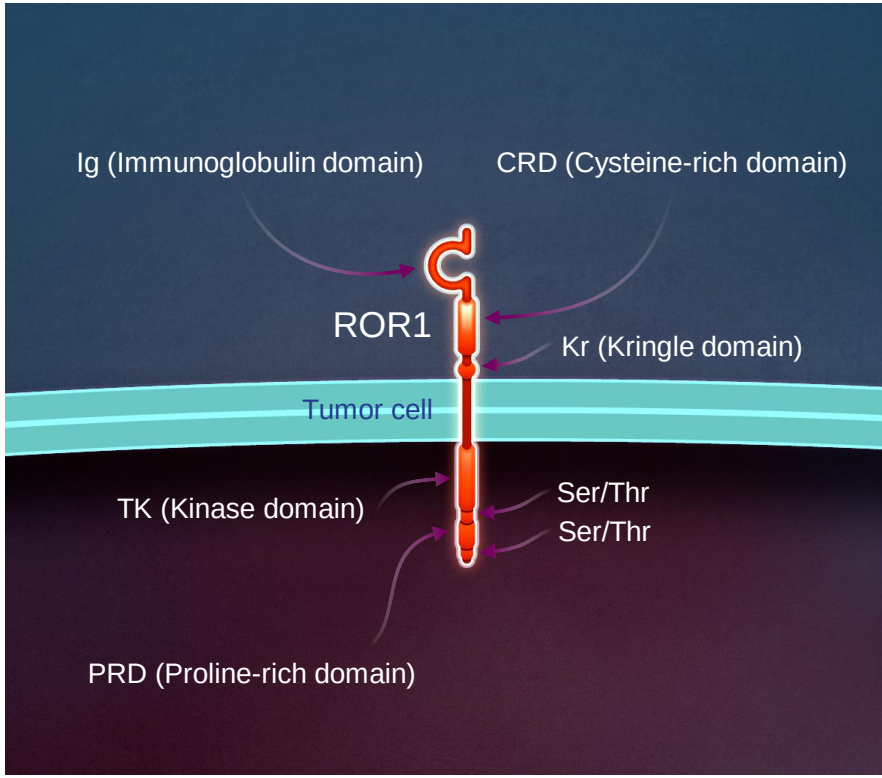
Receptor Tyrosine Kinase-Like Orphan Receptor 1 (ROR1)

ROR1 is an oncofetal antigen, typically present only during fetal development and absent following birth, which can later be expressed on cancer cells

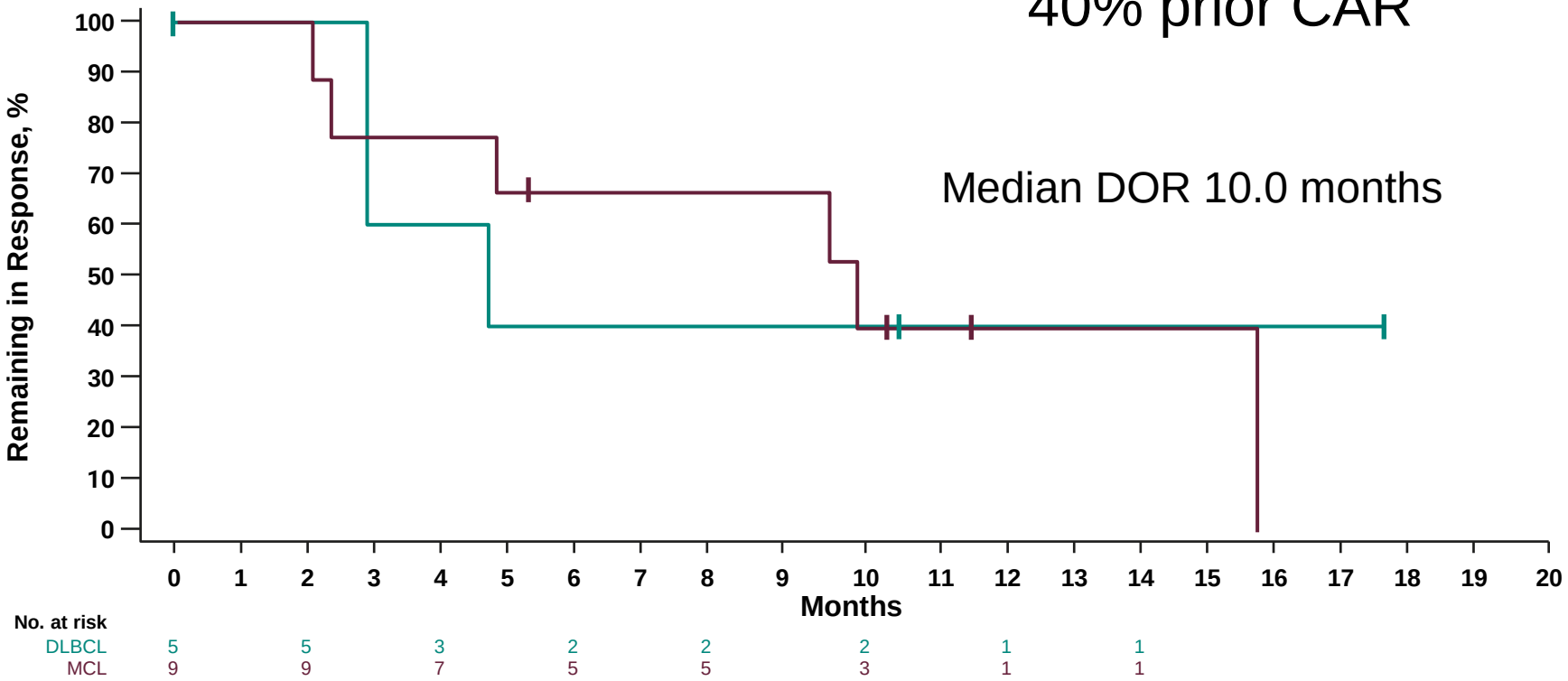
- Appears as a marker of cancer stem cells (CSCs) and of epithelial-mesenchymal transition (EMT)
- Is broadly expressed on hematologic and solid tumors
- Is NOT expressed on normal adult tissues*
- Can be targeted with antibody-drug-conjugates (ADC's) and bispecific antibodies (BiAb's)



Shabani et al. Expert Opin Ther Targets. 2015 Jul;19(7):941-55.
Zhang et al. Proc Natl Acad Sci USA. 2014 Dec 2;111(48):17266-71.
Cui et al. Cancer Res. 2013 Jun 15;73(12):3649-60.

VLS-101, ROR1 ADC

N=17
52.9% ORR
11% CR
40% prior CAR



Wang et al, ASH 2021

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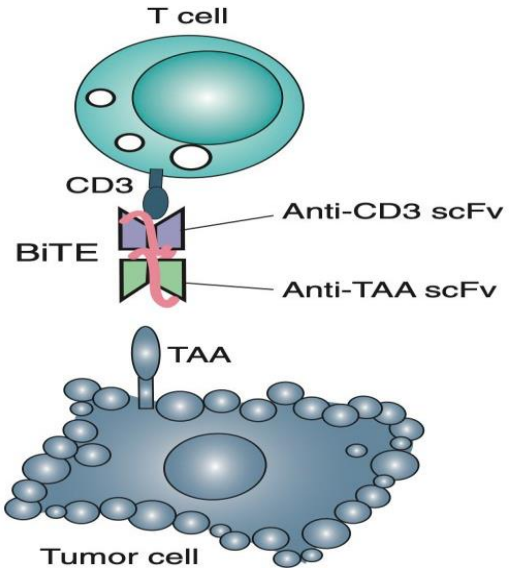
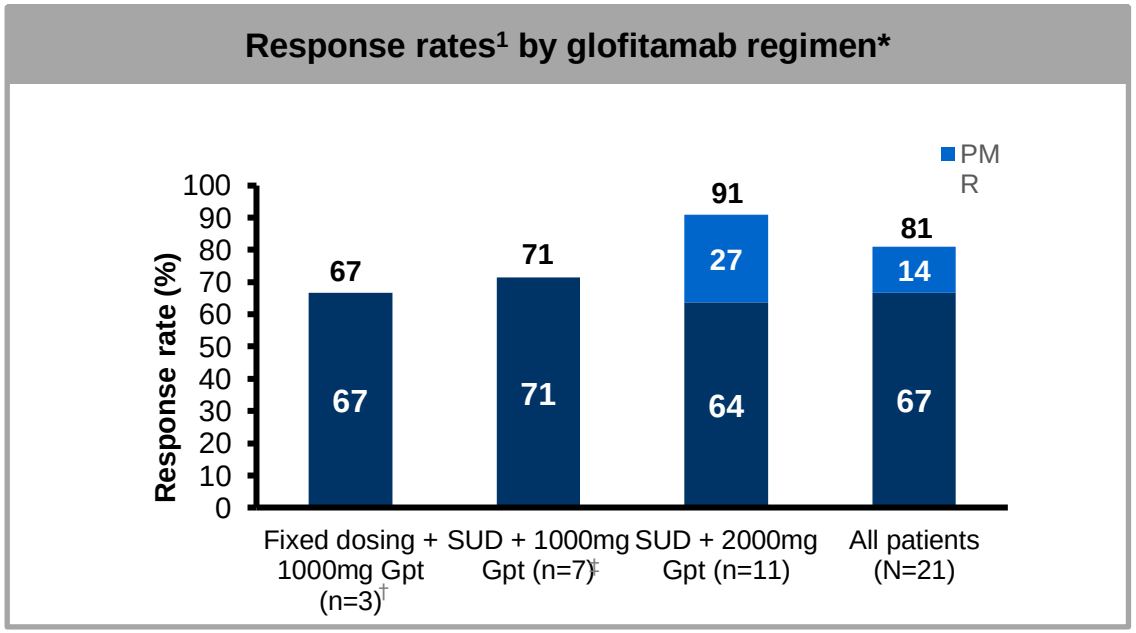
Bispecific Antibodies

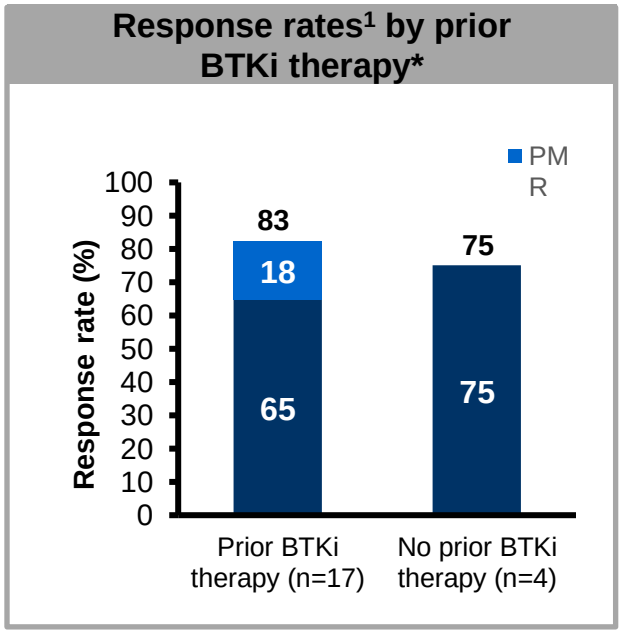


- Engineered antibodies
- Combine specificity of 2 antibodies to simultaneously bind different antigens
- Bind antigen on a cancer cell (CD19, CD20) and a T-cell surface glycoprotein CD3e-chain(CD3)
- Induces T-cell mediated cytotoxic activity against CD20 expressing B-cells
- “Off-the-Shelf” therapies

Golay J et al. *J Immunol.* 2014;193(9):4739-4747. Smith EJ et al. *Sci Rep*. 2015; 5:17943. Budde LE et al. *Hematol Oncol.* 2019;37(suppl 2):564-566.

Response rates





Glofitamab resulted in high response rates in patients with R/R MCL

*21/29 patients were efficacy-evaluable: the secondary efficacy-evaluable population includes all patients who had a response assessment performed (investigator-assessed), or who were still on treatment at the time of their first scheduled response assessment (Lugano 2014 criteria)[1]. †Due to a data issue, the response (CR) from one patient is reported as missing, and two patients treated with a combination of glofitamab and obinutuzumab (G-combo); ‡One patient treated with G-combo. CMR, complete metabolic response; PMR, partial metabolic response.

1. Cheson, BD et al. J Clin Oncol 2014

Phillips et al ASH 2021

Cytokine release syndrome

n (%) of patients with ≥1 AE unless stated	Glofitamab fixed dosing + 1000mg Gpt (n=3)	Glofitamab SUD + 1000mg Gpt (n=7)	Glofitamab SUD + 2000mg Gpt (n=19)	
Any CRS	3 (100)	5 (71.4)	9 (47.4)	17 (58.6)
Grade 1	3 (100)	2 (28.6)	5 (26.3)	10 (34.5)
Grade 2	0	2 (28.6)	4 (21.1)	6 (20.7)
Grade 3	0	0	0	0
Grade 4[†]	0	1 (14.3)	0	1 (3.4)
Serious AE of CRS (any grade)	2 (66.7)	5 (71.4)	4 (21.1)	11 (37.9)
Median time to first CRS event, hrs (range)	5.5 (3.0–32.7)	9.6 (6.6–21.7)	12.1 (7.7–19.8)	9.9 (3.0–32.7)
Tocilizumab use in patients with CRS	0	4 (57.1)	3 (15.8)	7 (24.1)
CRS events resolved	3 (100)	4 (80)	6 (66)[‡]	13 (76.5)[§]
Median time to CRS resolution, hrs (range)	23.0 (10.9–171.4)	38.8 (20.6–49.0)	51.4 (3.8–142.0)	38.8 (3.8–171.4)

Most common AE CRS

58.6% All Grade

3.4% Grade 3-4

3.4% Grade 1 ICANS

No Grade ≥2 ICANS AEs

27.6% neutropenia

No treatment discontinuations due to toxicity

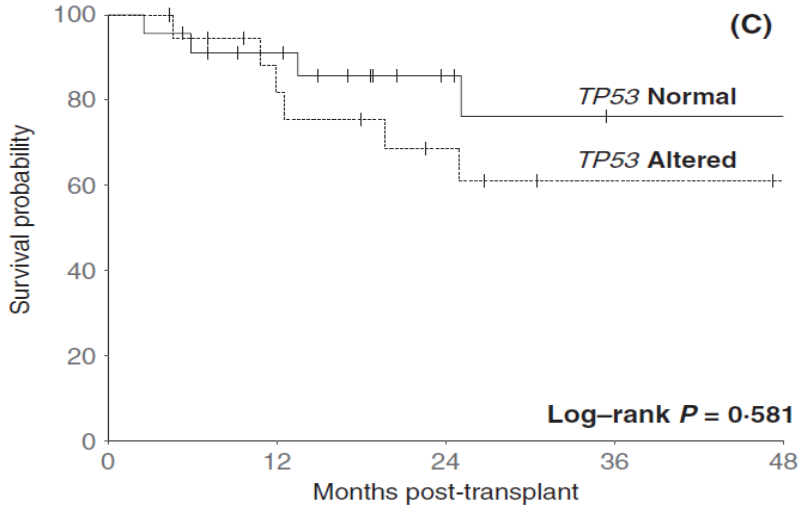
Most CRS events occurred during C1, were Grade 1 or 2 and resolved

*By American Society for Transplantation and Cellular Therapy (ASTCT) criteria[1]; [†]Grade 4 CRS in the SUD + 1000mg Gpt cohort (patient died due to cardiopulmonary insufficiency as a result of rapid PD; at time of death CRS was persisting). [‡]3/3 remaining CRS events resolved post data cut off; [§]3/4 remaining CRS events resolved post data cut-off; [¶]Patients in the fixed-dosing cohort (n=3) did not receive glofitamab on C1D8.

1. Lee, DW et al. Biol Blood Marrow Transplant 2019

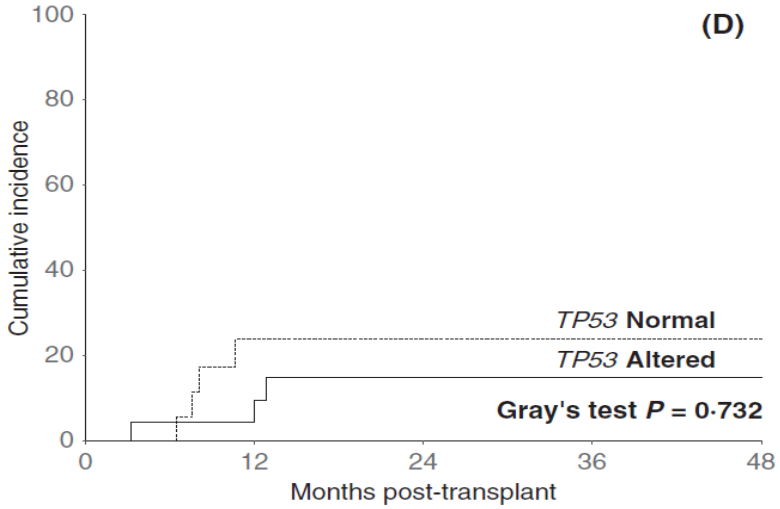
Phillips et al ASH 2021

Allogeneic Transplant in TP53



Risk Table

TP53 Status	0-month	12-month	24-month	36-month	48-month
Negative	23	18	10	7	7
Positive	19	13	9	6	5



Risk Table

TP53 Status	0-month	12-month	24-month	36-month	48-month
Negative	23	16	8	5	5
Positive	19	10	7	5	5

2-year PFS 78% 2-year OS 61%

Lin et al BJH 2019

Conclusions

- Chemoimmunotherapy for majority of patients 1L therapy
  - ASCT role may be evolving, rituximab maintenance
  - ? Novel therapy role in combinations and maintenance
- BTKi preferred relapse
  - Role of combination therapy unclear
- CART
  - Promising earlier in high risk
  - ? Role of sequencing
- High risk disease by TP53 no clear answer ?(BOVEN)
- Novel targeted and immune therapies
- Role of risk adapted approach