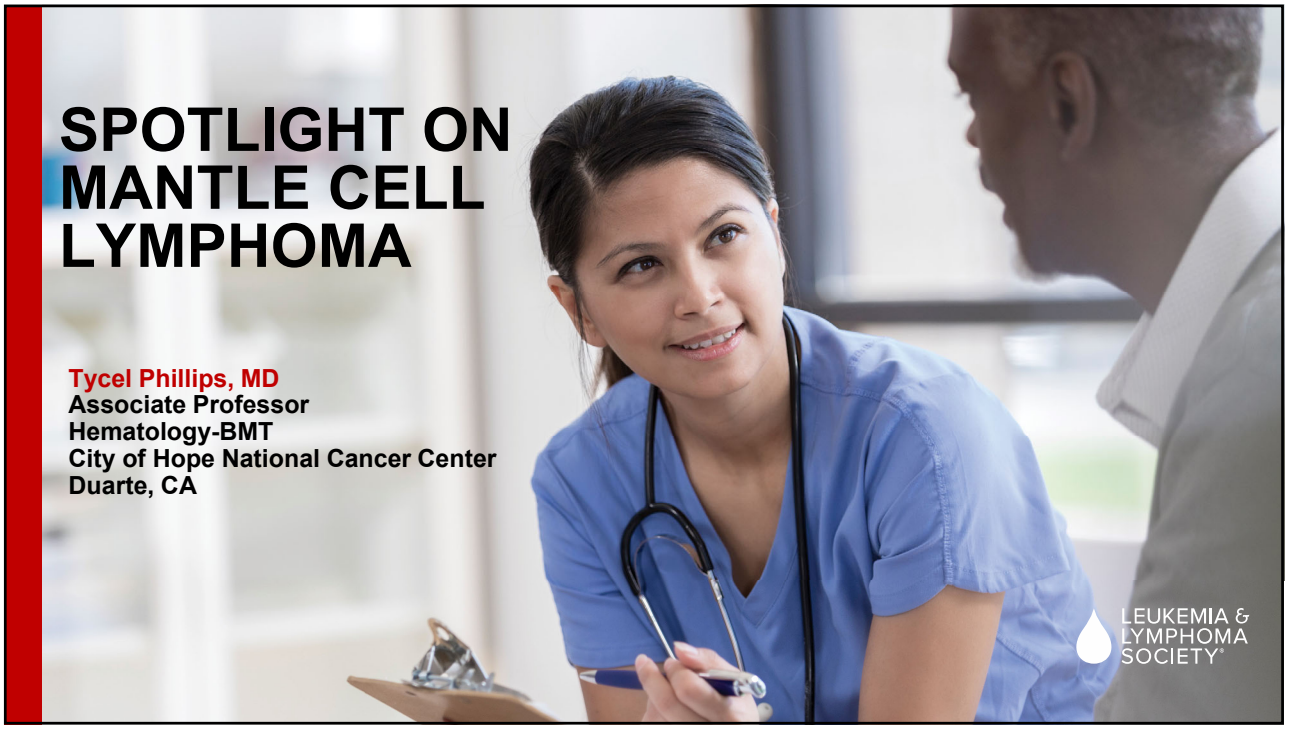
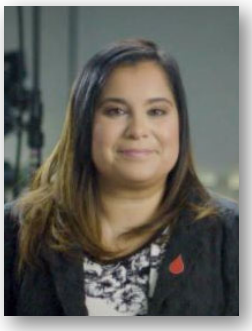


1

WELCOMING REMARKS

SPOTLIGHT ON MANTLE CELL LYMPHOMA



Lizette Figueroa-Rivera, MA
Sr. Director, Education & Support
The Leukemia & Lymphoma Society

LEUKEMIA &
LYMPHOMA
SOCIETY

2

FACULTY

SPOTLIGHT ON MANTLE CELL LYMPHOMA

Tycel Phillips, MD
Associate Professor
Hematology-BMT
City of Hope National Cancer Center
Duarte, CA

LEUKEMIA & LYMPHOMA SOCIETY®

3

DISCLOSURES

SPOTLIGHT ON MANTLE CELL LYMPHOMA

Tycel Phillips, MD has financial relationship(s) with:
AbbVie, Astra Zeneca, ADC Therapeutics, Bayer, BeiGene, BMS, Eli Lily, Genmab, Genetech, IPSEN, Incyte, MorphoSys, Pharmacyclics, Sobi, Xencor *(Consultant)*

LEUKEMIA & LYMPHOMA SOCIETY®

4

Management and Treatment of Mantle Cell Lymphoma

Tycel Phillips, MD
Associate Professor
City of Hope

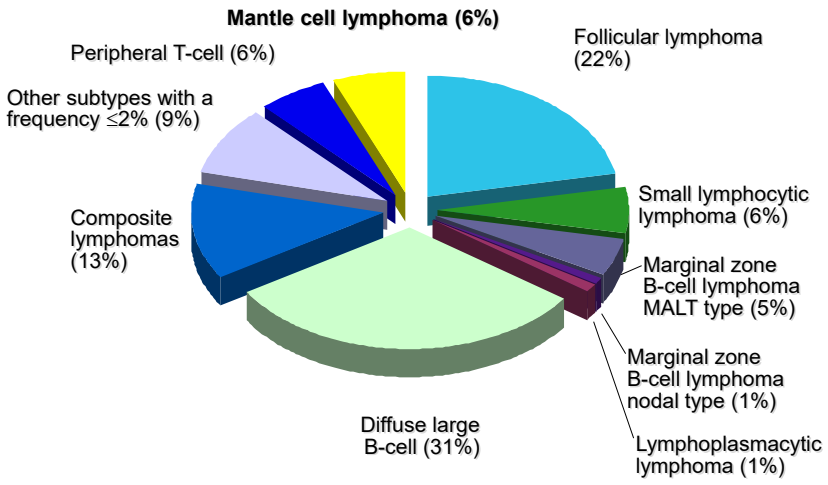
5

Outline

- Background
  - Pathology
  - Clinical Features
- Treatment options and survival
- Therapeutic Monitoring
- New therapy options
  - Targeted Therapies
  - Clinical Studies
  - Conclusion

6

Frequency of Non-Hodgkin lymphoma (NHL) subtypes in Adults

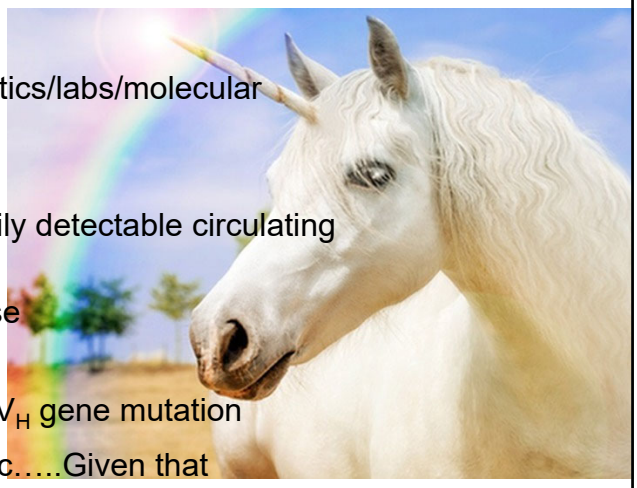


City of Hope

7

Indolent MCL

- How do we find these patients?
- Currently no definitive physical characteristics/labs/molecular findings
  - What the textbooks tell us…
  - Elevated white blood cell count with easily detectable circulating malignant cells
  - With little or no evidence of nodal disease
  - +/- splenomegaly ?
  - Lack expression of SOX 11 and have IgV_H gene mutation
- But that's not what I always see in my clinic…..Given that



City of Hope

8

Observation (Active Surveillance) becomes important

- I generally defer treatment on asymptomatic patients
  - Treat the patient not the pictures/and or white count
  - Exception with blastoid/pleomorphic patients
- With that being said most will need treatment within a few years of diagnosis but….during that time you have already accomplished the goal to treatment.
  - You are living symptom free from this incurable cancer but w/o any side effects from treatment.
  - Plus your remission clock has not started.
- But won't my cancer and in turn outcome be worse??

9

Observation (I am glad you asked)

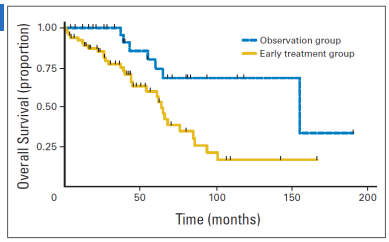


Fig 2. Overall survival (OS) of observation versus early treatment groups. The median OS of the early treatment group was 64 months (95% CI, 45 to 85 months). With median follow-up of 55 months for the observation group, the median OS is not yet reached and is significantly superior to that of the early treatment group ($P = .0038$).

Adjusted in respect to time to start treatment →

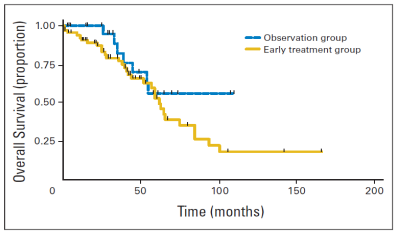


Fig 3. Overall survival of the observation versus early treatment groups from start of first systemic therapy.

JCO-Martin-2009-1209-27

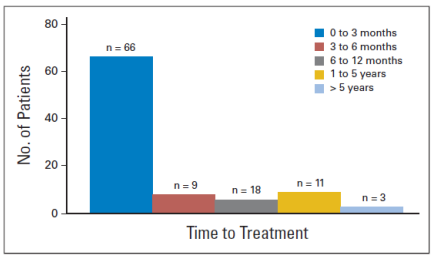


Fig 1. Time from diagnosis to first treatment in 97 patients with mantle-cell lymphoma.

- Some of you might notice this is an older citation
- No worries here is a newer article that supports this practice

Cohen JB et al. Deferred therapy is associated with improved overall survival in patients with newly diagnosed mantle cell lymphoma. Cancer. 2016 Aug 1;122(15):2356-63. doi: 10.1002/cncr.30068. Epub 2016 May 6. PMID: 27153197.

10

Elderly Unfit patients

- Historical data indicated that CHOP was ineffective.
  - Outcomes improved with addition of rituximab
- R-CHOP compared to FR followed by maintenance rituximab vs. interferon
  - Demonstrated improvement in PFS with maintenance rituximab after R-CHOP
- German study (Rummel et al.) and Bright Trial (US)
  - Demonstrated that BR is a superior regimen to R-CHOP in MCL only
- VR-CAP
  - Improved PFS vs. R-CHOP in randomized study (24.7 months vs 14.4 months)
- BRAC (Italian Regimen)
  - ORR > 90%
  - Toxicity??

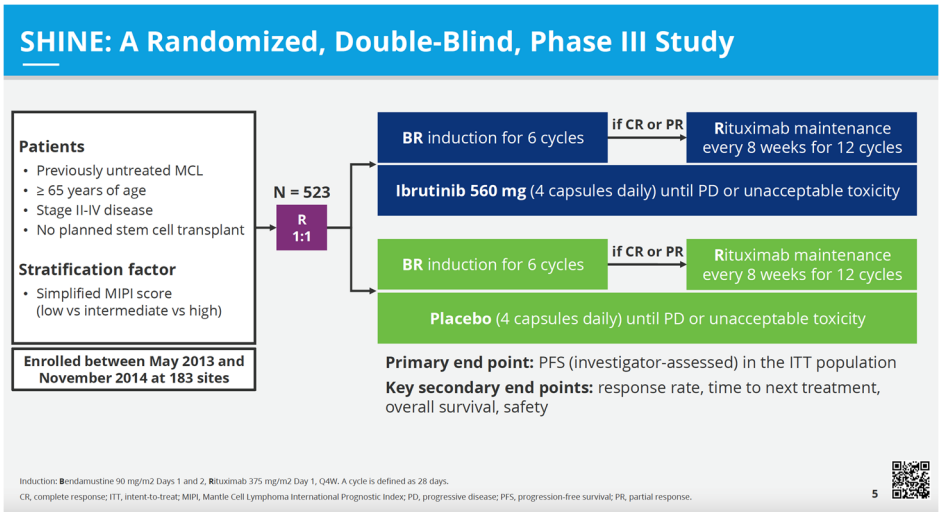
NCCN Guidelines Version 5.2023

CHOP – Cytoxan, Adriamycin, Vincristine, Prednisone
B – Bendamustine
R - Rituximab
V – Velcade
CAP – Cytoxan, Adriamycin, Prednisone
AC - Cytarabine

City of Hope

11

SHINE

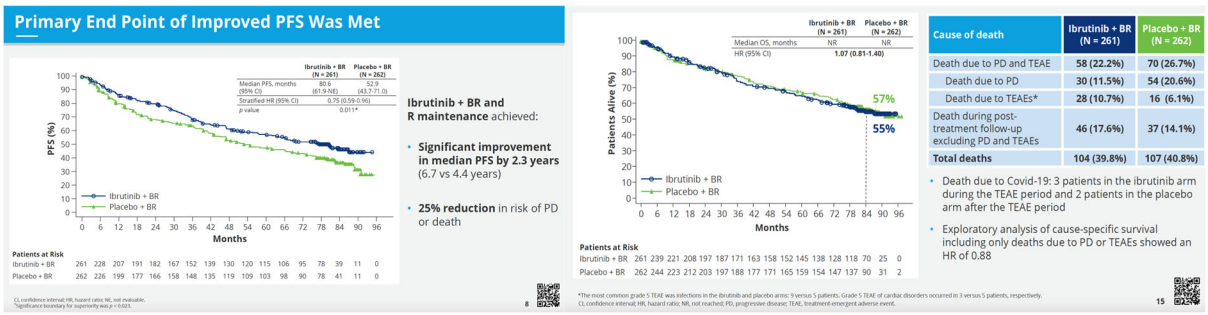


Wang et al. ASCO 2022

City of Hope

12

SHINE



13

Treatment Options (Outcomes with intensive induction for MCL)

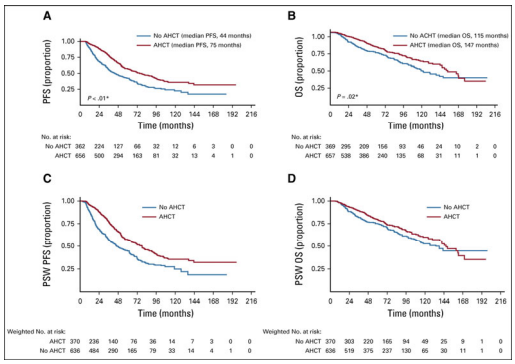
REGIMEN	EFFICACY	TOXICITY
Nordic (R-maxiCHOP/R-araC) followed by auto-HCT[1]	Median PFS: 8.5 years Median OS: 12.5 years	NRM: 7.5% MDS/AML: 3.1%
RCHOP/RDHAP followed by auto-HCT[2]	Median PFS: 9.1 years Median OS: 9.8 years	NRM: 3.4% MDS/AML: 2.4%
Any induction followed by auto-HCT (CIBMTR real world data)[3]	5 yr PFS: 52% 5 yr OS: 61%	NRM: 3%
R-HyperCVAD (without auto-HCT)[4]	Median PFS: 4.6 years 10 yr OS: 64%	NRM: 8% MDS/AML: 5%

1. Eskelund CV, BJH 2016, 2. Hermaine O, Lancet 2016, 3. Fenske T, JCO 2014, 4. Romaguera JE, BJH 2010

14

Does (ASCT) improve outcomes

- Retrospective study in 1029 patients
  - 25 centers; restricted to patients who would have been transplant eligible
  - 2/3 got auto up front; 1/3 did not
  - On initial analysis, PFS and OS benefit in favor of ASCT
  - After propensity weight analysis, clear PFS benefit but OS benefit not significant



Survival	HR	95% CI	P
PFS (n = 1,003)	0.70	0.59 to 0.84	< .01
OS (n = 1,003)	0.87	0.69 to 1.10	.24

Gerson JN, JCO 2019

City of Hope

15

Maintenance

- Data from LYMA Group has demonstrated benefit of maintenance rituximab after stem cell transplantation
  - Improved PFS
  - Most recent update reveals that OS no longer present
  - Hints that maintenance R does not overcome high risk disease maintenance
- After R-CHOP and BR
  - Data indicates benefit after R-CHOP (indefinite maintenance)
  - Randomized study did not show benefit but retrospective study hints that R maintains benefit after BR.
    - Most people recommend maintenance

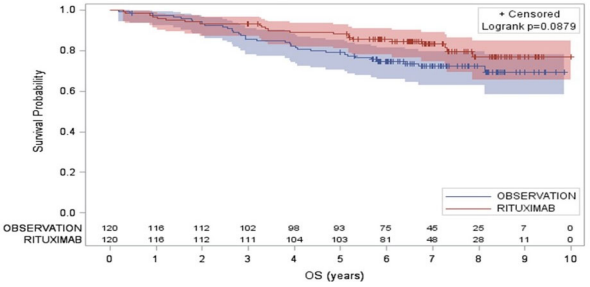
Le Gouill et al. N Engl J Med 2017; 377:1250-1260

City of Hope

16

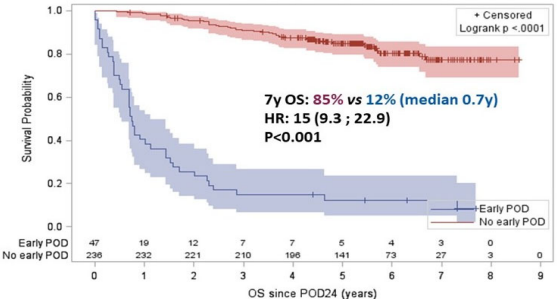
Long-Term Follow-Up From the LYMA Trial of Rituximab Maintenance After ASCT in Patients With MCL: OS

OS From Randomization (ITT)



	No. of Subjects	Event	Censored	Median Survival (95%CL)
OBSERVATION	120	27.5 % (33)	72.5 % (87)	NA (NA ; NA)
RITUXIMAB	120	18.3 % (22)	81.7 % (98)	NA (NA ; NA)

OS According to POD24 (POD Set)



	No. of Subjects	Event	Censored	Median Survival (95%CL)
Early POD	47	89.4 % (42)	10.6 % (5)	0.7 (0.6 ; 1.1)
No early POD	236	17.4 % (41)	82.6 % (195)	NA (NA ; NA)

Ghoulli S, et al. ASCO 2023. Abstract 7508. Sarkozy C, et al. EHA 2023. Abstract P1079. and ICML 2023. Abstract 100.

City of Hope

17

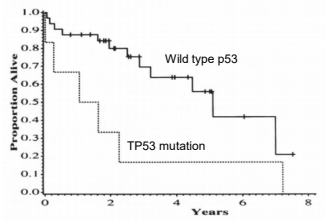
RISK

- MIPI used for prognosis.
  - Updated to include Ki-67 but overall scoring system complex and not easily tabulated (PC or App).
  - Not best for identifying patients with truly high-risk disease
- So, what helps truly ID poor risk
  - P53 alterations
    - Mutation appears worse than deletion
  - Blastoid/Pleomorphic, Ki-67 ≥ 50% (myc amplification), complex cytogenetics, other mutations such as Notch.

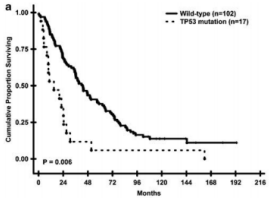
City of Hope

18

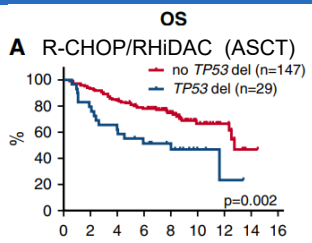
Data



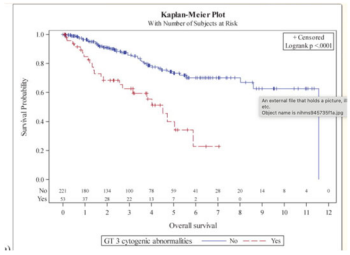
Greiner TC, Blood 1996



Halldórsdóttir A M, Leukemia 2011



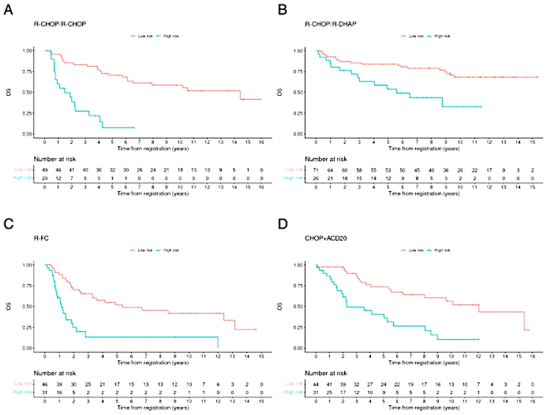
Eskelund CW, Blood 2017

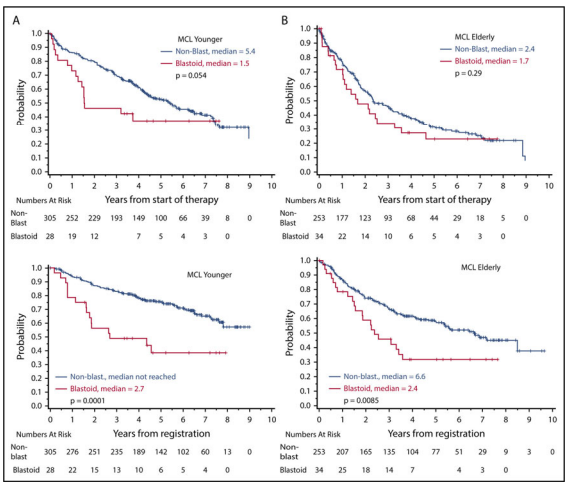


Scheubeck G, Leukemia 2023[14]

19

Fig. 3: Prognostic impact of high MIPI-c or high p53 expression on overall survival stratified by treatment groups of the MCL Younger and the MCL Elderly trial.





20

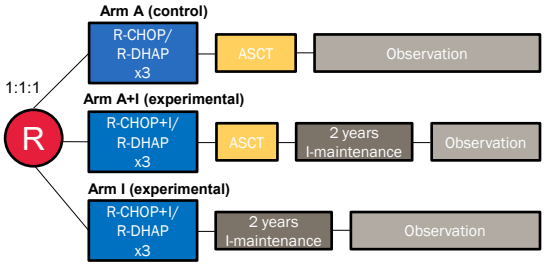
Upfront use of small molecules

- Can small molecules overcome high risk features?

21

TRIANGLE Phase 3 Study of Ibrutinib + SOC as a Substitute for ASCT in Younger Patients With MCL: Study Design and Patients

Key Eligibility Criteria
- Previously untreated stage II-IV MCL
- Age <66 years
- Suitable for HA and ASCT
- ECOG PS 0-2



Primary endpoint: FFS
Secondary endpoints: Response rates, PFS, RD, OS, safety

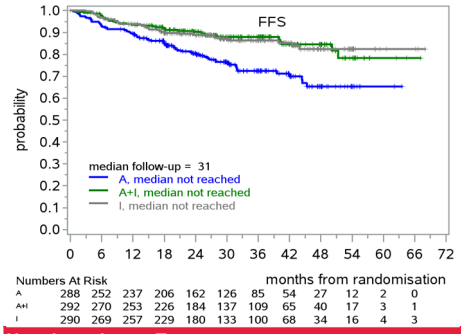
- R maintenance (± I) was added in all 3 trial arms, following national guidelines. It was initiated in 168 (58%) patients in Arm A; 165 (57%) patients in Arm A+I; and 158 (54%) patients in Arm I

[a]2 patients aged 66 & 68 years were randomized. [b]1 CLL, 1 FL. [c]1 NHL NOS, 1 HD, 2 MZL. [d]1 HCL, 1 DLBCL.
Dreyling M, et al. ASH 2022. Abstract 1.

22

TRIANGLE Phase 3 Study of Ibrutinib + SOC as a Substitute for ASCT in Younger Patients With MCL: Efficacy (cont'd)

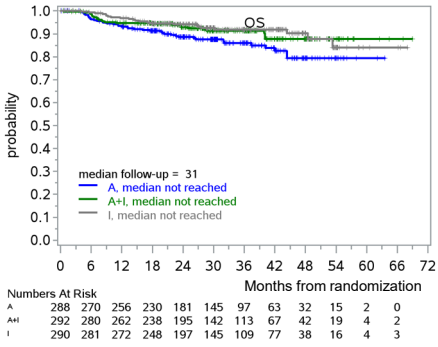
FFS of A vs A+I vs I



- Test for A+I vs I FFS is ongoing

Next Lymphoma Treatment After 1st Treatment Failure, n (%)	A (n=68)	A+I (n=35)	I (n=37)
With ibrutinib	34 (79)	4 (24)	3 (11)
Without ibrutinib	9 (21)	13 (76)	24 (89)
No treatment	25	18	10

Overall Survival



- 3-year OS: A 86%; A+I 91%; I 92%
- Too early to determine statistical significance

Dreyling M, et al. ASH 2022. Abstract 1.

23

WINDOW STUDY

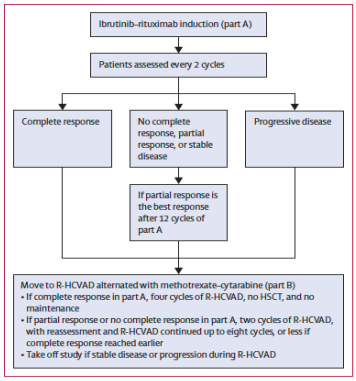
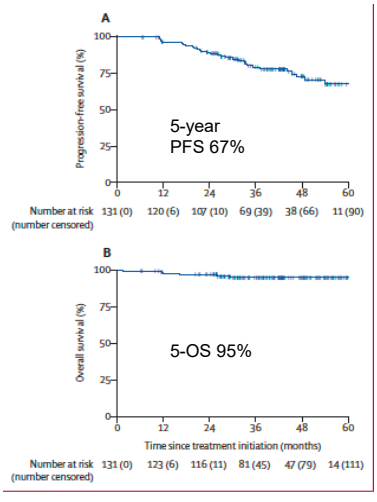


Figure 1: **Treatment schema**
This study involves induction with an ibrutinib–rituximab combination (part A) followed by R-HCVAD alternated with methotrexate–cytarabine (part B). Movement to part B was based on reaching complete response in part A or partial response in part A after receiving 12 cycles, whichever occurred earlier. Patients who progressed on part A were given part B chemotherapy if clinically fit enough to receive intensive chemoimmunotherapy. HSCT=haematopoietic stem-cell transplantation. R-HCVAD=rituximab plus hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone.

	Patients with positive PET-CT at baseline (n=97)*	All patients (n=131)
Part A best response†		
Evaluable patients	93‡	129
Overall response	93/131 (71%)	129 (98%)
Complete response	91/131 (69%)	114 (87%)
Partial response	2/131 (2%)	15 (11%)
Time to complete response in part A, months	--	5 (4-7)
Overall response after part A	--	129 (98%)
Complete response	--	114 (87%)
Partial response	--	15 (11%)
Part B best response§		
Evaluable patients	108	118
Overall response	108 (82%)	118 (90%)
Complete response	108 (82%)	117 (89%)
Partial response	0	1 (1%)
Overall response after part A and part B	--	117 (89%)
Complete response	--	90 (77%)
Partial response	--	1 (<1%)
Minimal residual disease-negative at best response¶	--	86 (65%)
Duration of response, months	--	28 (18-41)

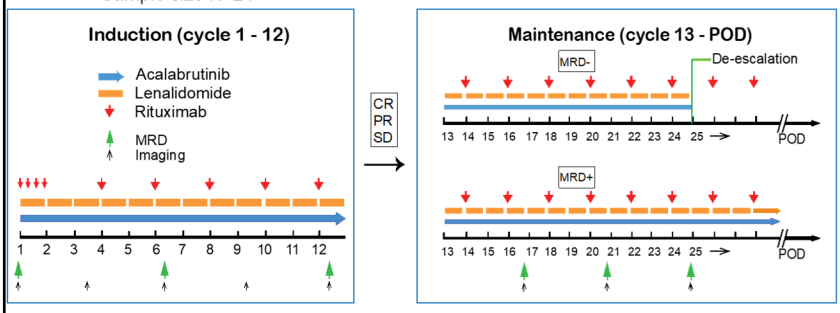


Wang et al. Lancet Oncol. 2022 Mar;23(3):406-415.

24

Study Design

Sample size N=24



Response	End of Induction* (12 cycles)	
	No. Pt	ITT
ORR	24	100%
CR	20	**83%**
PR	4	17%
SD	0	0
PD	0	0
Median Follow-up	23 months (range 12-36)	

"*": EOI following 12 cycles of treatment; response per Lugano criteria

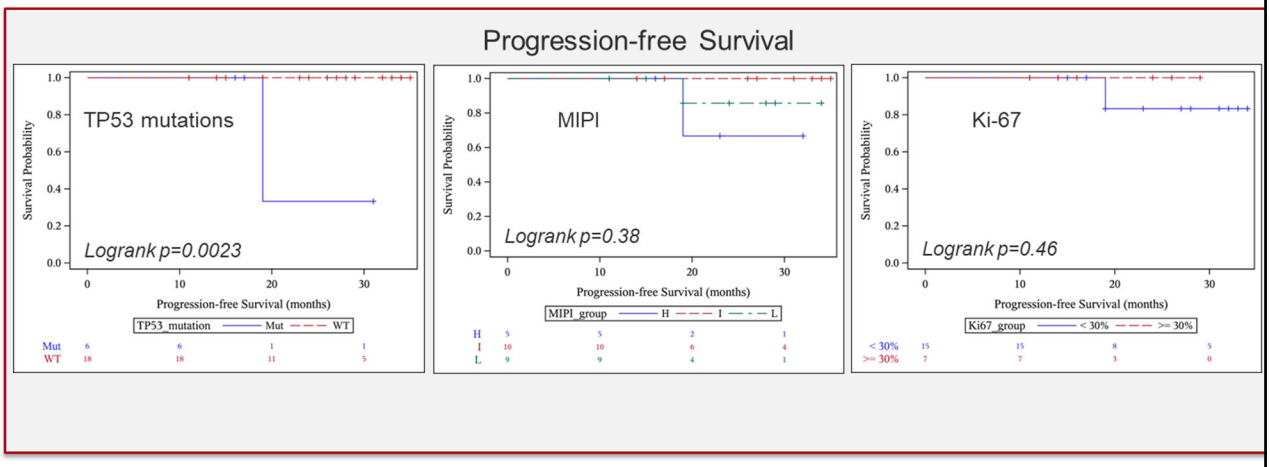
1st – CR rate after induction
2nd – ORR, safety and survival
Exploratory: MRD, NGS

- Acalabrutinib and lenalidomide can be discontinued after 24 cycles of treatment for subjects achieving MRD-negative CR during maintenance.
- Imaging studies: PET/CT is required at baseline and time to confirm CR.

City of Hope

25

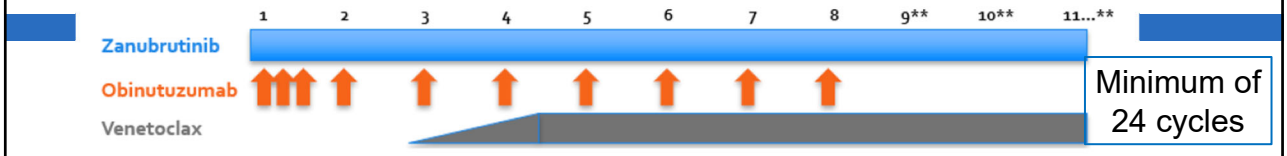
Efficacy: Survival



City of Hope

26

Study Design for **BOV**en



Dosing:

Zanubrutinib 160 mg oral twice daily

Obinutuzumab 1000 mg IVPB
Cycle 1: day 1, 8, 15
Cycle 2-8: day 1

Venetoclax 400mg oral daily
5-week ramp-up: 1 week each of 20mg; 50mg; 100mg; 200mg; 400 mg oral daily

After 24 cycles, MRD-driven approach to limit treatment duration in selected patients:

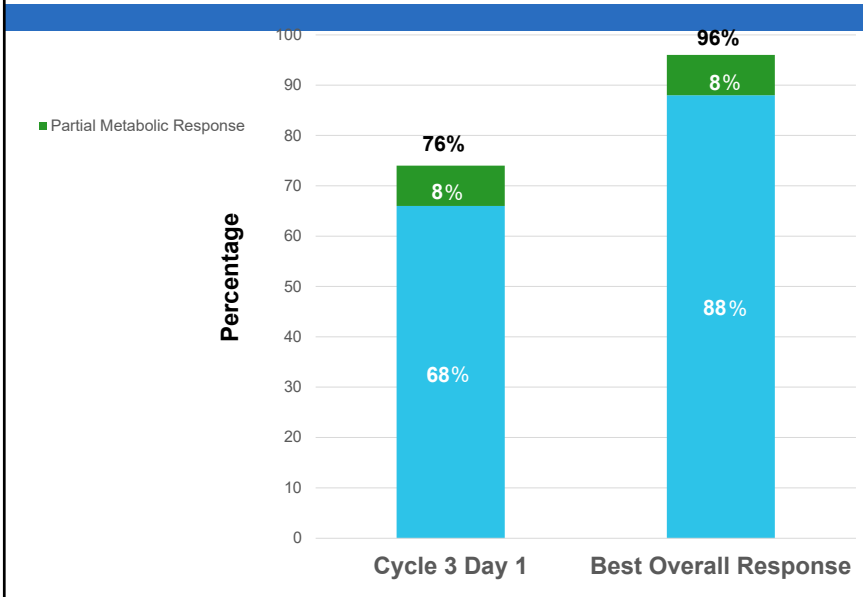
CR and uMRD	→ Stop treatment
<CR and/or dMRD	→ Continue ZANU and VEN

Key Eligibility Criteria:
- Previously untreated MCL (except localized RT prior)
- *TP53* mutation (of any variant allele frequency)
- ECOG ≤2, adequate organ and hematologic function (ANC >1, PLT >75, HGB ≥9 (unless due to MCL))

Primary Endpoint:
- 2-year progression-free survival.
- A promising 2-yr PFS rate ≥55% and an unacceptable rate ≤30%
- If ≥11 patients were progression-free at 2 years, the treatment regimen would be declared effective

27

Response Rates By Timepoint

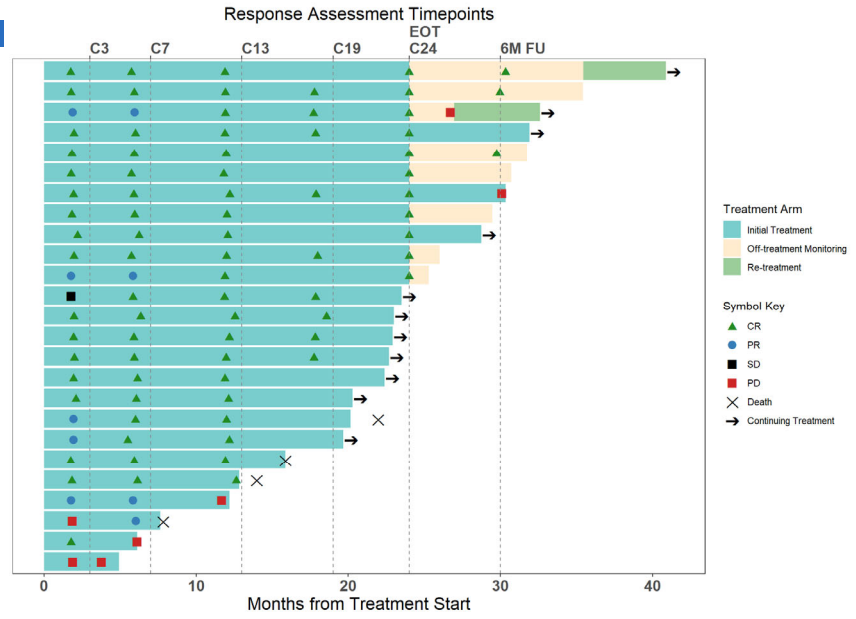


- **High Metabolic Response Rates after 2 cycles of Zanu+Obin**
- **High Overall Metabolic Response Rate with Zanu+Obin+Ven**

City of Hope

28

Response timing and duration

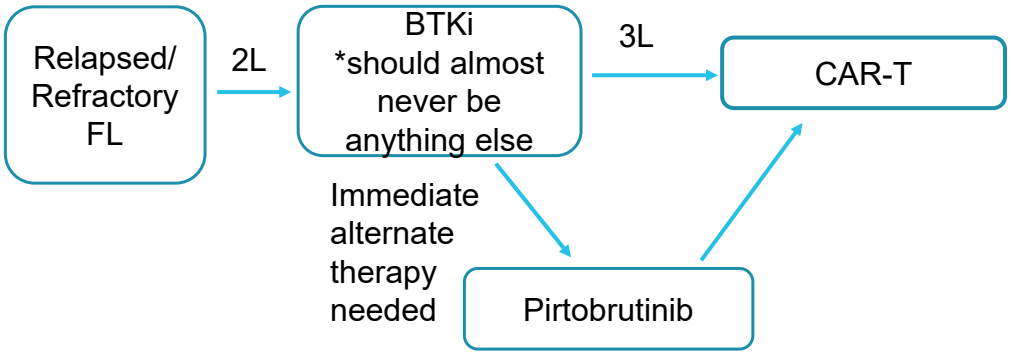


- Median follow up:
  - 23.3 months
- There were 9 events:
  - 5 progressions
  - 4 deaths
    - 2 COVID-related
    - 1 unknown
    - 1 PNA / respiratory failure
- The 4 deaths occurred in patients in ongoing response at time of death

29

R/R MCL

- **Outcomes in R/R MCL remain poor especially after BTKi failure**



30

Relapsed/Refractory MCL

- The primary endpoint was investigator-assessed ORR according to the 2014 Lugano Classification[1]
- Only 1.6% of patients required dose reductions and only 6.5% of patients discontinuing acalabrutinib due to adverse events.
- Atrial fibrillation was not observed. The most common side effects were headaches (36%) and diarrhea (38%), both of which were typically grades 1-2 and self-limited.
- Bleeding events were usually grade 1-2 and consisted of bruising and petechiae; there was 1 case of grade 3 gastrointestinal hemorrhage

Acalabrutinib

ORR using the 2014 Lugano Classification

	N=124	
	Investigator assessed	**IRC assessed**
	n (%)	**n (%)**
ORR (CR + PR)	100 (81)	99 (80)
Best response		
CR	49 (40)	49 (40)
PR	51 (41)	50 (40)
SD	11 (9)	9 (7)
PD	10 (8)	11 (9)
Not evaluable	3 (2)	5 (4)

Wang M, et al. Acalabrutinib in relapsed or refractory mantle cell lymphoma (ACE-LY-004): a single-arm, multicentre, phase 2 trial. *Lancet* 2018;391(10121):659-667

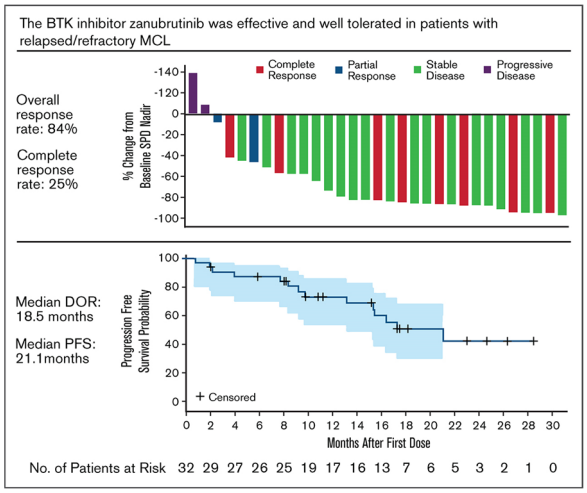
Wang M, et al. ASH 2017

City of Hope

31

Zanubrutinib in R/R MCL

Response assessment	**Investigator-assessed response (N = 32)**	**IRC-assessed response (N = 32)**
ORR 95% CI*	29 (90.6) (75.0-98.0)	27 (84.4) (67.2-94.7)
Best response		
CR	10 (31.3)	8 (25.0)
PR	19 (59.4)	19 (59.4)
Stable disease	1 (3.1)	2 (6.3)
PD	2 (6.3)	2 (6.3)
Unknown†	0	1 (3.1)



Constantine S. Tam, et al., Zanubrutinib for the treatment of relapsed or refractory mantle cell lymphoma, Blood Adv, 2021,

City of Hope

32

SYMPATICO Study Design

– SYMPATICO (NCT03112174) is multinational, randomized, double-blind, placebo-controlled, phase 3 study

SYMPATICO (N=267)
- Age ≥18 years
- R/R MCL
- 1–5 prior therapies for MCL
- ≥1 prior rituximab/ anti-CD20-containing regimen
- ECOG PS 0–2

Randomized 1:1

Ibrutinib + venetoclax (n=134)
Ibrutinib 560 mg once daily + venetoclax 5-week ramp-up to 400 mg once daily for 24 months

Ibrutinib + placebo (n=133)
Ibrutinib 560 mg once daily + placebo once daily for 24 months

Single-agent ibrutinib 560 mg once daily until PD or unacceptable toxicity

Stratification: ECOG PS, prior lines of therapy, TLS risk[a]

- **Primary endpoint:**
  - PFS by investigator assessment using Lugano criteria

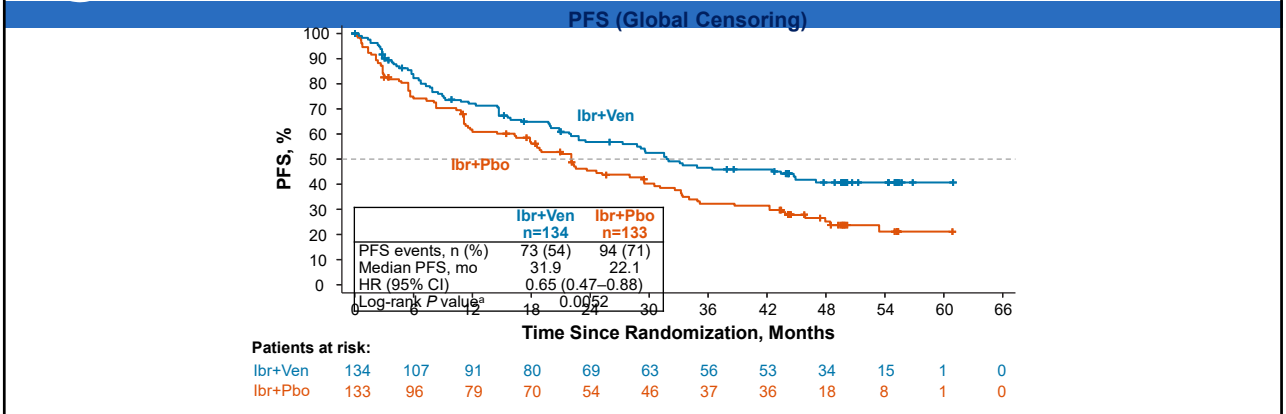
- **Secondary endpoints (tested hierarchically in the following order):**
  - CR rate by investigator assessment
  - TTNT[b]
  - OS (interim analysis)
  - ORR by investigator assessment

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; PFS, progression-free survival; ORR, overall response rate; OS, overall survival; TLS, tumor lysis syndrome; TTNT, time to next treatment.
[a]Increased TLS risk was defined as at least 1 lesion >10 cm, or at least 1 lesion >5 cm with circulating lymphocytes >25,000 cells/mm^3, and/or creatinine clearance <60 mL/min. [b]For hierarchical testing per US FDA censoring, TTNT was tested after OS.

City of Hope

33

Primary Endpoint: Investigator-Assessed PFS Was Significantly Improved With Ibrutinib + Venetoclax Versus Ibrutinib + Placebo



Median PFS, mo	Global Censoring[b]				US FDA Censoring[c]			
	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]
Investigator assessment	31.9	22.1	0.65 (0.47–0.88)	0.0052	42.6	22.1	0.60 (0.44–0.83)	0.0021
IRC assessment	31.8	20.9	0.67 (0.49–0.91)	0.0108	43.5	22.1	0.63 (0.45–0.87)	0.0057

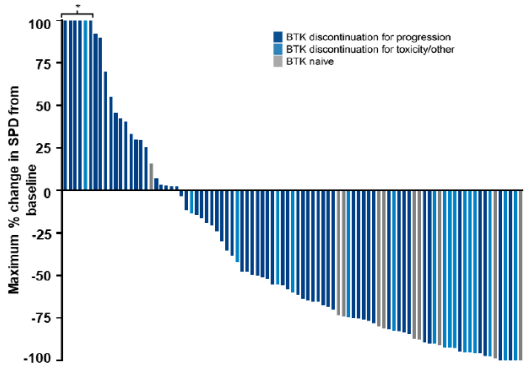
HR, hazard ratio; Ibr, ibrutinib; Pbo, placebo; Ven, venetoclax.
[a]*P* values were determined by stratified log-rank test (stratification factors: prior lines of therapy [1–2 vs ≥3] and TLS risk category [low vs increased risk]). [b]Censoring at last non-PD assessment for patients without PD or death. [c]Patients were censored at last non-PD assessment before start of subsequent anticancer therapy or missing ≥2 consecutive visits prior to a PFS event, whichever occurred first.

City of Hope

34

Pirtobrutinib (Post BTKi Outcomes)

Pirtobrutinib Efficacy in Mantle Cell Lymphoma



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)

Data cutoff date of 16 July 2021. Data for 20 MCL patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. [a]Efficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. [b]ORR includes patients with a best response of CR and PR. Response status per Lugano 2014 criteria based on investigator assessment. Total % may be different than the sum of the individual components due to rounding.

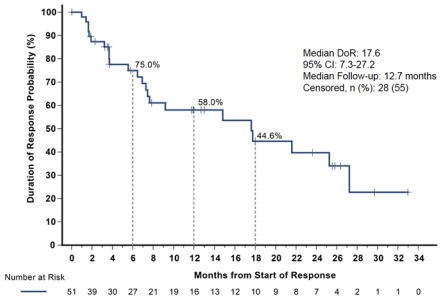
Wang et al. ASH 2021

City of Hope

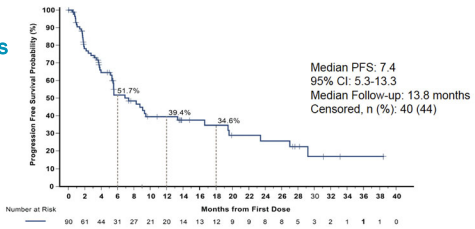
35

Updated Results and Subgroup Analysis From the BRUIN Phase 1/2 Study of Pirtobrutinib in Patients With R/R MCL: DOR, PFS, and OS

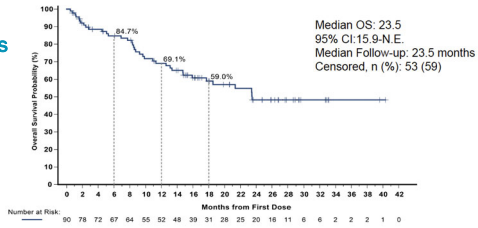
DOR in Prior cBTKi Patients



PFS in Prior cBTKi Patients



OS in Prior cBTKi Patients



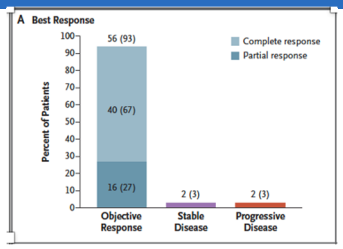
- Median DOR, PFS, and OS were not reached in the cBTKi-naïve cohort
- 18-month rates (95% CI)
  - DOR: 100% (100)
  - PFS: 92.3% (56.6-98.9)
  - OS: 92.3% (56.6-98.9)

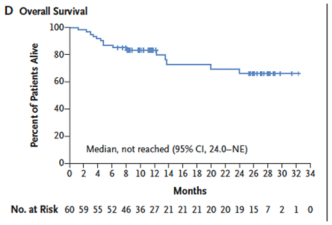
Shah NN, et al. ASCO 2023. Abstract 7514. Jurczak J, et al. EHA 2023. Abstract P1087. Cheah CY, et al. ICML 2023. Abstract 102.

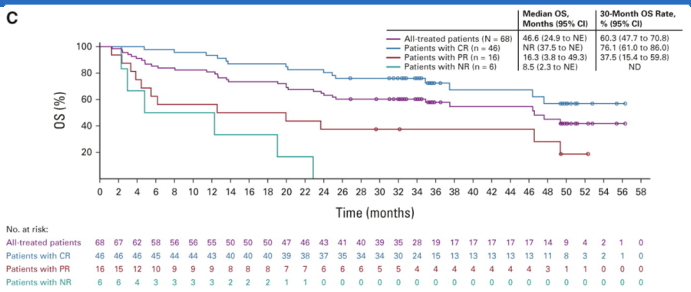
City of Hope

36

Brexucabtagene autoleucel







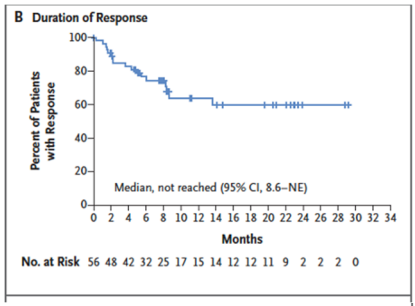
- Median PFS and median OS were not reached after a median follow-up of 12.3 months
- The median DOR has not been reached after a median follow-up of 12.3 months
- 57% of all patients and 78% of patients with a CR remain in remission

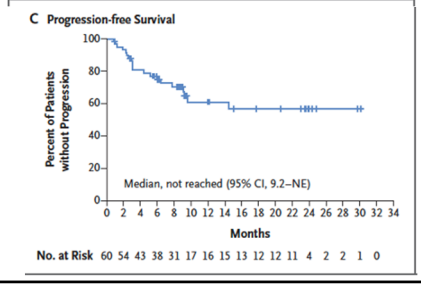
Wang M et al, KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2020 Apr 2;382(14):1331-1342. doi: 10.1056/NEJMoa1914347. PMID: 32242358; PMCID: PMC7731441.

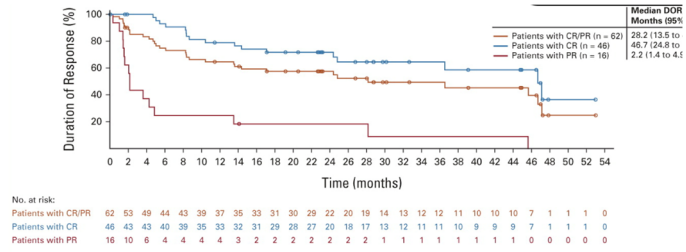
City of Hope

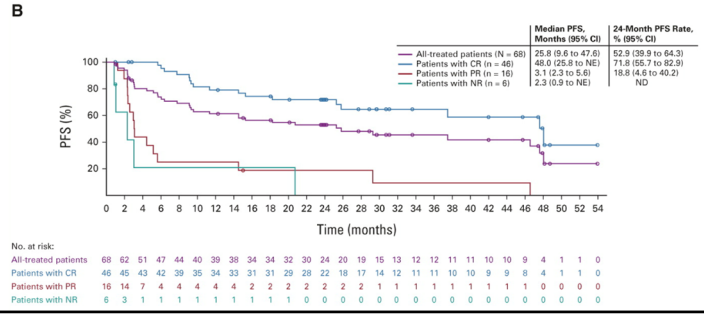
37

Then vs. Now









City of Hope

38

Cytokine Release Syndrome/Neurotoxicity

- No Grade 5 CRS occurred

Parameter	N = 68
CRS, n (%)[a]	
Any grade	62 (91)
Grade ≥ 3	10 (15)
Most common any grade symptoms of CRS, n (%)	
Pyrexia	62 (91)
Hypotension	35 (51)
Hypoxia	23 (34)
AE management, n (%)	
Tocilizumab	40 (59)
Corticosteroids	15 (22)
Median time to onset (range), days	2 (1 – 13)
Median duration of events, days	11
Patients with resolved events, n (%)	62/62 (100)

Parameter	N = 68
Neurologic events, n (%)[a]	
Any grade	43 (63)
Grade ≥ 3	21 (31)
Most common any grade symptoms, n (%)	
Tremor	24 (35)
Encephalopathy	21 (31)
Confusional state	14 (21)
AE management, n (%)	
Tocilizumab	18 (26)
Corticosteroids	26 (38)
Median time to onset (range), days	7 (1 – 32)
Median duration of events, days	12
Patients with resolved events, n (%)	37/43 (86)[b]

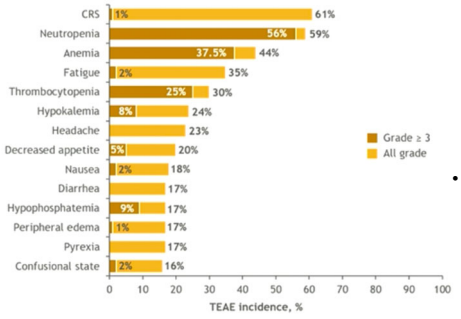
Wang M et al, KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2020 Apr 2;382(14):1331-1342. doi: 10.1056/NEJMoa1914347. PMID: 32242358; PMCID: PMC7731441.

City of Hope

39

Primary Analysis Results From the TRANSCEND-NHL-001 Study of Liso-cel in Patients With R/R MCL: Safety

TEAEs (Liso-cel-Treated Set, n=88)

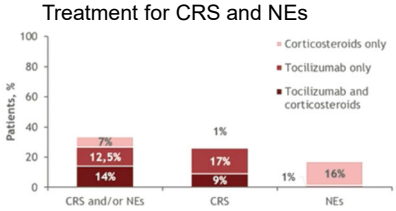


- MTD was not reached; 2 patients with a DLT among 31 DLT-evaluable patients (both at DL2)
  - Grade 5 TLS in a patient with high tumor burden
  - Grade 3 neutropenia/grade 4 thrombocytopenia
- Grade 5 TEAEs in 4 (4.5%) patients
  - 3 were considered related to liso-cel
  - 1 was considered unrelated

CRS and NEs (Liso-cel-Treated Set, n=88)		CRS	NEs
Any grade, n (%)		54 (61)	27 (31)
Grade 1/2		53 (60)	19 (22)
Grade 3		0	7 (8)
Grade 4		1 (1)	1 (1)
Grade 5		0	0
Median time to: (range), days	Onset	4.0 (1-10)	8.0 (1-25)
	Resolution	4.0 (1-14)	5.0 (1-45)

Other AEs of Special Interest, n (%)	Liso-cel-Treated Set (n=88)
Prolonged cytopenias	35 (40)
Grade ≥3 infections	13 (15)
Hypogammaglobulinemia	6 (7)

Treatment for CRS and NEs



Wang M, et al. ICML 2023. Abstract LBA3.

CRS – Cytokine Release Syndrome
DLT – Dose limiting Toxicity
MTD – Maximum Tolerated Dose, NE – Neurological Event

City of Hope

40

Glofitamab

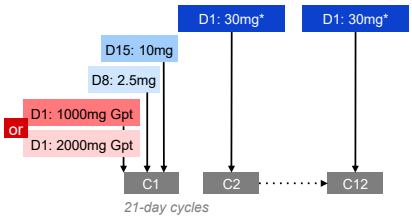
Glofitamab dosing schedules

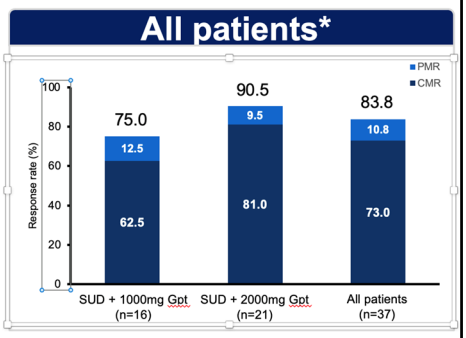
Phase I dose escalation in R/R MCL

Glofitamab IV administration
- Fixed-duration treatment: maximum 12 cycles

CRS mitigation
- Obinutuzumab pretreatment (1 x 1000mg or 1 x 2000mg)
- C1 step-up dosing
- Monitoring after first dose (2.5mg)

Population characteristics:
- Age ≥18 years
- ≥1 prior systemic therapy
- ECOG PS ≤1





Clinical cut-off date: March 14, 2022; *In the glofitamab SUD + 1000mg Gpt cohort, two patients had 16mg glofitamab as their target dose.

Phillips et al. ASH 2022

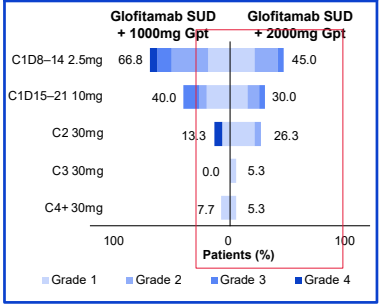
41

Adverse Events

Cytokine release syndrome*

n (%) of patients with ≥1 AE unless stated	Glofitamab SUD + 1000mg Gpt (n=16)	Glofitamab SUD + 2000mg Gpt (n=21)	All patients (N=37)
Any CRS	14 (87.5)	14 (66.7)	28 (75.7)
Grade 1	4 (25.0)	7 (33.0)	11 (29.7)
Grade 2	6 (37.5)	5 (23.8)	11 (29.7)
Grade 3	2 (12.5)	2 (9.5)	4 (10.8)
Grade 4	2 (12.5)	0 (0.0)	2 (5.4)
Serious AE of CRS (any grade)	10 (62.5)	5 (23.8)	15 (40.5)
Median time to CRS onset, hours (range)	7.55 (4.4–14.0)	9.77 (5.0–20.8)	9.31 (4.4–20.8)
Tocilizumab for CRS management	11 (68.8)	6 (28.6)	17 (45.9)
Corticosteroid for CRS management	8 (50.0)	6 (28.6)	14 (37.8)

CRS by cycle, grade and regimen



Higher Gpt (2000mg) was associated with a lower rate of CRS, with no Grade 4 events reported in this group

AE, n (%)	All grades (N=37)	Grade ≥3 (N=37)
ICANS (derived)†	5 (13.5)‡	0 (0.0)‡

Lee et. Al. Biol Blood Marrow Transplant 2019, Phillips et al. ASH 2022

42

Future Directions/Conclusions

- MCL is a disease with an evolving treatment and response algorithm.
  - How do we better segregate patients (observation vs. treatment)
  - What is the best management for high-risk patients
  - MRD? How do we incorporate this into our practice?
- Clinical trials remain very important in this disease.

43

Thank you

44

ASK A QUESTION
SPOTLIGHT ON MANTLE CELL LYMPHOMA

Ask a question by phone:

Press star (*) then the number 1 on your keypad.

Ask a question by web:

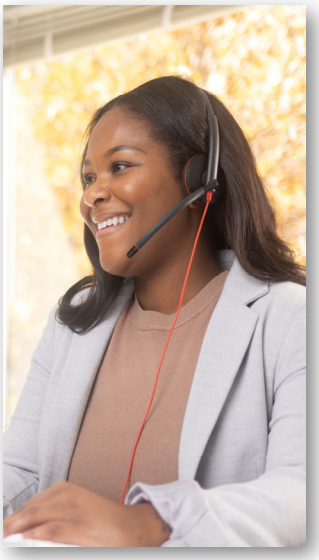
Click "Ask a question"
Type your question
Click "Submit"

Due to time constraints, we can only take one question per person. Once you've asked your question, the operator will transfer you back into the audience line.

LEUKEMIA & LYMPHOMA SOCIETY®

45

LLS EDUCATION & SUPPORT RESOURCES

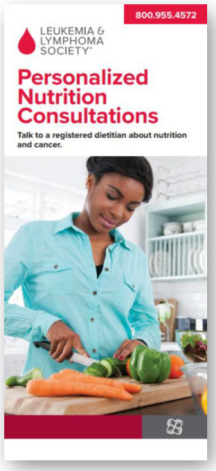


HOW TO CONTACT US:

To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:
www.LLS.org/InformationSpecialists

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
Email: www.LLS.org/ContactUs
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation

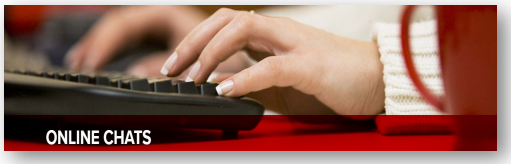


NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLSNutrition.org

LEUKEMIA & LYMPHOMA SOCIETY®

46

LLS EDUCATION & SUPPORT RESOURCES

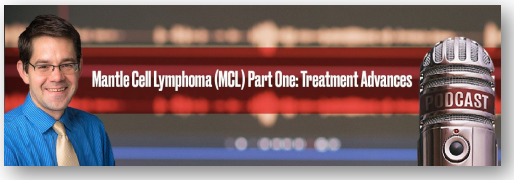


Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit www.LLS.org/Chat

Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit www.LLS.org/EducationVideos



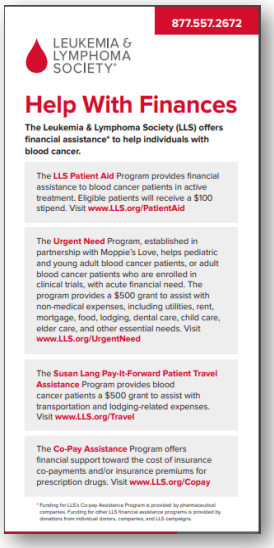
Patient Podcast

The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit www.TheBloodline.org

LEUKEMIA & LYMPHOMA SOCIETY®

47

LLS EDUCATION & SUPPORT RESOURCES


877.557.2672

LEUKEMIA & LYMPHOMA SOCIETY®

Help With Finances

The Leukemia & Lymphoma Society (LLS) offers financial assistance* to help individuals with blood cancer.

The **LLS Patient Aid** Program provides financial assistance to blood cancer patients in active treatment. Eligible patients will receive a $100 stipend. Visit **www.LLS.org/PatientAid**

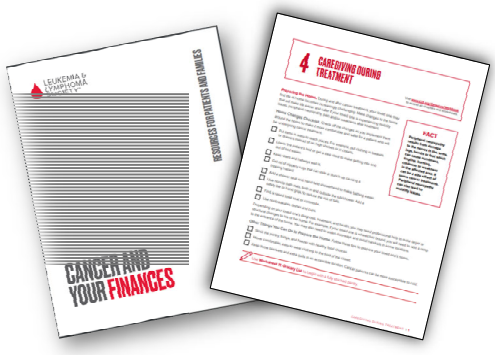
The **Urgent Need** Program, established in partnership with Moppie's Love, helps pediatric and young adult blood cancer patients, or adult blood cancer patients who are enrolled in clinical trials, with acute financial need. The program provides a $500 grant to assist with non-medical expenses, including utilities, rent, mortgage, food, lodging, dental care, child care, elder care, and other essential needs. Visit **www.LLS.org/UrgentNeed**

The **Susan Lang Pay-It-Forward Patient Travel Assistance** Program provides blood cancer patients a $500 grant to assist with transportation and lodging-related expenses. Visit **www.LLS.org/Travel**

The **Co-Pay Assistance** Program offers financial support toward the cost of insurance co-payments and/or insurance premiums for prescription drugs. Visit **www.LLS.org/Copay**

* Funding for LLS's Co-pay Assistance Program is provided by pharmaceutical companies. Funding for other LLS financial assistance programs is provided by donations from individual donors, companies, and LLS campaigns.

The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers: **www.LLS.org/Finances**



To order free materials: www.LLS.org/Booklets

LEUKEMIA & LYMPHOMA SOCIETY®

48


THANK YOU
PLEASE PROVIDE US WITH FEEDBACK,
CLICK FOR SURVEY:
We have one goal: A world without blood cancers
LEUKEMIA &
LYMPHOMA
SOCIETY®

49