POST-SAN DIEGO 2023
Novità dal Meeting della Società Americana di Ematologia

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Verona
Palazzo della Gran Guardia
15-16-17 Febbraio 2024

Linfoma Mantellare

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AO SS Antonio e Biagio e Cesare Arrigo, Alessandria

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DISCLOSURE INFORMATION

Marco Ladetto

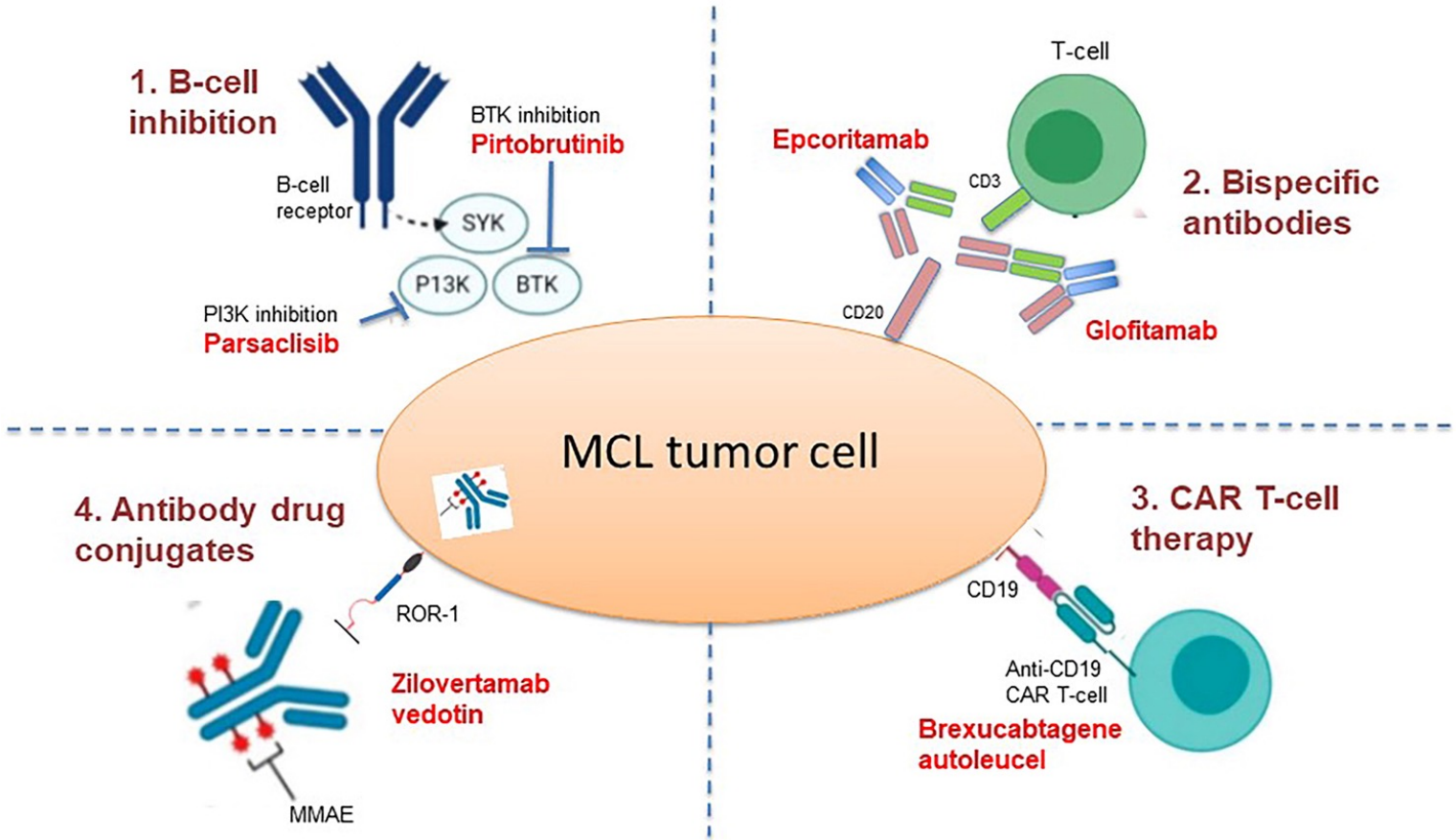
I declare in the last five years the following relationships in terms of consultancy, participation to advisory boards, invitation to scientific meetings, institutional research support and contracts with: AbbVie, Acerta, Amgen, ADC Therapeutics, BeiGene, Celgene/BMS, Eusapharma, GSKI, Gentili, Gilead/Kite, Lilly, Novartis, Incyte J&J, Jazz, Regeneron, Roche, Sandoz.

Non-financial interests:
PI or strategic investigator in studies supported by: Celgene, J&J, BeiGene, ADC Therapeutics

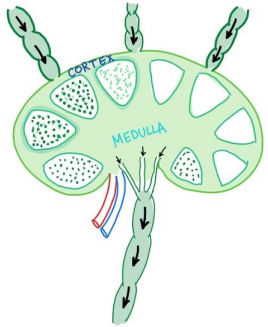
Leadership roles:
President of Fondazione italiana linfomi (FIL)
Member of the EHA Guideline Committee up to 2023
Member of the ESMO Guidelines Committee up to Dec 2018
Member of the ESMO Educational Committee

THE STATE OF THE ART

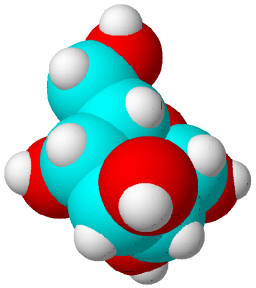
- ASH 2023 was another important ASH for MCL (but not as ASH2022)
- Further shift towards biological and T-cell engaging treatments.



Mantle cell Lymphoma



1st Line



MOLECULES

ACALABRUTINIB-R

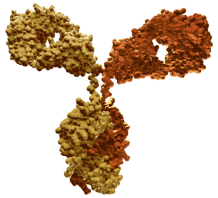
Jain P et al., *Blood* (2023) 142 (Supplement 1): 3036

ACALABRUTINIB-R-ASCT

Hawkes et al., *Blood (2023) 142 (Supplement 1): 735.*

ZANUBRUTINIB-OBINU-VEN

VEN-R-BAC



MONOCLONAL ANTIBODIES

R/R

PIRTOBRUTINIB

Cohen J et al., *Blood (2023) Volume 142 (Supplement 1): Page 981*

IBRUTINIB + VEN

MOSUNETUZUMAB + POLATUZUMAB VEDOTIN

New therapies in development

Updated results

R/R MCL

Ibrutinib Combined with Venetoclax in Patients with Relapsed/Refractory Mantle Cell Lymphoma: Primary Analysis Results from the Randomized Phase 3 Sympatico Study

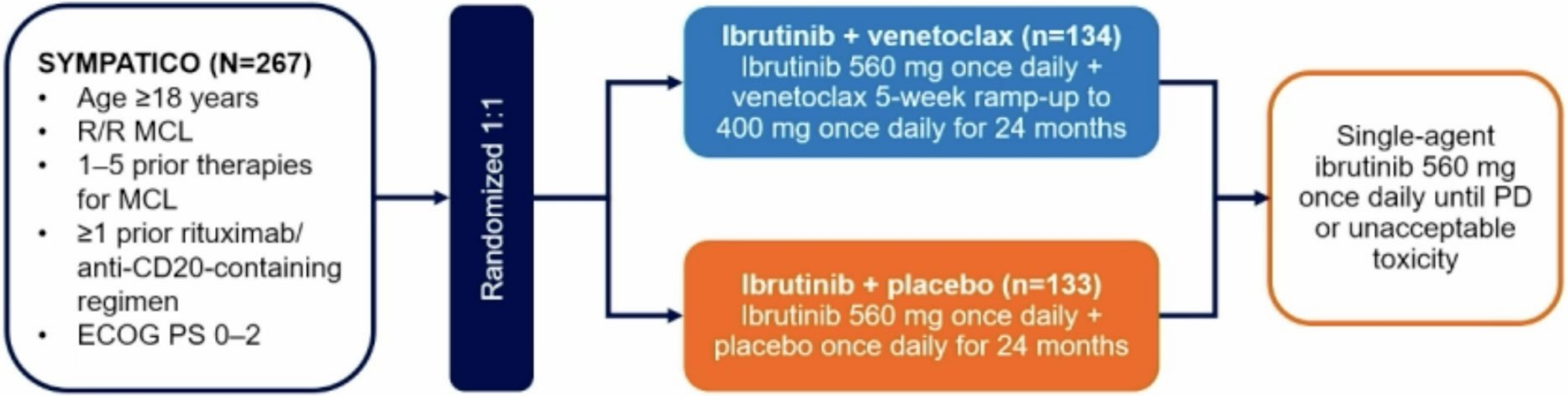
Michael Wang, Wojciech Jurczak, Marek Trněný, David Belada, Tomasz Wrobel, Nilanjan Ghosh, Mary-Margaret Keating, Tom van Meerten, Ruben Fernandez Alvarez, Gottfried von Keudell, Catherine Thieblemont, Frederic Peyrade, Marc Andre, Marc Hoffmann, Edith Szafer Glusman, Jennifer Lin, James P. Dean, Jutta K. Neuenburg, Constantine S. Tam

1. Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX

Blood, Volume 142, Supplement 2, 2023, Page LBA-2

SYMPATICO Study Design

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



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.

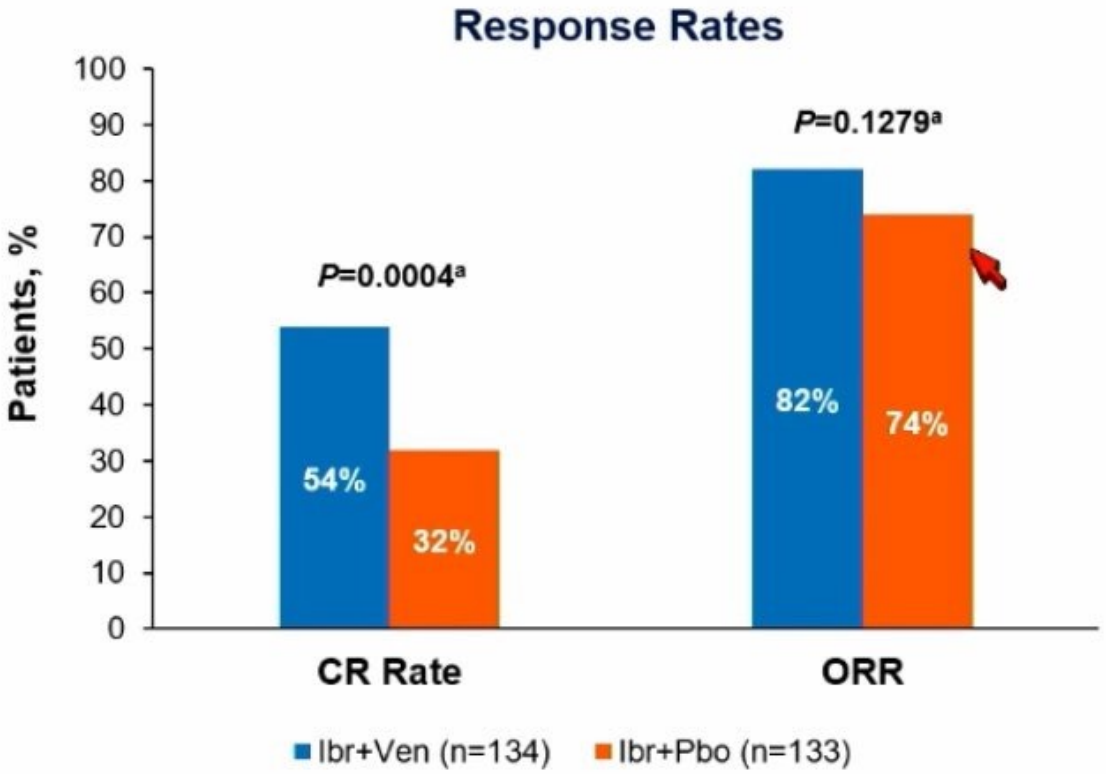
Baseline Characteristics

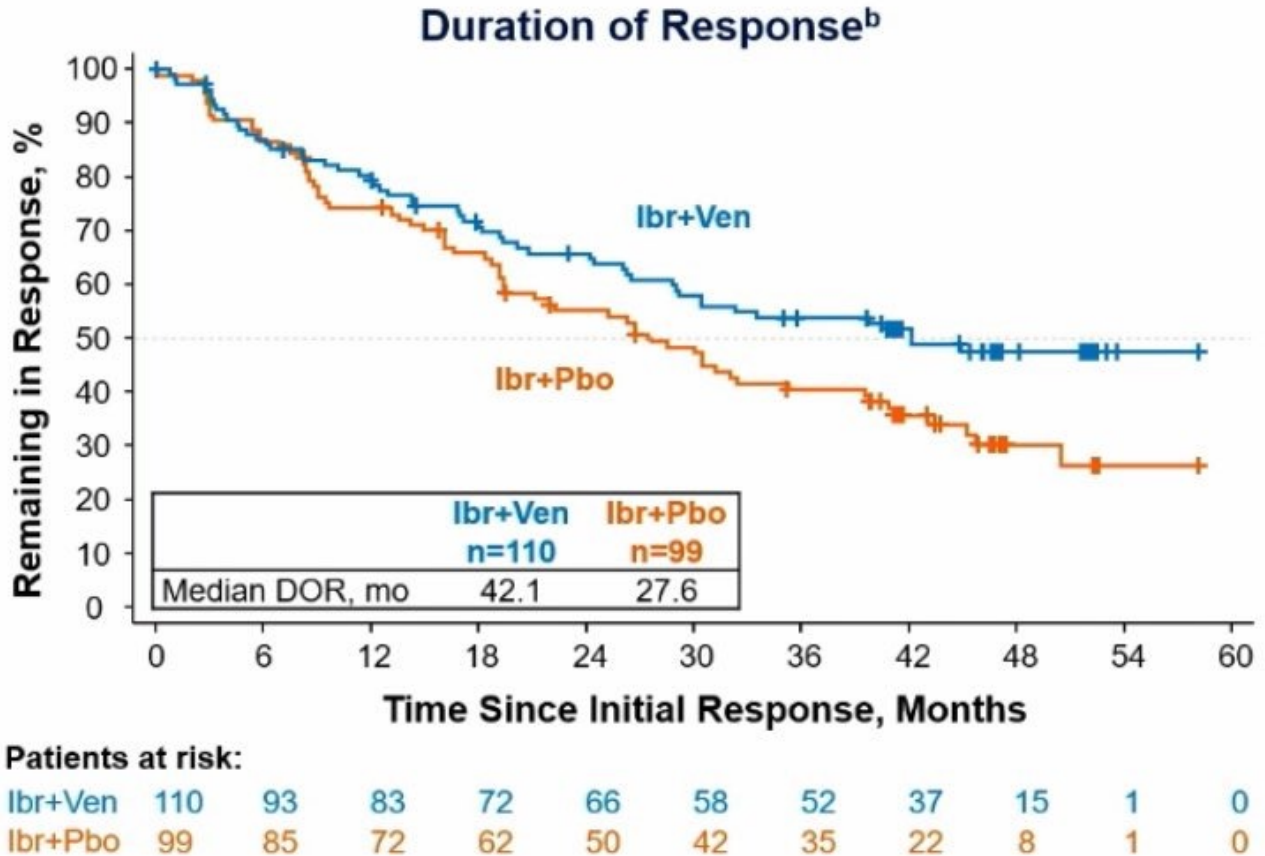
Characteristic	Ibrutinib + venetoclax n=134	Ibrutinib + placebo n=133
Age		
Median (range), years	69 (42–84)	67 (44–88)
≥65 years, n (%)	93 (69)	86 (65)
ECOG PS, n (%)		
0	74 (55)	74 (56)
1–2	60 (45)	59 (44)
Prior lines of treatment, n (%)		
1	80 (60)	79 (59)
2	32 (24)	31 (23)
≥3	22 (16)	23 (17)
MCL histology, n (%)		
Typical	88 (66)	95 (71)
Blastoid	19 (14)	17 (13)
Pleomorphic	8 (6)	6 (5)
Round cell (CLL-like)	1 (1)	0
Other	18 (13)	15 (11)

Characteristic	Ibrutinib + venetoclax n=134	Ibrutinib + placebo n=133
Simplified MIPI score, n (%)		
Low risk	18 (13)	23 (17)
Intermediate risk	63 (47)	68 (51)
High risk	51 (38)	41 (31)
***TP53* status, n (%)**		
Mutated	40 (30)	37 (28)
Not mutated	66 (49)	57 (43)
Missing	28 (21)	39 (29)
Bulky disease, n (%)		
≥5 cm	62 (46)	53 (40)
≥10 cm	13 (10)	10 (8)
Extranodal disease, n (%)	64 (48)	61 (46)
BM involvement, n (%)	62 (46)	54 (41)
Splenomegaly, n (%)	42 (31)	33 (25)

BM, bone marrow; MIPI, MCL International Prognostic Index.

CR Rate Was Significantly Improved With Ibrutinib + Venetoclax





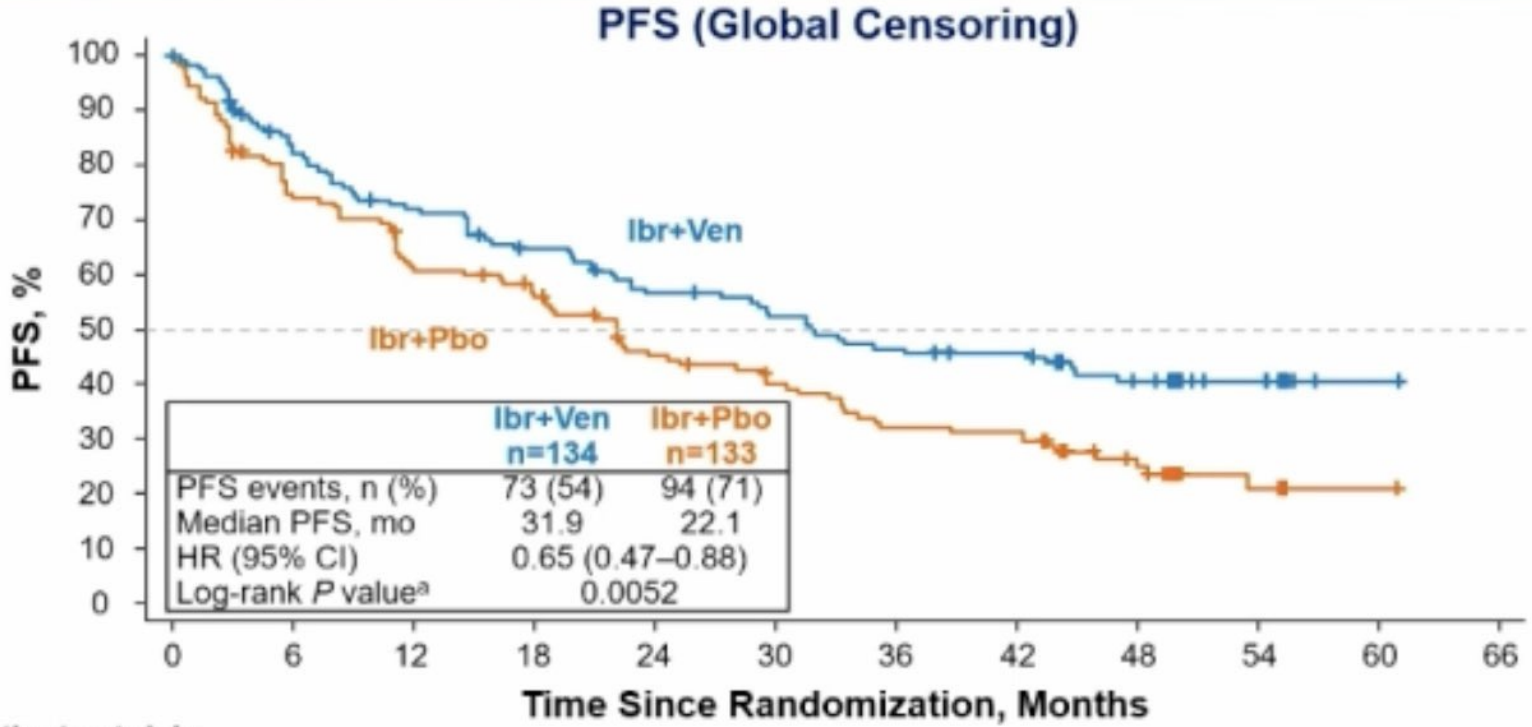
Patients at risk:

Ibr+Ven	110	93	83	72	66	58	52	37	15	1	0
Ibr+Pbo	99	85	72	62	50	42	35	22	8	1	0

DOR, duration of response.

[a]*P* values were determined by stratified Cochran-Mantel-Haenszel test (stratification factors: prior lines of therapy [1–2 vs ≥3] and TLS risk category [low vs increased risk]). [b]Global censoring (censoring at last non-PD assessment for patients without PD or death).

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

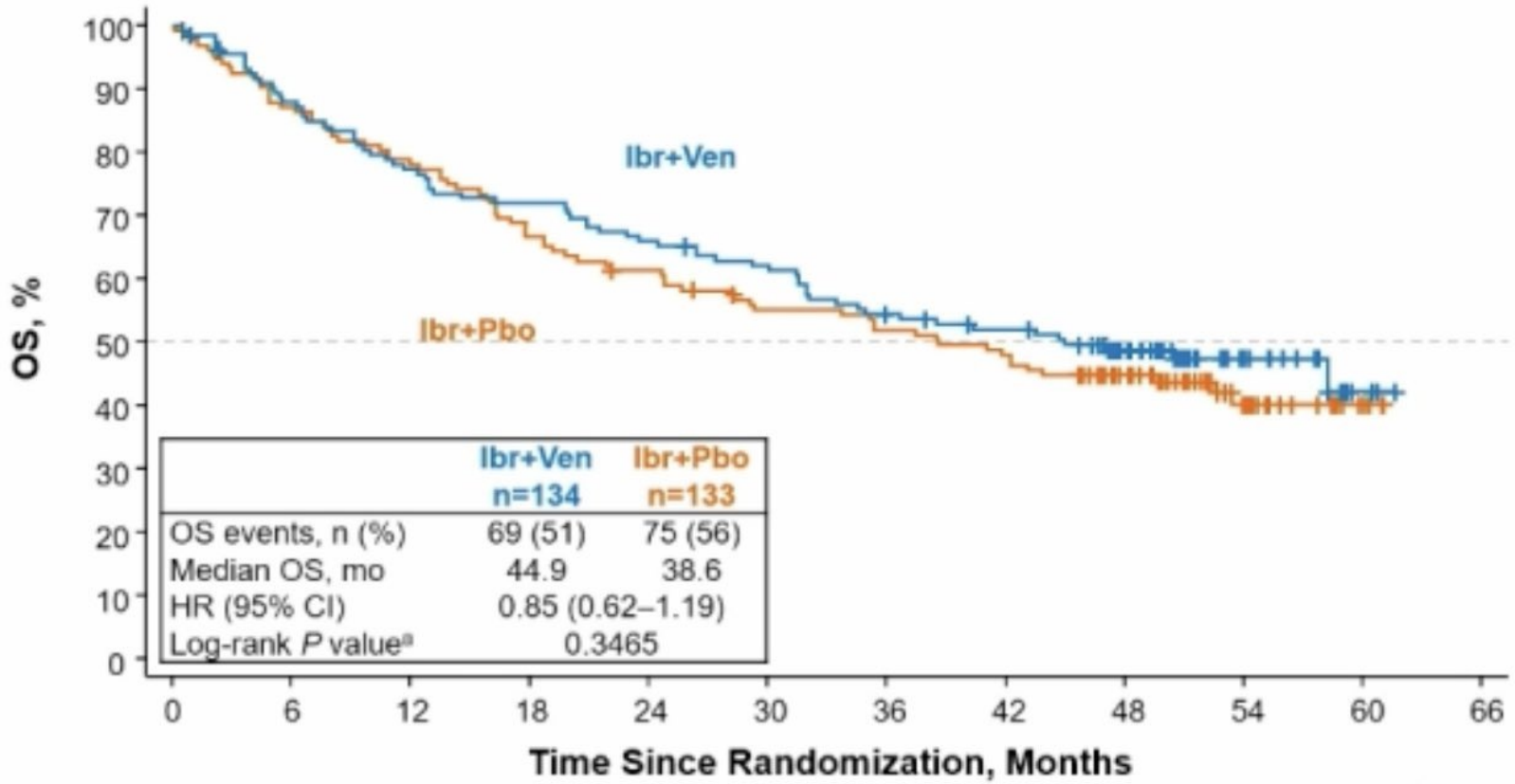


Median PFS, mo	Global Censoring[b]				US FDA Censoring[c]			
	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]
Investigator assessment	31.9	22.1	0.65 (0.47–0.88)	0.0052	42.6	22.1	0.60 (0.44–0.83)	0.0021
IRC assessment	31.8	20.9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

OS Was Numerically Improved At This Interim Analysis



	Ibr+Ven n=134	Ibr+Pbo n=133
OS events, n (%)	69 (51)	75 (56)
Median OS, mo	44.9	38.6
HR (95% CI)	0.85 (0.62–1.19)	
Log-rank *P* value[a]	0.3465	

Patients at risk:

Ibr+Ven	134	116	102	95	87	81	70	65	48	20	3	0
Ibr+Pbo	133	115	103	88	80	70	66	61	46	20	4	0

Safety Was Consistent With Known AEs of Each Single Agent

- Median overall treatment duration:
  - Ibrutinib + venetoclax, 22.2 months (range, 0.5–60.4)
  - Ibrutinib + placebo, 17.7 months (range, 0.1–58.9)

AE, n (%)	Ibrutinib + venetoclax n=134	Ibrutinib + placebo n=132
Grade ≥3 AEs	112 (84)	100 (76)
Serious AEs	81 (60)	79 (60)
AEs leading to discontinuation	41 (31)	48 (36)
Ibrutinib only	11 (8)	10 (8)
Venetoclax/placebo only	2 (1)	7 (5)
Both	28 (21)	31 (23)
AEs leading to dose reduction	48 (36)	29 (22)
Ibrutinib only	17 (13)	14 (11)
Venetoclax/placebo only	14 (10)	7 (5)
Both	17 (13)	8 (6)
AEs leading to death	22 (16)	18 (14)
Ibrutinib-related[a]	3 (2)	2 (2)
Venetoclax/placebo-related[a]	0	1 (1)
Tumor lysis syndrome		
Laboratory	7 (5)	3 (2)
Clinical	0	0

AE, n (%)	Ibrutinib + venetoclax n=134	Ibrutinib + placebo n=132
Most frequent any-grade AEs[b]		
Diarrhea	87 (65)	45 (34)
Neutropenia	46 (34)	19 (14)
Nausea	42 (31)	22 (17)
Fatigue	39 (29)	36 (27)
Anemia	30 (22)	16 (12)
Pyrexia	28 (21)	26 (20)
Cough	27 (20)	36 (27)
Muscle spasms	11 (8)	32 (24)
Most frequent grade ≥3 AEs[c]		
Neutropenia	42 (31)	14 (11)
Pneumonia	17 (13)	14 (11)
Thrombocytopenia	17 (13)	10 (8)
Anemia	13 (10)	4 (3)
Diarrhea	11 (8)	3 (2)
Leukopenia	10 (7)	0
MCL[d]	9 (7)	16 (12)
Atrial fibrillation	7 (5)	7 (5)
COVID-19	7 (5)	1 (1)
Hypertension	6 (4)	12 (9)

[a]Per investigator opinion. [b]Occurring in ≥20% of patients in either arm. [c]Occurring in ≥5% of patients in either arm. [d]Worsening of MCL without meeting criteria for PD.

Fixed Duration Mosunetuzumab Plus Polatuzumab Vedotin Has Promising Efficacy and a Manageable Safety Profile in Patients with BTKi Relapsed/Refractory Mantle Cell Lymphoma: Initial Results from a Phase Ib/II Study

Michael L. Wang, Sarit Assouline, Manali Kamdar, Nilanjan Ghosh, Seema Naik, Shazia K. Nakhoda, Julio C. Chavez, Ting Jia, Song Pham, Ling-Yuh Huw, Jing Jing, Wahib Ead, Iris To, Connie Lee Batlevi, Michael C. Wei, L. Elizabeth Budde

1. University of Texas MD Anderson Cancer Center, Houston, TX

Blood (2023) Volume 142, Supplement 1, Page 734

Study design: Phase II dose expansion

Key inclusion criteria

- R/R MCL
- ECOG PS 0–2
- ≥2 prior therapies (including an anti-CD20 antibody, anthracycline or bendamustine therapy, and BTKi)

Objectives

- Primary: efficacy of mosun-pola (best ORR[1] by IRC)
- Secondary: efficacy by INV, durability of response, and safety

Mosun-pola fixed duration administration (NCT03671018)

Mosun

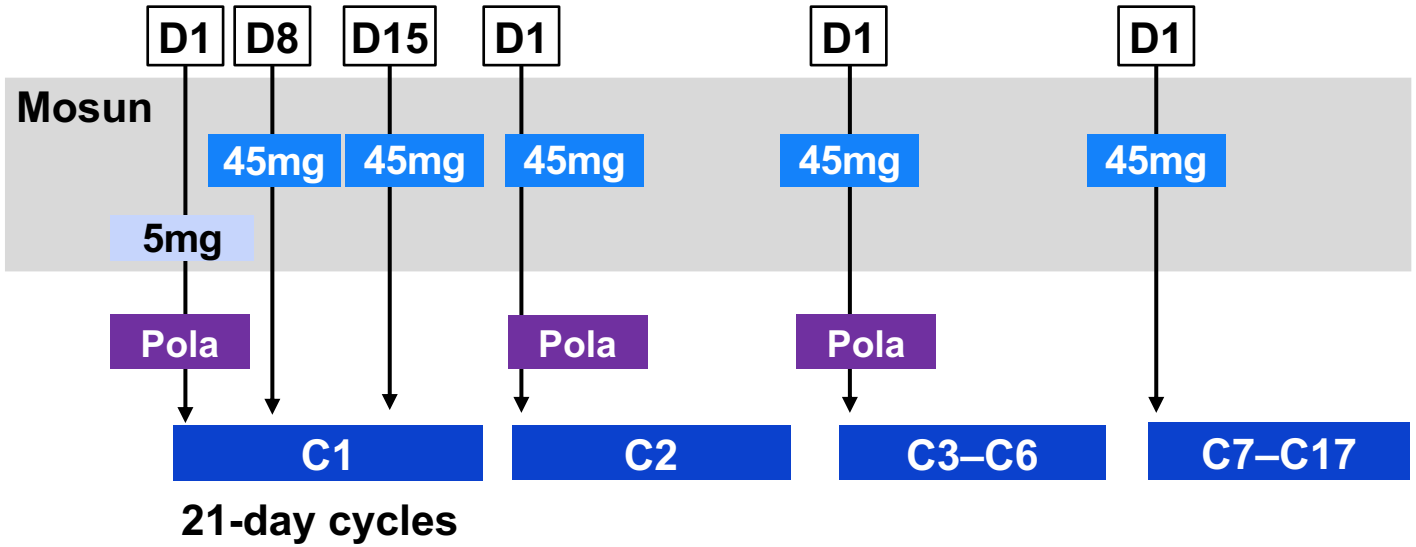
- SC administered in 21-day cycles with step-up dosing in Cycle (C) 1; total of 17 cycles

Pola

- 1.8mg/kg IV on Day [D],1 of C1–6

No mandatory hospitalization

All patients received corticosteroid premedication prior to each dose in C1*



*From C2 and beyond, premedication was optional for patients who did not experience CRS in the previous cycle; corticosteroid premedication consisted of 20mg of dexamethasone or 80mg of methylprednisolone, either IV or orally.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

Baseline characteristics

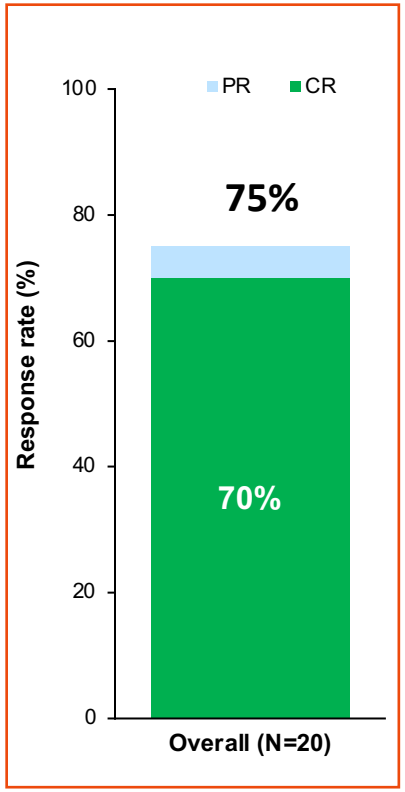
n (%), unless stated	N=20
Median age, years (range)	68 (44–82)
Male sex	15 (75)
ECOG PS score	
0	12 (60)
1	5 (25)
2	3 (15)
Ann Arbor stage III–IV	19 (95)
Extranodal involvement	17 (85)
Elevated LDH	9 (45)
Median lines of prior therapy, n (range)	3 (2–9)
Number of prior lines of therapy	
2	5 (25)
3	6 (30)
≥4	9 (45)

n (%), unless stated	N=20
Prior therapy	
BTKi	20 (100)
CAR T	7 (35)
ASCT	6 (30)
Refractory to last prior therapy	17 (85)
TP53 aberration at study entry	
Mutation/deletion	5/12 (42)*
Wildtype	7/12 (58)
Unknown	8
Ki-67	
≥30%	13 (65)†
≥50%	12 (60)
MIPI score ≥6	8 (40)
Blastoid/pleomorphic	10 (50)
Bone marrow involvement	9 (45)

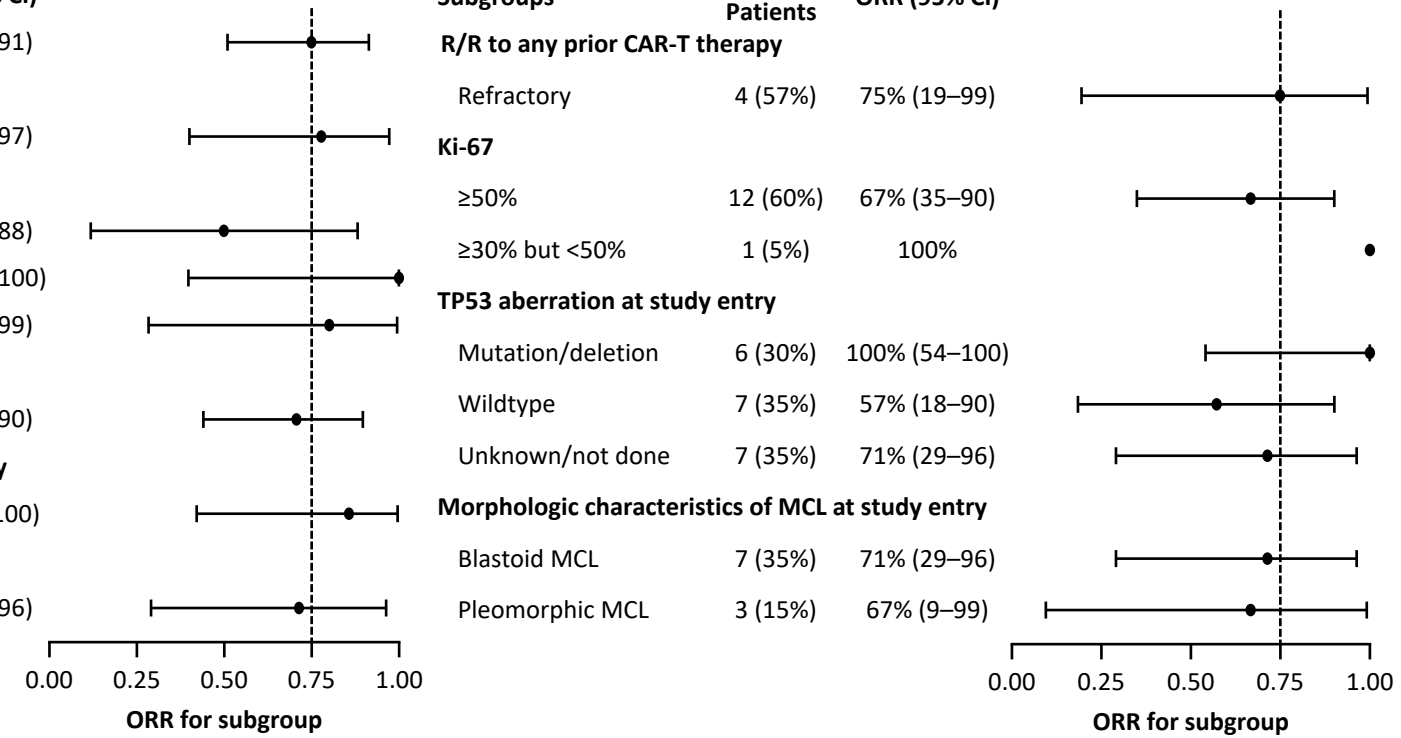
Clinical cut-off date: July 6, 2023. *One additional patient had a TP53 mutation confirmed after the clinical cut-off date.
†1 patient (5.0%) had Ki-67 ≥30–<50%.
MIPI, MCL International Prognostic Index; TP53, tumor protein 53.

INV-assessed best ORR

ORR and CR rates in the overall population were 75% and 70%, respectively



Subgroups	No. Patients	ORR (95% CI)
Overall	20 (100%)	75% (51–91)
Age group, in years		
≥70	9 (45%)	78% (40–97)
No. of prior lines of therapy		
3	6 (30%)	50% (12–88)
4	4 (20%)	100% (40–100)
≥5	5 (25%)	80% (28–99)
R/R to last prior therapy		
Refractory	17 (85%)	71% (44–90)
Relapse within 12 months of first prior therapy		
Yes	7 (35%)	86% (42–100)
Received prior CAR-T therapy		
Yes	7 (35%)	71% (29–96)
R/R to any prior CAR-T therapy		
Refractory	4 (57%)	75% (19–99)
Ki-67		
≥50%	12 (60%)	67% (35–90)
≥30% but <50%	1 (5%)	100%
TP53 aberration at study entry		
Mutation/deletion	6 (30%)	100% (54–100)
Wildtype	7 (35%)	57% (18–90)
Unknown/not done	7 (35%)	71% (29–96)
Morphologic characteristics of MCL at study entry		
Blastoid MCL	7 (35%)	71% (29–96)
Pleomorphic MCL	3 (15%)	67% (9–99)

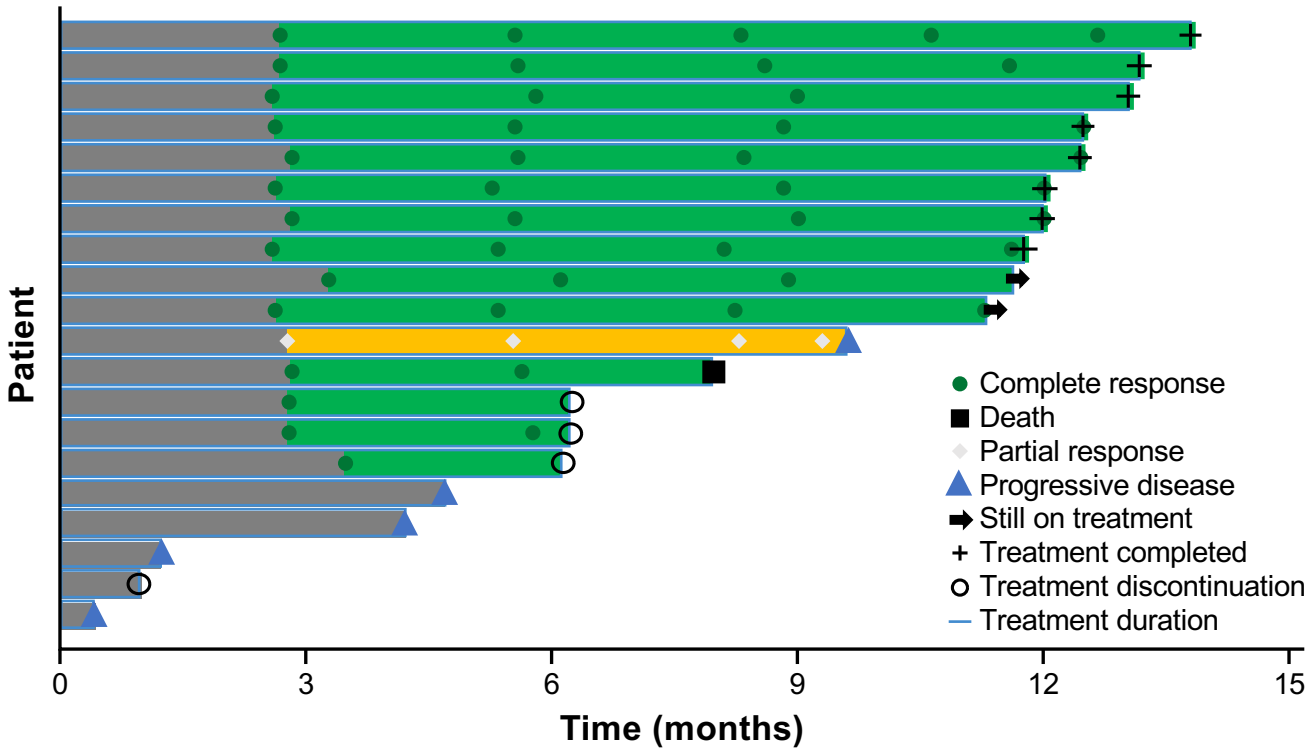


Best ORR rates were generally consistent across high-risk MCL subgroups

Clinical cut-off date: July 6, 2023.

Durability of response

Swimlane plot



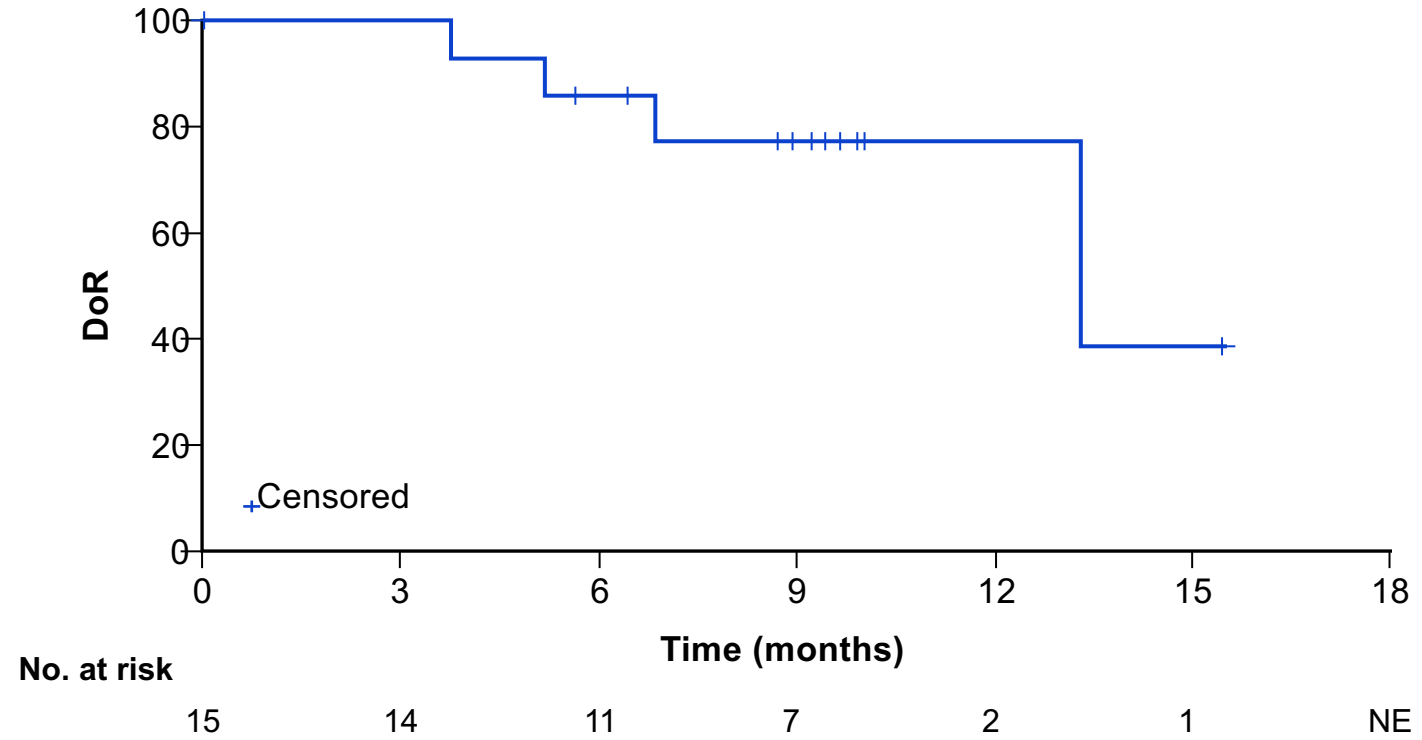
- Median follow-up: 15.8 months (range: 0–25)
- Median time to first response: 2.8 months (range: 2.6–3.4)
- Of 14 patients with CR, 11 remain in remission*

Complete remission was achieved early and remained durable

Clinical cut-off date: July 6, 2023. *Out of the three patients who were not in remission, 1 patient had progressive disease, and two died from non-lymphoma causes.

Duration of response (DoR)

Median DoR: 13.3 months (95% CI: 13.3–NE)



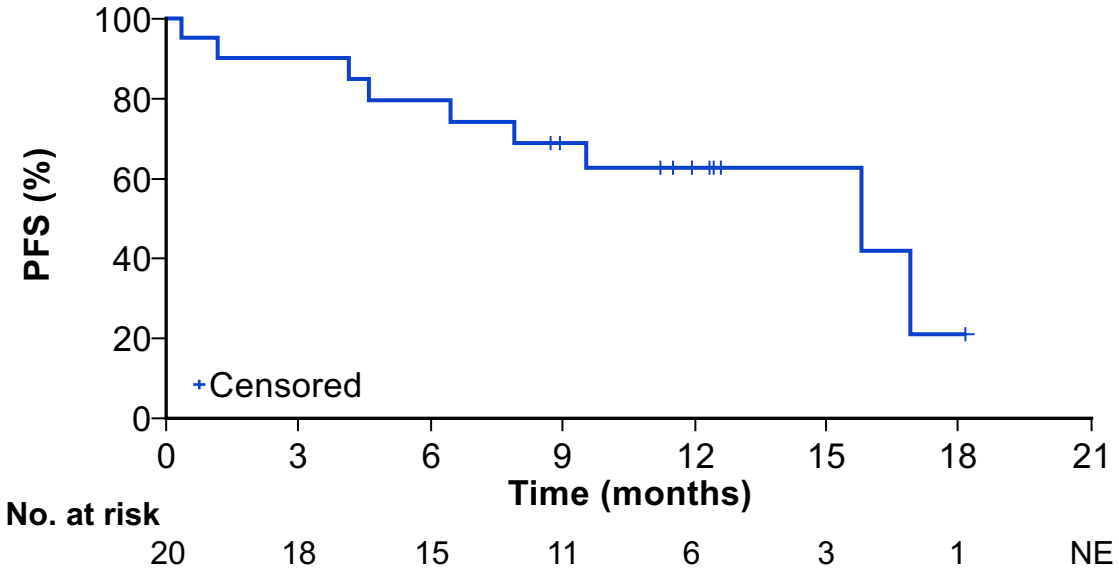
Promising durability of responses observed

Clinical cut-off date: July 6, 2023. Duration of complete response was 13.3 months (95% CI: 13.3–NE).

PFS and OS

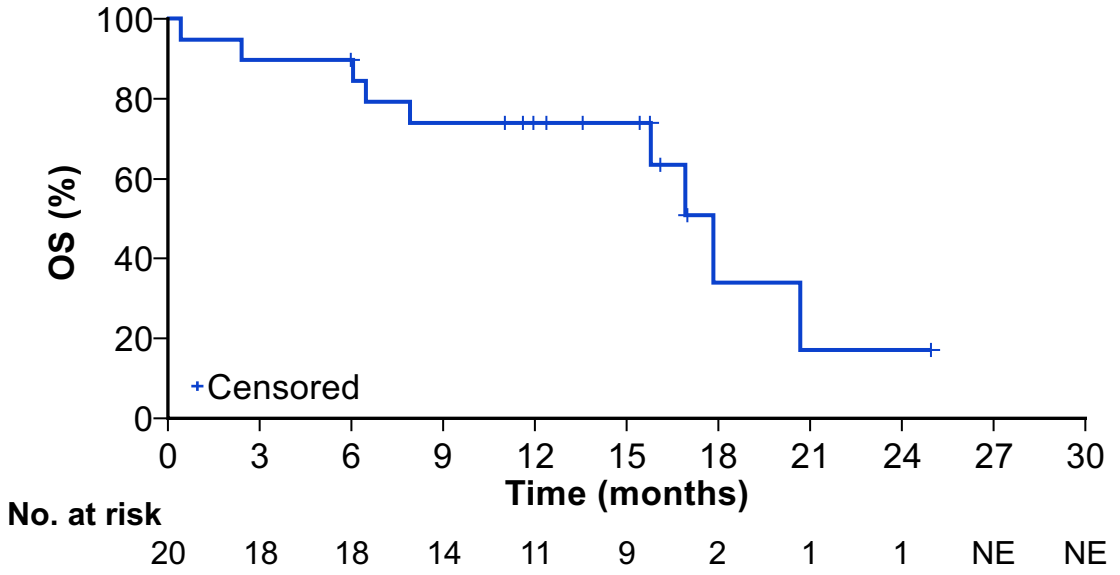
Median follow-up: 15.8 months (95% CI: 12.4–NE)

PFS



	N=20
Median PFS, months (95% CI)	15.8 (8.0–NE)
9-month event-free rate, % (95% CI)	68.8% (48.1–89.6)

OS



	N=20
Median OS, months (95% CI)	17.9 (15.8–20.7)
9-month event-free rate, % (95% CI)	74.1% (54.5–93.7)

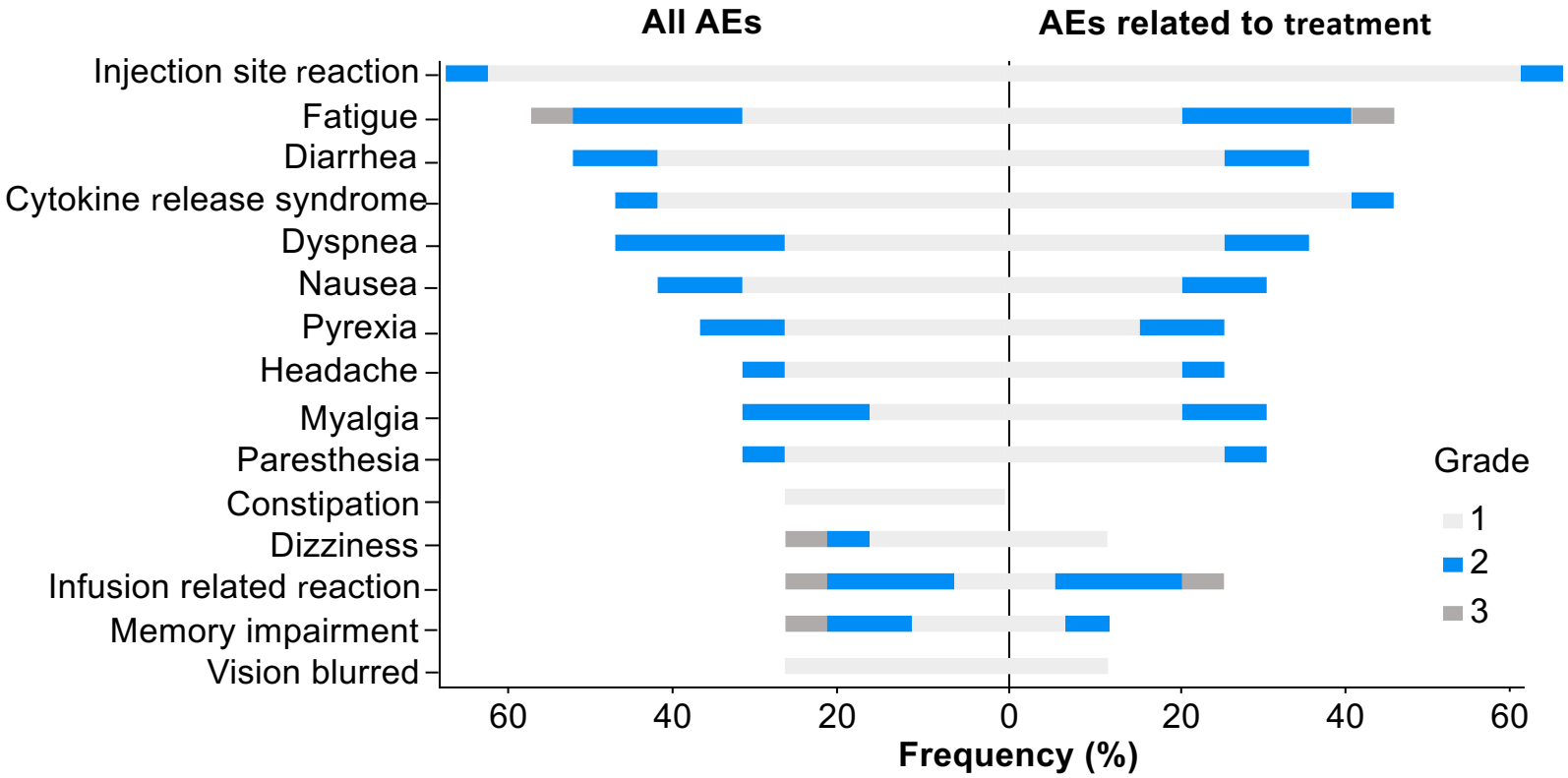
Promising PFS and OS benefits from longer follow up

Clinical cut-off date: July 6, 2023.

Safety profile

AE summary, n (%)	N=20
AE	20 (100)
Treatment-related	18 (90)
Grade 3/4 AE	12 (60)
Treatment-related	9 (45)
Serious AE	13 (65)
Treatment-related	9 (45)
Grade 5 (fatal) AE	3 (15)*
Treatment-related	0
AE leading to treatment discontinuation	4 (20)†
Treatment-related	2 (10)

AEs (≥20%) by grade



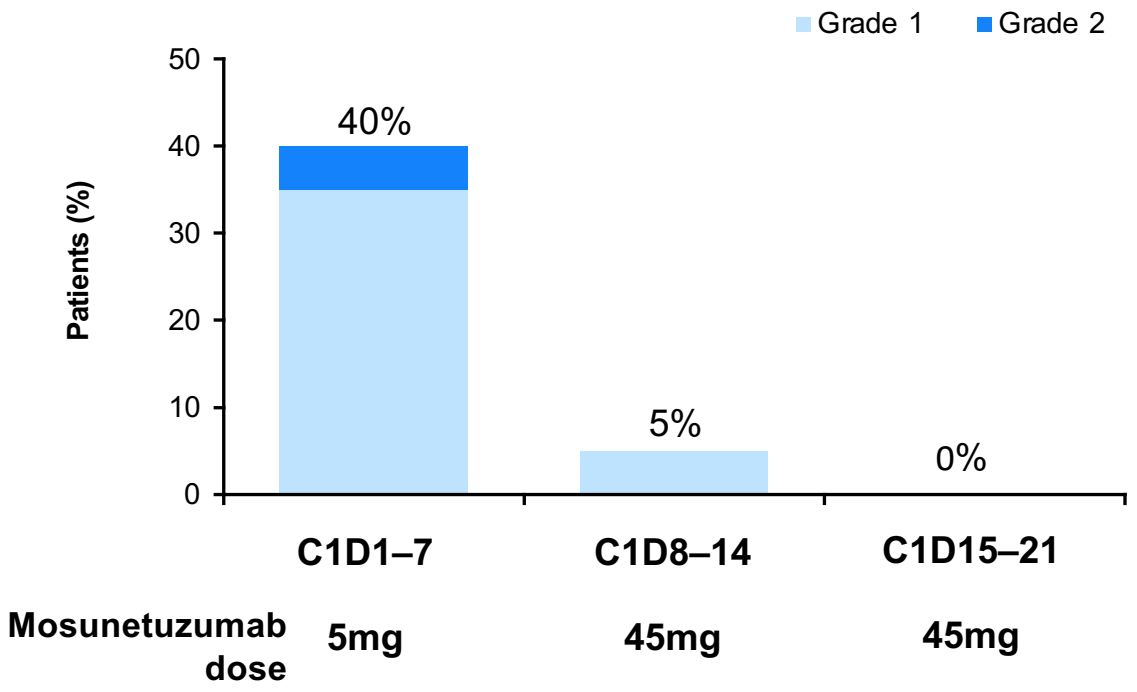
No new safety signals observed; SC injection site reaction (all grade 1–2) was the most common AE

Clinical cut-off date: July 6, 2023. *Includes COVID-19 pneumonia (n=2) and COVID-19 (n=1).
†Includes Grade 5 COVID-19 pneumonia (n=2; not treatment related), Grade 3 uveitis (n=1; mosun- and pola-related), Grade 3 pneumonitis (n=1; mosun- and pola-related; pola-discontinuation) and *Clostridioides difficile* (n=1; mosun-related; mosun-discontinuation).

CRS summary

CRS by ASTCT criteria[1]	N=20
Any grade, n (%) Grade 1 Grade 2* Grade 3+	9 (45) 8 (40) 1 (5) 0
Median time to first CRS onset relative to last dose, days (range)	1 (0–2)
Median CRS duration, days (range)	3 (1–9)
CRS management, n (%) Corticosteroids Tocilizumab Low-flow oxygen	 1 (5) 1 (5) 1 (5)

CRS by cycle and grade



All CRS events were low grade and resolved within C1

Clinical cut-off date: July 6, 2023. *This patient experienced Grade 2 fever, confusion, and hypoxia on D3; management included tocilizumab, low-flow oxygen, acetaminophen, and broad-spectrum antibiotics.
ASTCT, American Society for Transplantation and Cellular Therapy

1. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

Other adverse events of interest

AE summary, n (%)	N=20
ICANS*	
Any grade	4 (20)
Grade 3–4	0
Peripheral neuropathy	
Any grade	2 (10.0)
Grade 3–4	0
Tumor flare	
Any grade	2 (10.0)
Grade 3–4	0

AE summary, n (%)	N=20
Serious infections	
Any grade	8 (40.0)
Grade 3–4	3 (15.0)
Grade 5†	3 (15.0)
Neutropenia	
Any grade	4 (20.0)
Grade 3–4	3 (15.0)
Febrile Neutropenia	1 (5.0)

Mosun-pola demonstrated a manageable safety profile consistent with that of the individual agents in patients with R/R MCL, including those with high-risk features

Clinical cut-off date: July 6, 2023. *Treatment-related neurologic AEs potentially consistent with ICANS; patient cases included two cases of memory impairment (Grade 1 and Grade 2), amnesia (Grade 2), agitation (Grade 1), confusional state (Grade 1).
†Grade 5 infections included 2 cases of COVID-19 pneumonia and 1 case of COVID-19.

First-line MCL

A Multicenter Phase 2 Trial of Zanubrutinib, Obinutuzumab, and Venetoclax (BOVen) in Patients with Treatment-Naïve, TP53-Mutant Mantle Cell Lymphoma

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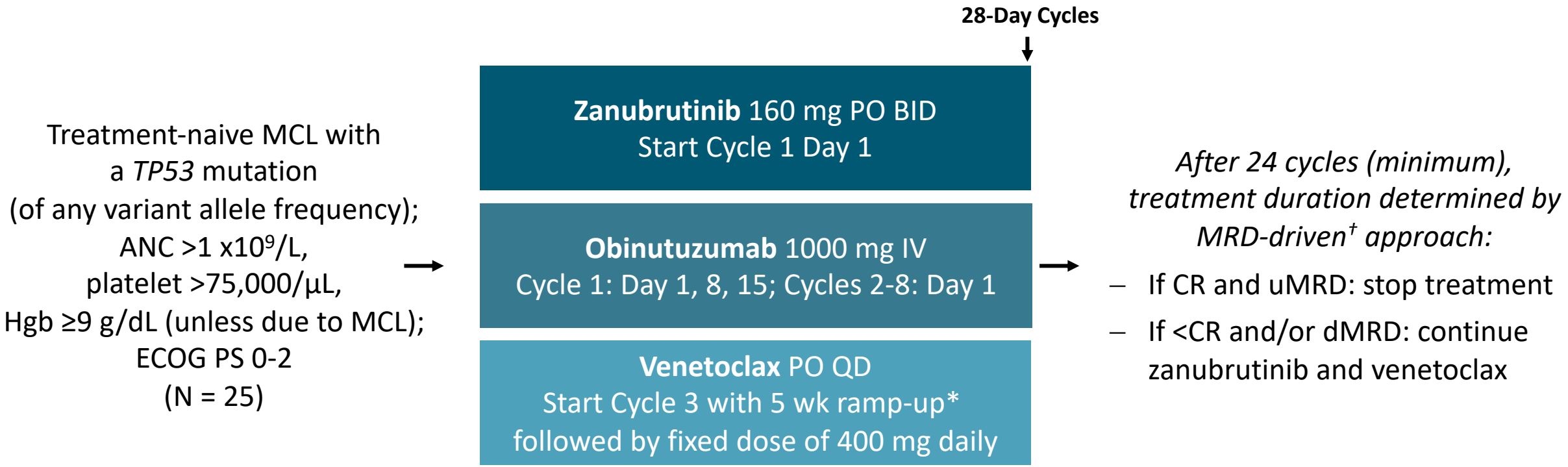
BOVen: Study Design

- Open-label, multicenter, single-arm phase II trial (median follow-up : 23.3 mo)



*5 wk ramp-up: 1 wk each of 20 mg, 50 mg, 100 mg, 200 mg, 400 mg. †MRD assessment in PB by Adaptive clonoSEQ®.

- **Primary endpoint:** 2-yr PFS
  - Treatment considered effective if ≥11 patients are progression-free at 2 yr

Kumar. ASH 2023. Abstr 738. NCT03824483.

BOVen: Baseline Characteristics

Characteristic	All Patients (N = 25)
Enrollment site, n (%)	
▪ MSKCC	13 (52)
▪ MGH	12 (48)
Median age, yr (range)	68 (60-73)
Male, n (%)	19 (76)
MCL histology, n (%)	
▪ Classical	15 (60)
▪ Non-nodal leukemic	5 (20)
▪ Blastic/blastoid	2 (8)
▪ Pleomorphic	3 (12)
Stage IV, n (%)	25 (100)
Ki-67 proliferation rate, n (%)	
▪ <30%	8 (38)
▪ ≥30% and <50%	6 (29)
▪ ≥50%	7 (33)
▪ Unknown	4

Characteristic	All Patients (N = 25)
MIPI classification, n (%)	
▪ Low	1 (4)
▪ Intermediate	7 (28)
▪ High	17 (68)
Bone marrow involvement, n (%)	22 (88)
Peripheral blood involvement,* n (%)	20 (80)
GI involvement,† n (%)	8 (32)
TP53 overexpression by IHC,‡ n (%)	
▪ Positive	18 (86)
▪ Negative	3 (14)
▪ Unknown	4
IgHV mutation, n (%)	
▪ Mutated	5 (28)
▪ Unmutated	13 (72)
▪ Unknown	7
17p deletion by FISH/SNP array	11 (44)

*Abnormal B-cells in PB detected via flow cytometry. †Evidence of MCL by endoscopy. ‡*TP53* expression defined as ≥30% tumor nuclei staining with strong intensity.

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Slide credit: clinicaloptions.com

BOVen: Response

Response, %	Complete Metabolic Response	Partial Metabolic Response	Overall
Cycle 3 Day 1	68	8	76
Best overall	88	8	96

Survival Outcome	All Patients (N = 25)
PFS	
▪ **2-yr, % (95% CI) (Primary Endpoint)**	**72 (56-92)**
▪ Median, mo	NR
OS	
▪ 2-yr, % (95% CI)	75 (58-93)
▪ Median, mo	NR
DFS	
▪ 2-yr, % (95% CI)	88 (76-100)
▪ Median, mo	NR

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BOVen: Safety

Treatment-Related AEs, n (%)	All Patients (N = 25)
Any AE	24 (96)
▪ Grade ≥3	12 (48)
Serious AE	12 (48)
Deaths	5 (20)
Hospitalizations	12 (48)

Serious AE, n (%)	All Patients (N = 25)					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Overall
COVID-19 infection	**-**	**3 (12)**	**-**	**-**	**2 (8)**	**5 (20)**
Atrial fibrillation	-	-	1 (4)	-	-	1 (4)
Fever	1 (4)	-	-	-	-	1 (4)
Lung infection	-	-	1 (4)	-	-	1 (4)
Nocardia	-	1 (4)	-	-	-	1 (4)
Organizing pneumonia	-	1 (4)	-	-	-	1 (4)
Maculopapular rash	-	-	1 (4)	-	-	1 (4)
Tumor lysis syndrome	-	-	-	1 (4)	-	1 (4)

- 3 patients at high risk for TLS at Cycle 3 required inpatient venetoclax ramp-up
  - No clinically significant TLS occurred during ramp-up
- Grade 4 TLS occurred in 1 patient after initial dose of obinutuzumab

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Rituximab, Bendamustine and Cytarabine Followed By Venetoclax (V-RBAC) in High-Risk Older Patients with Mantle Cell Lymphoma: A Phase 2 Study By the Fondazione Italiana Linfomi (FIL)

Carlo Visco, Valentina Tabanelli, Maria Vittoria Sacchi, Andrea Evangelista, Isacco Ferrarini, Maria Chiara Tisi, Anna Merli, Stefano Fiori, Vittorio Ruggero Zilioli, Alessandro Re, Claudia Castellino, Francesco Piazza, Paolo Corradini, Stefan Hohaus, Gerardo Musuraca, Francesca Gaia Rossi, Benedetta Puccini, Federica Cavallo, Filippo Ballerini, Roberta Sciarra, Alice Di Rocco, Annalisa Arcari, Carola Boccomini, Francesco Merli, Guido Gini, Monica Tani, Riccardo Bruna, Vincenzo Pavone, Andrés José María Ferreri, Armando Santoro, Caterina Patti, Giacomo Loseto, Marco Ladetto, Michele Merli, Michele Spina, Pier Luigi Zinzani, Piero Maria Stefani, Sara Usai, Stefano Pileri, Monica Balzarotti

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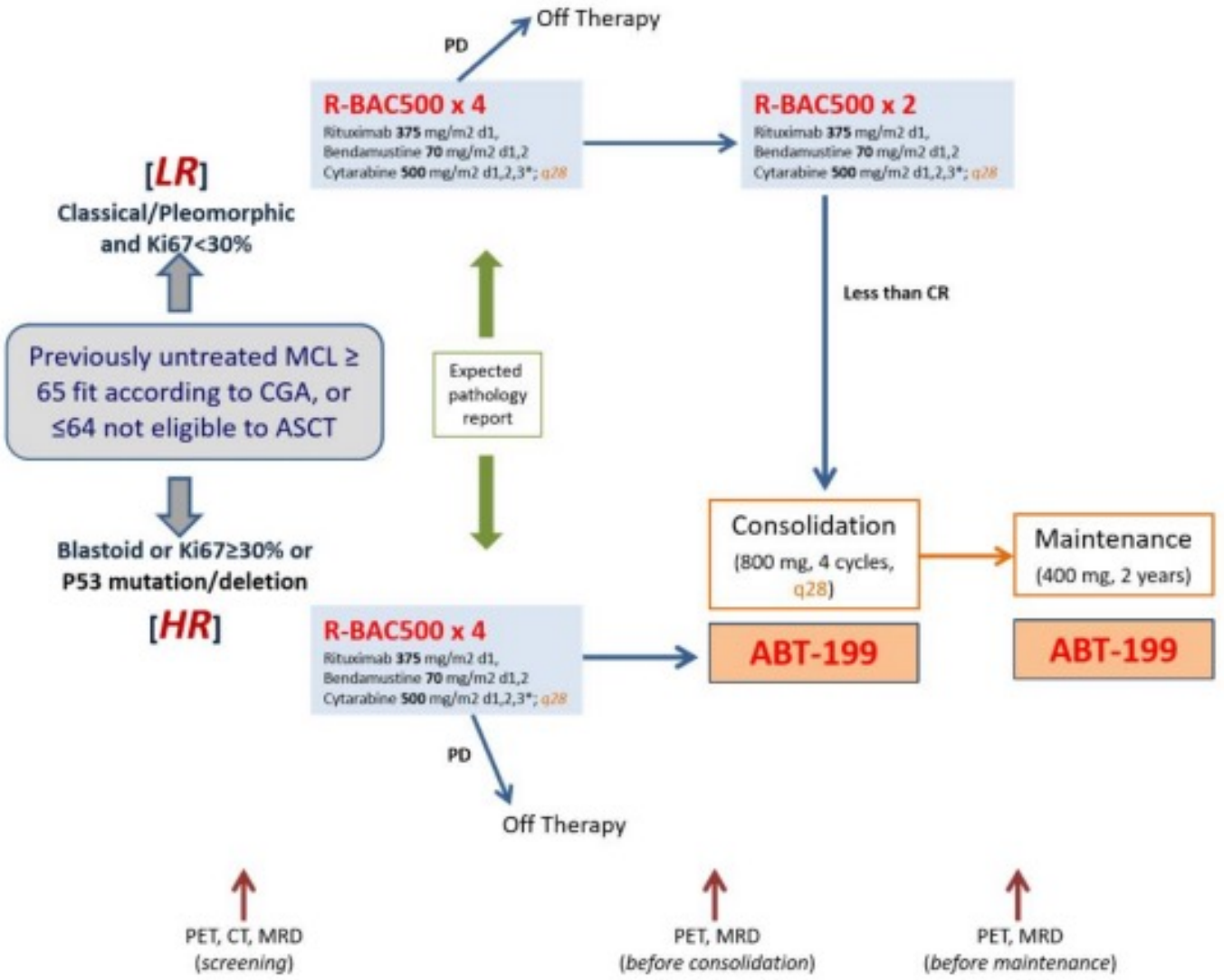

Off Therapy
PD
R-BAC500 x 4
Rituximab 375 mg/m2 d1,
Bendamustine 70 mg/m2 d1,2
Cytarabine 500 mg/m2 d1,2,3*; q28
R-BAC500 x 2
Rituximab 375 mg/m2 d1,
Bendamustine 70 mg/m2 d1,2
Cytarabine 500 mg/m2 d1,2,3*; q28
[LR]
Classical/Pleomorphic
and Ki67<30%
Less than CR
Previously untreated MCL ≥
65 fit according to CGA, or
≤64 not eligible to ASCT
Expected
pathology
report
Consolidation
(800 mg, 4 cycles,
q28)
Maintenance
(400 mg, 2 years)
Blastoid or Ki67≥30% or
P53 mutation/deletion
[HR]
R-BAC500 x 4
Rituximab 375 mg/m2 d1,
Bendamustine 70 mg/m2 d1,2
Cytarabine 500 mg/m2 d1,2,3*; q28
ABT-199
ABT-199
PD
Off Therapy
PET, CT, MRD
(screening)
PET, MRD
(before consolidation)
PET, MRD
(before maintenance)

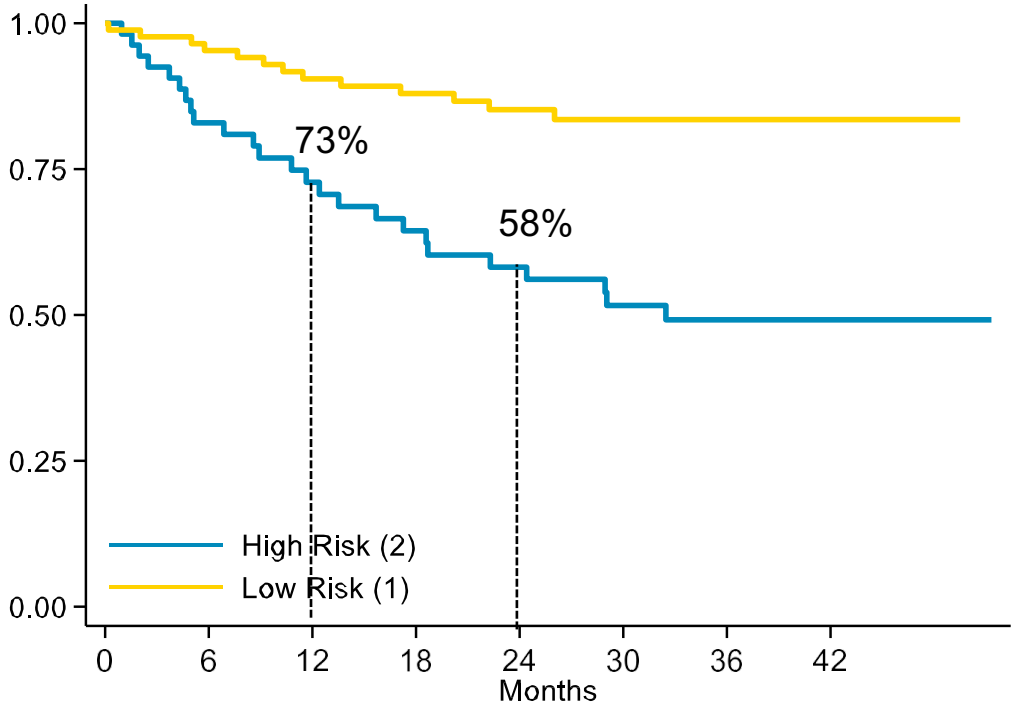
Patients allocation and disease characteristics

		Low Risk	High Risk	p-value
N		**86 (61%)**	**54 (39%)**	
Sex	Male	67 (78%)	40 (74%)	0.60
Age, median (IQR)		72 (69, 74)	73 (69, 76)	0.12
Systemic B symptoms	Present	16 (19%)	10 (19%)	0.98
Ann Arbor Stage	III-IV	82 (96%)	50 (94%)	0.53
ECOG Performance Status	0-1	83 (98%)	50 (92%)	0.35
	2	3 (3%)	4 (8%)	
Bone marrow involvement	Positive	60 (71%)	40 (74%)	0.51
LDH abnormal	Yes	18 (22%)	24 (46%)	0.003
MIPI score	Low (0-3)	9 (10.8%)	1 (1.9%)	0.017
	Intemediate (4-5)	43 (51.8%)	20 (38.5%)	
	High (6-11)	31 (37.3%)	31 (59.6%)	
SUV max of lesion	Median (IQR)	8.8 (6.9, 12.2)	10.9 (8.8, 15.6)	0.051

*Missing value: LDH and MIPI score in 5 patients; SUVmax in 60 patients; bone marrow was not performed in 8 patients (7 LR, 1 HR)

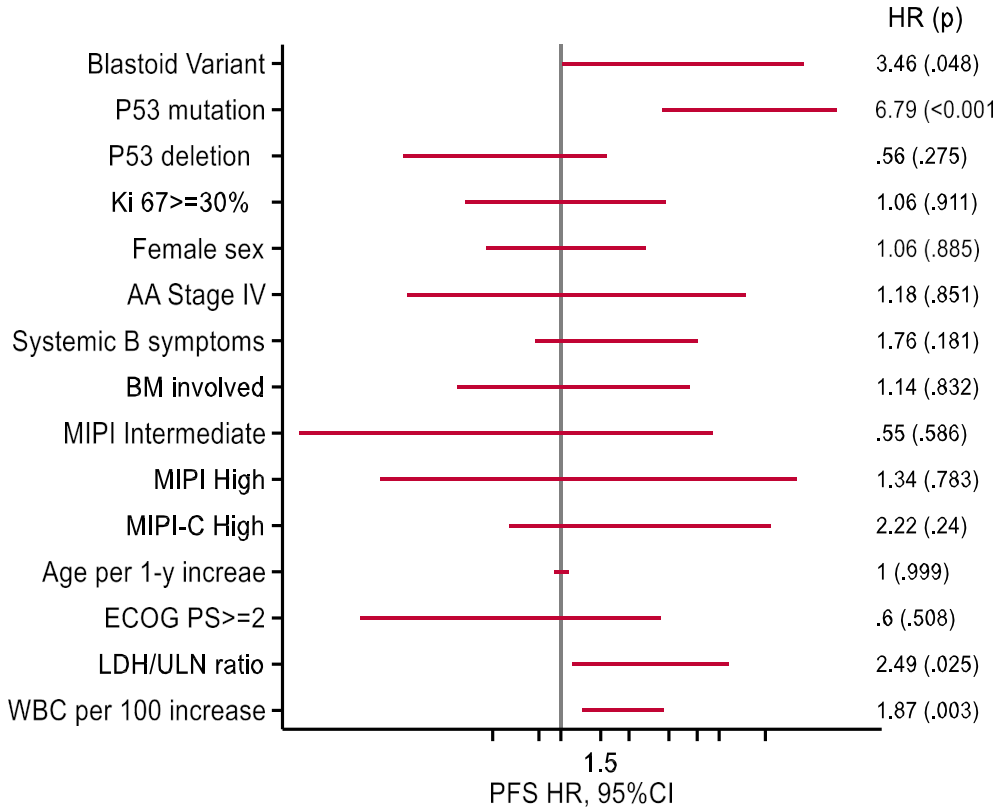
V-RBAC

Progression-free Survival by risk group



At risk:								
High Risk (2)	54	42	35	31	28	22	15	10
Low Risk (1)	86	81	73	70	56	42	26	13

Time	Survivor Function	Std. Error	[95% Conf.	Int.]
Low Risk (1)				
12	0.9046	0.0321	0.8182	0.9511
24	0.8519	0.0396	0.7534	0.9133
High Risk (2)				
12	0.7274	0.0624	0.5829	0.8289
24	0.5819	0.0701	0.4329	0.7046



MRD analysis

Timepoint	BM			PB		
	N	N pos	% pos	N	N pos	% pos
MRD-0 (Screening)	39	38	97.4%	38	37	97.4%
MRD-1 (before Consolidation therapy)	33	8	24.2%	35	7	20.0%
MRD-2 (before Maintenance therapy)	30	4	13.3%	31	3	9.7%
MRD-3 (half of Maintenance therapy)	-	-	-	19	0	0.0%
MRD-4 (end of Maintenance therapy)	10	1	10.0%	13	2	15.4%
MRD-5 (+6 month after Maintenance therapy)	-	-	-	7	0	0.0%
MRD-6 (Relapse/progression - before new treatment)	2	1	50.0%	2	0	0.0%

CONCLUSION

- The introduction of novel therapies has transformed the treatment of MCL.
- Preliminary results confirm the highly encouraging clinical activity of novel combinations, including in pts with high-risk features.
- Novel fixed-duration, chemotherapy-free combinations offer a convenient means for pts and have a manageable early safety profile.
- Advancing BTKi into the first-line setting offers potential benefits in chemotherapy-naïve pts.
- Incorporation of these potent novel therapies into frontline therapy may improve outcomes without sacrificing efficacy to reduce treatment complications.

Acalabrutinib with Rituximab As First-Line Therapy for Older Patients with Mantle Cell Lymphoma – a Phase II Clinical Trial

Preetesh Jain, Chi Young OK, Loretta J. Nastoupil, Jason Westin, Holly A Hill, Ranjit Nair, Swami P. Iyer, Ahmed Fetooh, Hun Ju Lee, Sairah Ahmed, Rashmi Kanagal-Shamanna, Fatima Z Jelloul, Luis Enri Malpica Castillo, Yang Liu, Yijing Li, Jovanny Vargas, Lei Feng, Maria Badillo, Selvi Thirumurthi, Guofan Xu, Anita Deswal, Cezar Iliescu, Vinh Quang Nguyen, Guilin Tang, Keyur P. Patel, Francisco Vega, L. Jef Medeiros, Michael L. Wang, Christopher R. Flowers

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- 50 pts, med age 69, lots of extranodal
- ORR 94% (CR 90%)
- 2-yr PFS 92%, OS 96%
- 9 pts OFF STUDY- (5 AEs, 3 PD, 1 personal choice)

-The most common all-grade toxicities were fatigue (82%), myalgia (64%), headache (38%), bruising (28%) and <1% were grade 3 or higher.