Transforming Relapsed/Refractory MCL Exploring New Options for Your Patients

Presenting Faculty

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Content Outline

- Part 1: The evolving landscape of treatment options for R/R MCL
  (expert commentary)

- Part 2: Case Studies
  (expert discussion regarding patient case and choice selection)
  - Case Study 1 (R/R with or without prior BTKi exposure)
  - Case Study 2 (Treatment sequencing)
  - Case Study 3 (Mitigating a treatment-emergent event)

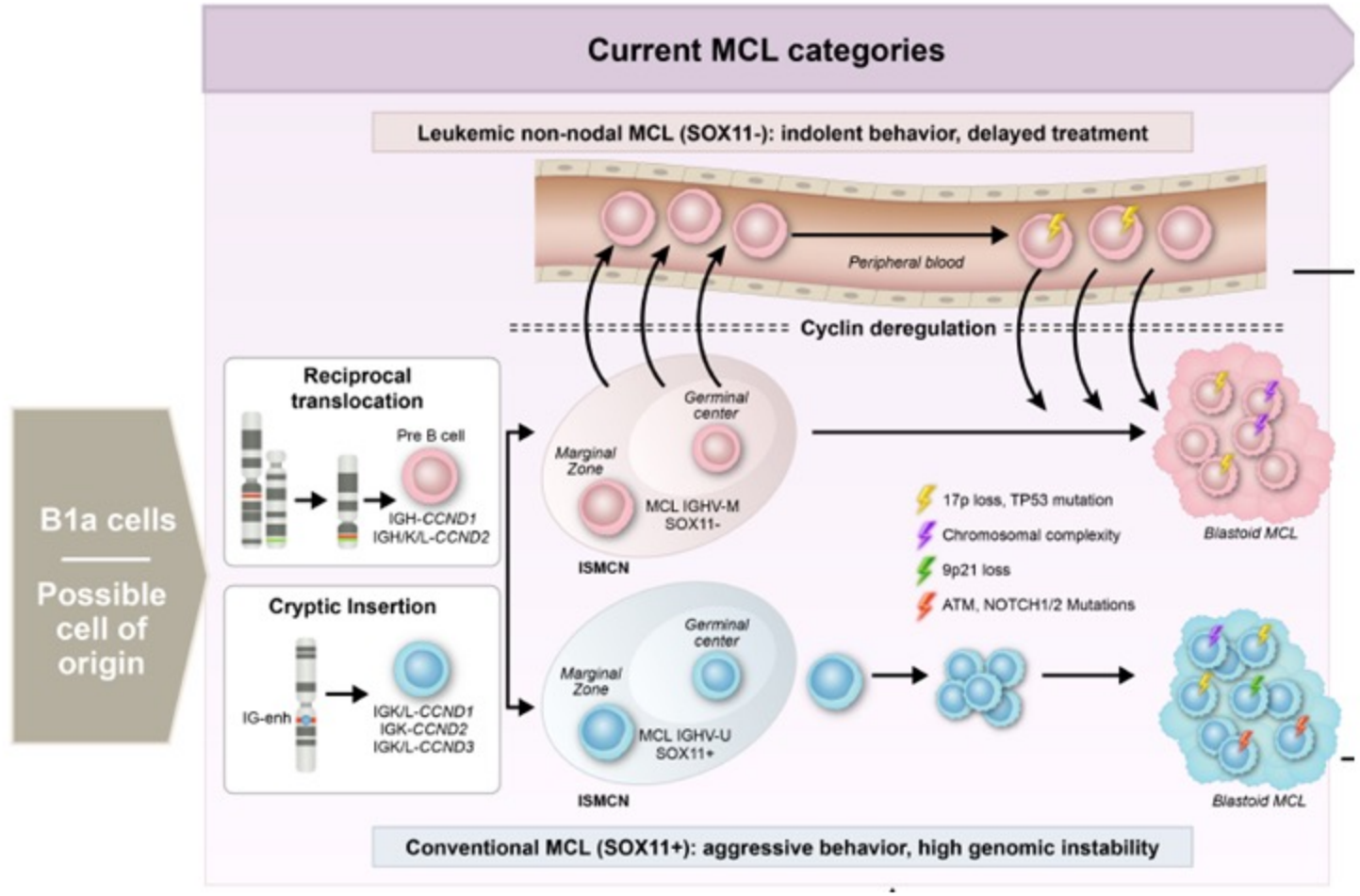
- Part 3: The importance of collaboration between providers and patients
  (expert commentary)

Educational Objectives

- Implement appropriate treatment options across multiple lines of therapy
- Evaluate the use of emerging therapies, including their potential benefits and risks
- Optimize communication between providers and patients to improve overall care and outcomes

Mantle Cell Lymphoma Presentation and Pathogenesis

- Rare, aggressive B cell non-Hodgkin's lymphoma
  - 5%–7% of malignant lymphoma in Western Europe
- Varied clinical presentation and heterogeneous disease course
  - Ranges from an indolent non-nodal leukemic variant to a blastoid version that is highly proliferative
- Historically poor prognosis
  - Risk stratification at the time of diagnosis is critical



1. Dreyling et al. Ann Oncol 2017(Supplement 4):iv62-iv71. 2. Jain et al. American J Hematol 2022. 3. Wilson et al. Bf J Haem 2023.

Clinical, Molecular and Histological Features of MCL at Diagnosis

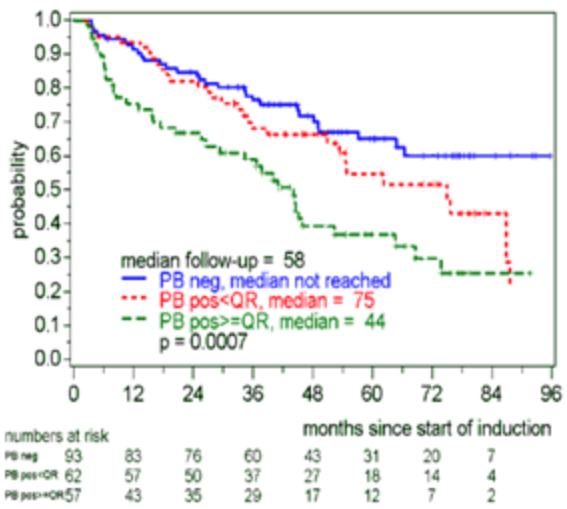
	Ultra-high-risk MCL	High-risk MCL	Standard risk classic/nodular MCL	Non-nodular indolent MCL
Molecular features	TP53 mutated with other high-risk gene mutations (KMT2D, NSD2,CCND1, NOTCH1, CDKN2A, NOTCH2, SMARCA4)	High karyotype complexity TP53 mutated with high variant allele frequency (>10%) or del(17p) by FISH	Normal karyotype	Low karyotype complexity
	Few or no mutations of IGHV			Hypermutated IGHV
	High expression of SOX11	High expression of SOX11	High expression of SOX11	Very low or no expression of SOX11
Histology	De novo blastoid/pleomorphic histology K-i67 >30% issues with blastoid/ pleomorphic histology	Blastoid/pleomorphic histology Ki-67 >30% in classic histology	Classical histology Ki-67 <30%	Restricted to mantle zone of lymphoid follicles However, blood and spleen involvement may be noted
Clinical features	Bulky disease, clinically aggressive course	Bulky disease, clinically aggressive course	Bulky or non-bulky disease	Low-risk MIPI Leukemic non-nodal disease

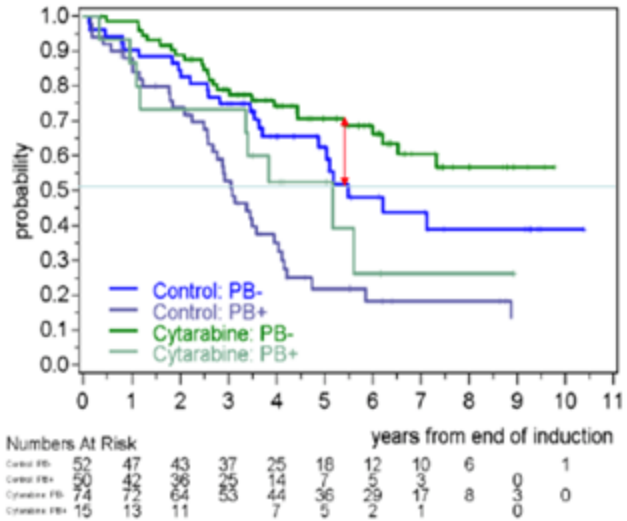
1. Jain P et al. *Am J Hematol*. 2019(94):710–725. 2. Fernandez V et al. *Cancer Res*. 2010(70):1408–1418. 3. Sakhdari A. *Ann Diagn Patho*. 2019(41):38–42.

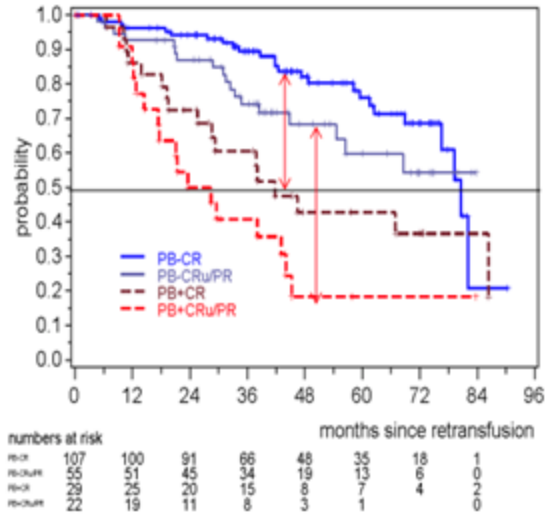
The Role of MRD in MCL: What Can We Learn From Current Data?

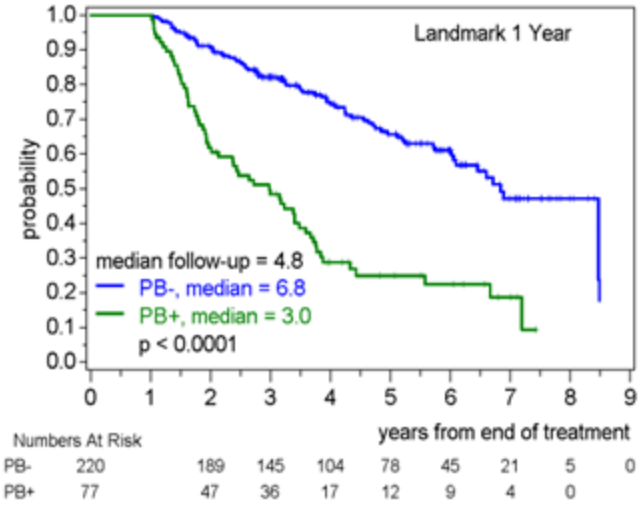
MRD for Prognostication

Mid induction → End of induction → Post ASCT → During maintenance



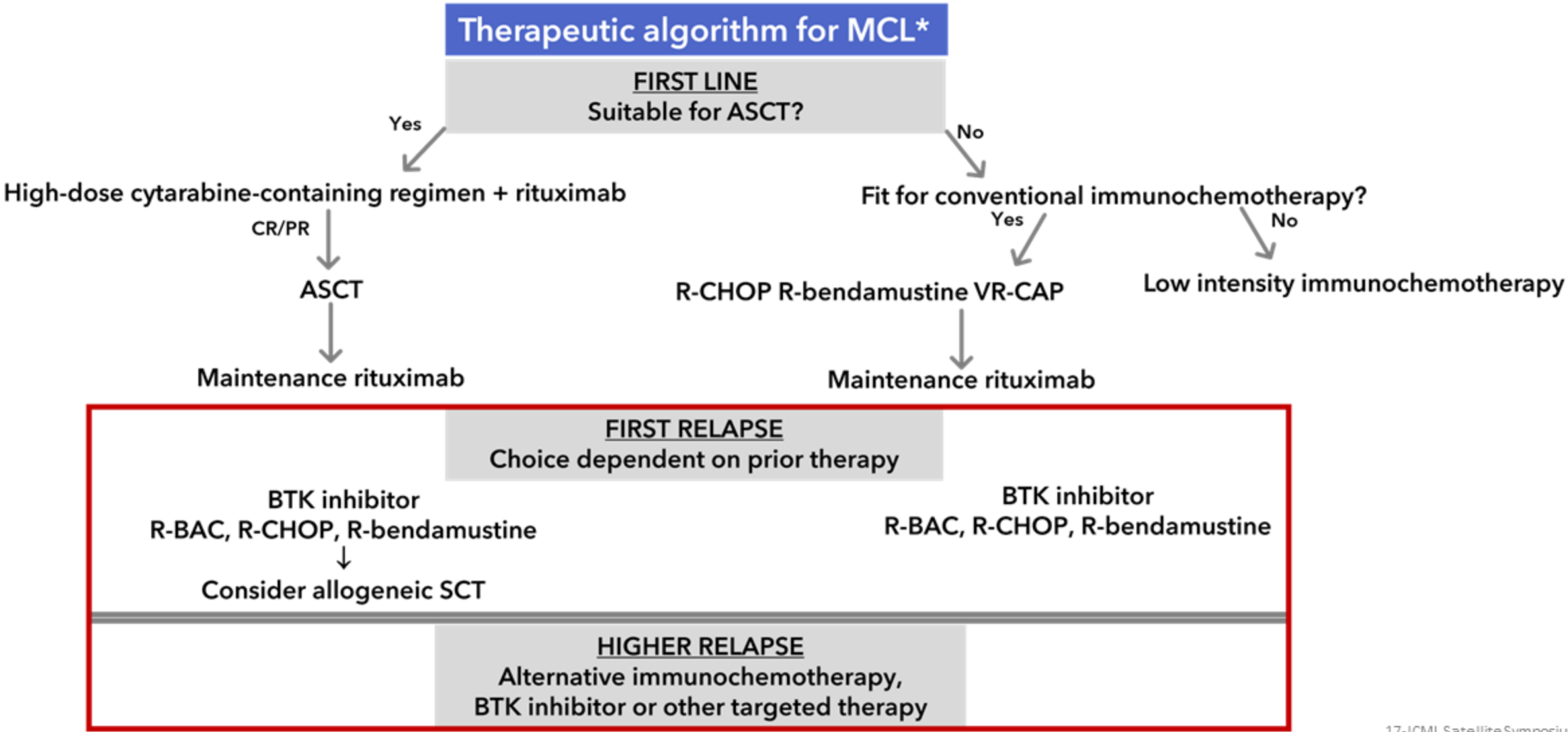






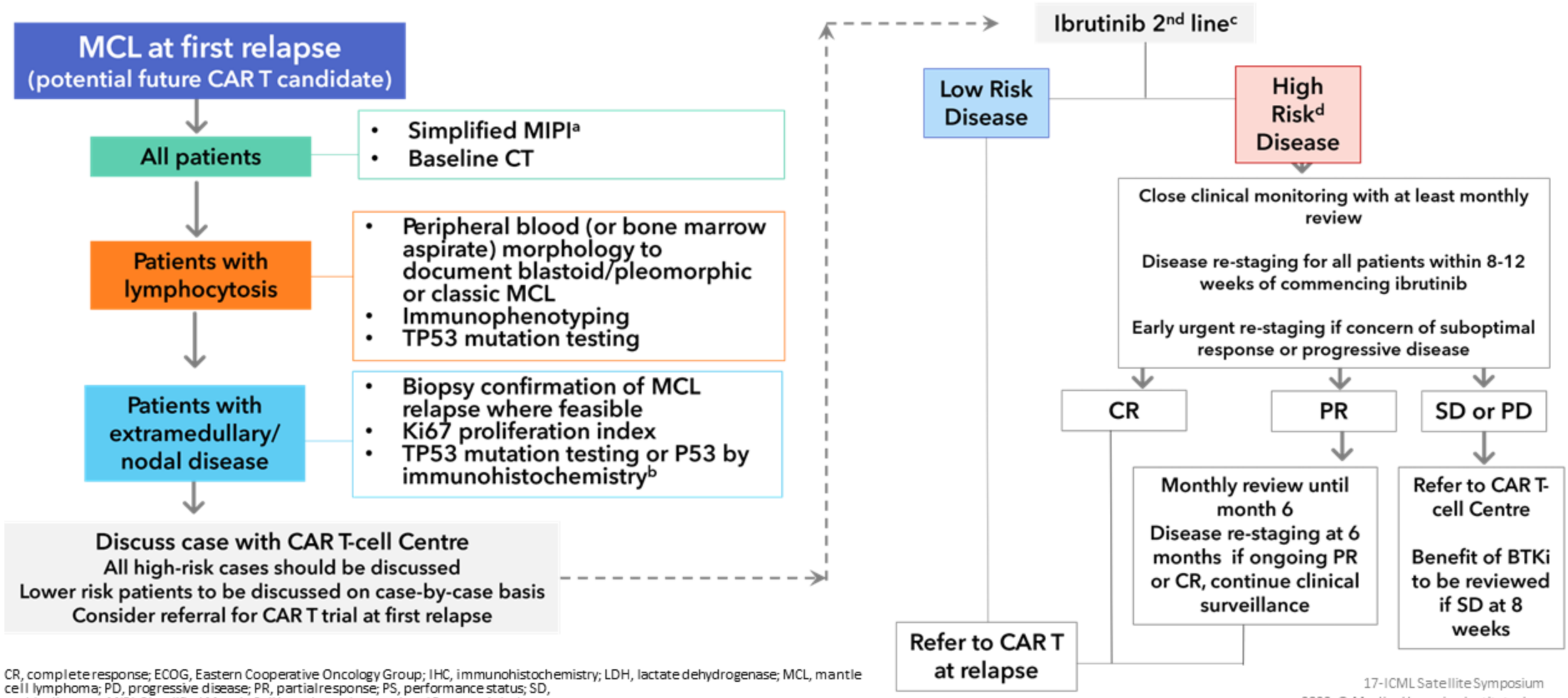
Pott et al. The European MCL Network. 2016, 2018, 2023.

British Society for Hematology Clinical Practice Guidelines



McKay P et al. *Br J Haematol*. 2018(182):46-62.

British Society for Hematology Clinical Practice Guidelines (Addendum)

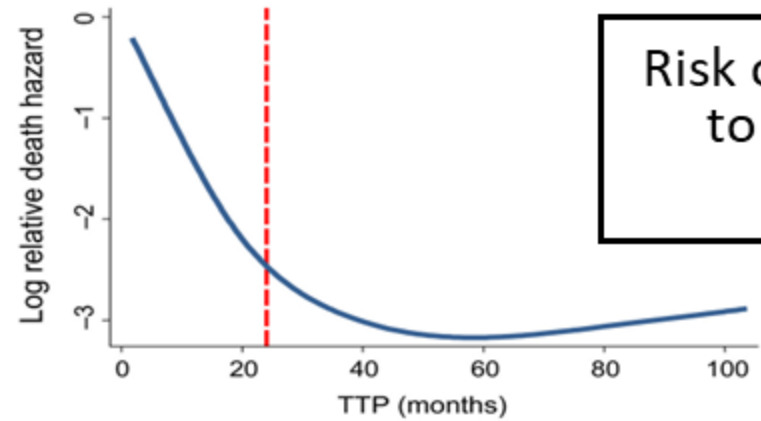


CR, complete response; ECOG, Eastern Cooperative Oncology Group; IHC, immunohistochemistry; LDH, lactate dehydrogenase; MCL, mantle cell lymphoma; PD, progressive disease; PR, partial response; PS, performance status; SD, stable disease; sMIPI, Simplified Mantle Cell Lymphoma International Prognostic Index.

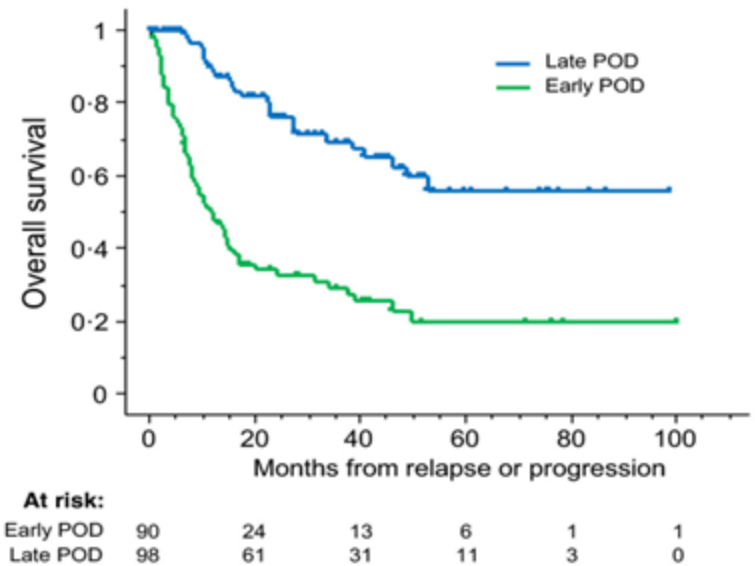
O'Reilly MA et al. Br J Haematol. 2022(199):40-44.

Early vs. Late Relapse of MCL: Impact on Patient Survival

- Early relapse after treatment induction is associated with poor survival outcomes
- Identification of patients with MCL who are likely to relapse early or not respond to initial induction is imperative
  - Biological subsets of MCL
  - Prospective clinical trials to assess high-risk groups



Risk of death and time to first relapse or progression



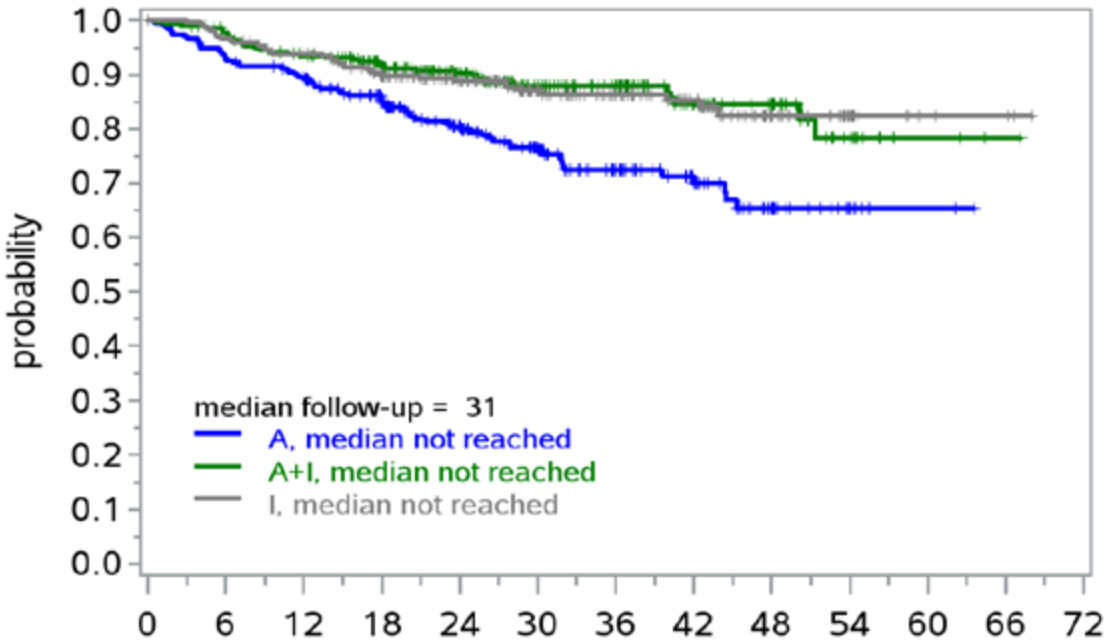
OS-2 according to early POD vs late POD

MCL, mantle cell lymphoma; OS, overall survival; POD, progression of disease.

1. Visco C et al. Br J Haematol. 2019(5):940-944. 2. Cabirta A et al. Blood. 2021(Supplement 1):1357.

TRIANGLE and SHINE Studies

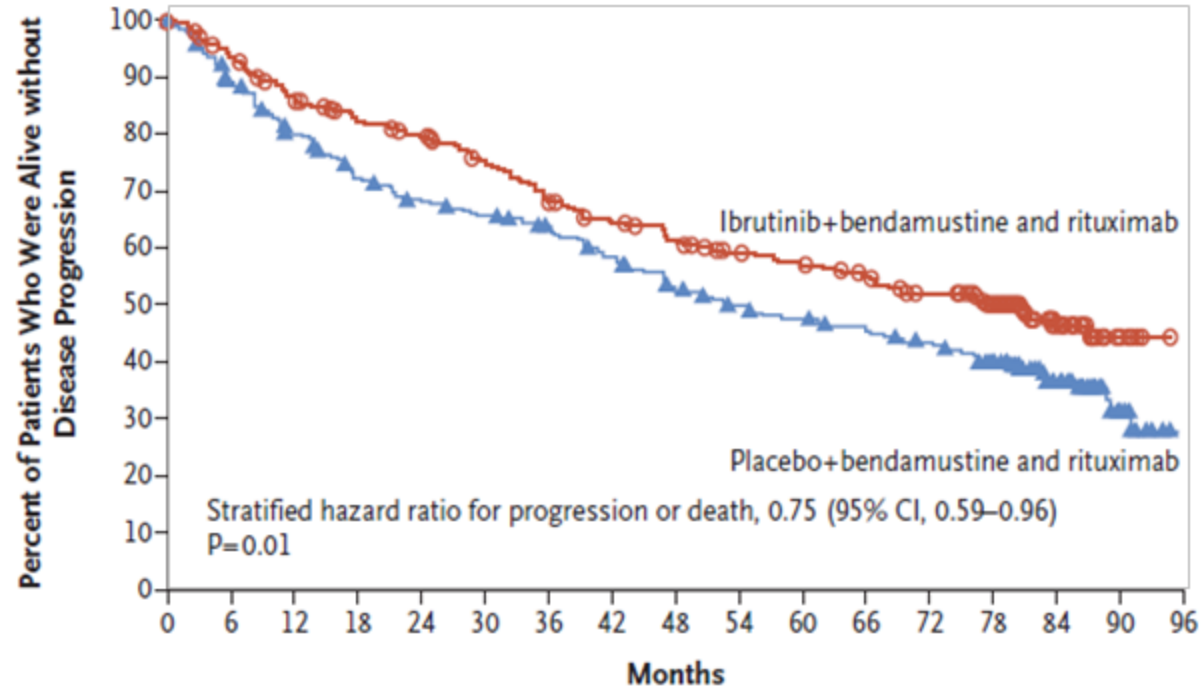
TRIANGLE:
Failure Free Survival



Numbers At Risk

A	288	252	237	206	162	126	85	54	27	12	2	0
A+I	292	270	253	226	184	137	109	65	40	17	3	1
I	290	269	257	229	180	133	100	68	34	16	4	3

SHINE:
Progression Free Survival



No. at risk

I+B and R	261	228	207	191	182	167	152	139	130	120	115	106	95	78	39	11	0
Placebo+B and R	262	226	199	177	166	158	148	135	119	109	103	98	90	78	41	11	0

A, Ara-C; B, bendamustine; CI, confidence interval; I, ibrutinib; No, number.

1. Dreyling M et al. Presented at ASH 2022. 2. Wang ML. *N Engl J Med*. 2022;30(26):2482-2494.

Factors to Consider When Choosing a Therapy For R/R MCL

Age

Performance status

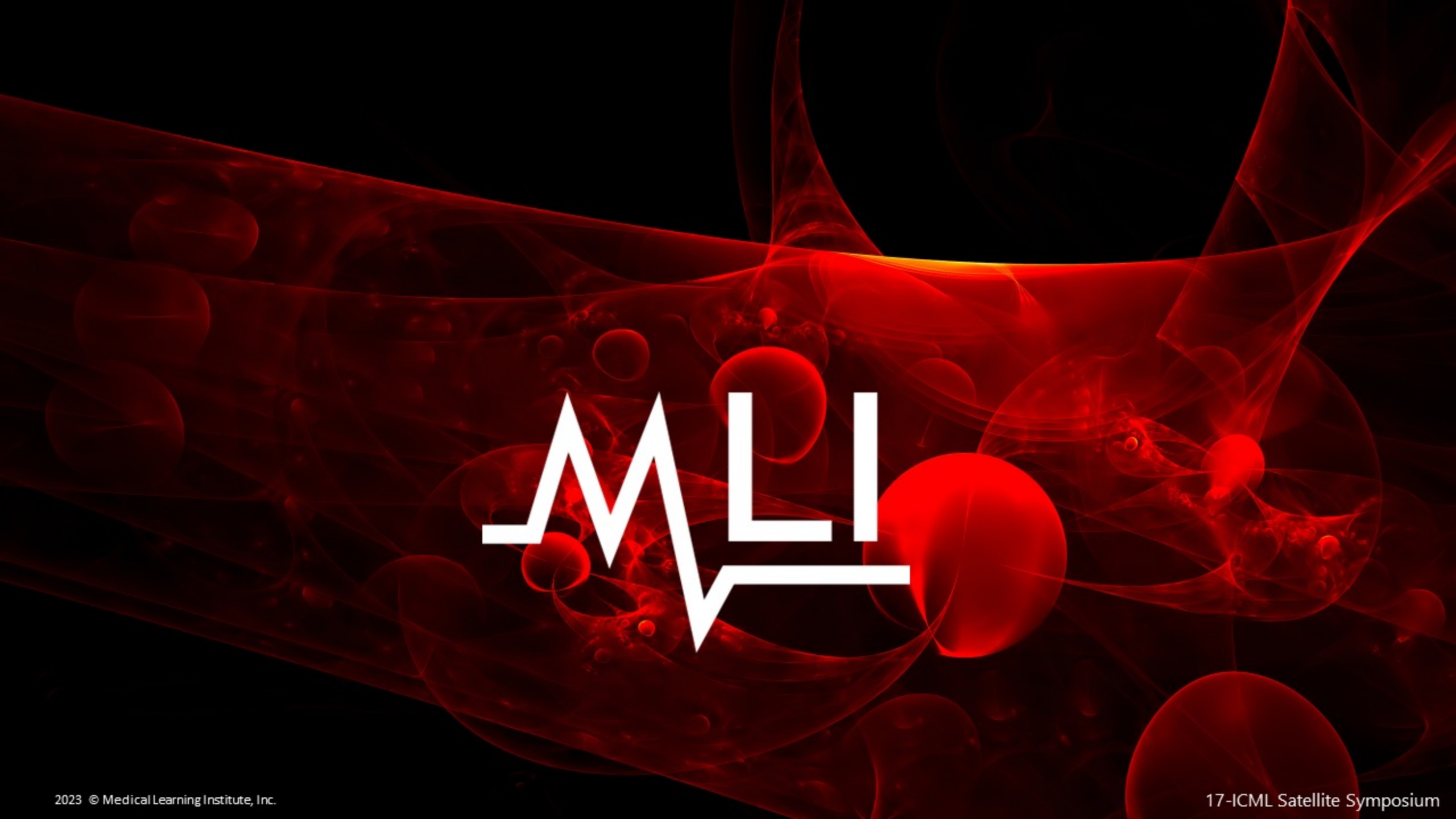
Comorbidities

Tumor biology and histologic subtype

Level of bone marrow reserve

Agents used in first line

Duration of response to 1L therapy



Patient Cases with R/R MCL

Mr. Åkerfeldt

69-year-old fit male from Sweden

Ms. Stanić

58-year-old fit female from Croatia

Mr. Dupont

78-year-old frail male from France

Mr. Åkerfeldt
69-year-old fit male from Sweden
Retired carpenter

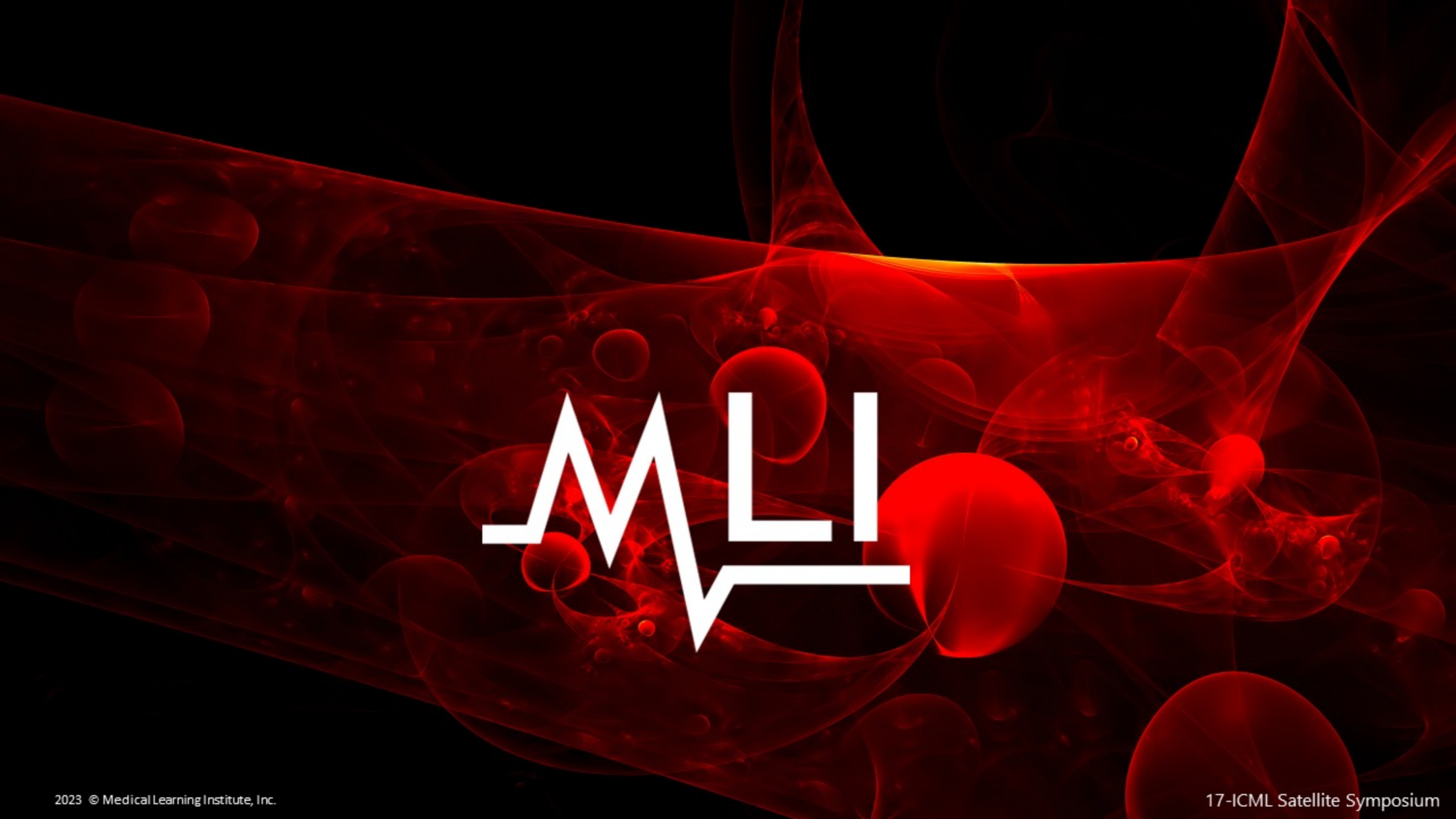
- **Medical History**
  - Hypertension (controlled on metoprolol)
  - No family history of cancer
  - Enjoyed cycling, hiking, and walking; continued activities until relapse
- **Initially diagnosed with stage II indolent extranodal localization of MCL**
  - IGHV mutated
  - TP53 not performed
  - SOX11 negative
  - Classic histology
  - Low proliferation index by Ki-67
- **Watch and wait for 2 years; 66-years-old when received initial induction of bendamustine and rituximab with rituxumab maintenance and relapsed 3 years after start**
- **Current symptoms:**
  - Splenomegaly (5 cm below right costal margin)
  - GI involvement (25% via lower endoscopy; received radiotherapy)
  - Moderately elevated LDH (290 U/L)
  - ECOG PS: 0
- **Subjective symptoms:**
  - Fatigue
  - GI discomfort

Ms. Stanić
58-year-old fit female from Croatia
Marketing Executive

- **Medical History**
  - S/P bilateral salpingo-oophorectomy age 47
  - Mother history of ovarian cancer; brother history of glioma
  - Marathon runner prior to diagnosis; continues to be an avid walker
- **Initially diagnosed with stage III indolent, extranodal localization of MCL**
  - IGHV mutated
  - TP53 unmutated
  - SOX11 negative
  - Low proliferation index by Ki-67
  - Classic histology
  - Chromosomal translocation of (11;14)(q13;32)
- **54 years old when received initial induction of rituximab and cytarabine with ASCT consolidation and rituximab maintenance; relapsed 4 years after start and received ibrutinib and became intolerant**
- **Current symptoms:**
  - Lymphadenopathy (2 cm nodes on neck and axilla)
  - Neuropathy
  - Moderate lower back pain
  - ECOG PS: 1
- **Subjective symptoms:**
  - Weakness and loss of reflexes
  - Pain

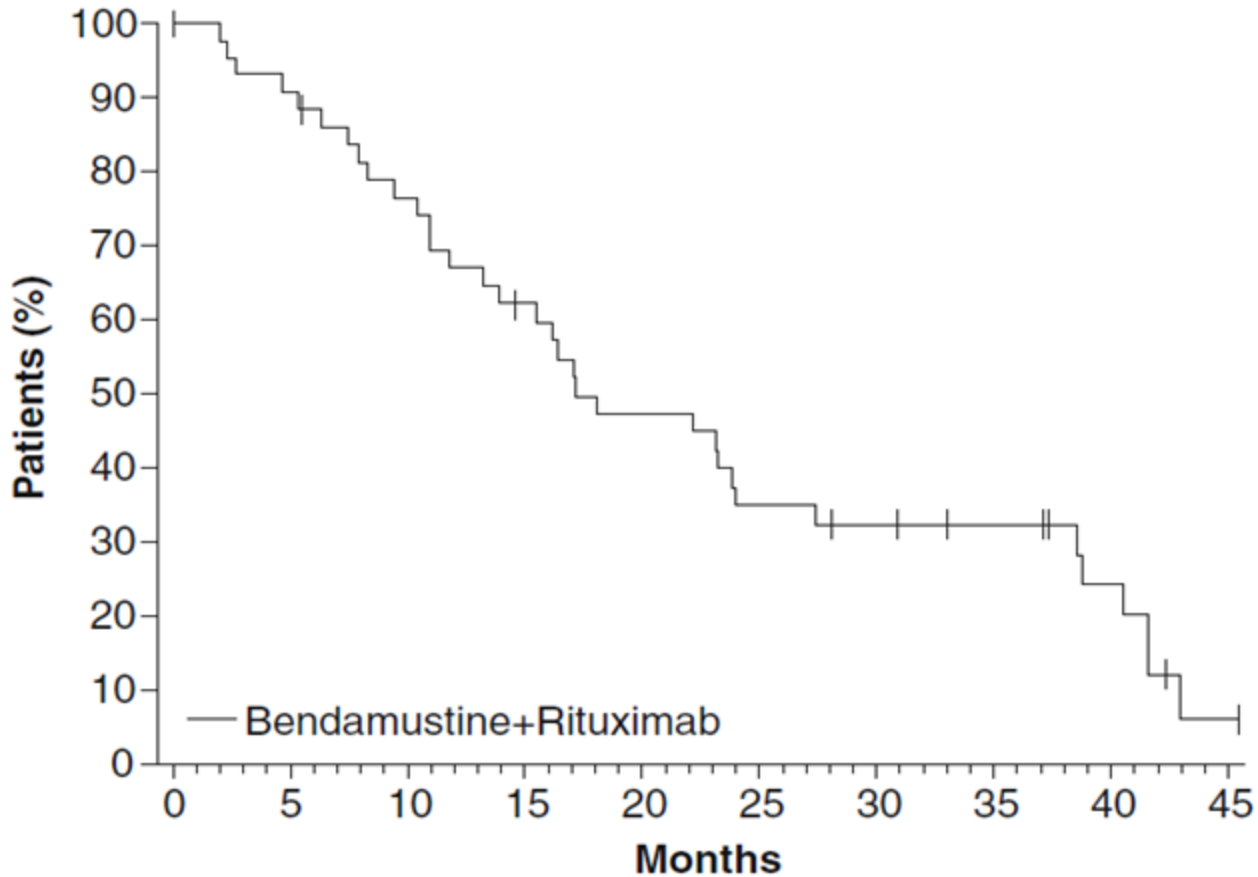
Mr. Dupont
78-year-old frail male from France
Retired architect, currently a volunteer gardener

- **Medical History**
  - Hypertension (controlled on furosemide)
  - Type 2 diabetes (controlled on metformin)
  - S/P prostatectomy at age 69 for benign prostatic hyperplasia
  - Father history of melanoma; mother, sister, and 2 aunts history of breast cancer
  - Former smoker; prior to relapse enjoyed attending grandchildren's sporting events and gardening
- **Initially diagnosed with stage IV aggressive, nodal MCL**
  - IGHV unmutated
  - TP53 mutated; TP53 deletion positive
  - SOX11 positive
  - Blastoid histology
  - High proliferation index by Ki-67
- **Relapsed 6 months after initial induction of R-CHOP**
- **Current symptoms:**
  - Lymphadenopathy (3 cm nodes on axillae)
  - Lymphocytosis (3,000/mcL)
  - Elevated LDH (350 U/L)
  - Elevated PSA (4 ng/ml)
  - Rapid weight loss and chronic fatigue
  - ECOG PS: 2
- **Subjective symptoms**
  - Fatigue
  - Loss of appetite



Bendamustine + Rituximab

Phase II, multicenter, open-label, single-arm, trial evaluating the efficacy of **bendamustine + rituximab (n=45)** for patients with R/R MCL

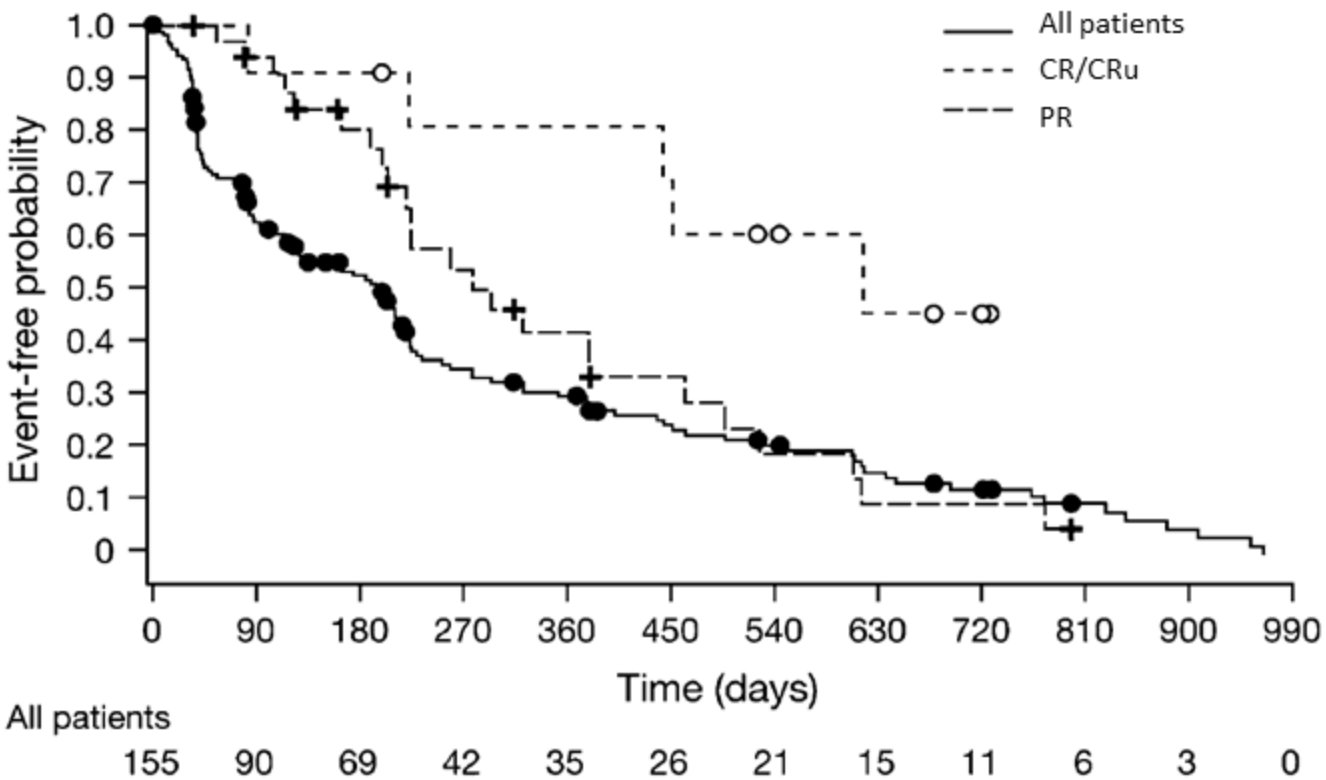


PFS	Median PFS (95% CI), mo
Median PFS	17.2 (0.03 – 45.37)
1-year PFS	67.0

B-R; bendamustine + rituximab; CI, confidence interval; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.
Czuczman MS et al. *Ann Hematol*. 2015;94(12):2025-2032.

Bortezomib Monotherapy

Phase II, multicentre, time-to-event PINNACLE study evaluating the efficacy of **bortezomib (n=155)** in patients with R/R MCL



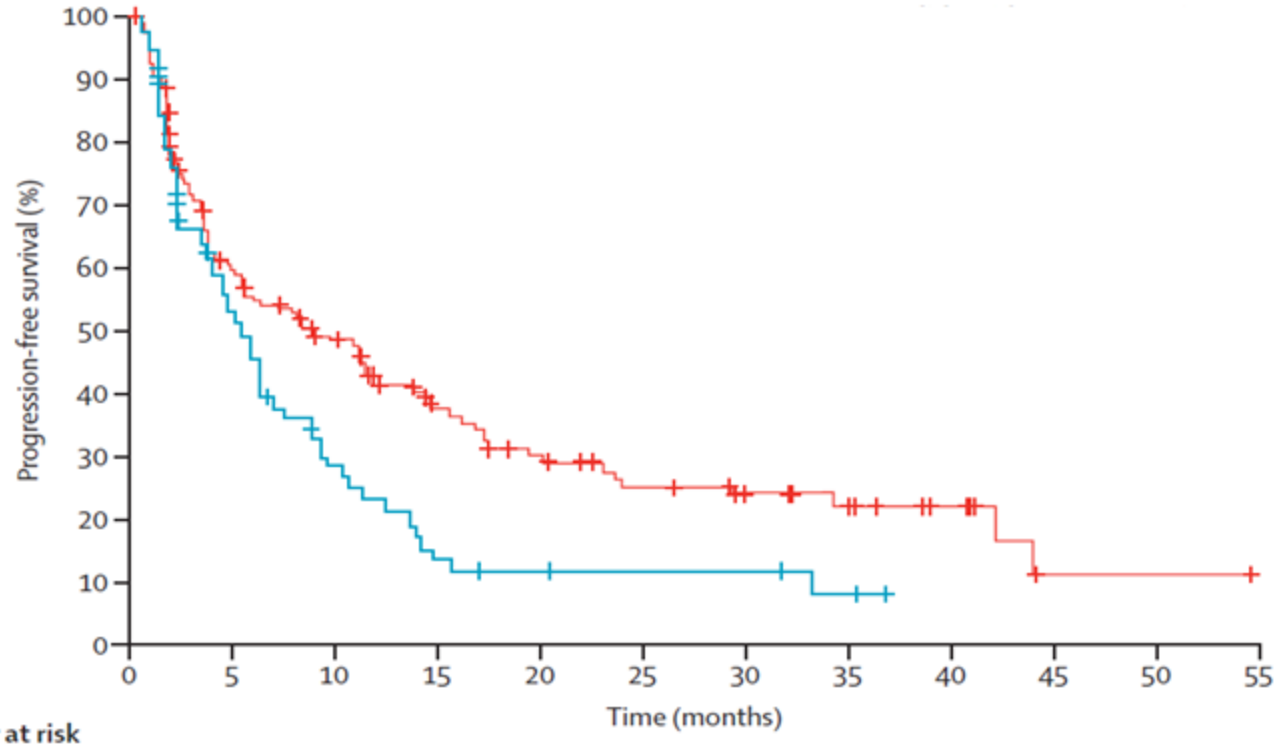
PFS	Median PFS (95% CI), mo
All patients	6.5 (4.0 – 7.3)
CR/CRu (n=11)	20.3 (14.6 – NE)
PR (n=34)	9.7 (7.2 – 15.2)

CI, confidence interval; CR, complete response; CRu, unconfirmed complete response; MCL, mantle cell lymphoma; mo, months; NE, not estimatable; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory.

Goy A et al. *Ann Oncol*. 2009(3):520-525.

Lenalidomide Monotherapy (1/2)

Phase II, randomized, multicenter, SPRINT study evaluating the efficacy of **lenalidomide (n=170)** vs **investigators choice (n=84)** in patients with R/R MCL



Number at risk												
Lenalidomide group	170	86	63	36	27	20	16	12	7	1	1	0
Investigator's choice group	84	31	15	7	5	4	4	2	0	0	0	0

PFS	Median PFS (95% CI), mo
Lenalidomide	8.7 (5.5 – 12.1)
Investigator's choice	5.2 (3.7 – 6.9)
HR (95% CI)	0.6 (0.4 – 0.8)

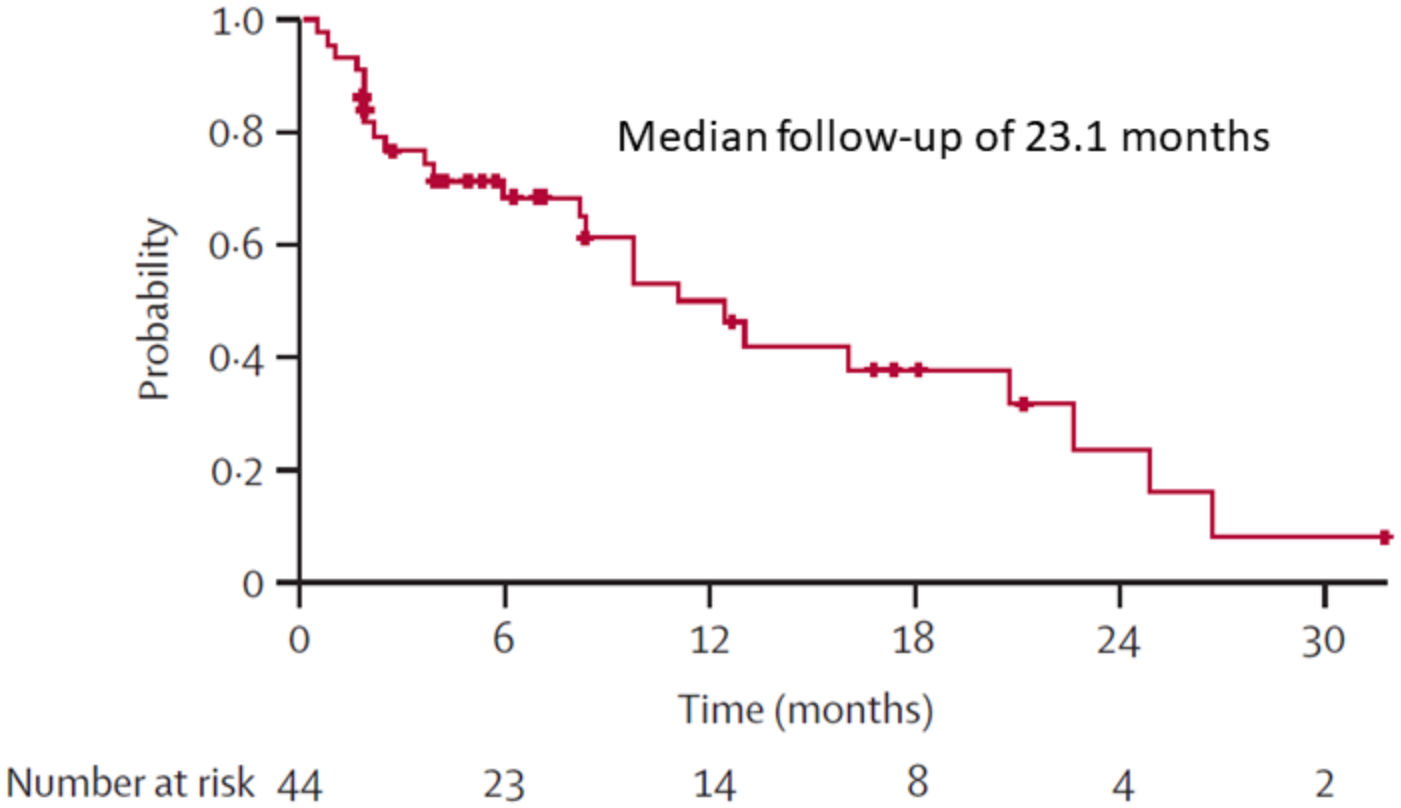
Investigator's choice included rituximab, gemcitabine, fludarabine, chlorambucil, or cytarabine

CI, confidence interval; HR, hazard ratio; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.

Trněný M et al. *Lancet Oncol*. 2016(3):319-331.

Lenalidomide + Rituximab (2/2)

Phase I/II, single-arm, open-label trial at a single-arm, evaluating the efficacy of **lenalidomide + rituximab (n=52)** in patients with R/R MCL



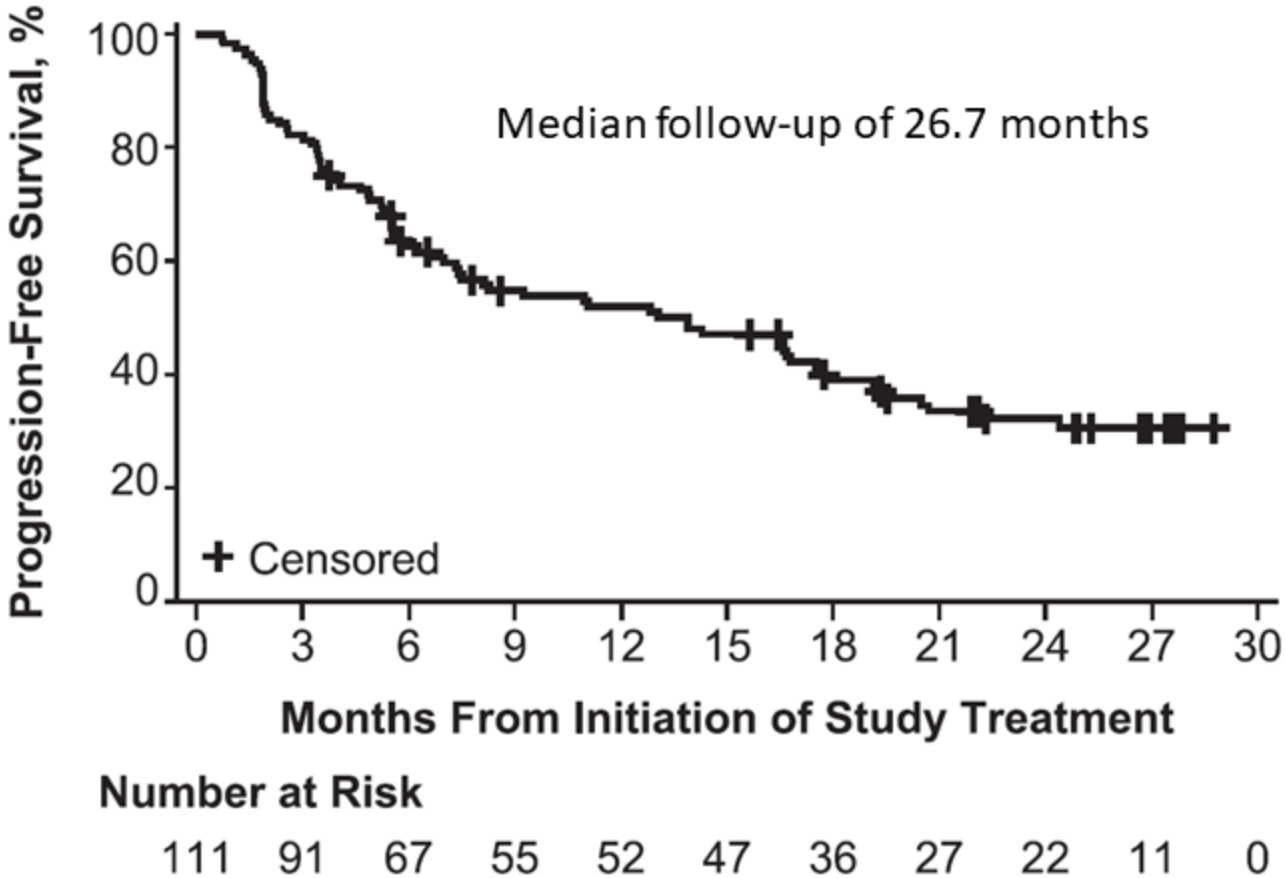
PFS	Median PFS (95% CI), mo
L-R	11.1 (8.3 – 24.9)

CI, confidence interval; L-R, lenalidomide + rituximab; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.

Wang M et al. *Lancet Oncol*. 2012(7):716-723.

Ibrutinib Monotherapy (1/7)

Phase II, open-label, multicenter study evaluating the efficacy of single agent **ibrutinib (n=111)** in patients with R/R MCL

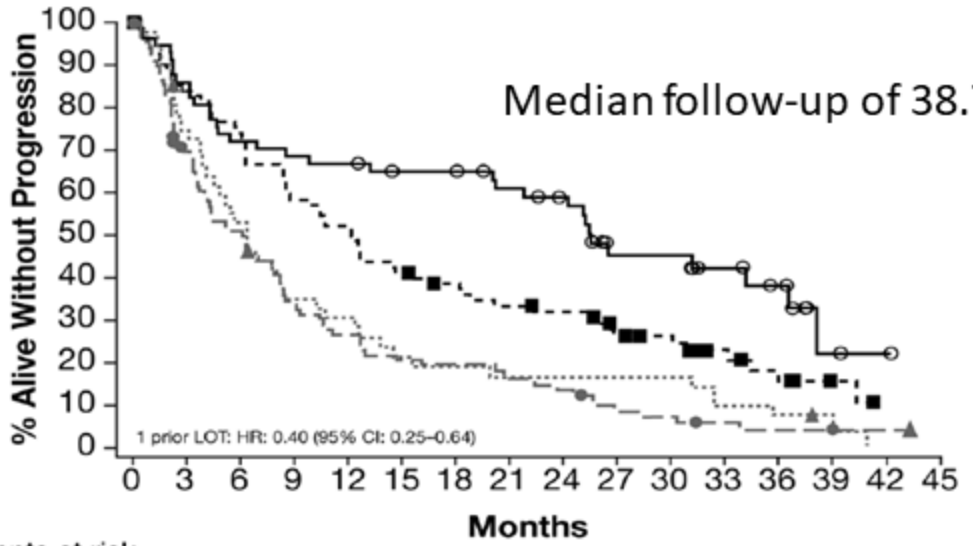


PFS	Median PFS (95% CI), mo
All treated patients	13.0 (7.0 – 17.5)

CI, confidence interval; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.
Wang M et al. *Blood*. 2015(6):739-745.

Ibrutinib vs Temsirolimus (2/7)

3-year follow-up, randomized, international, open-label RAY study evaluating the efficacy of **ibrutinib (n=139)** vs **temsirolimus (n=141)** in patients with R/R MCL



Median follow-up of 38.7 months

Patients at risk

Ibrutinib 1 prior	57	49	41	39	38	34	33	30	27	15	15	11	8	2	1	0
Temsirolimus 1 prior	50	34	24	15	13	9	8	7	7	7	7	4	3	1	1	0
Ibrutinib >1 prior	82	68	59	47	42	33	29	25	23	17	15	10	6	3	0	0
Temsirolimus >1 prior	91	59	43	27	22	17	16	13	11	6	5	3	2	1	0	0

PFS	Median PFS, mo
Ibrutinib	15.6
Temsirolimus	6.2
HR (95% CI)	0.45 (0.4 – 0.6)

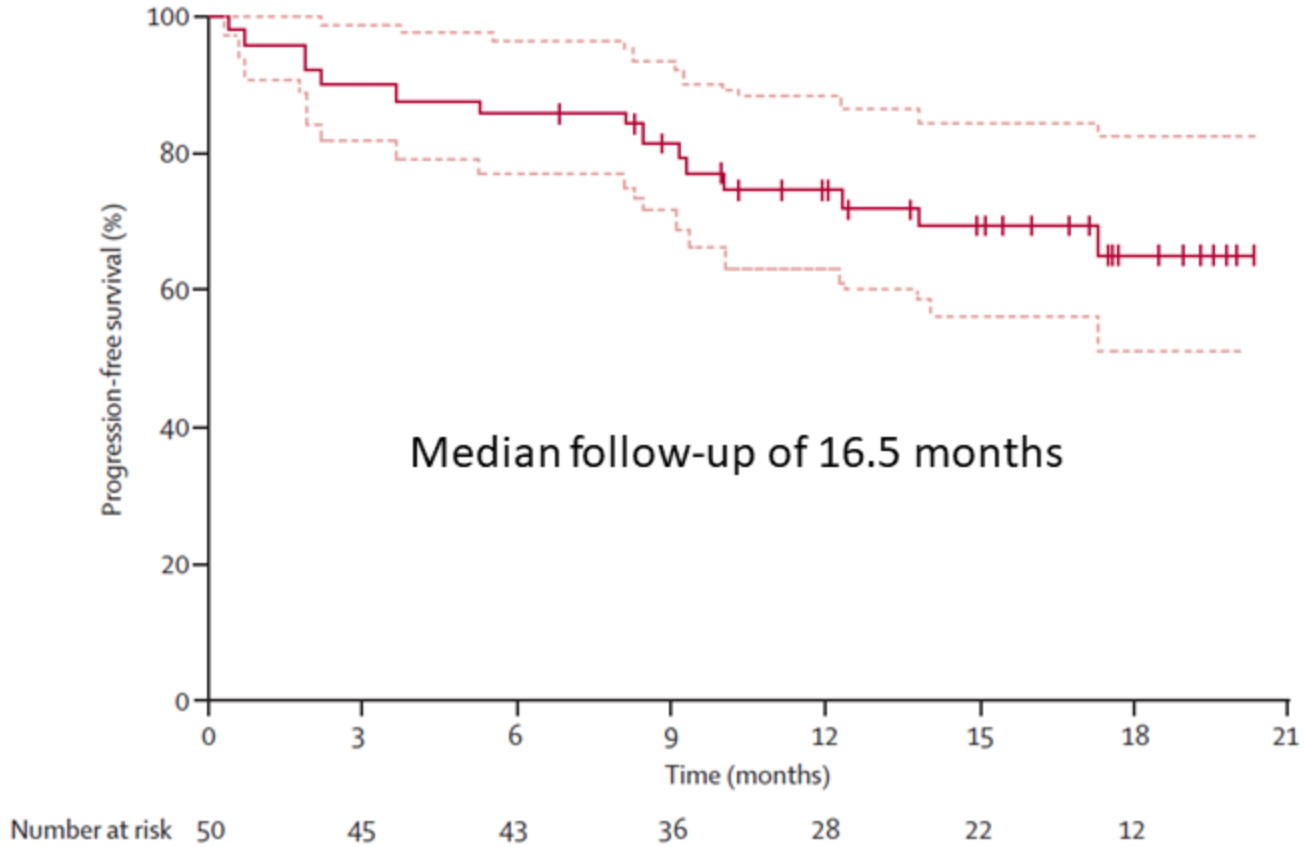
Ibrutinib 1 prior
Temsirolimus 1 prior
Ibrutinib >1 prior
Temsirolimus >1 prior

CI, confidence interval; HR, hazard ratio; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.

Rule S et al. *Leukemia*. 2018(8):1799-1803.

Ibrutinib + Rituximab (3/7)

Phase II, single-center, open-label study evaluating the efficacy of ibrutinib + rituximab (n=50) in patients with R/R MCL

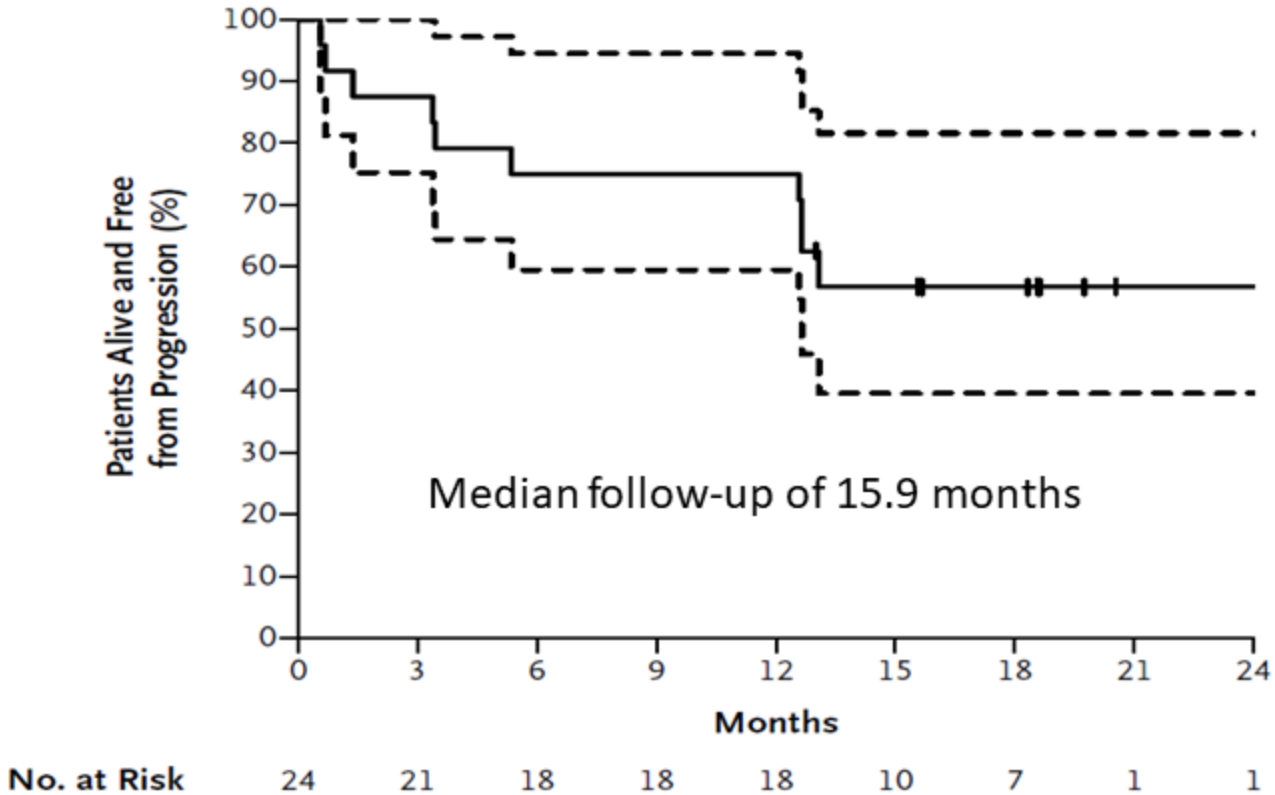


PFS	Median PFS (95% CI), mo
12-month PFS	75.0 (63.0 – 88.0)
15-month PFS	69.0 (57.0 – 84.0)

CI, confidence interval; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.
Wang M et al. *Lancet Oncol*. 2016(1):48-56.

Ibrutinib + Venetoclax (4/7)

Phase II, single group, open-label, AIM study evaluating the efficacy of **ibrutinib + venetoclax (n=24)** in patients with R/R MCL



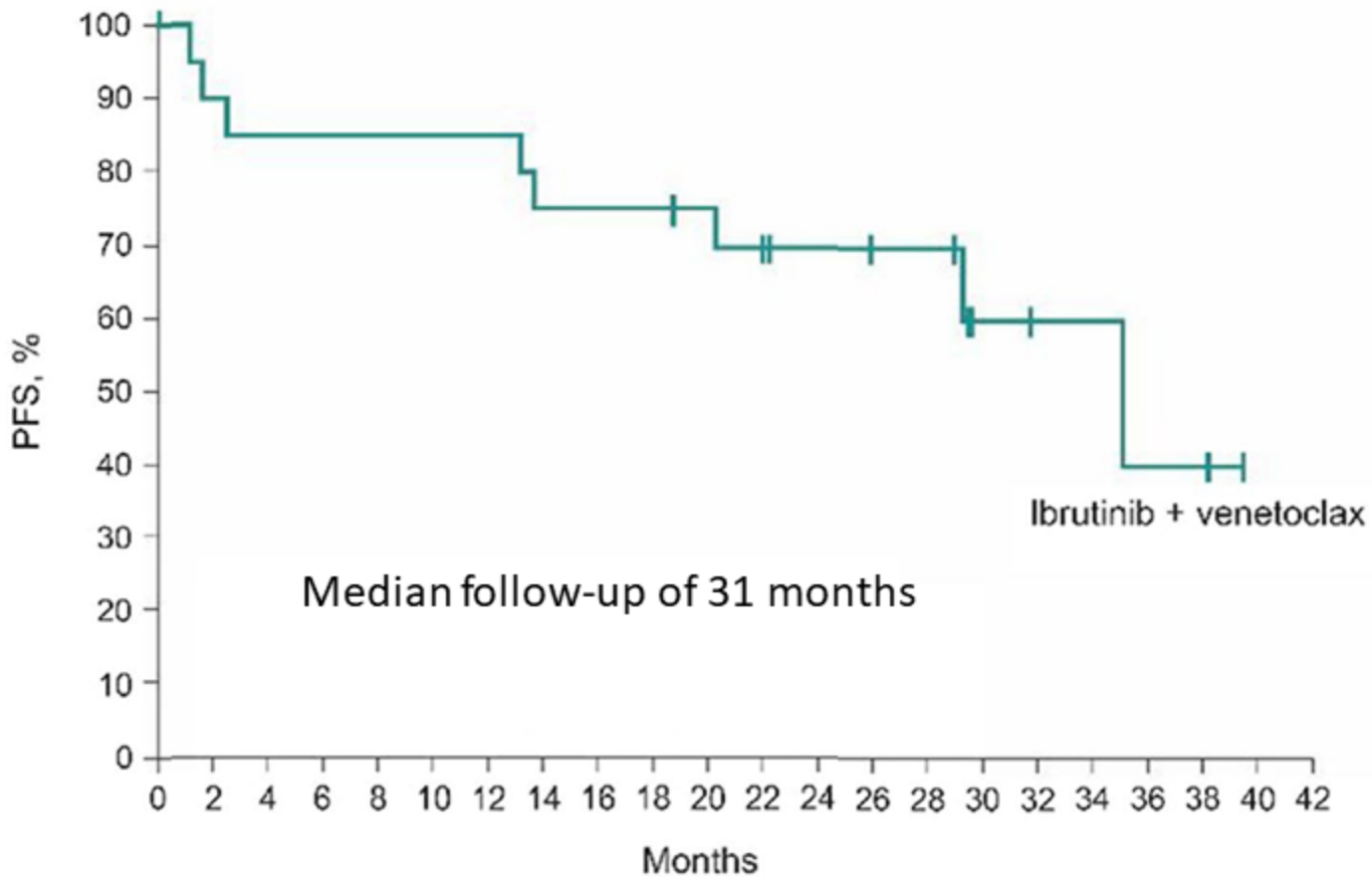
PFS	Median PFS (95% CI), mo
12-month PFS	75.0 (60.0 – 94.0)
18-month PFS	57.0 (40.0 – 82.0)

CI, confidence interval; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.

Tam C et al. *N Engl J Med*. 2018(13):1211-1223.

Ibrutinib + Venetoclax (5/7)

Phase III, multinational, open-label SRI cohort, SYMPATICO study evaluating the efficacy of concurrent **ibrutinib + venetoclax (n=24)** in patients with R/R MCL



PFS	Median PFS (95% CI), mo
12-month PFS	35.0 (13.7– NE)
30-month PFS	60.0 (31.0 – 80.0)

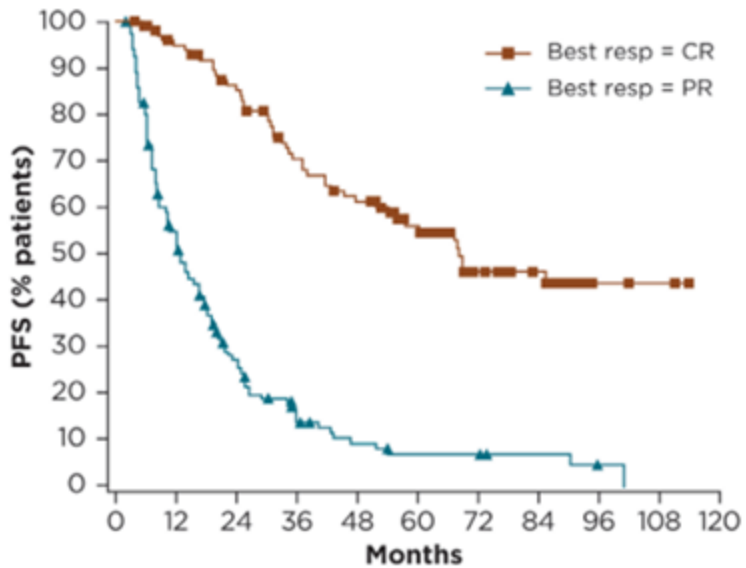
CI, confidence interval; MCL, mantle cell lymphoma mo, months; NE, not estimable; PFS, progression-free survival; R/R, relapsed/refractory; SRI, safety run-in.
Wang M et al. *J Hematol Oncol*. 2021;14(1):179.

Pooled Analyses of Ibrutinib (6/7)

Long-term Outcomes With Ibrutinib Treatment for Patients With R/R MCL: A Pooled Analysis of 3 Clinical Trials With Nearly 10 Years of Follow-up

PFS (n=99)	Median PFS (95% CI), mo
All Patients	12.5 (9.8 – 16.6)
Patients with CR	68.5 (51.7 – NE)
Patients with PR	12.6 (10.3 – 16.6)

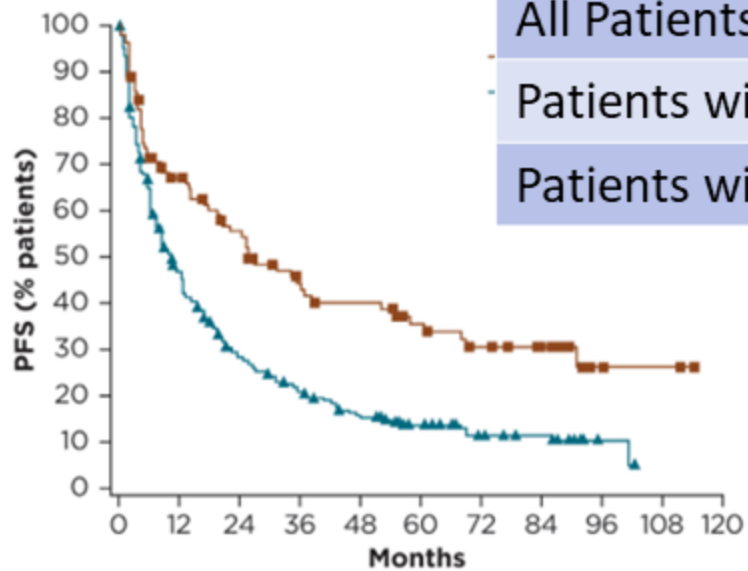
A



Patients at risk

Best resp = CR	102	90	77	61	52	39	25	19	3	2	0
Best resp = PR	156	80	35	16	8	5	5	3	1	0	0

B



Patients at risk

1 prior LOT	99	61	47	31	28	22	17	11	2	2	0
>1 prior LOT	271	117	67	47	33	23	14	11	2	0	0

1 Prior LOT
25.4 (17.5 – 51.8)

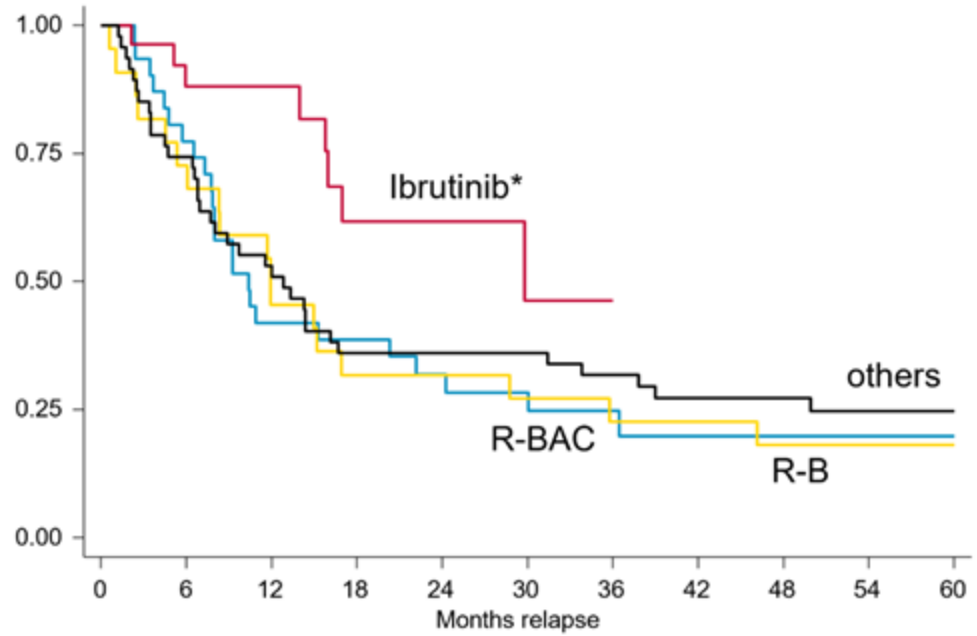
>1 Prior LOT
10.3 (8.1 – 12.5)

CI, confidence interval; CR, complete response; LOT, line of therapy; MCL, mantle cell lymphoma, NE, not estimable, PR, partial response; R/R, relapsed/refractory.
Dreyling M et al. *Hemasphere*. 2022;6(5): e712.

Comparison Among 2L Regimens (7/7)

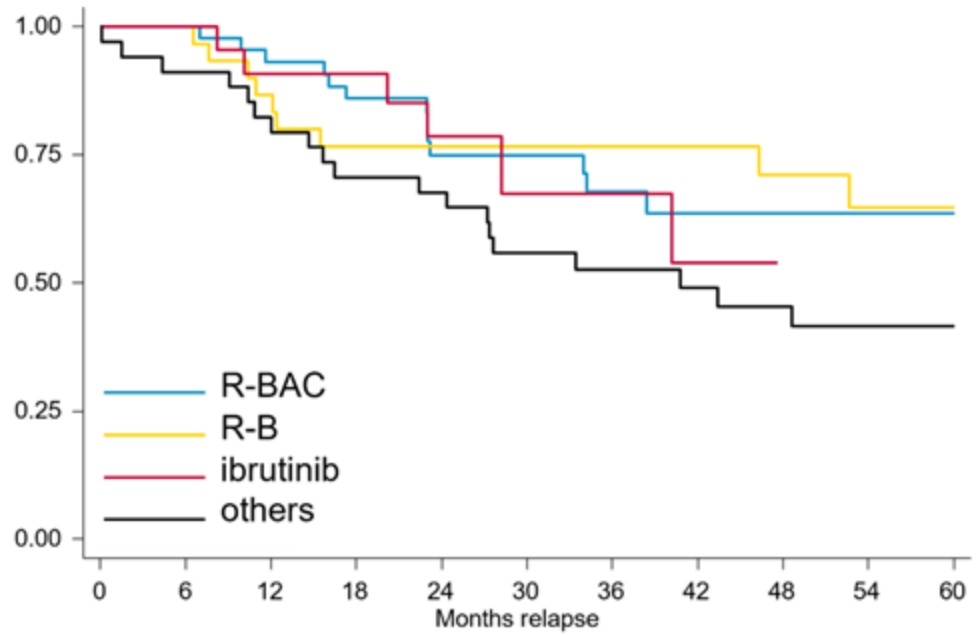
R-B (21%), R-BAC (29%), ibrutinib (19%), and others (31%)

Early POD



At risk:											
BAC	31	24	13	12	9	8	5	4	3	3	3
BR	22	16	10	7	7	6	5	5	4	3	2
ibru	27	21	16	8	5	3	0	0	0	0	0
other	47	35	24	17	17	17	15	11	11	10	6

Late POD



At risk:											
BAC	45	45	40	35	26	23	16	14	12	8	7
BR	32	30	26	23	22	20	16	15	13	10	9
ibru	23	22	20	18	10	6	6	4	0	0	0
other	34	31	27	24	23	19	16	13	12	8	7

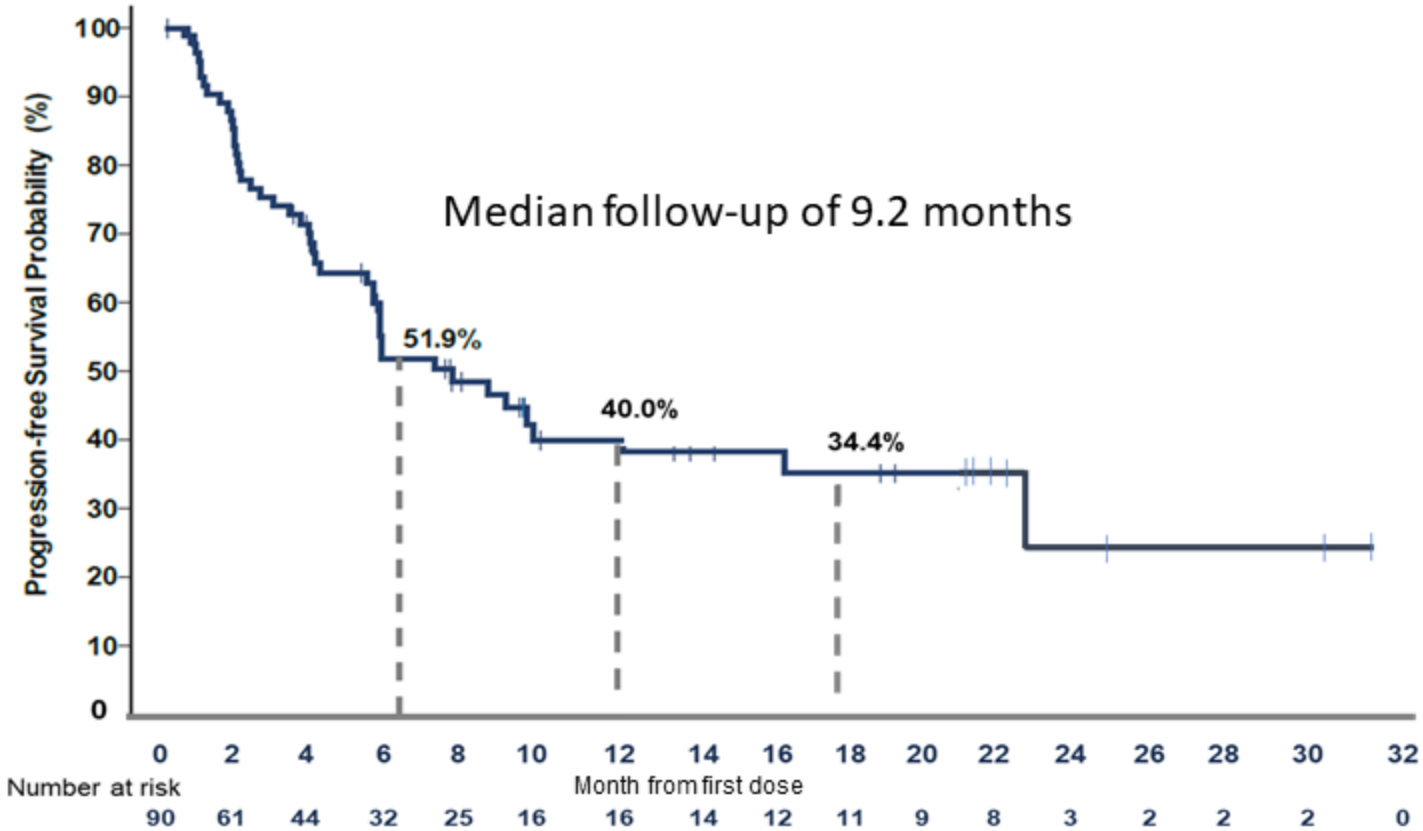
*Ibrutinib vs R-B and R-BAC (P=0.02); vs others (P=0.03)

MCL, mantle cell lymphoma; RB, rituximab-bendamustine; R-BAC, R-B and cytarabine; R/R, relapsed/refractory.

Visco C et al. *Leukemia*. 2021;35(3):787-795.

Pirtobrutinib Monotherapy

Phase I/II, first-in-human, open-label, multicenter, BRUIN study evaluating the efficacy of **pirtobrutinib (n=90)** in patients with covalent BTK inhibitor pretreated MCL



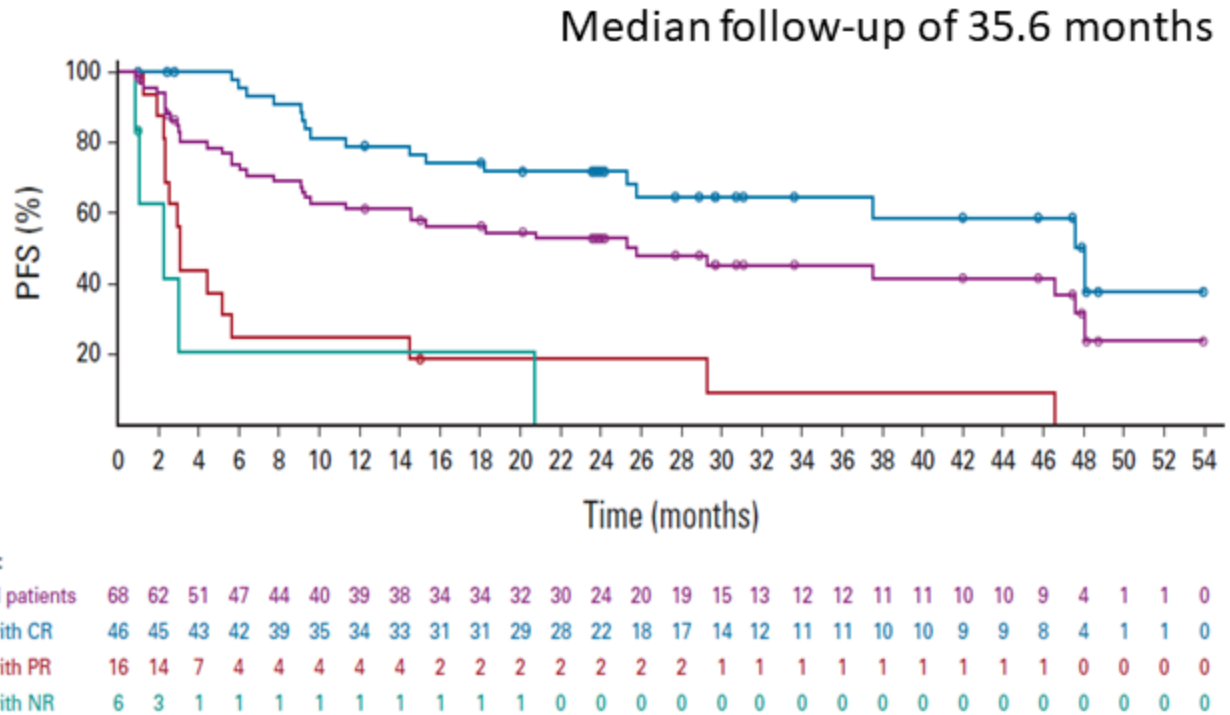
PFS	Median PFS (95% CI), mo
12-month PFS	7.4 (5.3 – 12.5)

Overall ORR (95% CI)
cBTKi pre-treated (n=90): 57.8% (46.9-68.1)
cBTKI naïve (n=14): 85.7% (57.2-98.2)

BTK, Bruton kinase; CI, confidence interval; MCL, mantle cell lymphoma mo, months; PFS, progression-free survival; R/R, relapsed/refractory.
Wang M et al. *J Clin Oncol*. 2023. Online ahead of print.

Brexacabtagene Autoleucel

3-year follow-up, ZUMA-2 study evaluating the efficacy of **brexacabtagene autoleucel (n=68)** in patients with R/R MCL, including high-risk subgroups



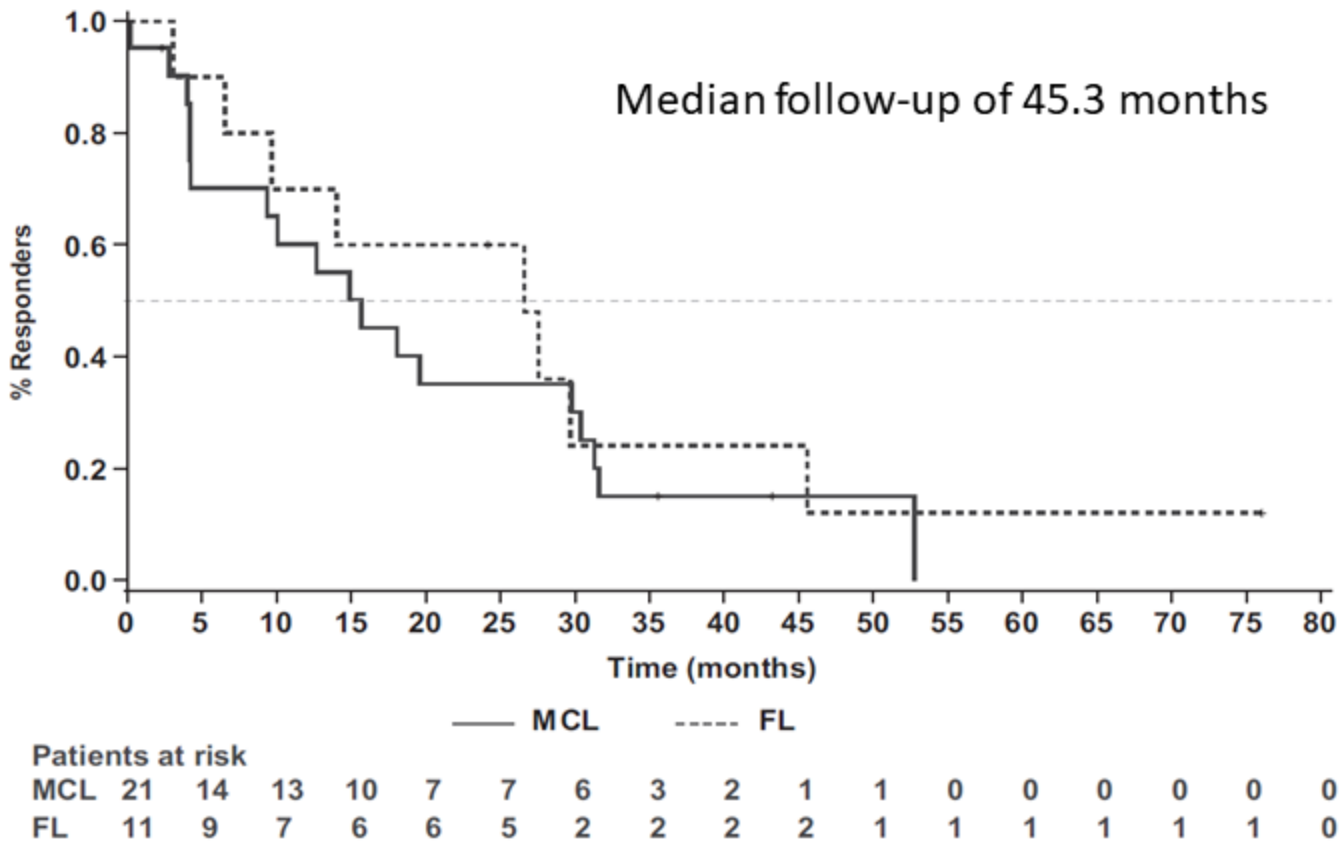
PFS	Median PFS (95% CI), mo
All treated patients	25.8 (9.6 – 47.6)
CR	48.0 (25.8 – NE)
PR	3.1 (2.3 – 5.6)
No response	2.3 (0.9 – NE)

CI, confidence interval; CR, complete response; MCL, mantle cell lymphoma mo, months; NE, not estimatable; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory.

Wang M et al. *J Clin Oncol*. 2022(41):555-567.

Venetoclax Monotherapy (1/2)

3-year follow-up, phase I, first-in-human, study evaluating the efficacy of **venetoclax monotherapy (n=106)** in patients with R/R NHL (R/R MCL; n=28)



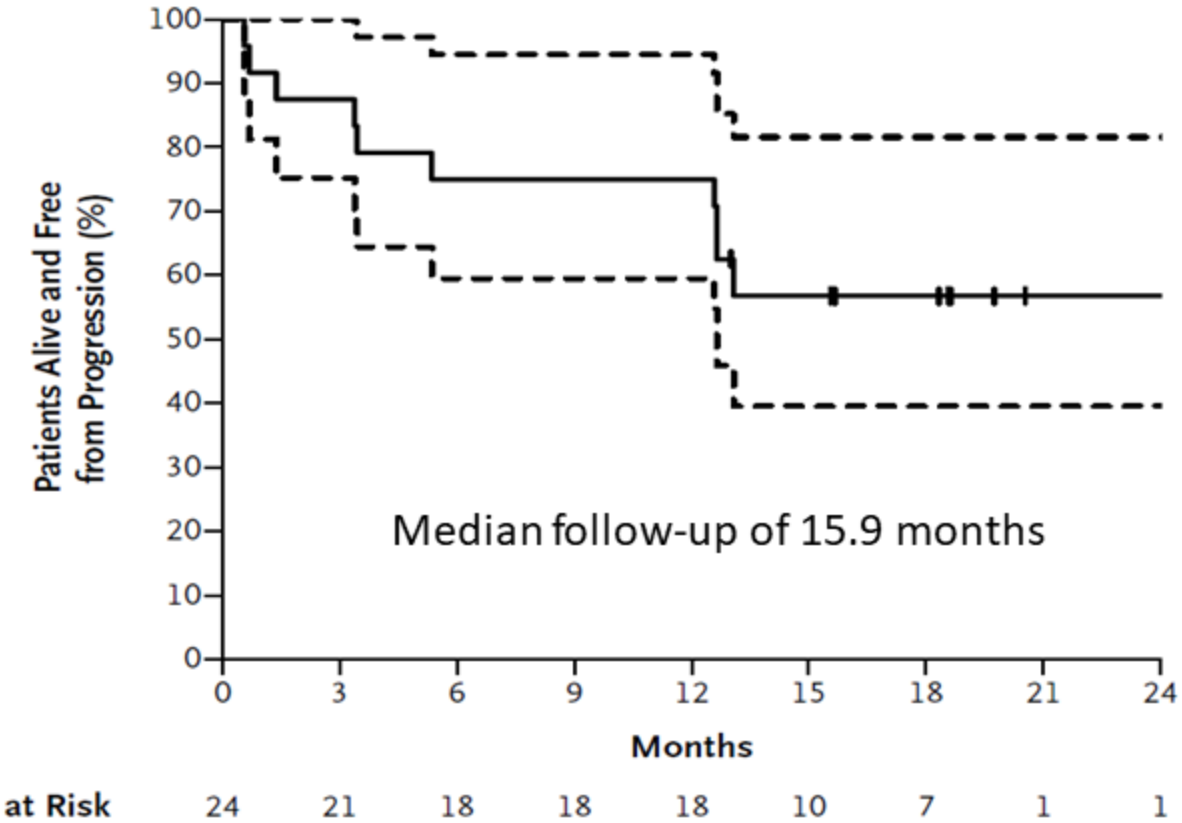
PFS	Median PFS (95% CI), mo
12-month PFS	11.3 (5.4 – 21.0)

CI, confidence interval; MCL, mantle cell lymphoma mo, months; PFS, progression-free survival; R/R, relapsed/refractory.

Davids MS et al. *Clin Cancer Res*. 2022(17):4690-4695.

Venetoclax + Ibrutinib (2/2)

Phase II, single group, open-label, AIM study evaluating the efficacy of **ibrutinib + venetoclax (n=24)** in patients with R/R MCL

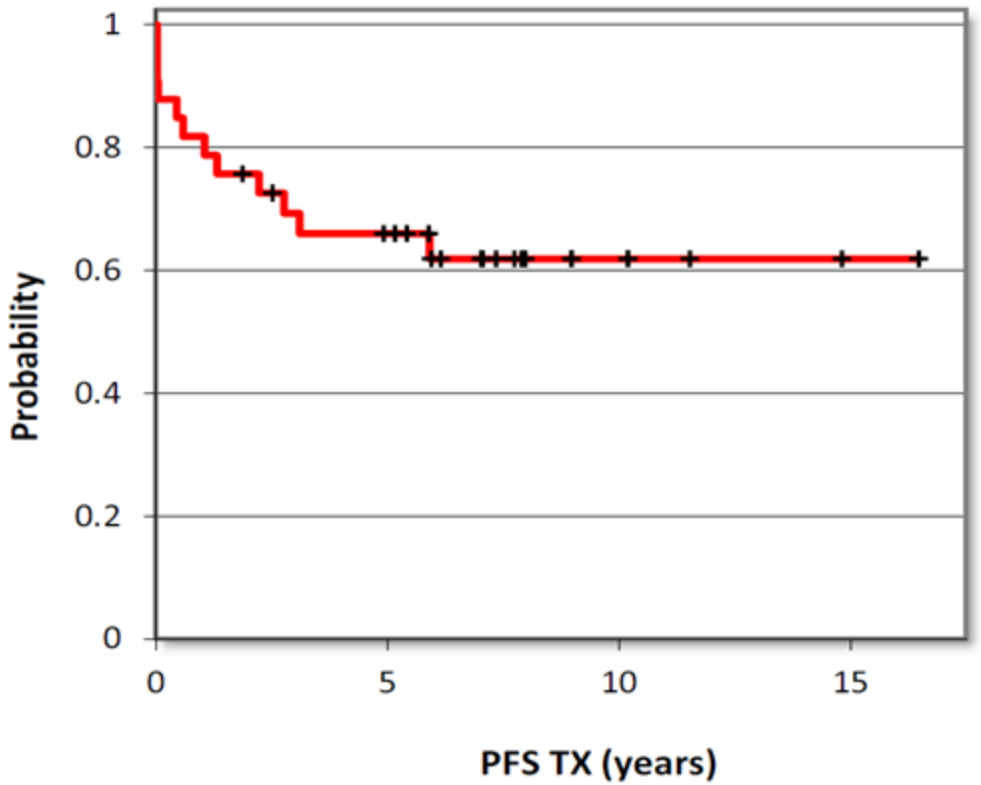


PFS	Median PFS (95% CI), mo
12-mo PFS	75.0 (60.0 – 94.0)
18-mo PFS	57.0 (40.0 – 82.0)

CI, confidence interval; MCL, mantle cell lymphoma; mo, months; PFS, progression-free survival; R/R, relapsed/refractory.
Tam C et al. *N Engl J Med*. 2018(13):1211-1223.

Allo-SCT (1/2)

OSHO studies evaluating the efficacy of **allogeneic STC (n=33)** in patients with de novo MCL and R/R MCL



Median follow-up of 16.5 years

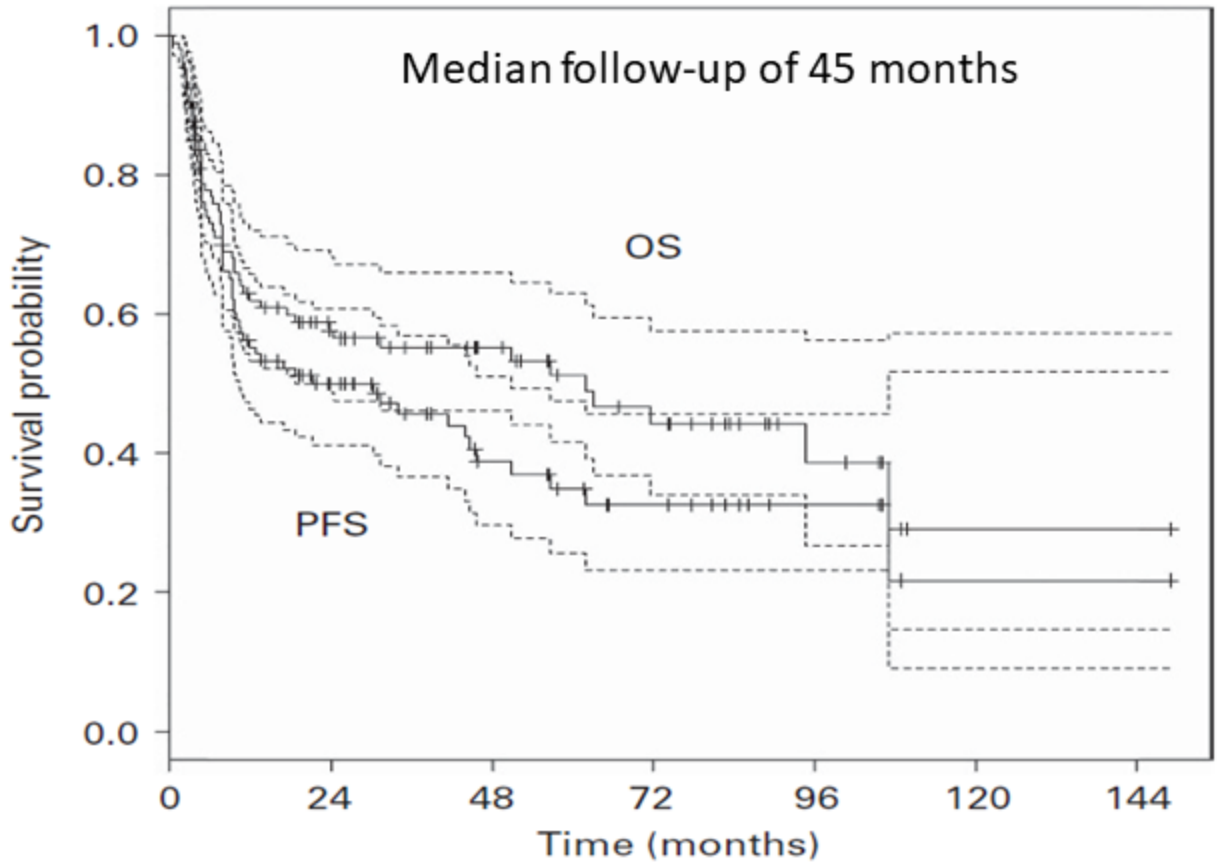
PFS	Median PFS (95% CI), yrs
All patients	5.9 (0.02 – 16.5)

50% survival was not reached

CI, confidence interval; MCL, mantle cell lymphoma; PFS, progression-free survival; R/R, relapsed/refractory; STC, stem cell transplant; TX, treatment; yrs, years.
Krüger WH et al. Ann Hematol. 2021(6):1569-1577.

Allo-SCT (2/2)

SFGM-TC study evaluating the efficacy of **allogeneic-STC (n=106)** in fit patients with R/R MCL who failed after autologous-SCT

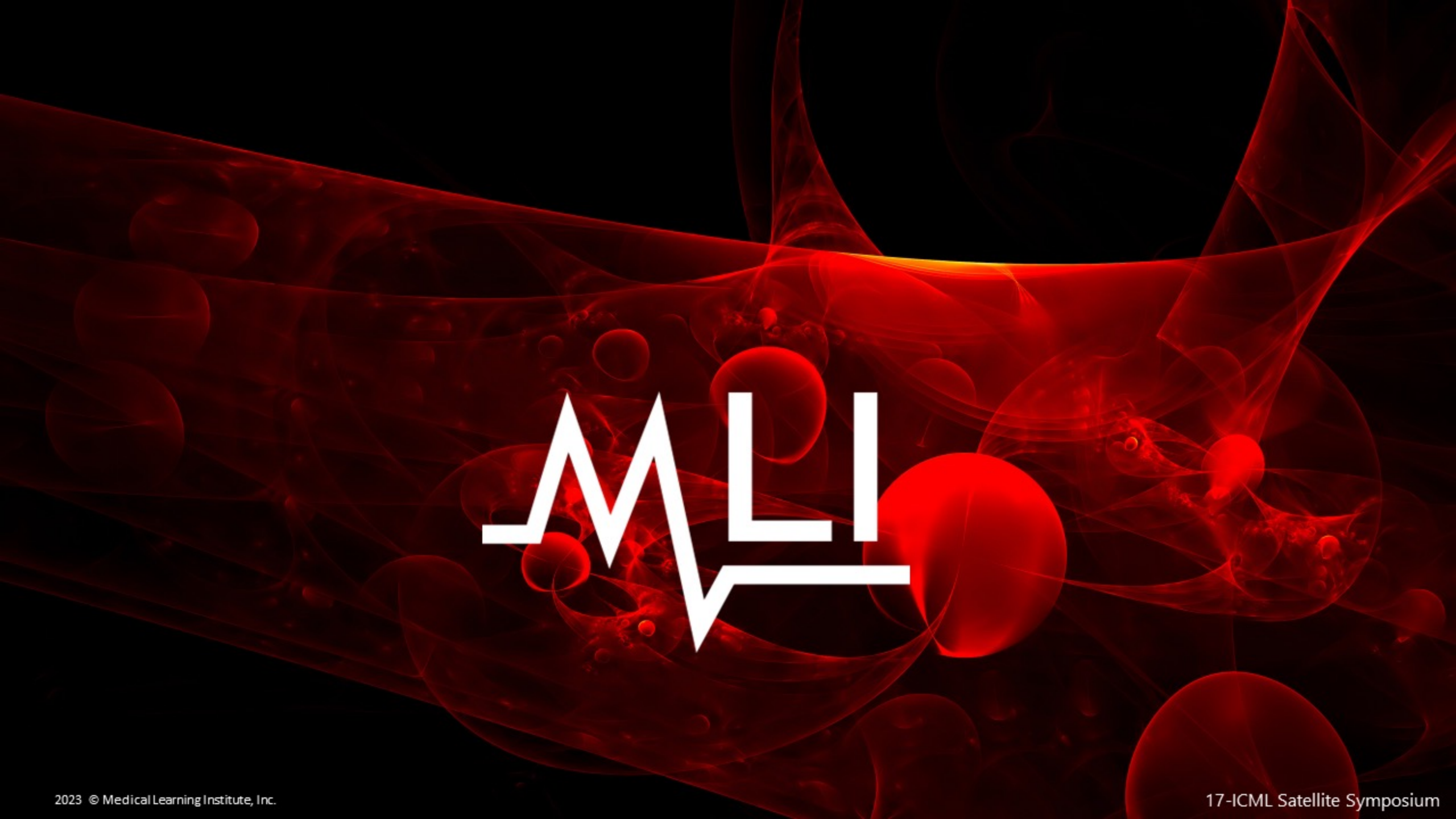


PFS	Median PFS (95% CI), mo
All patients	30.1
OS	**Median PFS (95% CI), mo**
All patients	62.0

TRM at 1 year and 3 years were 28% and 32%, respectively

Mo, months; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory; SCT, stem cell transplant; TRM, treatment-related mortality.

Tessoulin B et al. *Bone Marrow Transplant*. 2016;51(9):1184-1190.



Safety of Bendamustine + Rituximab

Grade 3/4 laboratory toxicities and adverse events (n=45)

Laboratory Hematologic Toxicities	n (%)
Lymphopenia	40 (89)
Leukopenia	20 (44)
Neutropenia	20 (44)
Thrombocytopenia	3 (7)
Anemia	2 (4)

Non-hematologic AEs Occurring in ≥2 Patients	n (%)
Hypokalemia	3 (7)
Muscle weakness	3 (7)
Hypotension	3 (7)
Pneumonia	2[a] (4)
Back pain	2 (4)
Decreased appetite	2 (4)
Device-related infection	2 (4)
Hyponatremia	2 (4)
Pleural effusion	2 (4)
Syncope	2 (4)
Weight decreased	2 (4)

[a]Once additional case of pneumonia was fatal.
AEs, adverse events; n, number.
Czuczman MS et al. *Ann Hematol*. 2015;94(12):2025-2032.

Safety of Bortezomib Monotherapy

Most Common Grade ≥3 Hematologic AE	n (%)
Lymphopenia	52 (34)

Most Common Grade ≥3 Non-Hematologic AE	n (%)
Peripheral neuropathy	20 (13)

AEs, adverse events; n, number.
Goy A et al. *Ann Oncol*. 2009(3):520-525.

Safety of Lenalidomide Monotherapy (1/2)

Treatment-Emergent Hematological AEs (≥10% Grade 1–2, ≥5% Grade 3–4)

	Lenalidomide (n=167) n (%)			Investigator's Choice (n=83) n (%)		
Hematological	Grade 1-2	Grade 3	Grade 4	Grade 1-2	Grade 3	Grade 4
Anemia	34 (20)	12 (7)	2 (1)	13 (16)	5 (6)	1 (1)
Thrombocytopenia	31 (19)	25 (15)	5 (3)	10 (12)	16 (19)	7 (8)
Leukopenia	15 (9)	11 (7)	2 (1)	9 (11)	5 (6)	4 (5)
Neutropenia	12 (7)	40 (24)	33 (20)	1 (1)	13 (16)	15 (18)
Febrile neutropenia	0	7 (4)	3 (2)	0	2 (2)	0

AEs, adverse events.

Trněný M et al. *Lancet Oncol*. 2016(3):319-331.

Safety of Lenalidomide Monotherapy (2/2)

Treatment-Emergent Non-Hematological AEs (≥10% Grade 1–2, ≥5% Grade 3–4)

Non-Hematological AEs	Lenalidomide (n=167) n (%)			Investigator's Choice (n=83) n (%)		
	Grade 1-2	Grade 3	Grade 4	Grade 1-2	Grade 3	Grade 4
Fatigue	33 (20)	2 (1)	0	4 (5)	0	0
Diarrhea	32 (19)	5 (3)	1 (1)	8 (10)	0	0
Constipation	28 (17)	1 (1)	0	5 (6)	0	0
Nasopharyngitis	25 (16)	0	0	5 (6)	0	0
Asthenia	24 (14)	2 (1)	0	11 (13)	0	0
Pyrexia	24 (14)	3 (2)	1 (1)	9 (11)	1 (1)	0
Upper RTI	19 (11)	1 (1)	0	4 (5)	1 (1)	0
Cough	19 (11)	0	0	3 (4)	1 (1)	0
Decreased appetite	18 (11)	1 (1)	0	3 (4)	0	0
Nausea	18 (11)	0	0	12 (14)	0	0
Rash	18 (11)	0	0	3 (4)	0	0
Peripheral edema	16 (10)	1 (1)	0	9 (11)	0	0
Vomiting	10 (6)	0	0	9 (11)	0	0
Pneumonia	5 (3)	5 (3)	1 (1)	2 (2)	2 (2)	0

AEs, adverse events; RTI, respiratory tract infection.
Trněný M et al. *Lancet Oncol*. 2016(3):319-331.

Safety of Lenalidomide + Rituximab (1/2)

Common AEs in phase 2 (n=44) after 379 cycles of lenalidomide plus rituximab

Hematological	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
Anemia	31 (70)	6 (14)	1 (2)	0
Neutropenia	20 (45)	22 (50)	16 (36)	13 (30)
Febrile neutropenia	1 (2)	7 (16)	2 (5)	0
Thrombocytopenia	23 (52)	9 (20)	8 (18)	2 (5)
Leukopenia	26 (59)	14 (32)	10 (23)	3 (7)
Lymphopenia	27 (61)	21 (48)	12 (27)	4 (9)

AEs, adverse events; n, number.

Wang M et al. *Lancet Oncol*. 2012(7):716-723.

Safety of Lenalidomide + Rituximab (2/2)

Common AEs in phase 2 (n=44) after 379 cycles of lenalidomide plus rituximab

Non-Hematological	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
Pruritus	19 (43)	3 (7)	0	0
Fatigue	39 (89)	17 (39)	2 (5)	0
Constipation	27 (61)	3 (7)	0	0
Neuropathy	27 (61)	5 (11)	1 (2)	0
Cough	17 (39)	1 (2)	1 (2)	0
Nausea	15 (34)	5 (11)	0	0
Vomiting	11 (25)	4 (9)	0	0
Memory impairment	11 (25)	2 (5)	0	0
Mood alteration	11 (25)	1 (2)	0	0
Ataxia	1 (2)	0	1 (2)	0
Dizziness	14 (32)	4 (9)	0	0
Diarrhea	22 (50)	7 (16)	0	0
Rash	21 (48)	6 (14)	2 (5)	0
Myalgia	20 (45)	8 (18)	2 (5)	0

AEs, adverse events; n, number.

Wang M et al. *Lancet Oncol*. 2012(7):716-723.

Safety of Ibrutinib Monotherapy (1/2)

Summary of SAEs (≥2% of Patients) Regardless of Attrition (N=111)

SAE*, n (%)	Any Grade	Grade 3-4	Grade 5
Disease progression†	11 (10)	3 (3)	8 (7)
Pneumonia	8 (7)	7 (6)	1 (1)
Atrial fibrillation	7 (6)	6 (5)‡	0
Urinary tract infection	4 (4)	3 (3)	0
Febrile neutropenia	3 (3)	3 (3)	0
Abdominal pain	3 (3)	3 (3)	0
Acute renal failure	3 (3)	2 (2)	1 (1)
Subdural hematoma	3 (3)	2 (2)	0
Pyrexia	3 (3)	1 (1)	0
Confusional state	3 (3)	1 (1)	0

*SAEs were updated with an estimated median follow-up of 26.7 months. †Mantle cell lymphoma reported as a SAE by investigators. ‡One additional patient had a grade 3 atrial fibrillation that was not considered an SAE.
SAEs, serious adverse events; n, number.
Wang M et al. *Blood*. 2015(6):739-745.

Safety of Ibrutinib Monotherapy (2/2)

Prevalence of Select AEs by 6-Month Intervals

Select AE*, n (%)	1-6 mo (n=111)	7-12 mo (n=72)	13-18 mo (n=51)	19-26 mo (n=41)	>24 mo (n=22)
Any diarrhea	49 (44)	21 (29)	15 (29)	8 (20)	6 (27)
Grade 3†	5 (5)	0	0	1 (2)	0
SAE	1 (1)	0	0	0	0
Any infection	76 (69)	43 (60)	30 (59)	22 (54)	9 (41)
Grade	20 (18)	11 (15)	6 (12)	5 (12)	1 (5)
SAE	16 (14)	9 (13)	4 (8)	5 (12)	1 (5)
Any bleeding	46 (41)	17 (24)	17 (33)	14 (34)	5 (23)
Major bleeding	6 (5)	1 (1)	3 (6)	2 (5)	2 (9)

*AEs were updated with an estimated median follow-up of 26.7 months. †No grade 4 or 5 diarrhea.
Mo, months; n, number; SAEs, serious adverse events
Wang M et al. *Blood*. 2015(6):739-745.

Safety of Ibrutinib vs Temsirolimus

TEAEs in ≥20% of Patients in Either Treatment Arm

Hematologic AEs	Ibrutinib (N=139)		Temsirolimus (N=139)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Thrombocytopenia	18.0	9.4	56.1	43.2
Anemia	19.4	8.6	43.9	20.1
Neutropenia	15.8	12.9	26.6	17.3

Non-Hematologic AEs	Ibrutinib (N=139)		Temsirolimus (N=139)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Diarrhea	33.1	3.6	30.9	4.3
Fatigue	23.7	5.0	28.8	7.2
Cough	23.0	0.7	22.3	0
Upper RTI	20.1	2.2	11.5	0.7
Pyrexia	18.7	0.7	20.9	2.2
Nausea	14.4	0	21.6	0
Peripheral edema	13.7	0	23.7	2.2
Epistaxis	9.4	0.7	23.7	1.4
Stomatitis	2.9	0	20.9	3.6

RTI, respiratory tract infection; TEAEs, treatment-emergent adverse events.

Rule S et al. *Leukemia*. 2018(8):1799-1803.

Safety of Ibrutinib + Rituximab

Treatment-Emergent Adverse Events (n=50)

Hematologic AEs n (%)	Grade 1-2	Grade 3	Grade 4
Thrombocytopenia	24 (48)	2 (4)	0
Anemia	24 (48)	0	0
Neutropenia	10 (20)	1 (2)	1 (2)
Leukopenia	5 (10)	0	0
Leucocytosis	2 (4)	1 (2)	0

Non-Hematologic AEs n (%)	Grade 1-2	Grade 3	Grade 4
Fatigue	47 (94)	2 (4)	0
Diarrhea	39 (78)	1 (2)	1 (2)
Myalgia	34 (68)	1 (2)	0
Hypertension	13 (26)	1 (2)	0
Pneumonitis	2 (4)	1 (2)	0
Non-itchy rash (arms)	1 (2)	2 (4)	0
Skin infection	1 (2)	1 (2)	0
Urinary tract infection	3 (6)	1 (2)	0
Atrial fibrillation	1 (2)	6 (12)	0
Acute renal failure	0	1 (2)	0

AEs, adverse events.

Wang M et al. *Lancet Oncol*. 2016(1):48-56.

Safety of Ibrutinib + Venetoclax (1/2)

Adverse Events and Serious Adverse Events*

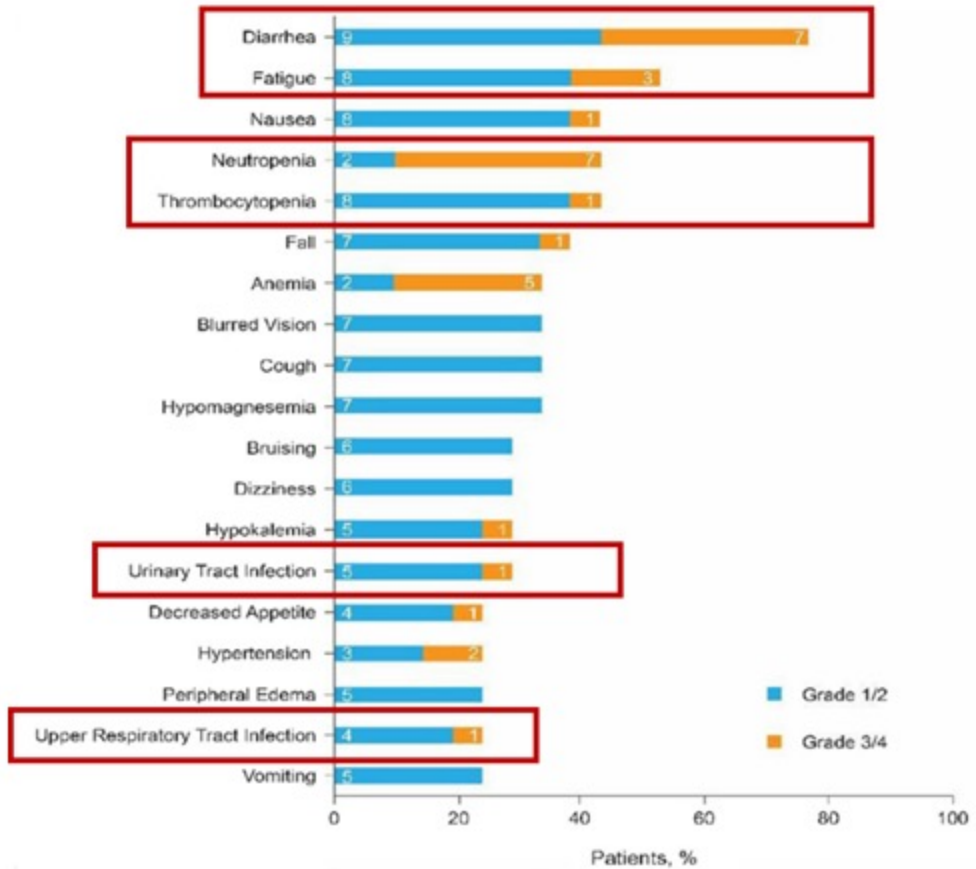
Event n (%)	Any Grade (N=24)	Grade ≥3 (N=24)
Any AE	24 (100)	17 (71)
Diarrhea	20 (83)	3 (12)†
Fatigue	18 (75)	0
Nausea or vomiting	17 (71)	0
Bleeding, bruising, post-operative hemorrhage	13 (54)	1 (4)
Cough or dyspnea	11 (46)	1 (4)
Soft tissue infection	10 (42)	2 (8)‡
Neutropenia	8 (33)	8 (33)
Anemia	7 (29)	3 (12)
Rash	7 (29)	0
Thrombocytopenia	5 (21)	4 (17)
Atrial fibrillation	2 (8)	2 (8)

Event n (%)	Any Grade (N=24)	Grade ≥3 (N=24)
Any serious AE§	14 (58)	--
Diarrhea	3 (12)¶	--
Tumor lysis syndrome	2 (8)	--
Atrial fibrillation	2 (8)	--
Pyrexia	2 (8)	--
Pleural effusion	2 (8)	--
Cardiac failure	1 (4)‡	--
Soft-tissue infection	1 (4)‡	--

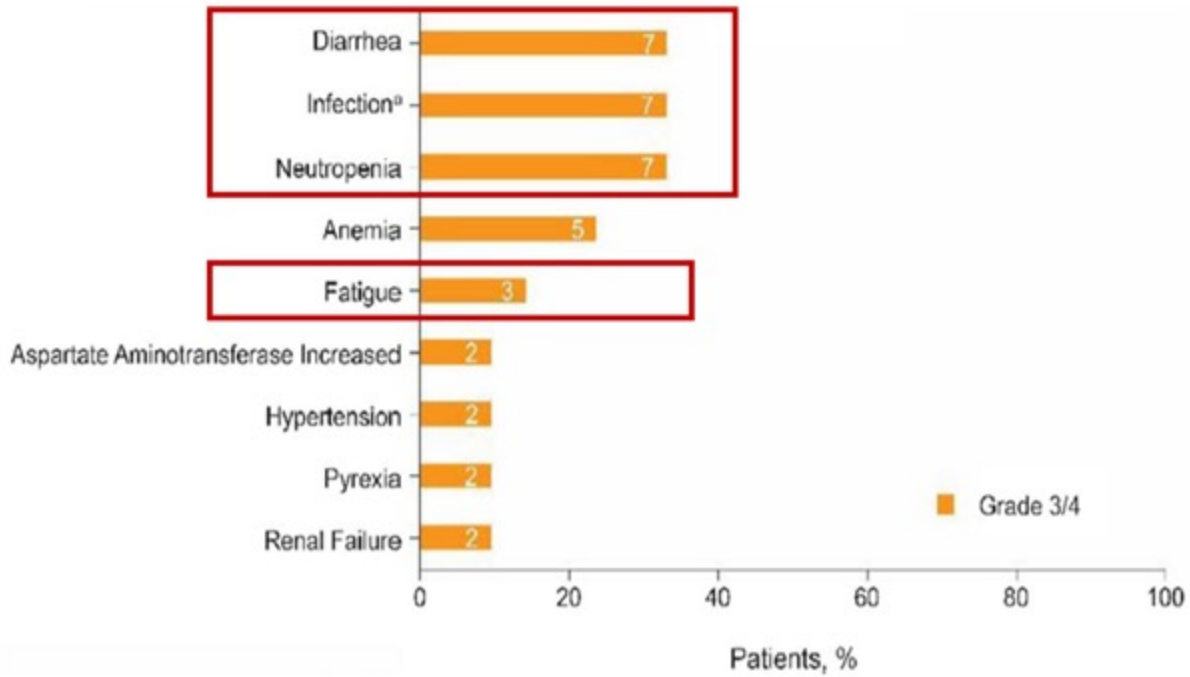
*Listed are the adverse events that were reported in at least 15% of the patients, as well as events of special interest (the tumor lysis syndrome and atrial fibrillation). †The three cases of grade 3 diarrhea lasted 4 days, 1 week, and 2 weeks. ‡Data include one fatal adverse event. The two fatal events that were considered by the investigators to be unrelated to disease progression were soft-tissue infection (malignant otitis externa) and cardiac failure. §Listed are the serious adverse events that were reported in at least two patients, as well as fatal events. ¶Data include one patient with microscopic colitis that had been diagnosed on the basis of colonoscopy and biopsy.
AEs, adverse events; n, number.
Tam C et al. *N Engl J Med*. 2018(13):1211-1223.

Safety of Ibrutinib + Venetoclax (2/2)

Any-grade treatment-emergent AE occurring in >20% of all patients



Grade 3/4 AE occurring in >5% of all patients



[a]AEs of infection were bronchitis (n = 1), candida infection (n = 1), cellulitis (n = 1), fungal abscesscentral nervous system (n = 1, recovered), infection (not specified, n = 1), pneumonia (n = 2), sepsis(n = 1), staphylococcal bacteremia (n = 1), upper respiratory tract infection (n = 1), and urinary tract infection (n = 1).
AEs, adverse events.
Wang M et al. *J Hematol Oncol*. 2021;14(1):179.

Safety of Pirtobrutinib Monotherapy

Adverse events in at least 10% of all MCL patients (n=164)

AEs of special interest[a]	TEAE (≥10%), %		TRAE	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Infections	59 (36)	28 (17)	24 (14)	5 (3)
Bleeding	45 (27)	6 (4)	26 (16)	1 (1)
Thrombocytopenia	24 (15)	11 (7)	2 (1)	0
Neutropenia[b]	23 (14)	22 (13)	15 (9)	14 (9)
Bruising[c]	27 (17)	0	19 (12)	0
Hemorrhage	25 (15)	6 (4)	11 (7)	1 (1)
Atrial fibrillation/atrial flutter[d]	6 (4)	2 (1)	1 (1)	0

AEs	TEAE (≥10%), %		TRAE	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Fatigue	49 (30)	4 (2)	34 (21)	4 (2)
Diarrhea	35 (21)	0	20 (12)	0
Dyspnea	27 (17)	3 (2)	15 (9)	1 (1)
Contusion	24 (15)	0	16 (10)	0
Anemia	21 (13)	8 (5)	10 (6)	4 (2)
Back pain	21 (13)	2 (1)	2 (1)	0
Cough	20 (12)	0	10 (6)	0
Pyrexia	19 (12)	0	6 (4)	0
Constipation	18 (11)	0	3 (2)	0
Nausea	18 (11)	0	7 (4)	0
Pneumonia	17 (10)	14 (9)	5 (3)	4 (2)
Myalgia	17 (10)	0	14 (9)	0

[a]Adverse events of special interest are those that were previously associated with cBTK inhibitors and are all composite terms.
[b]Combines neutrophil count decreased, neutropenia, febrile neutropenia, and neutropenic sepsis.
[c]Bruising includes contusion, petechia, ecchymosis, and increased tendency to bruise. [d]Of 6 total afib/aflutter TEAEs, 3 occurred in patients with a prior medical history of atrial fibrillation
MCL, mantle cell lymphoma; TEAE, treatment-emergent adverse events; TRAE, treatment-related adverse events.
Wang M et al. *J Clin Oncol*. 2023. Online ahead of print.

Safety of Brexacabtagene Autoleucel

Adverse Events Occurring After the Previous Report2 (July 24, 2019 Data Cutoff Date) in the All-Treated Population (N=68)

	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
CRS or neurologic events	2 (3)	1 (1)	0	1 (1)	0	0
CRS	0	0	0	0	0	0
Neurologic events	2 (3)	1 (1)	0	1 (1)	0	0
Serious neurological event	1 (1)	0	0	1 (1)	0	0

[a]CRS events were graded per revised Lee et al. 2014 grading system; all other AEs were graded per Common Terminology Criteria for Adverse Events version 4.03. [b]This serious neurologic event of encephalopathy began on day 397; the event resolved on day 408 and was considered unrelated to KTE-X19

AE, adverse events; CRS, cytokine release syndrome; N, number.

Wang M et al. *J Clin Oncol*. 2022(41):555-567.

Safety of Venetoclax Monotherapy

TEAEs	First events with onset ≤12 mo (N=64)				New events with onset 12-24 mo (N=33)				New events with onset >24 mo (N=15)			
	n/N	%	P-Y[c]	IR[b]	n/N	%	P-Y	IR	n/N	%	P-Y	IR
Any AE	62/64	97	3.1	1984.7	26/33	79	7.6	340.7	13/15	87	9.3	139.6
Hematologic[a]	18/64	28	37.1	48.5	5/33	15	21.8	22.9	0/15	0	40.1	0
Neutropenia	13/64	20	39.1	33.3	1/25	4	17.7	5.6	0/13	0	38.0	0
Thrombocytopenia	9/64	14	44.1	20.4	1/29	3	19.9	5.0	0/14	0	34.5	0
Anemia	7/64	11	45.3	15.4	2/31	7	21.0	9.5	0/13	0	36.6	0
Non-hematologic												
Nausea	34/64	53	21.4	158.5	1/11	9	6.1	16.3	1/2	50	2.9	34.3
Diarrhea	30/64	47	27.0	111.3	3/13	23	5.3	56.6	1/1	100	1.7	58.1
Fatigue	22/64	34	35.2	62.5	3/21	14	12.5	24.0	2/7	29	18.5	10.8
Upper RTI	15/64	23	39.7	37.8	1/20	5	13.9	7.0	3/8	38	11.2	26.7
Constipation	12/64	19	41.3	29.1	0/29	0	20.8	0	2/13	15	32.8	6.1
Headache	12/64	19	41.1	29.2	2/25	8	15.0	13.3	0/8	0	14.6	0
Vomiting	11/64	17	40.0	27.5	1/24	4	15.3	6.5	3/10	30	19.1	15.7
Decreased appetite	10/64	16	42.1	23.7	1/25	4	17.1	5.8	0/10	0	28.0	0
Cough	10/64	16	42.0	23.8	2/26	7	17.1	11.7	2/9	22	16.1	12.5

[a]Hematologic and nonhematologic adverse events ≥15% occurrence by incidence rate sorted by first events with onset ≤12 months. [b]Incidence rate ¼ number of patients with an event per 100 person-years at risk. [c]Person-years for the calculation of the incidence rate is the total time at risk of an event across all patients. Only new events not reported before this time period were counted in the summary of events with onset in one time period.
AE, adverse events; IR, incidence rate; mo, months; N, number PY, person-years; RTI, respiratory tract infection; TEAE, treatment-emergent adverse events.
Davids MS et al. *Clin Cancer Res*. 2022(17):4690-4695.

Safety of Allo-SCT (1/2)

Patient	OSHO Trial	G	Age at SCT (yrs)	Follow-up after allo-SCT	Causes of death
#1	#60	M	65	N/A	PD
#2	#60	M	64	Day +8	Infection in aplasia
#3	#60	M	61	Day +8	Kidney/lung toxicity IV plus pneumonia
#4	#60	M	64	Day +481	Septic cardiomyopathy
#5	#74	F	63	Day +15	Bleeding d/t Aspergillosis of CNS
#6	#74	M	69	Day +312	Infection
#7	#74	M	59	Day +9	Infection
#8	#74	M	59	Day +1009	Infection
#9	#74	M	63	Day +229	PD
#10	#60	M	60	Day +2168	PD

Incidence of chronic GVDH was 15% (limited disease n=5, extensive disease n=1) without dynamic or mortality since 2014

Allo-SCT; allogeneic stem cell transplant; d/t, due to; F, female; G, gender; GVHD, graft-versus-host-disease; M, male; N/A not applicable; PD, progressive disease.
Krüger WH et al. Ann Hematol. 2021(6):1569-1577.

Safety of Allo-SCT (2/2)

Patient Outcomes	n (%)
Relapse post RIC-allo-SCT, *number of patients (8)*	
Yes	24 (24)
aGVHD, *number of patients (1)*	
No aGVHD	48 (46)
I-II	37 (35)
III-IV	20 (19)
cGVHD*, *number of patients (13)*	
Yes	48 (59)
Extensive cGVHD	28 (58)
Toxicity-related mortality according to the period after RIC-allo-SCT, *percentage*	
6 months	17
1 year	29
3 years	32

*Limited to patients whose follow-up reached day 100.
aGVHD, acute GVHD; cGVHD, chronic GVHD; NA, not asserted; OS, overall survival; Ric-allo-SCT, reduced-intensity conditioning allogeneic stem cell transplantation.
Tessoulin B et al. *Bone Marrow Transplant*. 2016;51(9):1184-1190.

Chemotherapeutic Combination TEAEs

Hematological

- Neutropenia
- Thrombocytopenia
- Lymphopenia
- Leukopenia
- Anemia

Non-Hematological

- Pneumonia
- Infection

Commonly occurs with: Bendamustine

PREVENT

- Provide effective education at treatment start and throughout
- Assess prior treatment risk factors, which may place patient at increased risk (e.g., age, genetics, comorbidities)

MONITOR

- Assess during each visit and more frequently as needed
- Compare to similarly reported analyses to assess for manageability and reversibility

MITIGATE SYMPTOMS

- Consider prophylaxis for patients at increased risk of opportunistic infection
- Consider switching to another novel chemotherapy-free agent or clinical trial
- Dosing adjustment when using R-BAC or VR-CAP

TEAE, treatment-emergent adverse events.

1. Rummel MR et al. *Lancet Oncol*. 2016(1):57-66.

Lenalidomide TEAEs

Hematological

- Neutropenia
- Thrombocytopenia
- Anemia
- Leukopenia

Non-Hematological

- Rash
- Fatigue
- Diarrhea
- Pneumonia

PREVENT

- Provide effective education at treatment start and throughout
- Assess prior treatment risk factors, which may place patient at increased risk (e.g., age, genetics, comorbidities)

MONITOR

- Assess during each visit and more frequently as needed
- Compare to similarly reported analyses to assess for manageability and reversibility

MITIGATE SYMPTOMS

- Utilize patient self-reporting at early signs of rash
- Provide appropriate and prompt intervention by grading of rash symptoms

TEAE, treatment-emergent adverse events.

1. Trněný M et al. *Lancet Oncol*. 2016(3):319-331.
2. Wang M et al. *Lancet Oncol*. 2012(7):716-723.
3. Tinsley et al. Clin Lymphoma Myeloma Leuk. 2015(Suppl):S64-S69.

CAR T Therapy TEAEs

Non-Hematological

- CRS
- Neurological toxicity
- B cell aplasia
- Thrombocytopenia
- Neutropenia
- Immune-mediated pancytopenia

Commonly occurs with:

- Brexucabtagene autoleucel

PREVENT

- Provide effective education at treatment start and throughout
- Assess prior treatment risk factors, which may place patient at increased risk (e.g., age, genetics, comorbidities)

MONITOR

- Monitor and assess CRS and ICANs by grade
- Provide brain imaging for neurologic symptoms (MRI > CT)

MITIGATE SYMPTOMS

- Low-grade CRS and neurotoxicity can be managed by supportive care or corticosteroids
- Provide prophylactic antiseizure medication if needed
- Provide monthly immunoglobulin G for patients at risk of infection

CRS, cytokine release syndrome; TEAE, treatment-emergent adverse events.

1. Wang M et al. J Clin Oncol. 2022(41):555-567.
2. Adkins S. *J Adv Pract Oncol*. 2019(Suppl 3):21-28.

Covalent BTK Inhibitor TEAEs

Hematological

- Thrombocytopenia
- Neutropenia

Non-Hematological

- Atrial fibrillation/flutter
- Infection
- Bleeding
- Diarrhea
- Fatigue
- Rash
- Upper RTI

Commonly occurs with:

- Ibrutinib

PREVENT

- Provide effective education at treatment start and throughout
- Assess prior treatment risk factors, which may place patient at increased risk (e.g., age, genetics, comorbidities)

MONITOR

- Assess during each visit and more frequently as needed
- Monitor for signs of atrial fibrillation, bleeding, hypertension during treatment

MITIGATE SYMPTOMS

- Administer direct oral anticoagulants and discontinue BTK inhibitor if atrial fibrillation not controlled
- Use antihypertensive medication for hypertension
- Consider prophylaxis for patients at increased risk of opportunistic infection

BTK, Bruton kinase; RTI, respiratory tract infection; TEAEs, treatment-emergent adverse events.

1. Wang M et al. *J Clin Oncol*. 2023(3):555-567. 2. Wang M et al. *Leukemia*. 2019(11):2762-2766.
3. Tam CS et al. *Blood Adv*. 2021(12):2577-2585. 4. O'Brien SM et al. *Front Oncol*. 2021(11):720704.

Non-Covalent BTK Inhibitor TEAEs

Hematological

- Thrombocytopenia
- Neutropenia

Non-Hematological

- Atrial fibrillation/flutter
- Infection
- Bleeding
- Diarrhea
- Fatigue
- Pneumonia

Commonly occurs with:

- Pirtobrutinib

PREVENT

- Provide effective education at treatment start and throughout
- Assess prior treatment risk factors, which may place patient at increased risk (e.g., age, genetics, comorbidities)

MONITOR

- Assess during each visit and more frequently as needed
- Monitor for signs of hypertension during treatment

MITIGATE SYMPTOMS

- Administer direct oral anticoagulants and discontinue BTK inhibitor if atrial fibrillation not controlled
- Use antihypertensive medication for hypertension
- Suggest use of Imodium for diarrhea symptoms
- Provide appropriate and prompt intervention by grading of rash symptoms

TEAE, treatment-emergent adverse events.

1. Wang M et al. *J Clin Oncol*. 2023(3):555-567.

BCL2 Inhibitor TEAEs

Hematological

- Thrombocytopenia
- Neutropenia
- Anemia

Non-Hematological

- Diarrhea
- Fatigue
- Upper RTI
- Nausea
- Headache
- Vomiting

Commonly occurs with:

- Venetoclax

PREVENT

- Provide effective education at treatment start and throughout
- Assess prior treatment risk factors, which may place patient at increased risk (e.g., age, genetics, comorbidities)

MONITOR

- Assess during each visit and more frequently as needed
- Monitor for signs of infection and bleeding during treatment

MITIGATE SYMPTOMS

- Use prophylactic measures to reduce opportunistic infection and tumor lysis syndrome
- Delays between venetoclax cycles may be need to address cytopenia and neutropenia
- Consider venetoclax dosing adjustment to address cytopenia
- Avoid grapefruit products to avoid CYP3A4 inhibitors

RTI, respiratory tract infection; TEAE, treatment-emergent adverse events.

1. Davids MS et al. *Clin Cancer Res*. 2022(17):4690-4695.
2. Richard-Carpentier G et al. *Ther Adv Hematol*. 2019(10): 2040620719882822.

Allogeneic Stem Cell Transplant TEAEs

Non-Hematologic

- GVHD
- Infection
- Bleeding
- Anemia
- Mucositis
- Abdominal pain
- Diarrhea

PREVENT

- Provide effective education at treatment start and throughout
- Assess prior treatment risk factors, which may place patient at increased risk (e.g., age, genetics, comorbidities)

MONITOR

- Assess patient quality of life symptoms via patient-reported outcomes or other tools to identify impact of GVHD
- Monitor for signs of fibrillation or bleeding during treatment
- Assess infections that may be a result of graft failure

MITIGATE SYMPTOMS

- Provide therapies to prevent acute GVHD from occurring
- Use direct oral anticoagulants if needed to control bleeding
- Consider prophylaxis for patients at increased risk of opportunistic infection
- Use of human keratinocyte growth factor for mucositis

GVHD, graft-versus-host-disease; TEAEs, treatment-emergent adverse events.

1. Davids MS et al. *Clin Cancer Res*. 2022(17):4690-4695.

Part 3:
Collaboration Between Clinicians and Patients

Interdisciplinary Teams for Management of MCL in Europe

Variation among European countries is a challenge

- Governance
- Clinical standardization
- Awareness and education
- Reimbursement
- Infrastructure
- Evidence generation

European Alliance for Personalised Medicine

EHA LyG EHA Lymphoma Group

European MCL Network

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Differences Between European Countries

Mats Jerkeman, MD

Christiane Pott, MD

Carlo Visco, MD

Ongoing Clinical Trials in MCL Treatment

Bispecific antibodies
- Glofitamab ± obinutuzumab
- Glofitamab ± pirtobrutinib
- Epcoritamab
- Odronextamab
- Mosunetuzumab + polatuzumab

CAR T Therapy
- Lisocabtagene maraleucel

BCL2 antagonists

Zilovertamab vedotin

Proteolysis targeting chimeras (PROTACS)

BTK inhibitors (covalent)
- Acalabrutinib monotherapy
  - Approved in the US in 2017 for 2L treatment of MCL
- Zanubrutinib monotherapy
  - Approved in the US in 2019 for 2L treatment of MCL

1. Kumar A et al. *Am Soc Clin Oncol Educ Book*. 2022(42):1-15.

Shared-Decision Making with Patients

Joint process between healthcare providers and patients based on evidence-based information and a patient's preferences, beliefs, and values

- Outcomes
- Benefits
- Harms
- Uncertainties

Empowers patients to make decisions about the treatment and care that is right for them at that time, including choosing to continue with their current treatment or choosing no treatment at all

1. National Institute for Health and Care Excellence (NICE). Making Decisions About Your Care. 2023. https://www.nice.org.uk/about/nice-communities/nice-and-the-public/making-decisions-about-your-care/patient-decision-aids.
2. Council of Europe. Good Practice. 2023. https://www.coe.int/be/web/bioethics/-/shared-decision-making-tools-and-guidelines-uk

Increasing Patient Participation in Clinical Trials

Lack of diversity is a barrier to the interpretation of safety and efficacy data across population subgroups, which is imperative in reducing disparities and advancing health equity

Barriers

- Medical mistrust
- Trial availability
- Patient access
- Patient eligibility criteria
- Enrollment practices
- Negative beliefs, norms, and attitudes

Solutions

- Provide patient education to increase interest
- Incorporate engagement among academic, community, government, and industry stakeholders
- Increase clinical trial center locations
- Utilize digital tools to improve accessibility of clinical research
- Improve representation among investigators and clinical research staff

1. Gray DM et al. *Lancet Gastroenterol Hepatol*. 2021(8):605-607. 2. Kelsey MD et al. *Contemp Clin Trials*. 2022(116):106740.

Key Points

- As a heterogenous disease, MCL continues to be a complex disease to treat and manage
- Novel targeted therapies for R/R MCL have improved patient outcomes with promising options undergoing clinical trials
- Shared-decision making and communication between hematologists and patients are imperative in the treatment and management of MCL

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