Società Italiana di Ematologia

FORMAZIONE SIE

I linfomi: un nome con almeno 40 sfaccettature!

25 giugno 2026

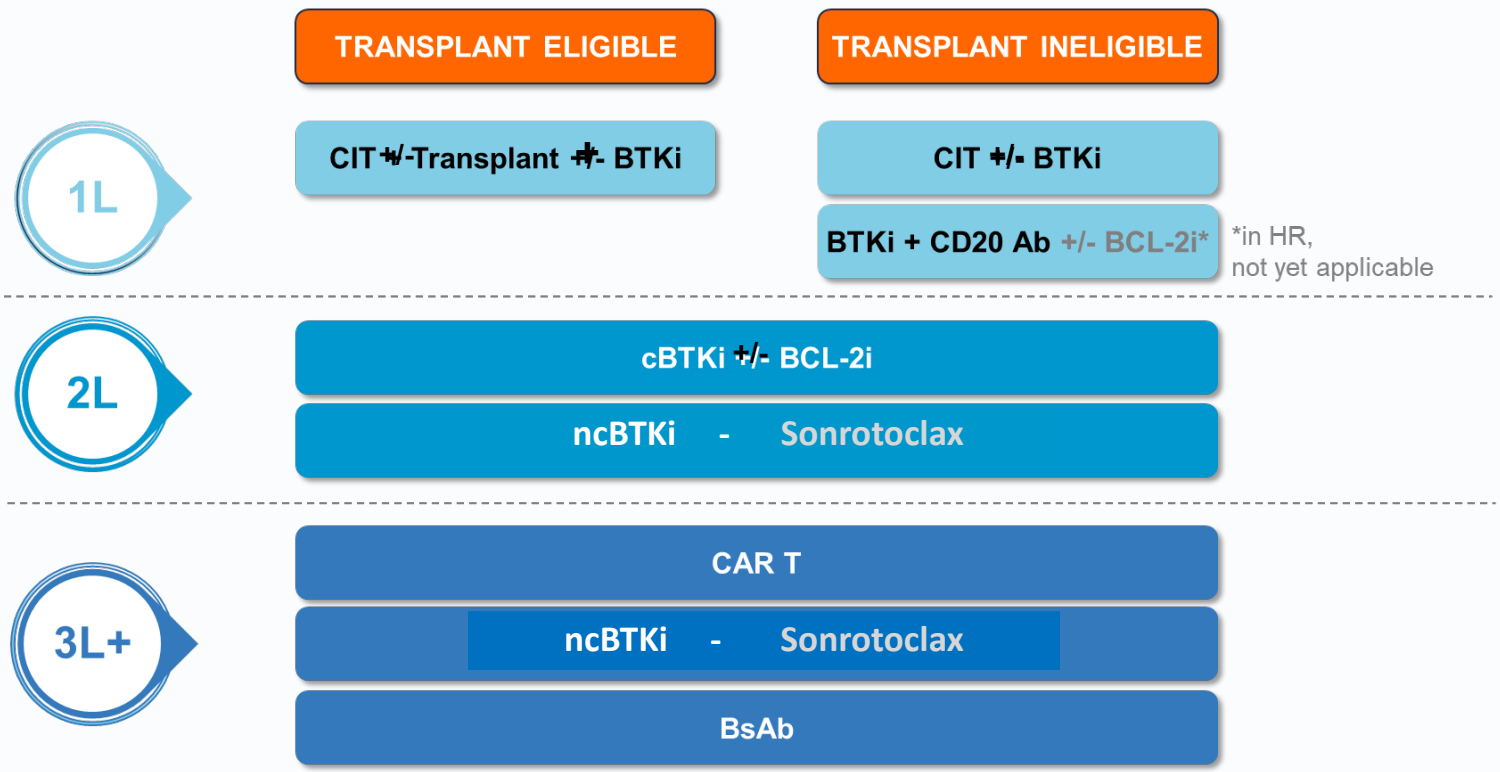
Bologna
Royal Hotel
Carlton

Linfoma mantellare

Disclosures of Carlo Visco

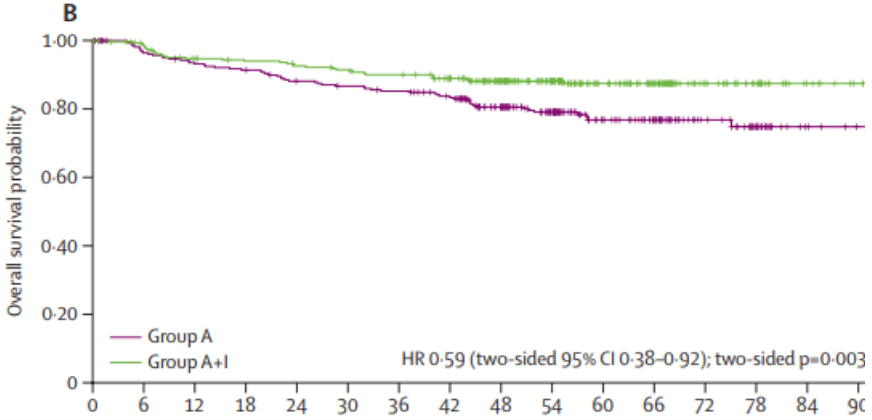
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
AbbVie	X				X	X	
Kite-Gilead					X	X	
Janssen	X		X		X	X	
Gentili					X	X	
Novartis						X	
Pfizer			X		X	X	
Roche					X	X	
Incyte					X	X	
Servier					X		
Astra Zeneca					X		
BMS						X	
Kyowa Kirin					X		
Beigene					X		
Lilly			X		X	X	

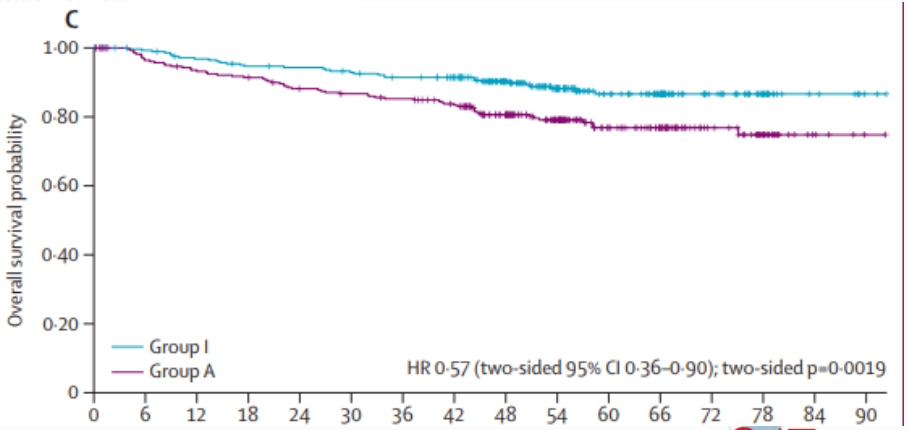
Evolving MCL Treatment Algorithm



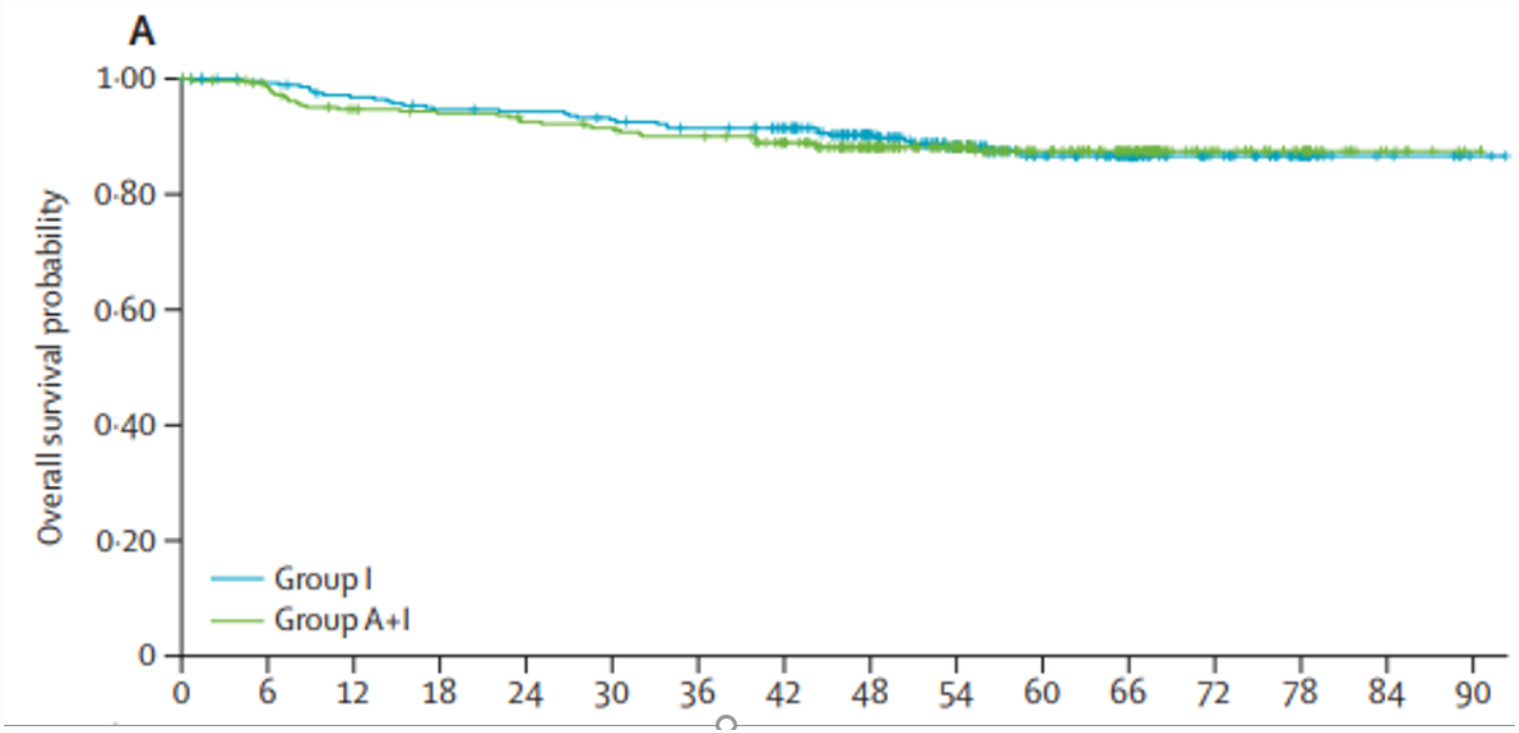
Addition of autologous stem-cell transplantation to an ibrutinib-containing first-line treatment in patients aged 18–65 years with mantle cell lymphoma (TRIANGLE): 4·5-year follow-up of a three-arm, randomised, open-label, phase 3 superiority trial of the European MCL Network

Martin Dreyling, Jeanette Doorduijn, Eva Giné, Mats Jerkeman, Jan Walewski, Martin Hutchings, Ulrich Mey, Jon Riise, Marek Trneny, Vibeke K J Vergote, Ofer Shpilberg, Maria Gomes da Silva, Sirpa Leppä, Linmiao Jiang, Stephan Stilgenbauer, Andrea Kerkhoff, Ron D Jachimowicz, Georg Heß, Tom van Meerten, Stefan Wirths, Peter Herhaus, Urban Novak, Judith Dierlamm, Mathias Hänel, Christine Hanoun, Kristina Sonnevi, Carlo Visco, Daniela Donnarumma, Andrés J M Ferreri, Caterina Patti, Piero Maria Stefani, Christiane Pott, Wolfram Klapper, Christian Schmidt, Michael Unterhalt, Tobias Tix, Marco Ladetto, Eva Hoster*, on behalf of the European Mantle Cell Lymphoma Network*



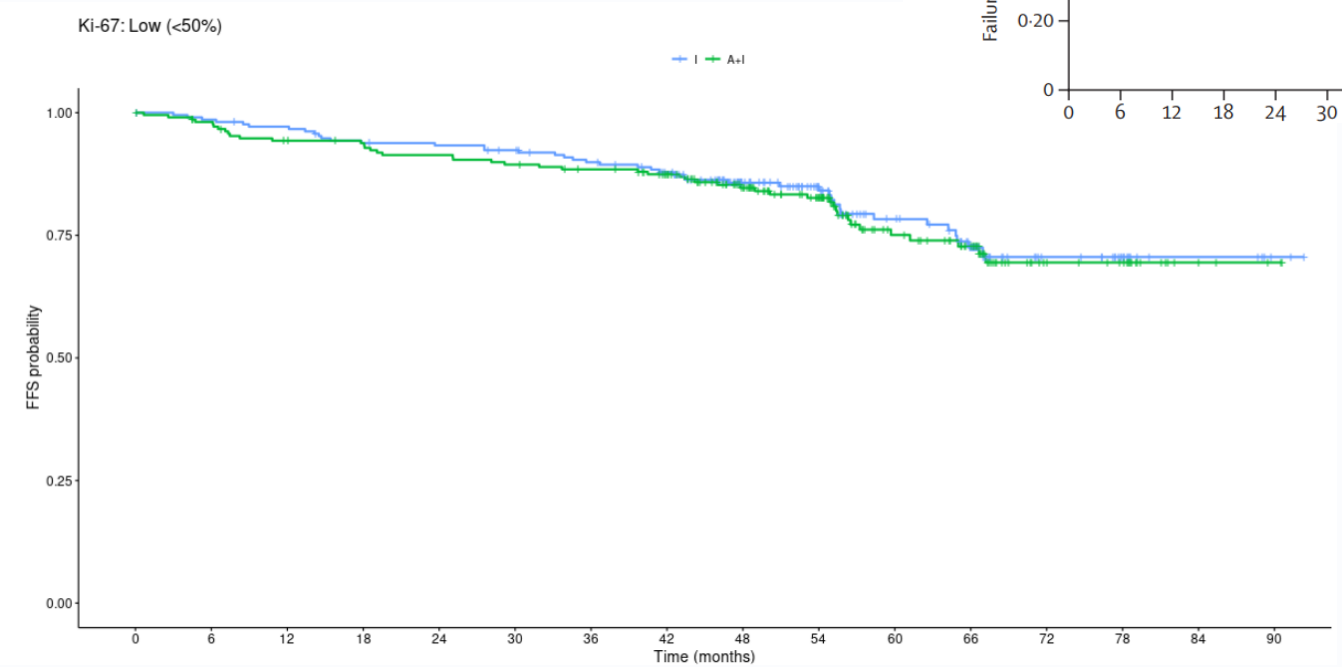


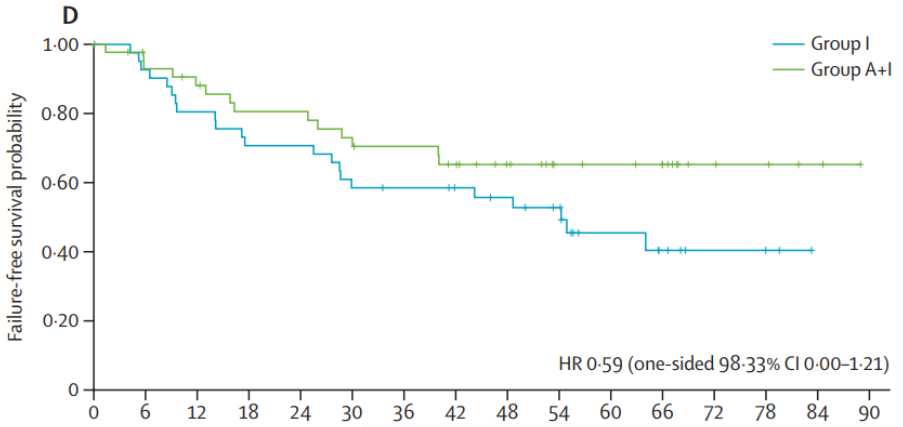
Overall Survival Probability



Ki-67 <50% vs high

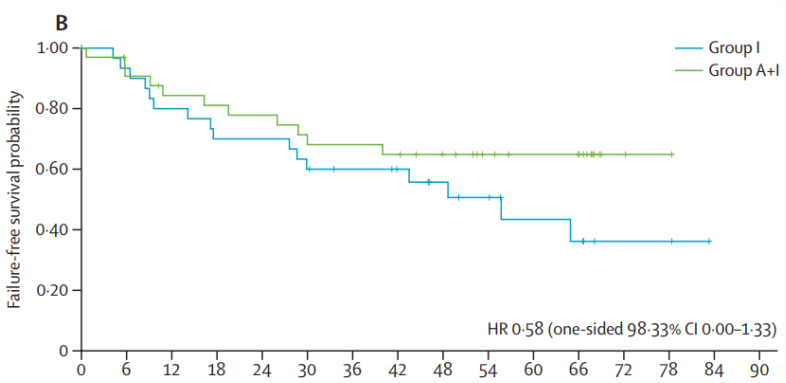
85%

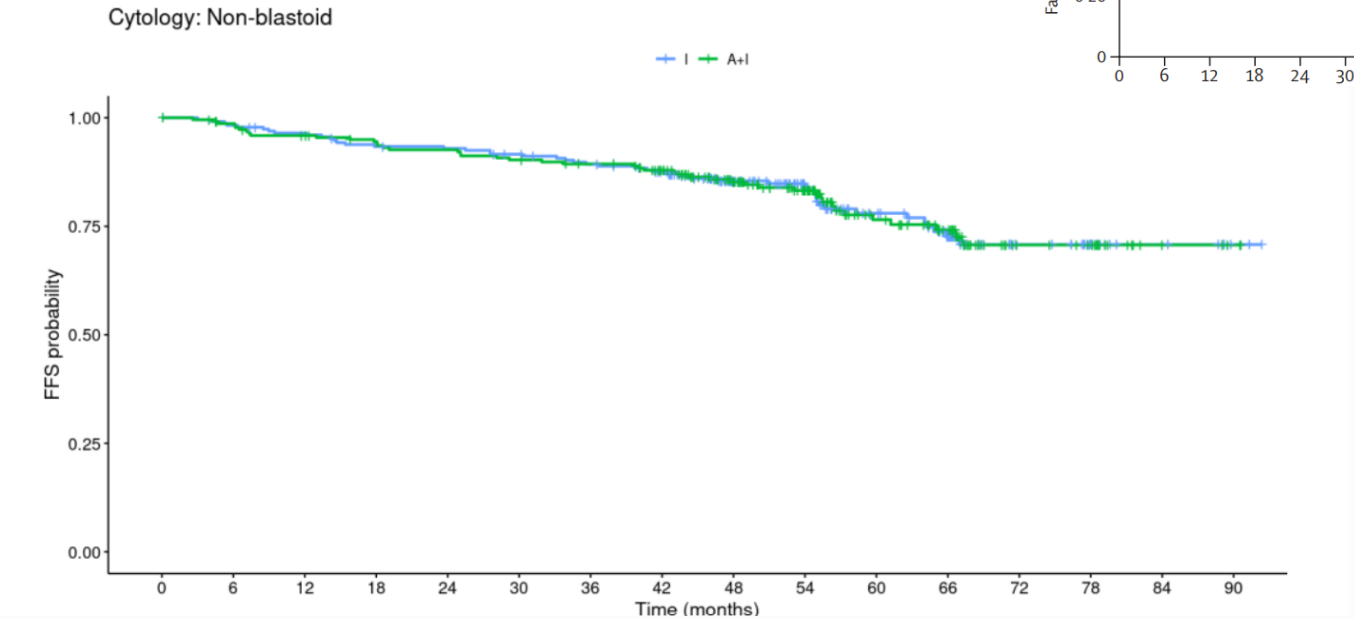




Non-blastoid vs Blastoid/PL

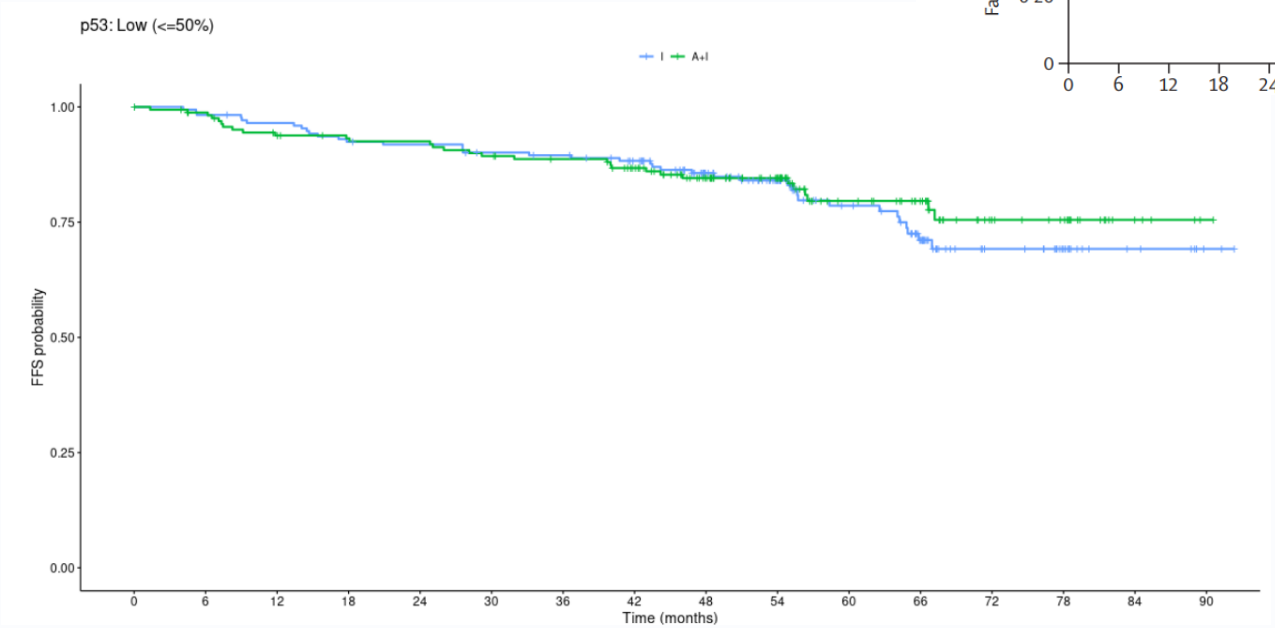
89%

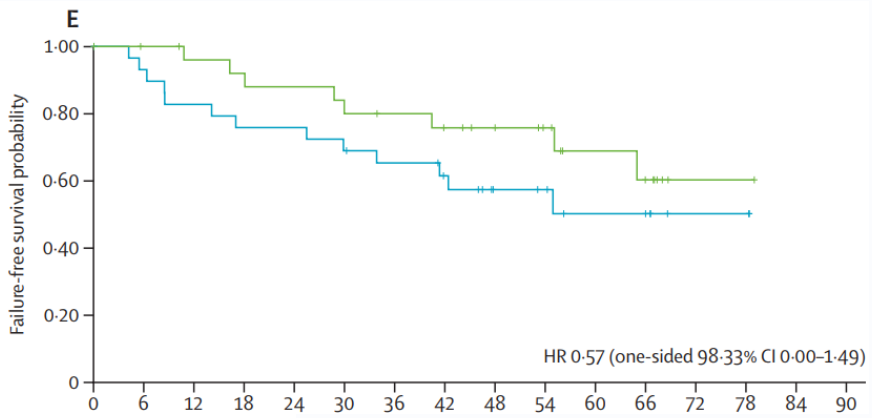




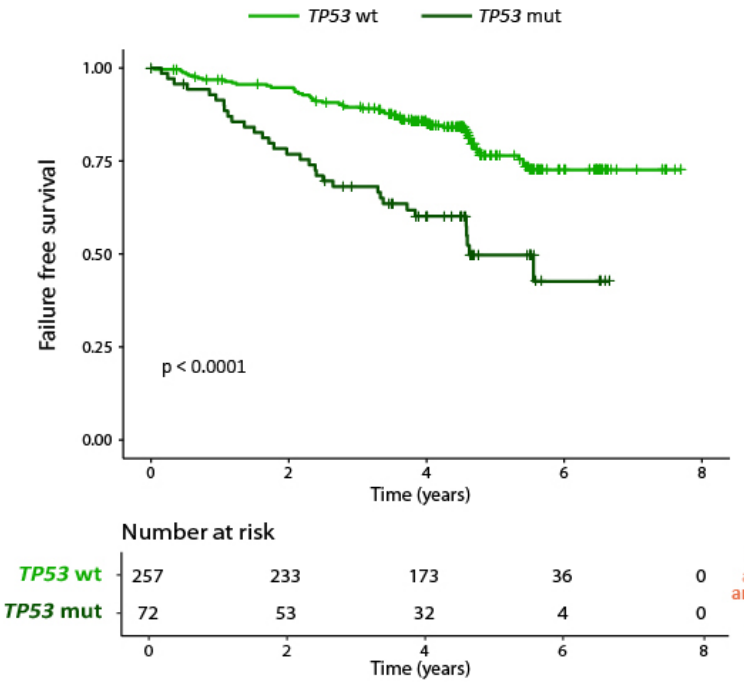
P53 IHC <=50% vs high

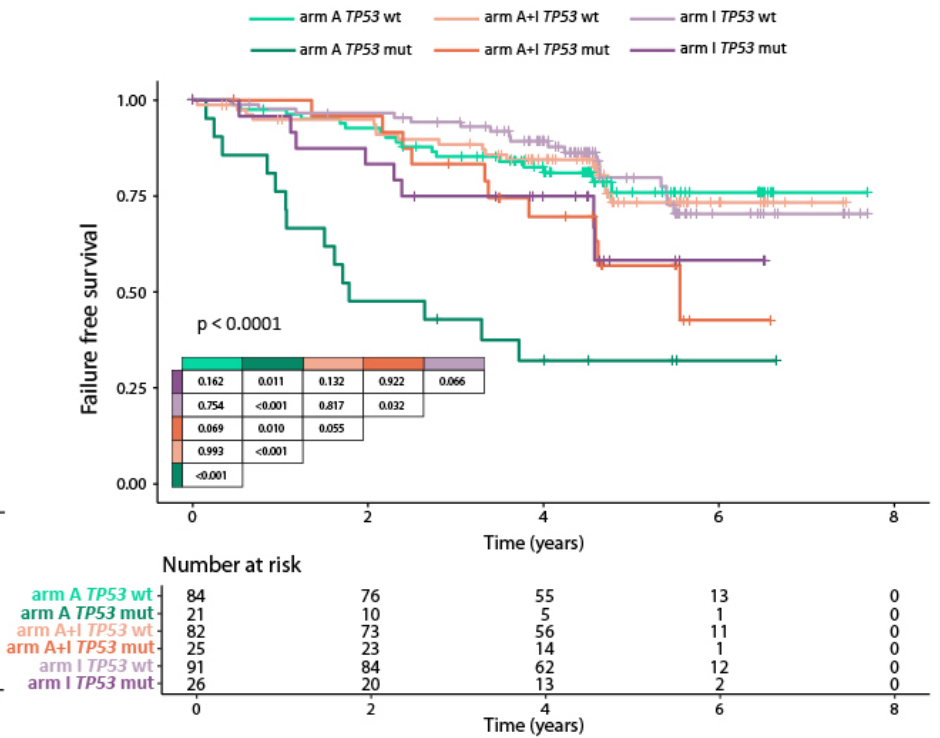
88%





TP53 mutation (first analysis at EHA)





ECHO Study Design

ECHO (NCT02972840): multicenter, double-blind, placebo-controlled, phase 3 trial

Primary endpoint:
- PFS (independent review committee)

Key secondary endpoints:
- ORR (independent review committee)
- OS

Safety

Untreated MCL (N=598)
- Age ≥65 years
- ECOG PS ≤2

Stratification

sMIPI score: Low vs intermediate vs high

Geographic region: North America vs Western Europe vs other

RANDOMIZE 1:1

ABR (N=299)

Bendamustine[a] + Rituximab[b] x 6 cycles → If ≥PR → Maintenance Rituximab (every 2 cycles x 2 years)

Acalabrutinib 100 mg BID, PO until PD or toxicity

PBR (N=299)

Bendamustine[a] + Rituximab[b] x 6 cycles → If ≥PR → Maintenance Rituximab (every 2 cycles x 2 years)

Placebo BID, PO until PD or toxicity

Crossover to acalabrutinib after PD was permitted

1 cycle = 28 days

Enrollment: April 2017 to March 2023
Sites: 195 globally

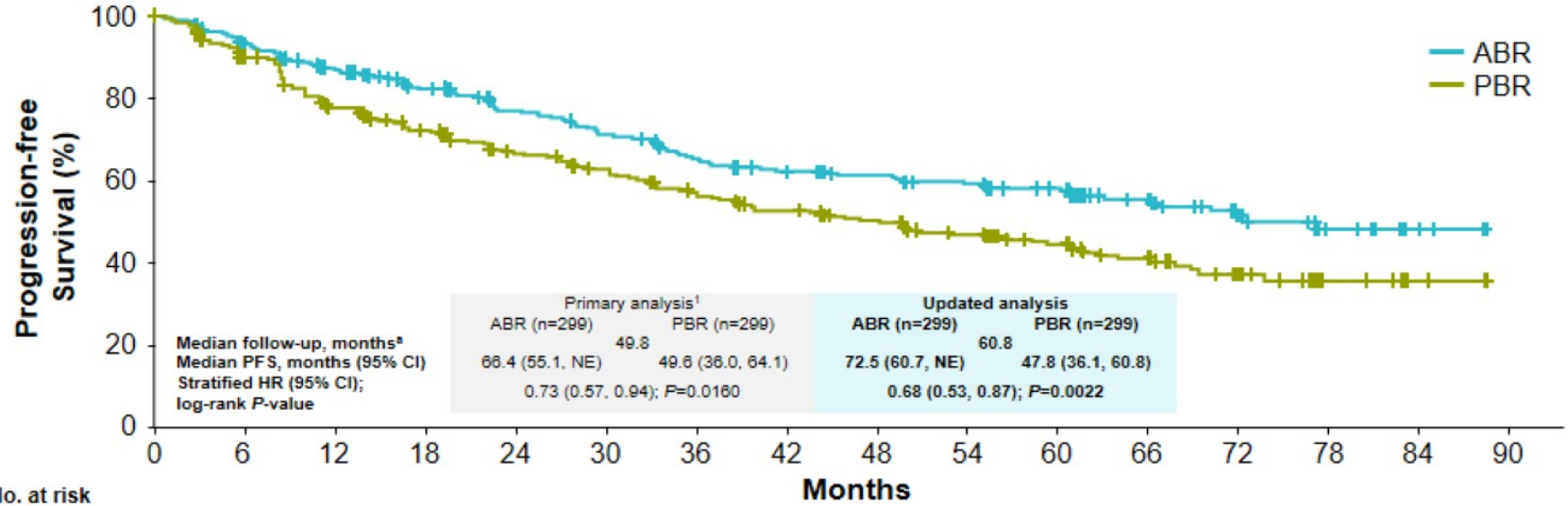
Updated Analysis (1 additional year of follow-up)

Data cutoff date: February 15, 2025

Median time on study: 51.9 (0.03–93.04) months

[a]Bendamustine 90 mg/m² on days 1 and 2. [b]Rituximab 375 mg/m² on day 1.
ABR, acalabrutinib plus bendamustine-rituximab; BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; KM, Kaplan-Meier; MCL, mantle cell lymphoma; PBR, placebo plus bendamustine and rituximab; PD, progressive disease; PFS, progression-free survival; PR, partial response; ORR, overall response rate; OS, overall survival; PO, orally; sMIPI, simplified MCL International Prognostic Index.

At 60.8 Months of Follow-up, PFS Further Improved With ABR vs PBR



No. at risk																
ABR	299	258	232	205	184	165	147	131	123	115	95	70	39	18	4	0
PBR	299	244	205	182	160	145	128	116	103	89	74	56	27	11	3	0

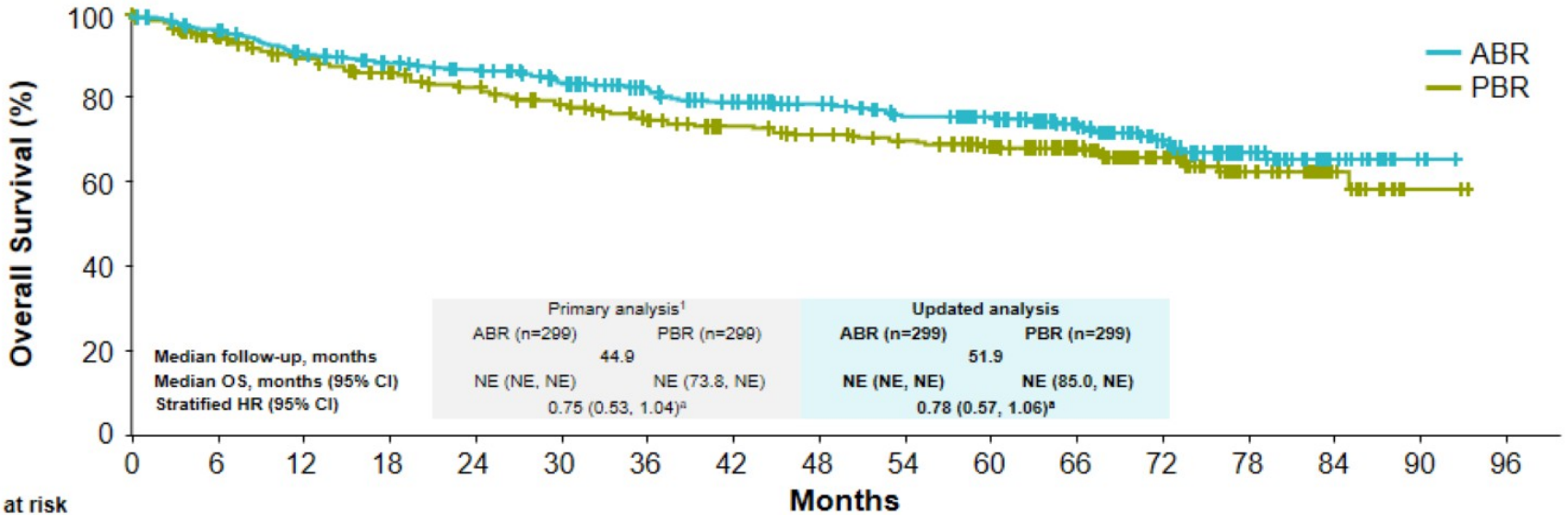
- PFS risk reduction with ABR vs PBR increased from 27% (primary analysis) to 32% (updated analysis)
- Median PFS was longer with ABR vs PBR (6 years vs 4 years)

[a]Median follow up for PFS estimated using the reverse K-M method.
ABR, acalabrutinib plus bendamustine-rituximab; CI, confidence interval; HR, hazard ratio; K-M, Kaplan-Meier; NE, not estimable; PBR, placebo plus bendamustine-rituximab; PFS, progression-free survival.

1. Wang M, et al. *J Clin Oncol*. 2025;43:2276-84.

ECHO Analysis

Prespecified OS Analysis Censoring for COVID-19 Deaths Showed Similar Trend as the Primary Analysis



No. at risk																
ABR	299	280	259	243	231	212	191	175	163	147	136	104	75	47	21	3	0
PBR	299	269	248	230	215	195	180	165	156	147	132	103	70	40	17	2	0

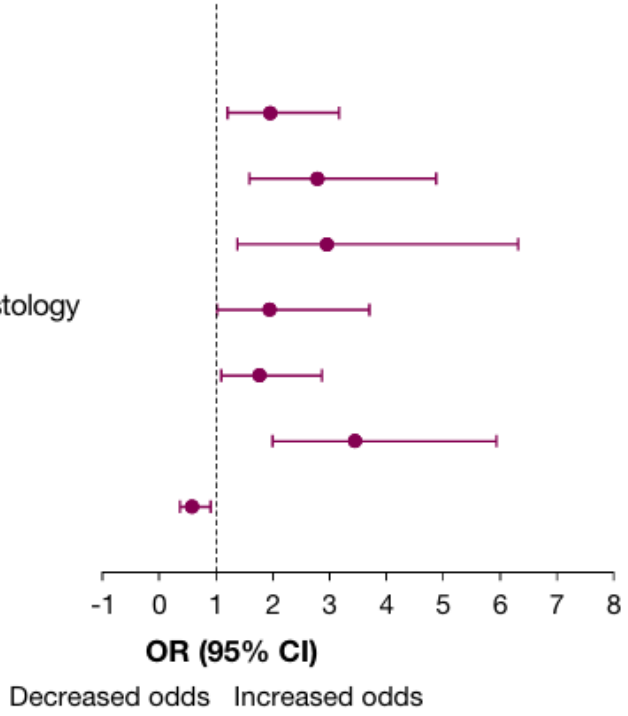
[a]This study was not powered to detect an OS benefit.
ABR, acalabrutinib plus bendamustine-rituximab; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PBR, placebo plus bendamustine-rituximab.

1. Wang M, et al. *J Clin Oncol*. 2025;43:2276-84.

ECHO Analysis

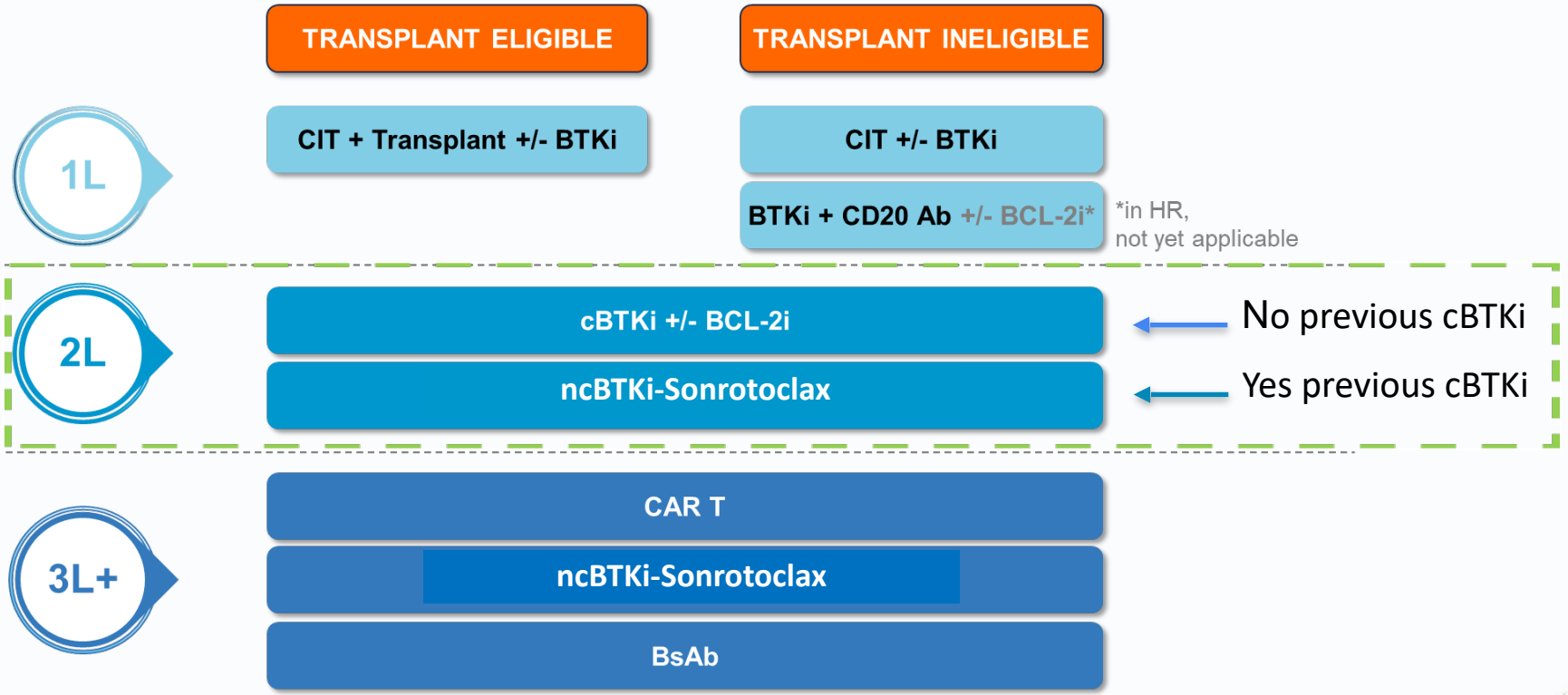
Factors impacting on **POD24 Status**

Comparison	OR	95% CI	*P*-value
Age ≥75 vs <75 y	1.950	1.200, 3.168	0.0070
Male vs female	2.782	1.587, 4.875	0.0004
Ann Arbor stage IV vs stage I–III	2.951	1.378, 6.320	0.0054
Blastoid/pleomorphic vs classic or other histology	1.943	1.020, 3.701	0.0434
Ki-67 ≥30% vs <30%	1.768	1.091, 2.864	0.0207
LDH ≥ULN	3.444	1.997, 5.939	<0.0001
Acalabrutinib vs Placebo	**0.577**	**0.366, 0.909**	**0.0177**

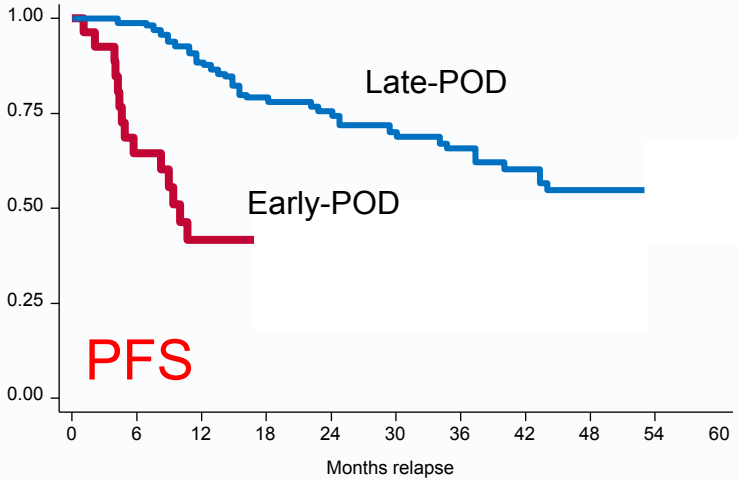


Cheah C, et al. ASH 2025

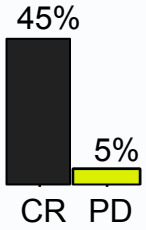
Evolving MCL Treatment Algorithm



Ibrutinib expected activity at the time of first relapse: survival and tumor response in late- versus early-POD, and management of the referral to CAR-T

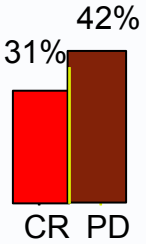


No previous cBTKi



Late-POD

Standard approach during BTKi
Refer to CAR-T centre if suboptimal response or high-risk features (i.e. TP53 mutation)



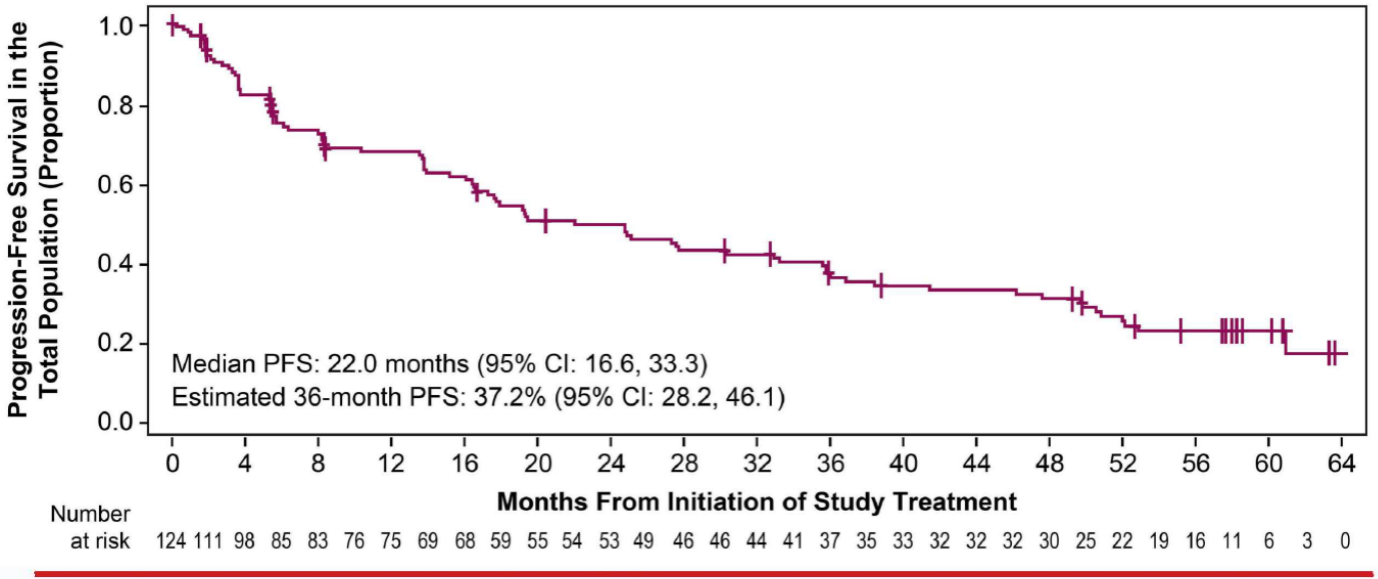
Early-POD

Refer to CAR-T centre at start of therapy
Close clinical monitoring
Restage 8-12 weeks

POD: progression of disease; PFS: progression-free survival; CR: complete response; PD: progressive disease

Visco C, modified from Leukemia 2020, and ICML-2023, Abstr 348 [https://doi.org/10.1002/hon.3164_348]

Final results and overall survival data from a phase II study of acalabrutinib monotherapy in patients with relapsed/refractory mantle cell lymphoma, including those with poor prognostic factors



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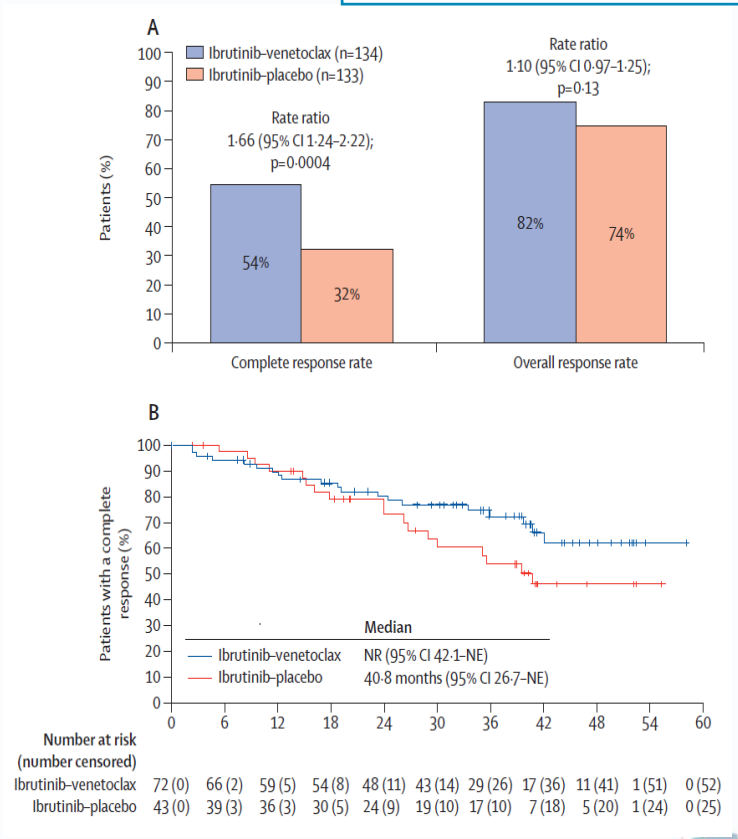
LeGouille S et al, Haematologica 2024

No previous cBTKi

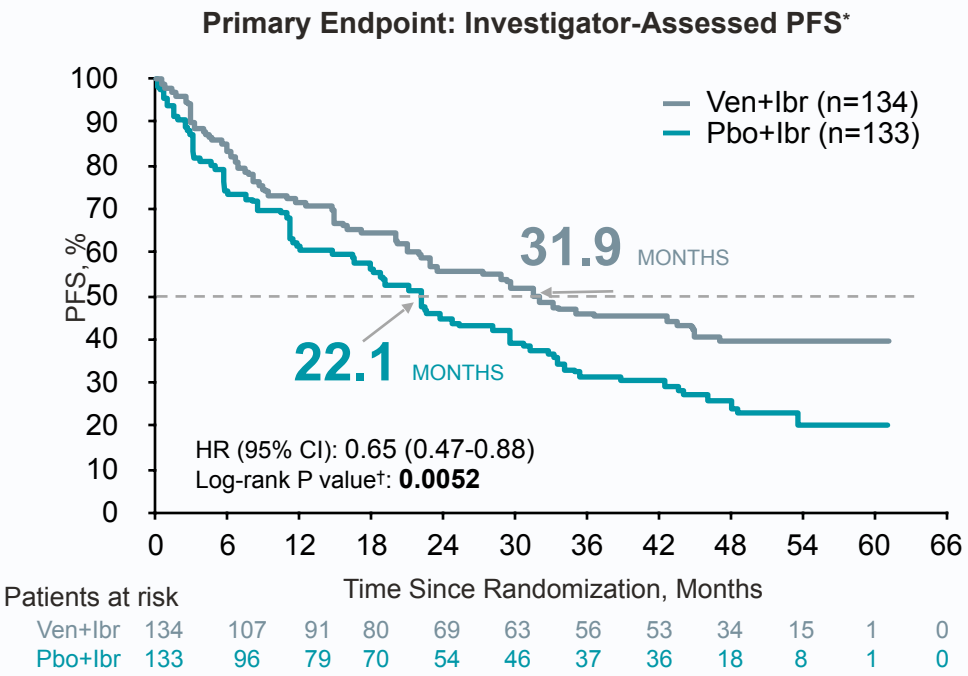
	Ibrutinib–venetoclax (n=134)	Ibrutinib–placebo (n=133)
Age, years	69 (62–74)	67 (60–73)
<65	41 (31%)	47 (35%)
≥65	93 (69%)	86 (65%)
Sex		
Female	31 (23%)	25 (19%)
Male	103 (77%)	108 (81%)
Race		
White	116 (87%)	115 (86%)
Asian	2 (1%)	3 (2%)
Black	1 (1%)	1 (1%)
Not reported	15 (11%)	14 (11%)
Ethnicity		
Hispanic, Latino, Latina, or Latinx	8 (6%)	7 (5%)
Other	112 (84%)	110 (83%)
Not reported	14 (10%)	16 (12%)
ECOG performance status		
0	74 (55%)	74 (56%)
1 or 2	60 (45%)	59 (44%)
Previous lines of therapy	1 (1–2)	1 (1–2)
1	80 (60%)	79 (59%)
2	32 (24%)	31 (23%)
≥3	22 (16%)	23 (17%)
Previous SCT	39 (29%)	50 (38%)



Wang M et al, Lancet Oncol 2025

Venetoclax + Ibrutinib: SYMPATICO

No previous cBTKi



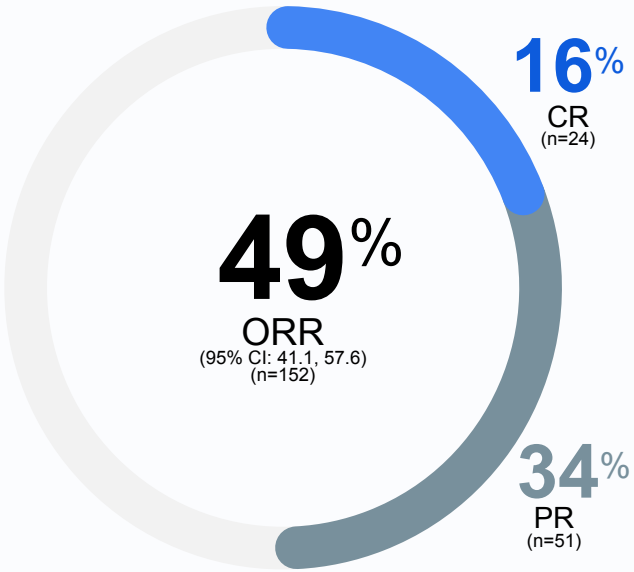
Most Frequent Adverse Events

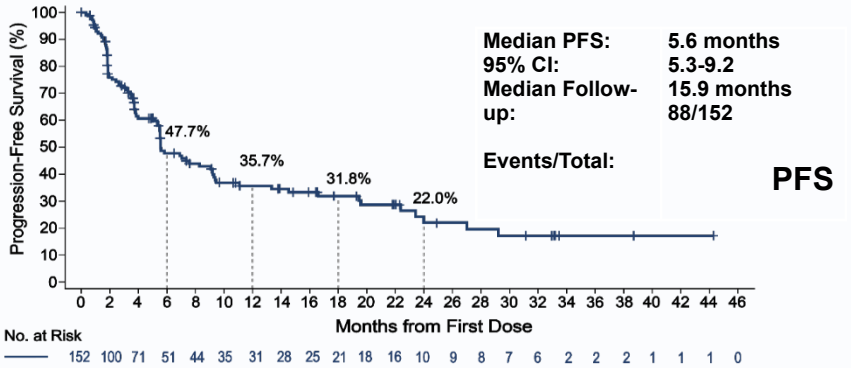
AE, n (%)	Ven+Ibr (n=134)	Pbo+Ibr (n=132)
Most frequent any-grade AEs‡		
Diarrhea	87 (65)	45 (34)
Neutropenia	46 (34)	19 (14)
Nausea	42 (31)	22 (17)
Fatigue	39 (29)	36 (27)
Anemia	30 (22)	16 (12)
Pyrexia	28 (21)	26 (20)
Cough	27 (20)	36 (28)
Asthenia	26 (20)	18 (14)
Thrombocytopenia	26 (20)	21 (15)
Most frequent grade ≥3 AEs§		
Neutropenia	42 (31)	14 (10)
Pneumonia	17 (13)	14 (11)
Thrombocytopenia	17 (13)	10 (7)
Anemia	13 (9)	4 (3)
Diarrhea	11 (8)	3 (2)
Leukopenia	10 (7)	0
MCL¶	9 (7)	16 (13)
Atrial fibrillation	7 (5)	7 (5)
Hypertension	6 (4)	12 (9)

Wang M et al, Lancet Oncol 2025

Pirtobrutinib in MCL previously treated with a cBTKi (n=152)

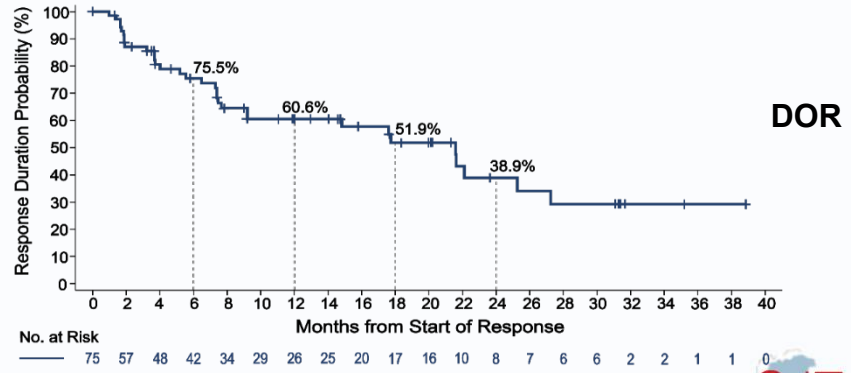
Yes previous cBTKi





Median PFS: 5.6 months
95% CI: 5.3-9.2
Median Follow-up: 15.9 months
Events/Total: 88/152

PFS



DOR

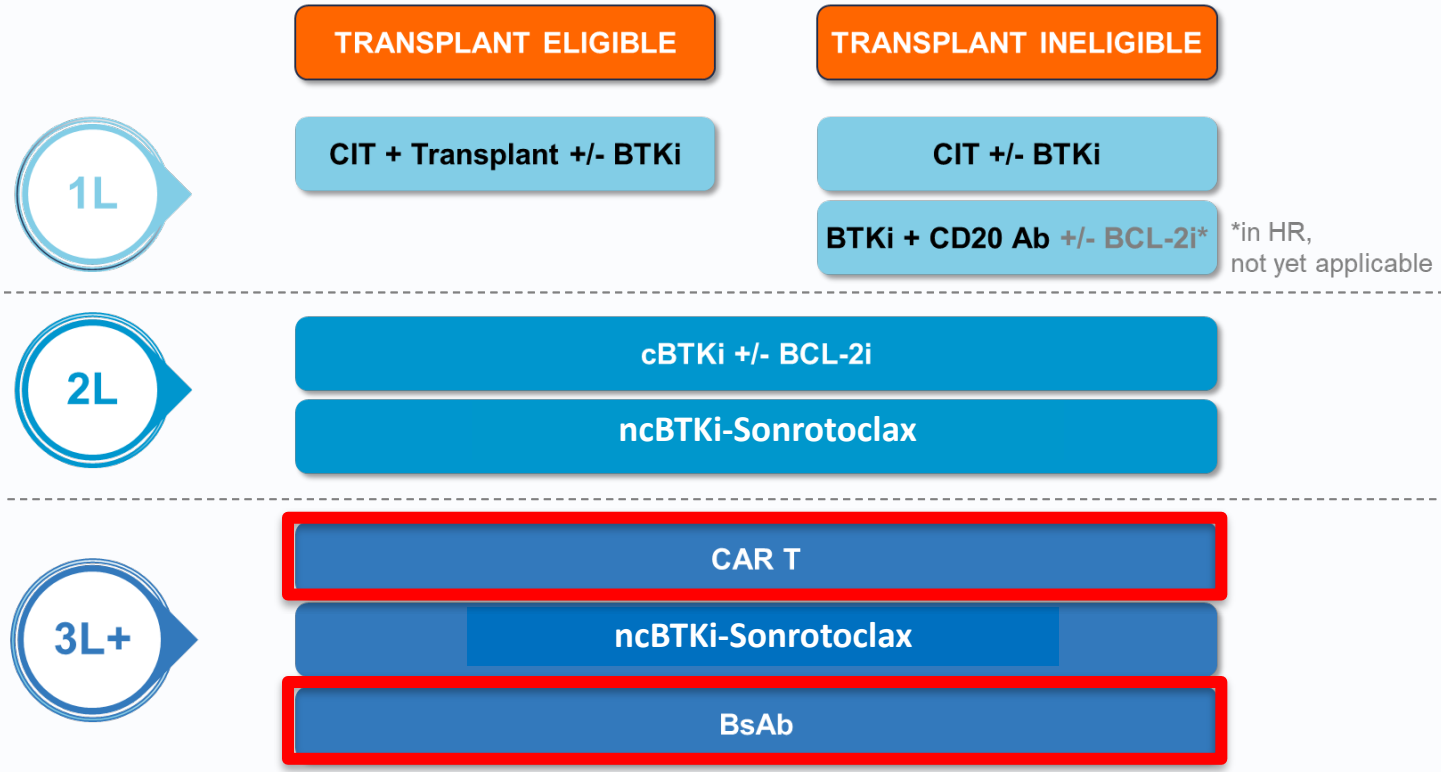
Cohen et al.; ASH 2023

Yes previous cBTKi

	Sonrotoclax	Venetoclax	Differences in Design
Potency (IC_{50})	0.014 nM[1]	0.20 nM[1]	14-fold more potent, which may potentially lead to deeper target inhibition
Selectivity (vs BCL-xL)	2000×[1]	325×[1]	Improved (6-fold) selectivity
Half-life in humans	≈5 hours[2]	26 hours[3]	Short half-life and no accumulation may potentially result in simplified TLS monitoring during sonrotoclax ramp-up

Wang M et al, ASH 2025

Evolving MCL Treatment Algorithm



Perspective in MCL

- In first line therapeutic shift ongoing….evolving field
- MCL patients with R/R disease are high-risk patients
- CarT the mainstay of the R/R algorithm
- Chemo-free options with clear results, some in development
- CIT (VR-CAP, BR, RBAC) left for debulking purposes

Thanks for your attention

FONDAZIONE ITALIANA LINFOMI

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