9th POSTGRADUATE
Lymphoma
Conference

ENRICH, SHINE, ECHO and beyond – BTKi in the FL-treatment of elderly patients

Florence,
March 20-21, 2025

Hotel Brunelleschi

President:
P.L. Zinzani

Disclosures G. Hess

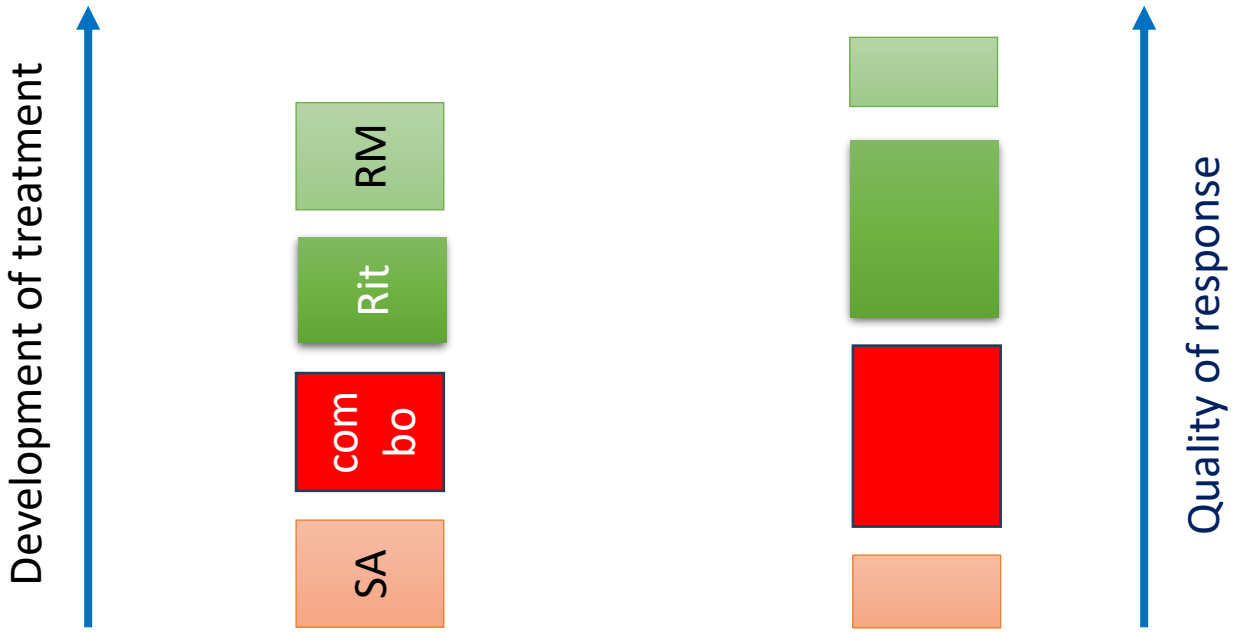
- Consultancy: Abbvie, ADC, AstraZeneca, Beigene, BMS, GileadKite, Incyte, Janssen, Lilly, Milenyie, MSD, Novartis, Pierre Fabre, Roche, Sobi
- Honoraria: Abbvie, ADC, AstraZeneca, Beigene, BMS, GileadKite, Incyte, Janssen, Lilly, Milenyie, MSD, Novartis, Roche, Sobi
- Research Funding (to institution): Abbvie, GileadKite, Janssen,Lilly
- Patents and Royalties: not applicable
- Membership on an entity's Board of Directors or advisory committees: not applicable
- Discussion of off-label drug use: not applicable
- Travel grants: Incyte, Janssen, Pierre-Fabre

JG|U UNIVERSITÄTSmedizin. MAINZ
Department of Haematology and Medical Oncology

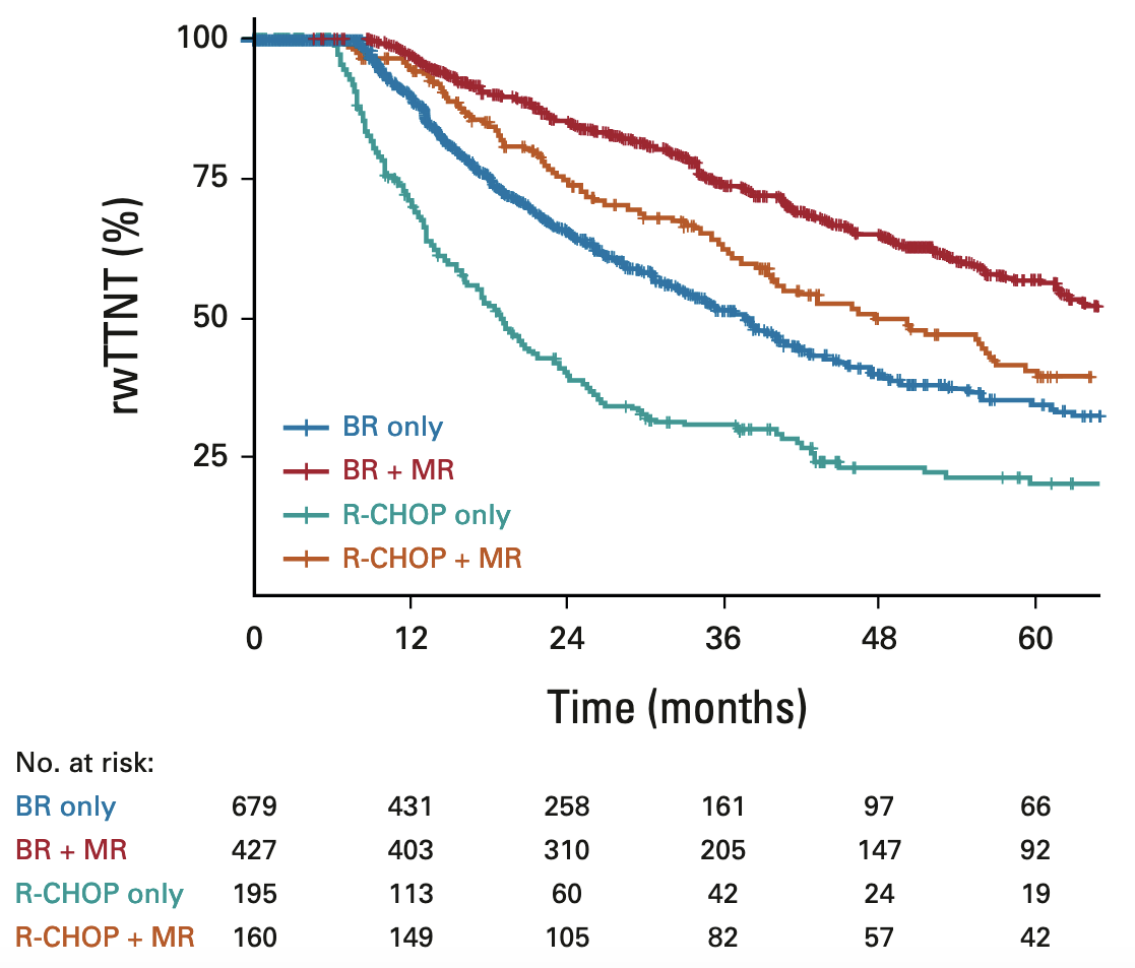
General considerations

Development of first line strategies

Development of novel options



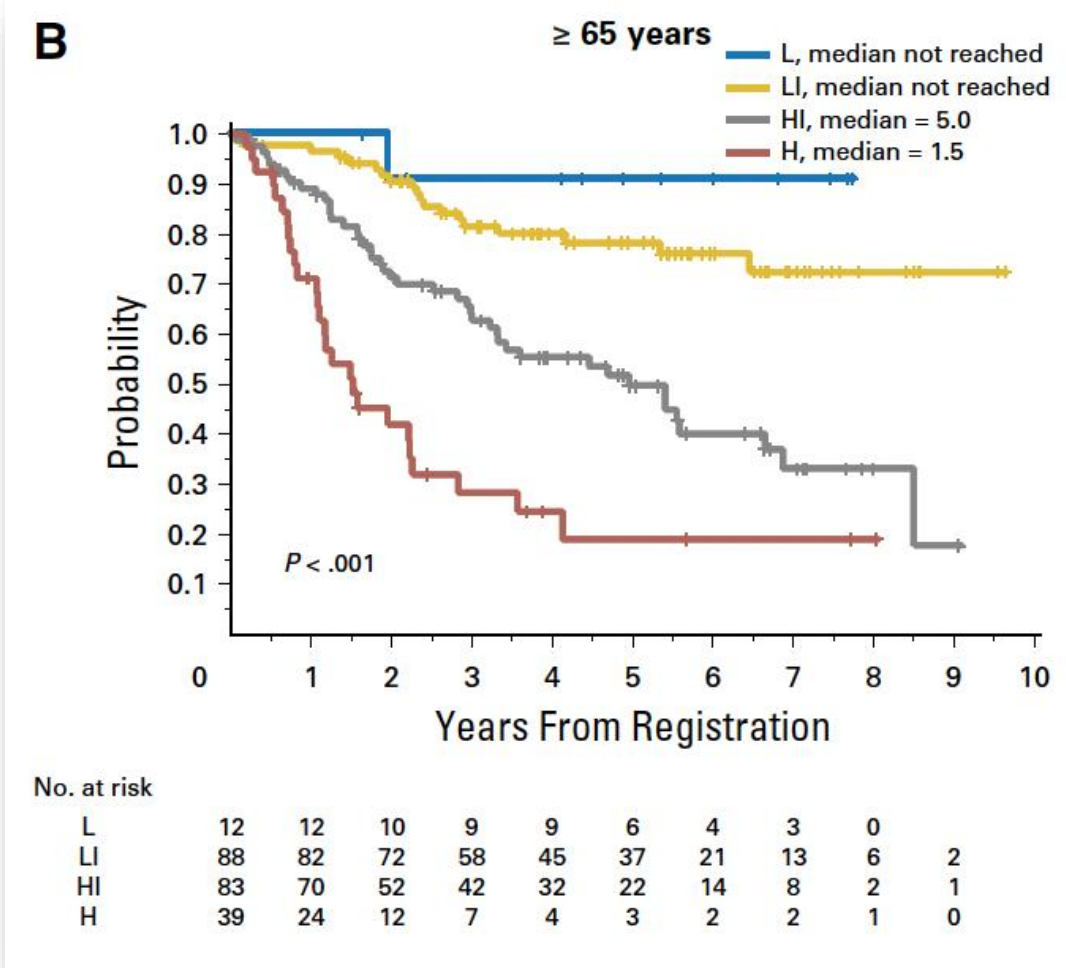
Results of standard regimen



No. at risk:

BR only	679	431	258	161	97	66
BR + MR	427	403	310	205	147	92
R-CHOP only	195	113	60	42	24	19
R-CHOP + MR	160	149	105	82	57	42

Martin et al., JCO; 2023



No. at risk

L	12	12	10	9	9	6	4	3	0	
LI	88	82	72	58	45	37	21	13	6	2
HI	83	70	52	42	32	22	14	8	2	1
H	39	24	12	7	4	3	2	2	1	0

Hoster el al., J Clin Oncol, 2016; 34(12):1386-94

Progressive shortening in response duration and survival

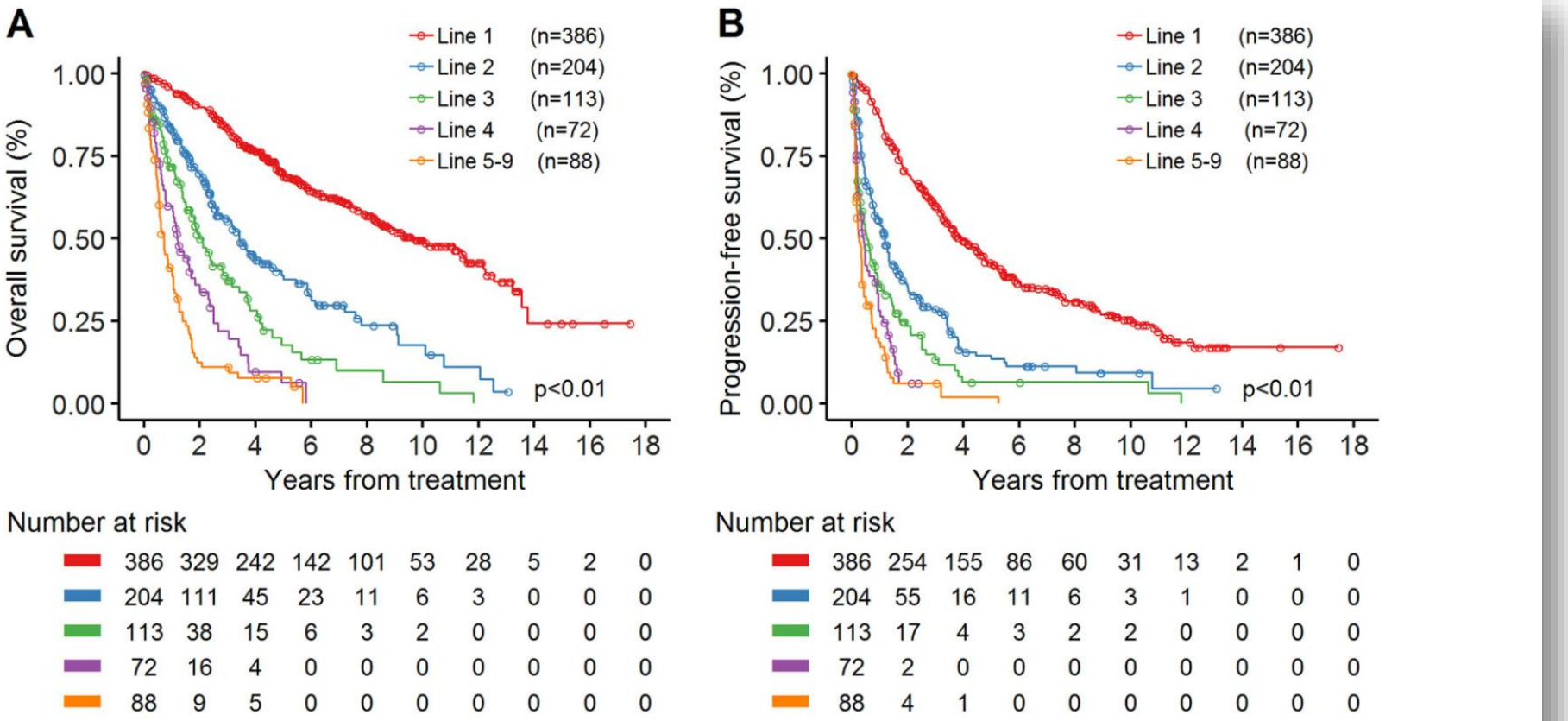


Fig. 5 Kaplan–Meier plots of overall survival (OS) and progression-free survival (PFS) in patients with mantle cell lymphoma after multiple lines of therapy. a, **b** OS and PFS after treatment with line 1, line 2, line 3, line 4, and line 5–9

Kumar et al. Blood Cancer J 2019; 9(6):50

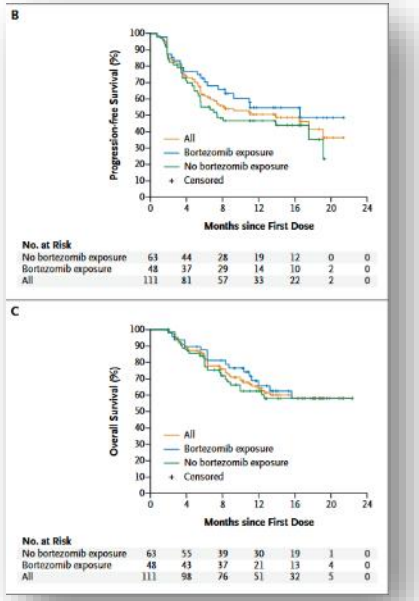
BTKi have changed the fate of relapsed MCL

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 8, 2013 VOL. 369 NO. 6

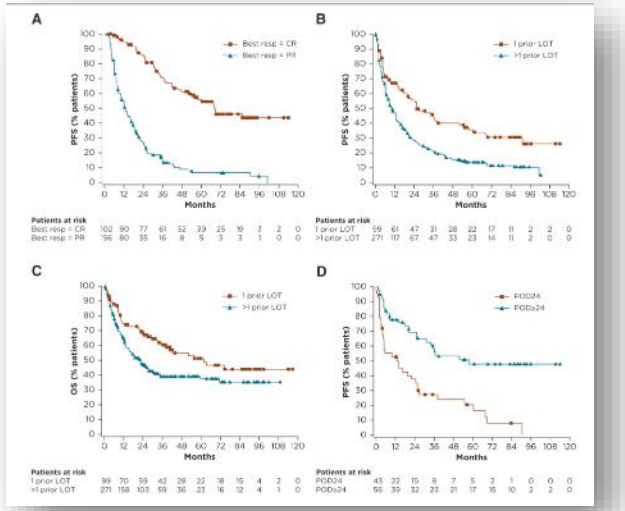
Targeting BTK with Ibrutinib in Relapsed or Refractory Mantle-Cell Lymphoma

Michael L. Wang, M.D., Simon Rule, M.D., Peter Martin, M.D., Andre Goy, M.D., Rebecca Auer, M.D., Ph.D., Brad S. Kahl, M.D., Wojciech Jurczak, M.D., Ph.D., Ranjana H. Advani, M.D., Jorge E. Romaguera, M.D., Michael E. Williams, M.D., Jacqueline C. Barrientos, M.D., Ewa Chmielowska, M.D., John Radford, M.D.,



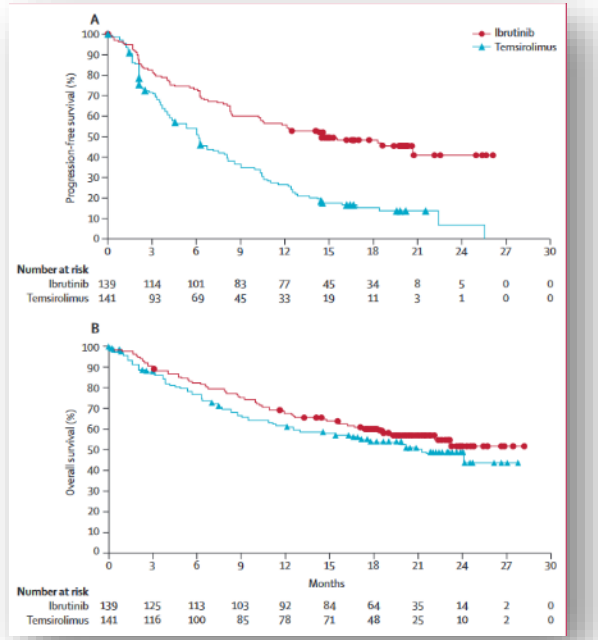
Long-term Outcomes With Ibrutinib Treatment for Patients With Relapsed/Refractory Mantle Cell Lymphoma: A Pooled Analysis of 3 Clinical Trials With Nearly 10 Years of Follow-up

Martin Dreyling[1], Andre Goy[2], Georg Hess[3], Brad S. Kahl[4], José-Ángel Hernández-Rivas[5], Natasha Schuier[6], Keqin Qi[7], Sanjay Deshpande[8], Angeline Zhu[8], Lori Parisi[8], Michael L. Wang[9]

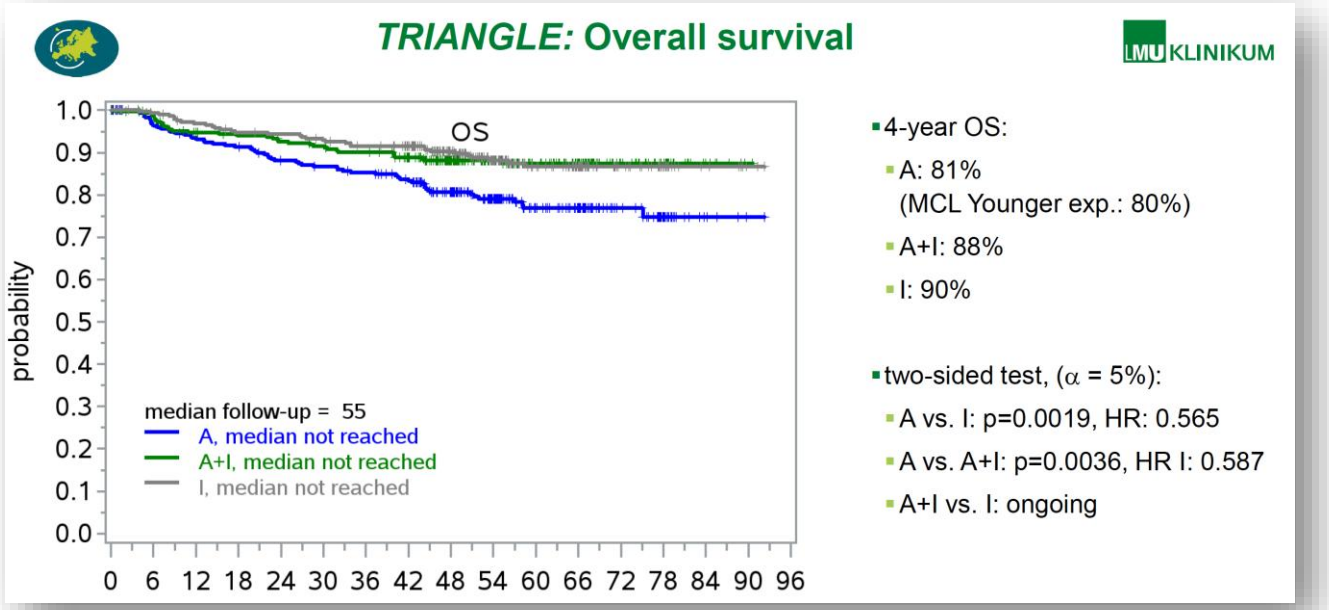


Ibrutinib versus temsirolimus in patients with relapsed or refractory mantle-cell lymphoma: an international, randomised, open-label, phase 3 study

Martin Dreyling*, Wojciech Jurczak*, Mats Jerkeman*, Rodrigo Santucci Silva, Chiara Rusconi*, Marek Trneny*, Fritz Offner*, Dolores Caballero*, Cristina Joao*, Mathias Witzens-Harig*, Georg Hess*, Isabelle Bence-Bruckler, Seok-Goo Cho, John Bothos, Jenna D Goldberg, Christopher Enny, Shana Traina, Sriram Balasubramanian, Nibedita Bandyopadhyay, Steven Sun, Jessica Vermeulen, Aleksandra Rizo, Simon Rule*

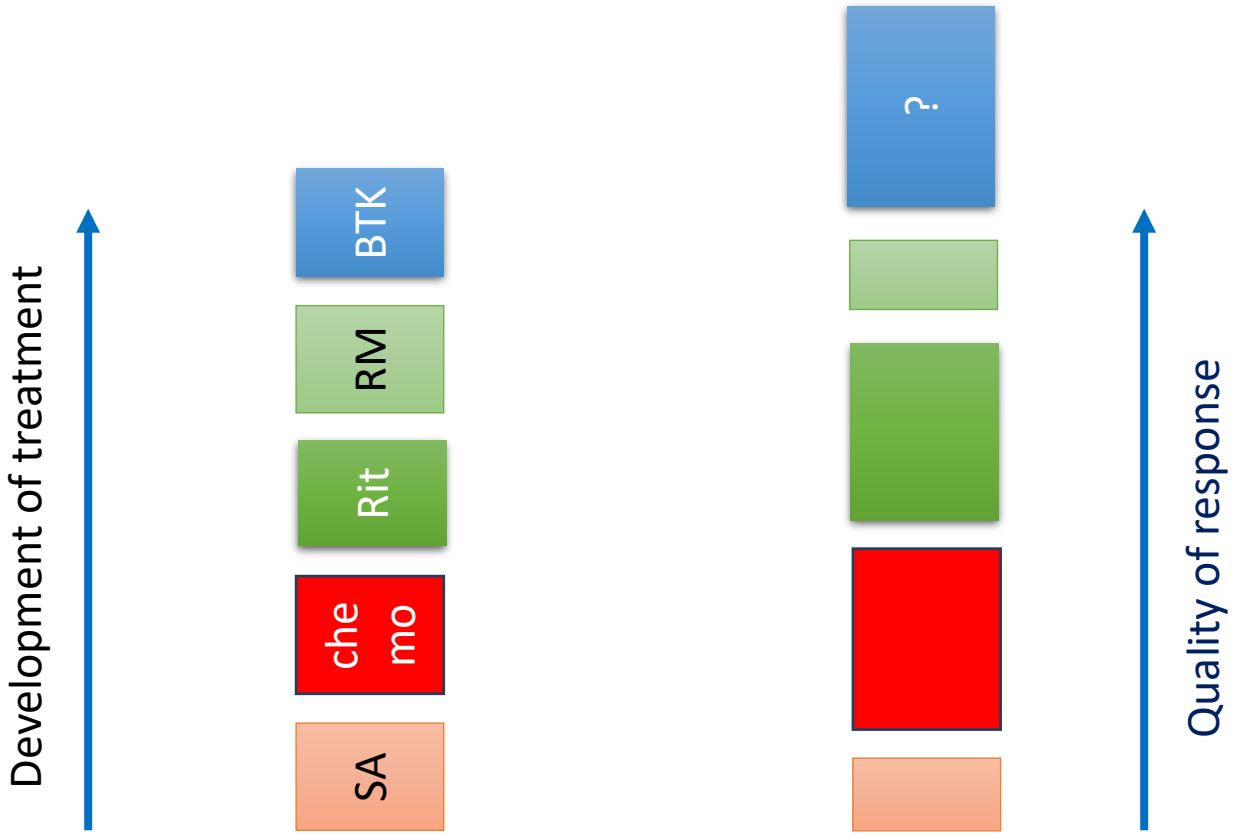


Add on strategies are of great benefit



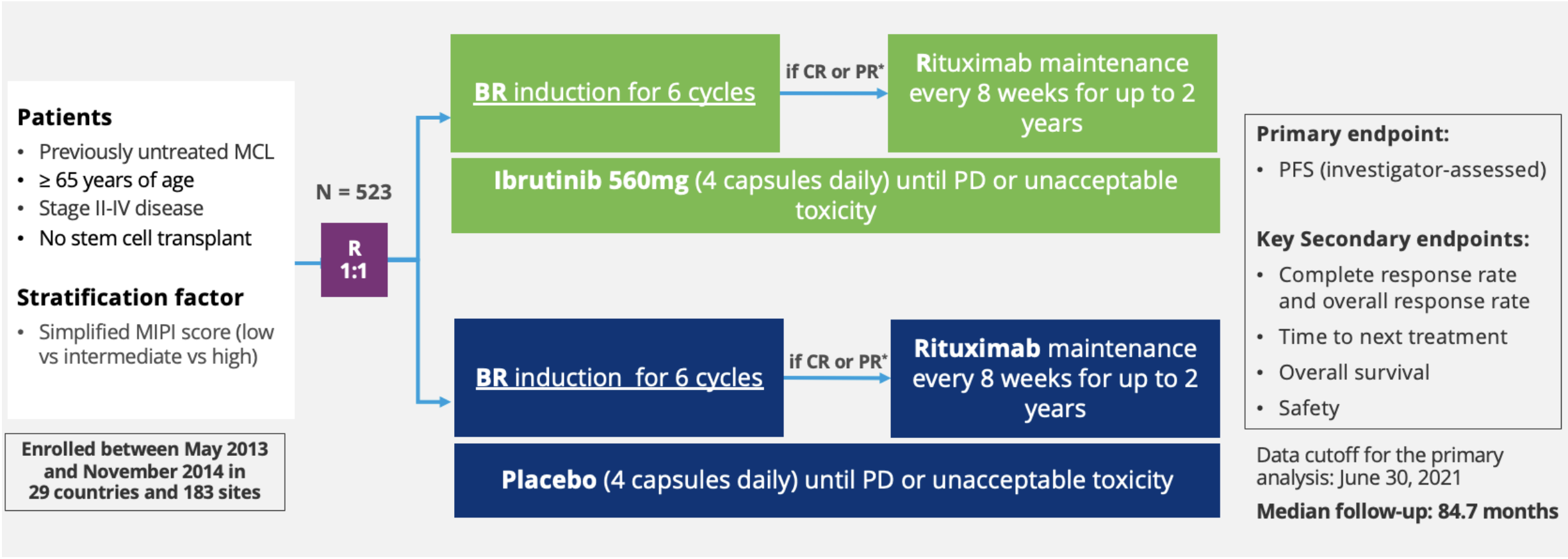
Similar impact on treatment of elderly patients?

Development of novel options



→ SHINE & ECHO

SHINE: Trial Design



Wang et al., EHA 2022; S209 (oral presentation; Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. Online ahead of print.

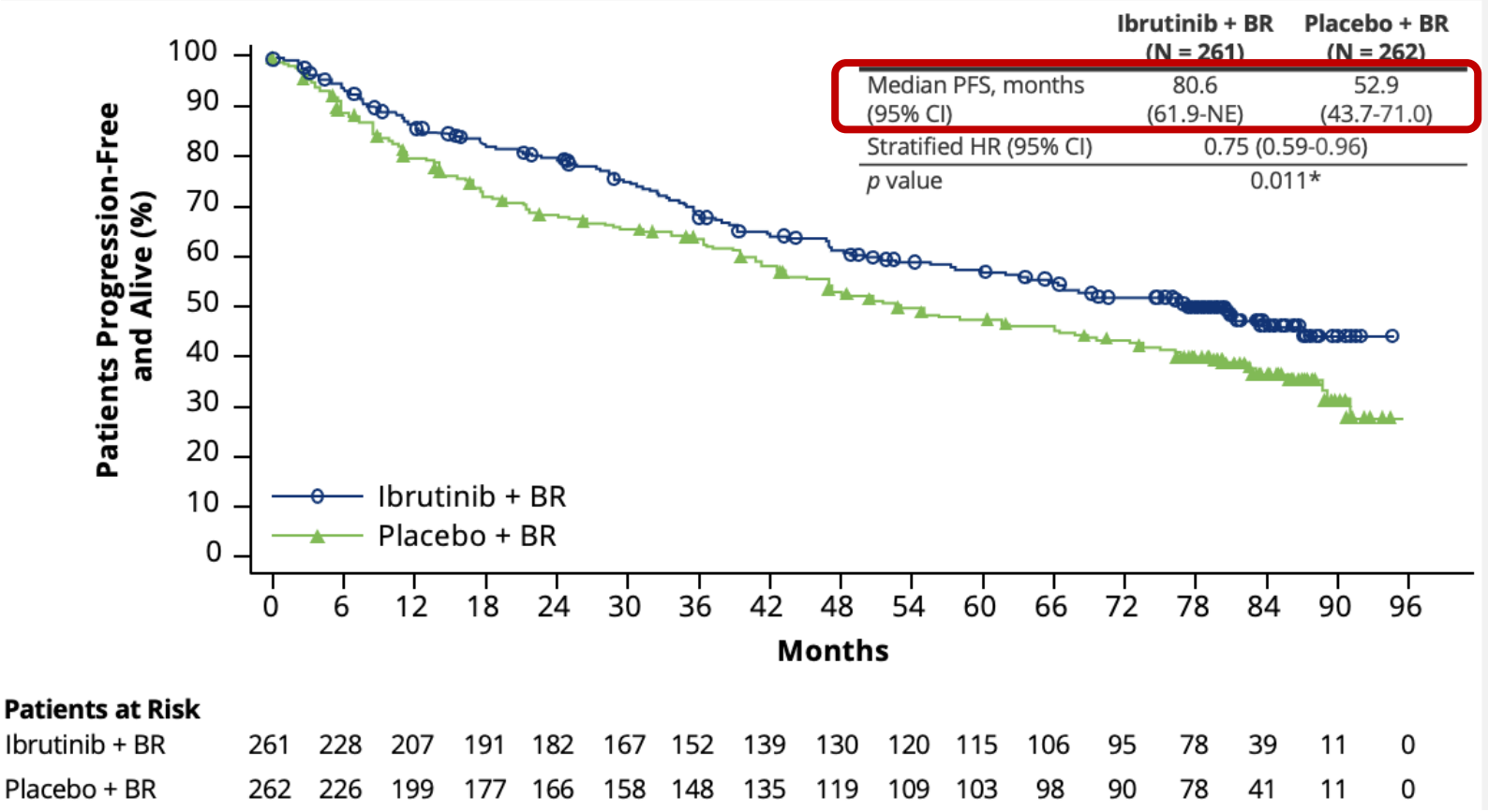
Response to treatment

Table S2. Antitumor Activity in the Intention-to-Treat Population.*

	Ibrutinib plus BR (N=261)	Placebo plus BR (N=262)	Relative Risk (95% CI)
Objective response — no. (%)	234 (89.7)	232 (88.5)	1.01 (0.95–1.07)
Best overall response — no. (%)			
Complete response	171 (65.5)	151 (57.6)	1.14 (1.00–1.30)**
Partial response	63 (24.1)	81 (30.9)	
Stable disease	1 (0.4)	6 (2.3)	
Progressive disease	3 (1.1)	10 (3.8)	
Could not be evaluated	23 (8.8)	14 (5.3)	
Duration of overall response — mo			
Median (95% CI)†	81.0 (64.2–NR)	63.5 (47.0–76.9)	
Undetectable MRD assessed among complete responders — no. (%)			
Yes	162 (62.1)	148 (56.5)	
Bone marrow	59 (22.6)	49 (18.7)	
Blood only	103 (39.5)	99 (37.8)	

Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. supplemtal data

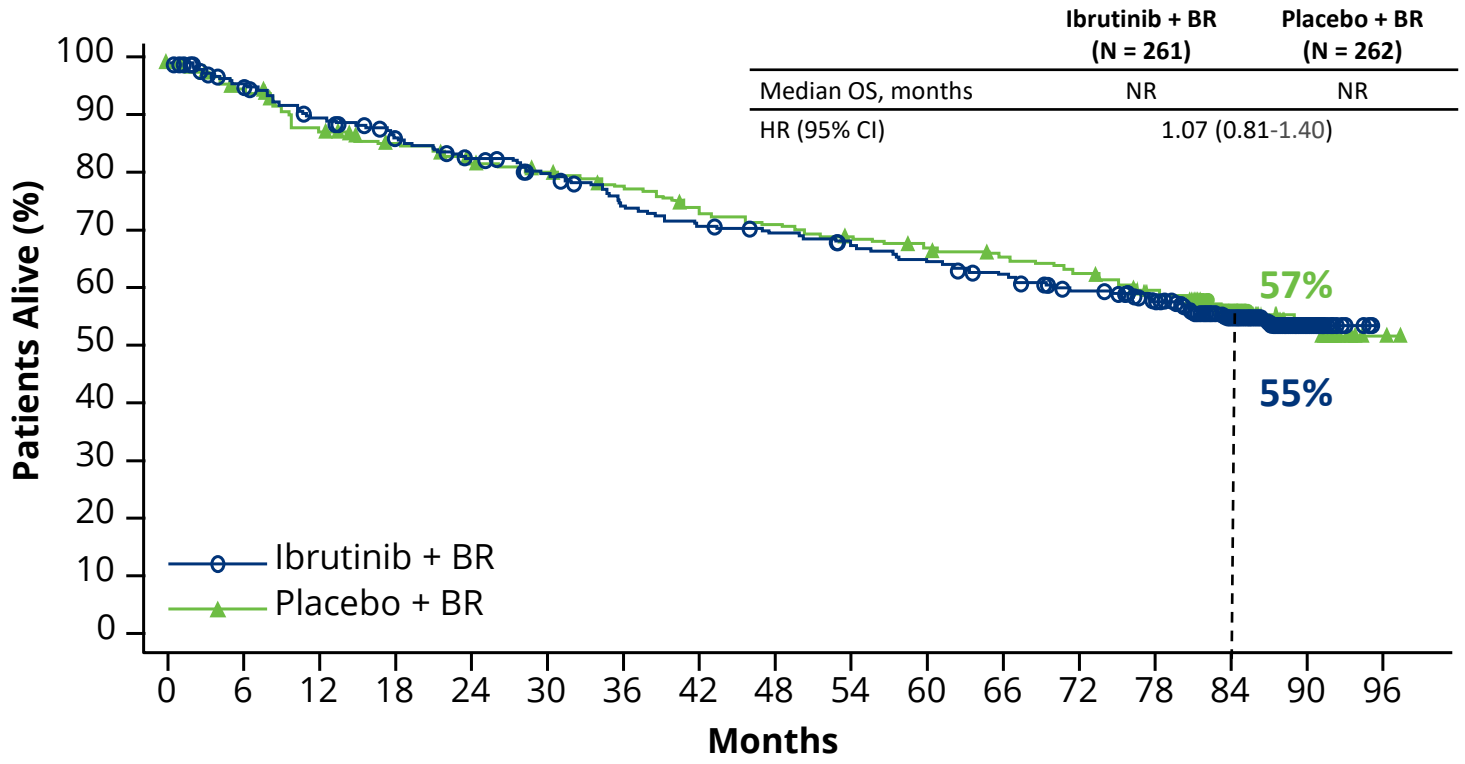
PFS



- Ibrutinib combined with BR and R maintenance demonstrated **a 25% reduction in the relative risk of disease progression or death** versus BR and R maintenance
- **Significant improvement in median PFS:** 80.6 month (6.7 years) versus 52.9 months (4.4 years) **(Δ=2.3 years)**

Wang et al., EHA 2022; S209 (oral presentation; Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. Online ahead of print.

Overall Survival Similar in Both Arms



Patients at Risk

Ibrutinib + BR	261	239	221	208	197	187	171	163	158	152	145	138	128	118	70	25	0
Placebo + BR	262	244	223	212	203	197	188	177	171	165	159	154	147	137	90	31	2

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

*The most common Grade 5 TEAE was infections in the ibrutinib and placebo arms: 9 vs 5 patients. Grade 5 TEAE of cardiac disorders in 3 vs 5 patients, respectively.

NR, not reached.

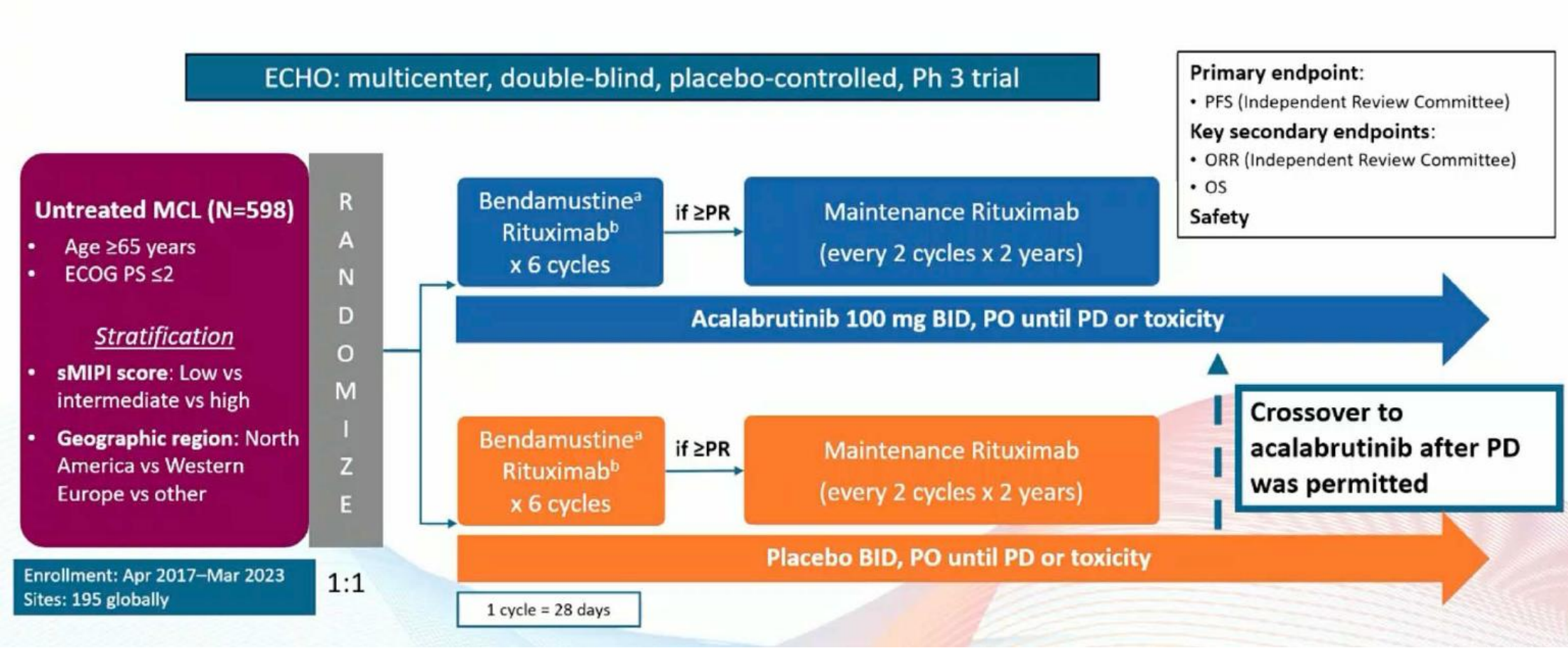
Wang et al., EHA 2022; S209 (oral presentation; Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. Online ahead of print.

Safety (AESI)

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

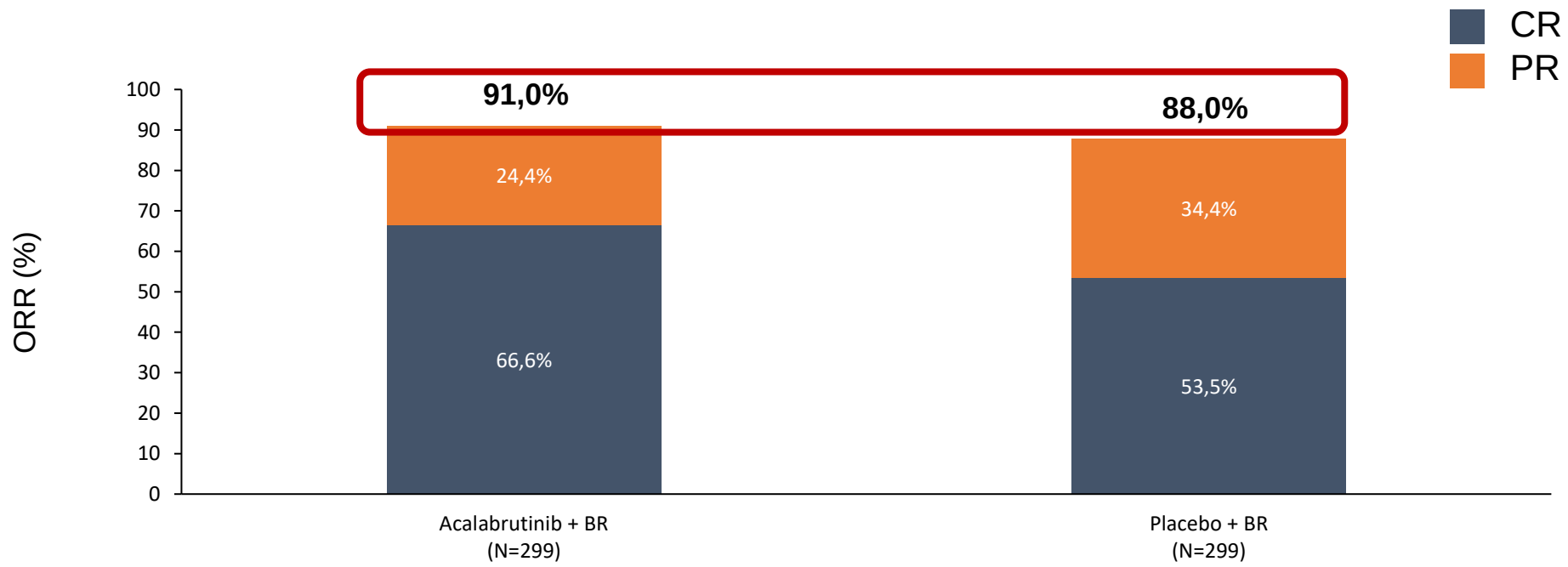
Wang et al., EHA 2022; S209 (oral presentation; Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. Online ahead of print.

ECHO-Trial: ACALABRUTINIB PLUS BENDAMUSTINE AND RITUXIMAB IN UNTREATED MANTLE CELL LYMPHOMA: RESULTS FROM THE PHASE 3, DOUBLE-BLIND, PLACEBO CONTROLLED



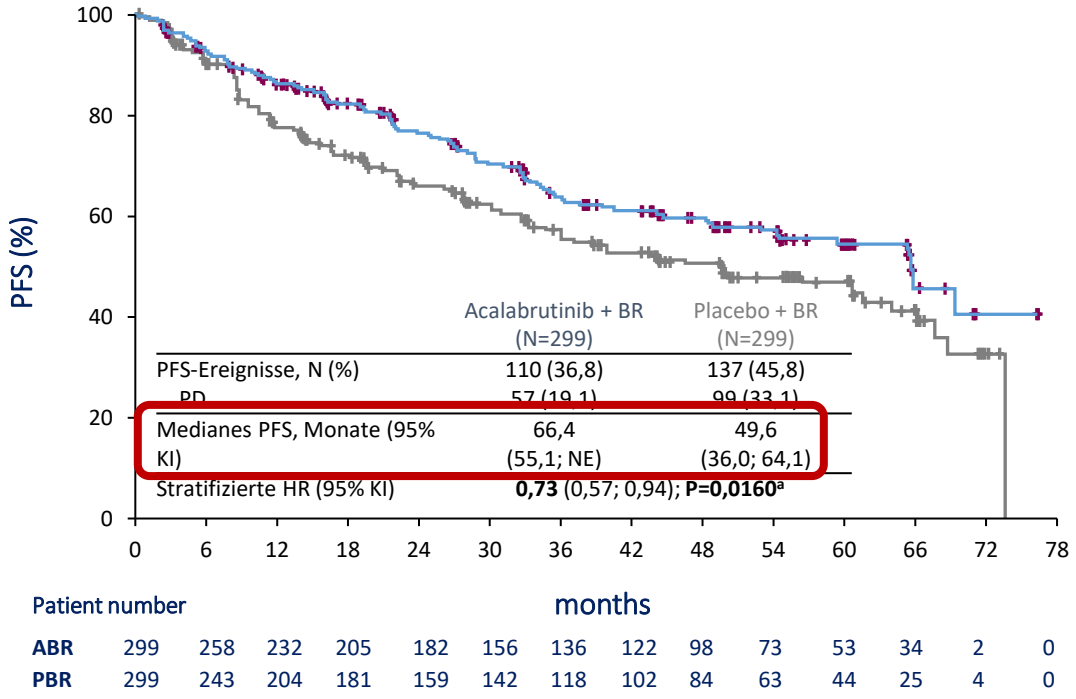
Wang, et al. EHA 2024 LB3439

Remission rates



PFS

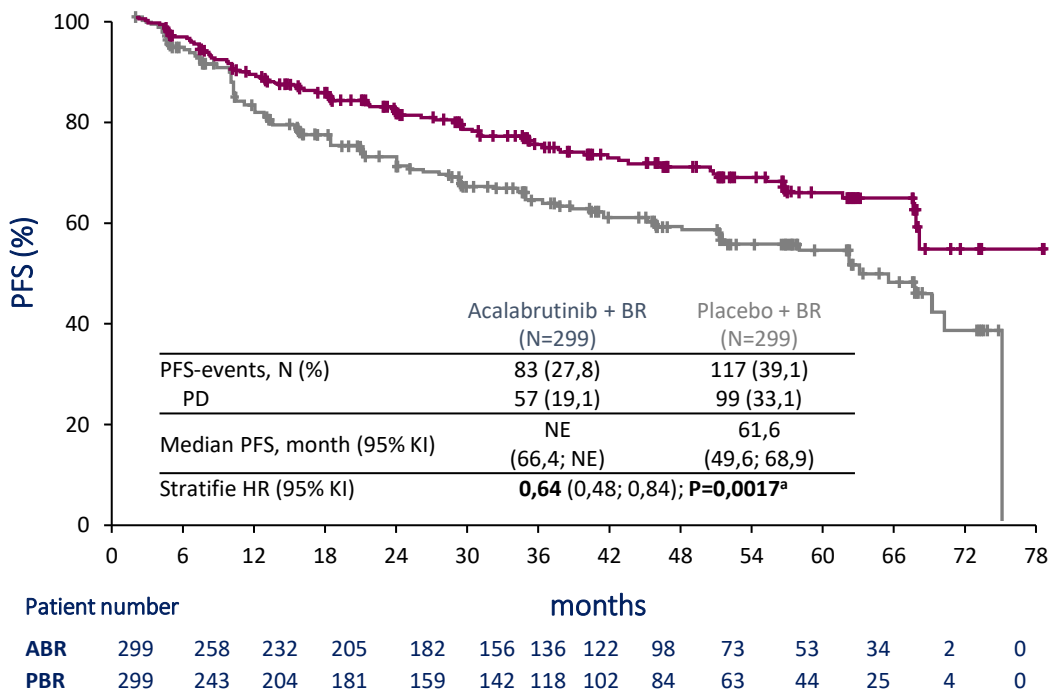
PFS: total trial population



Patient number

ABR	299	258	232	205	182	156	136	122	98	73	53	34	2	0
PBR	299	243	204	181	159	142	118	102	84	63	44	25	4	0

PFS: COVID-19-deaths censored

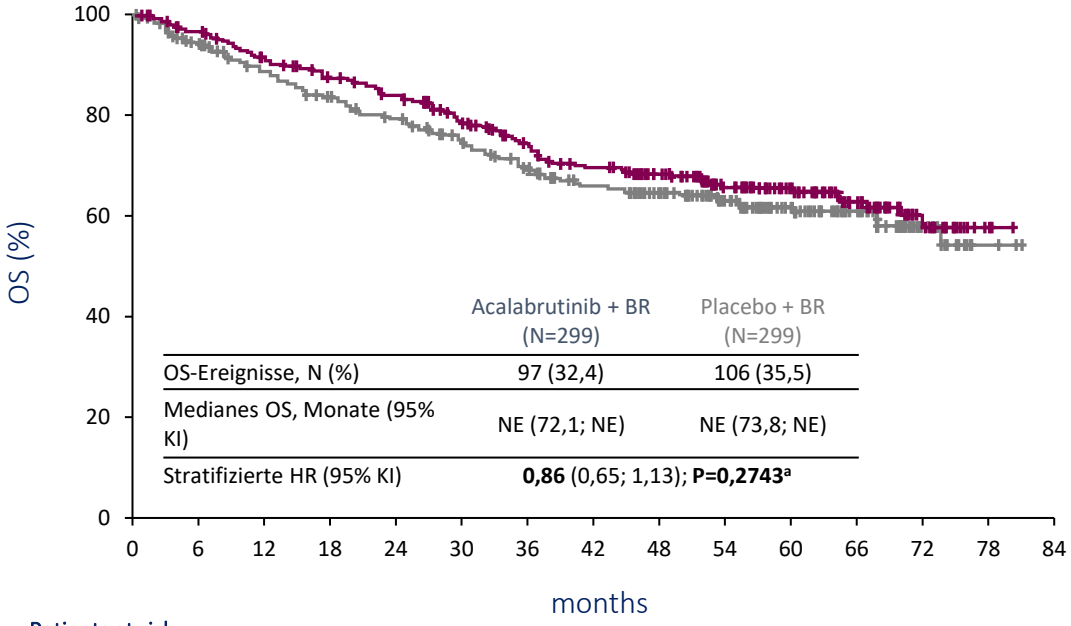


Patient number

ABR	299	258	232	205	182	156	136	122	98	73	53	34	2	0
PBR	299	243	204	181	159	142	118	102	84	63	44	25	4	0

Overall survival

OS: total (inkl. Cross-Over)

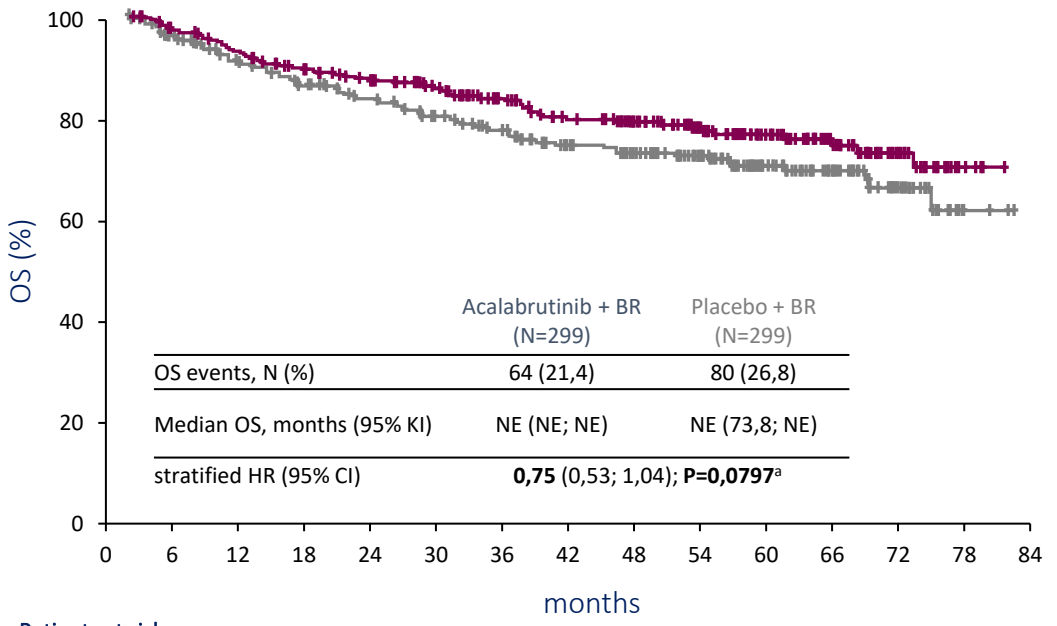


	Acalabrutinib + BR (N=299)	Placebo + BR (N=299)
OS-Ereignisse, N (%)	97 (32,4)	106 (35,5)
Medianes OS, Monate (95% KI)	NE (72,1; NE)	NE (73,8; NE)
Stratifizierte HR (95% KI)	**0,86** (0,65; 1,13); **P=0,2743**[a]	

Patients at risk

ABR	299	280	259	243	230	207	181	163	146	110	86	58	25	3	0
PBR	299	268	247	229	215	193	175	157	141	108	78	51	21	3	0

OS: COVID-19-deaths censored



	Acalabrutinib + BR (N=299)	Placebo + BR (N=299)
OS events, N (%)	64 (21,4)	80 (26,8)
Median OS, months (95% KI)	NE (NE; NE)	NE (73,8; NE)
stratified HR (95% CI)	**0,75** (0,53; 1,04); **P=0,0797**[a]	

Patients at risk

ABR	299	280	259	243	230	207	181	163	146	110	86	58	25	3	0
PBR	299	268	247	229	215	193	175	157	141	108	78	51	21	3	0

n (%)	Acalabrutinib + BR (n=297)	Placebo + BR (n=297)
Any TEAE	296 (99.7)	294 (99.0)
Grade ≥3	264 (88.9)	262 (88.2)
Grade 5	36 (12.1)	30 (10.1)
SAEs	205 (69.0)	184 (62.0)
Grade ≥3	191 (64.3)	166 (55.9)
TEAE related to acalabrutinib/ placebo	202 (68.0)	165 (55.6)
TEAE leading to acalabrutinib/ placebo discontinuation	127 (42.8)	92 (31.0)

	Acalabrutinib + BR (n=297)		Placebo + BR (n=297)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Event, n (%)				
Atrial fibrillation	18 (6.1)	11 (3.7)	13 (4.4)	5 (1.7)
Hypertension	36 (12.1)	16 (5.4)	47 (15.8)	25 (8.4)
Major bleeding[a]	7 (2.4)	6 (2.0)	16 (5.4)	10 (3.4)
Infections[b]	232 (78.1)	122 (41.1)	211 (71.0)	101 (34.0)
Second primary malignancies (excluding non-melanoma skin)[b]	29 (9.8)	16 (5.4)	32 (10.8)	20 (6.7)
Median treatment exposure (range), months	29 (0.1, 80.1)		25 (0.03, 76.4)	

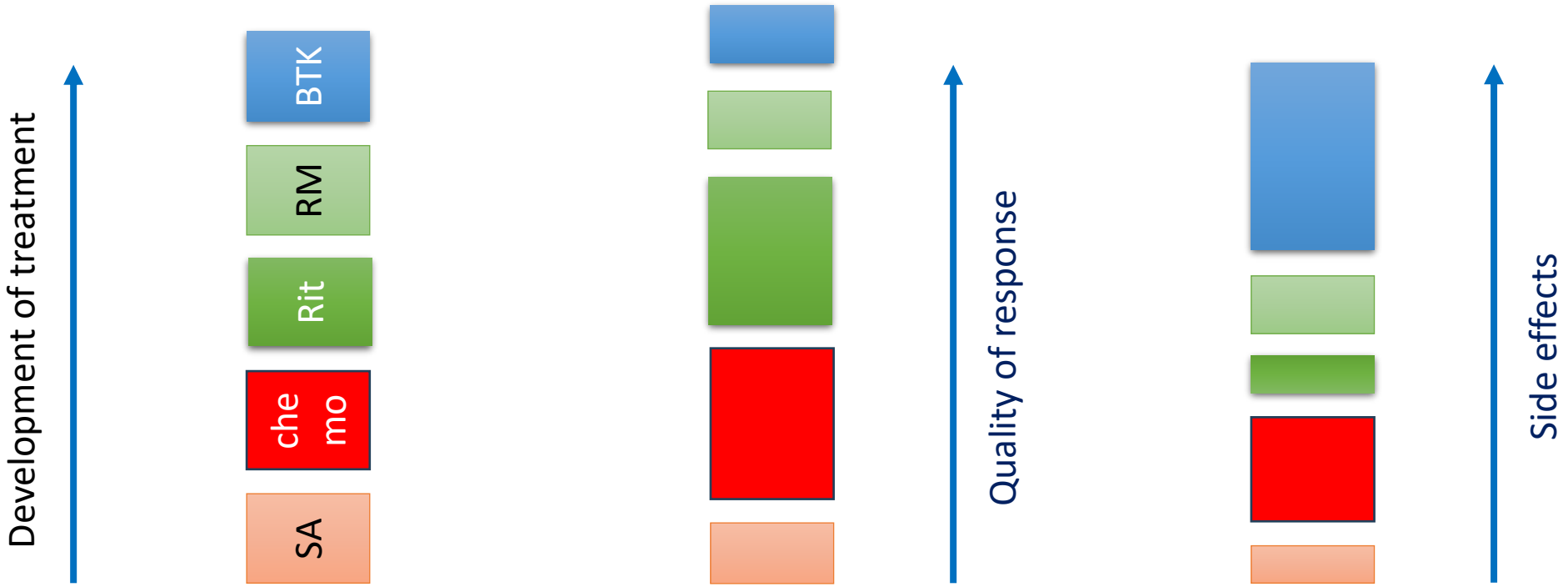
n (%)	COVID-19–related AEs	
	Acalabrutinib + BR (n=297)	Placebo + BR (n=297)
Any AE	121 (40.7)	88 (29.6)
Grade ≥3	60 (20.2)	50 (16.8)
Grade 5	28 (9.4)	20 (6.7)
SAEs	60 (20.2)	52 (17.5)
Grade ≥3	58 (19.5)	48 (16.2)
AE leading to acalabrutinib/ placebo discontinuation	31 (10.4)	19 (6.4)

Summary

- The addition of a BTK-inhibitor to BR improves ORR, CR and PFS
- There is not overall survival benefit
- However, many patients may not need any subsequent therapy

- There is added toxicity using this approach
- The design of the trials does not any longer reflect the urge for time limited treatments (especially with no risk stratification)

Development of novel options



BTKi based treatments w/o chemotherapy

Ibrutinib Rituximab - results

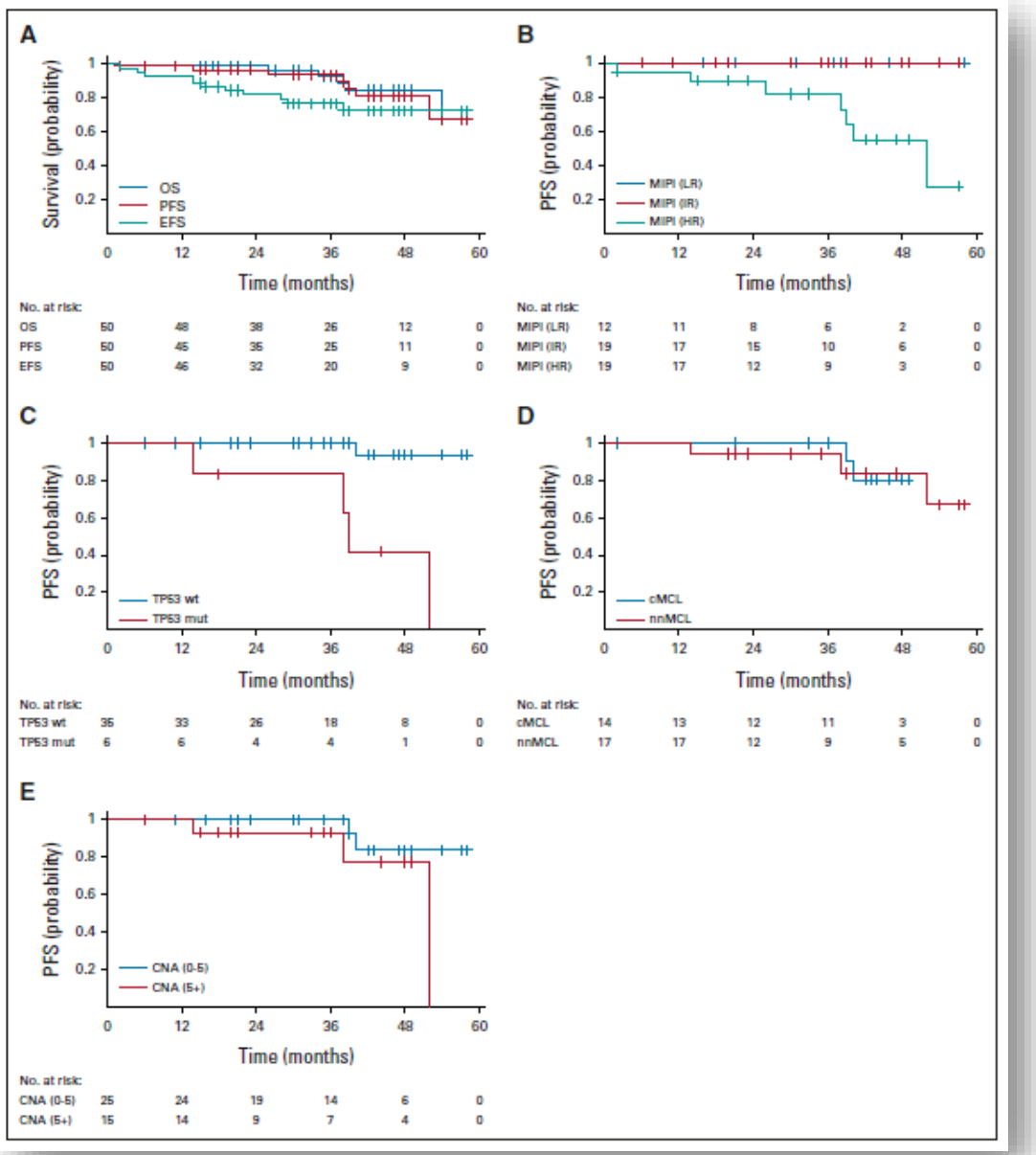
TABLE 3. Responses After 12 Cycles of IR Combination and According to Molecular Subtypes (nnMCL or cMCL) and *TP53* Mutational Status

		Gene Expression Profile L-MCL16		*TP53*	
Response	**All Patients (N = 50)**	**nnMCL (n = 17)**	**cMCL (n = 14)**	**Wild-Type (n = 35)**	**Mutated (n = 6)**
Overall response	42 (84, 74 to 94)	15 (88)	12 (86)	31 (89)	5 (83)
CR	40 (80, 69 to 91)	14 (82)	11 (79)	29 (83)	5 (83)
PR	2 (4, 0 to 9)	1 (6)	1 (7)	2 (6)	—
SD	3 (6, 0 to 10)	1 (6)	1 (7)	3 (8)	—
PD	1 (2, 0 to 6)	1 (6)	—	—	1 (17)
Nonevaluable[a]	4 (8, 0 to 15)	—	1 (7)	1 (3)	—

NOTE. Data are No. (%, 95% CI).

Abbreviations: cMCL, conventional MCL molecular subtype; CR, complete response; IR, ibrutinib, rituximab combination; MCL, mantle cell lymphoma; nnMCL, non-nodal MCL molecular subtype; PD, progressive disease; PR, partial response; SD, stable disease.

[a]Four patients were nonevaluable at 12 months of treatment because of treatment discontinuation: severe aplastic anemia, skin rash, and withdrawal consent because of treatment intolerance and unrelated event with vertebral fractures.



Ibrutinib-rituximab is superior to rituximab-chemotherapy in previously untreated older mantle cell lymphoma patients: Results from the international randomized controlled trial, Enrich

Aim

To investigate if chemotherapy-free treatment can replace chemotherapy in patients with MCL

Design

Phase 3: BR plus maintenance or R-CHOP plus maintenance vs IR (until progression)

B, bendamustine; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; I, ibrutinib; MCL, mantle cell lymphoma; R, rituximab.
Lewis DR, et al. ASH 2024. Oral presentation 235.

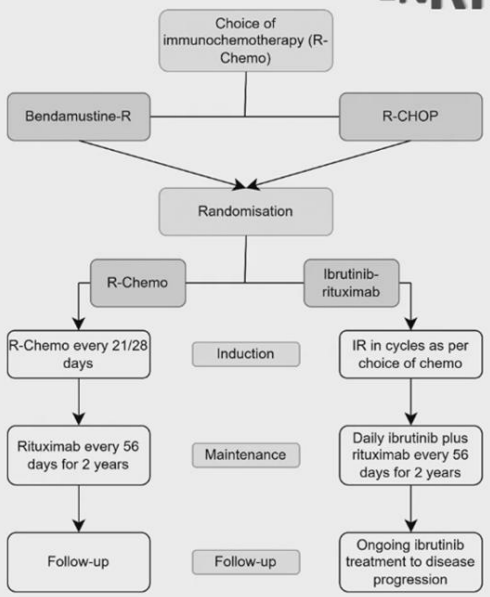
ENRICH: Results from the international randomized controlled trial

Trial design

Inclusion criteria
- 60 years or older
- Pathologically confirmed MCL, including either cyclin D1 overexpression or t(11;14)(q13;q32)
- Previously untreated, measurable (>1.5cm), stage II-IV MCL in need of treatment
- ECOG 0-2

Exclusion criteria
- Considered fit for stem cell transplantation
- CNS involvement
- Known serological positivity for HBC/HCV/HIV

Rituximab 375mg/m²
Ibrutinib - 560mg od
Bendamustine 90mg/m² D1+D2 of 28 day cycle
CHOP - (Cyclophosphamide 750mg/m², Doxorubicin 50mg/m², Vincristine 1.4mg/m², Prednisolone 100mg *5 days) 21 day cycle
Maintenance rituximab - 1400mg sc every 56 days

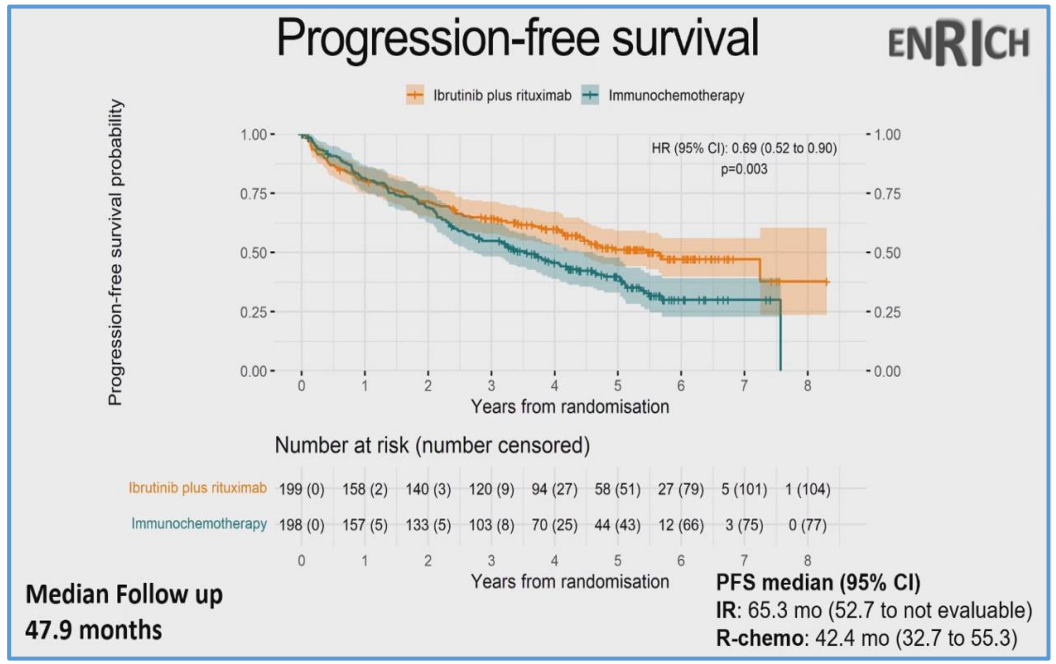


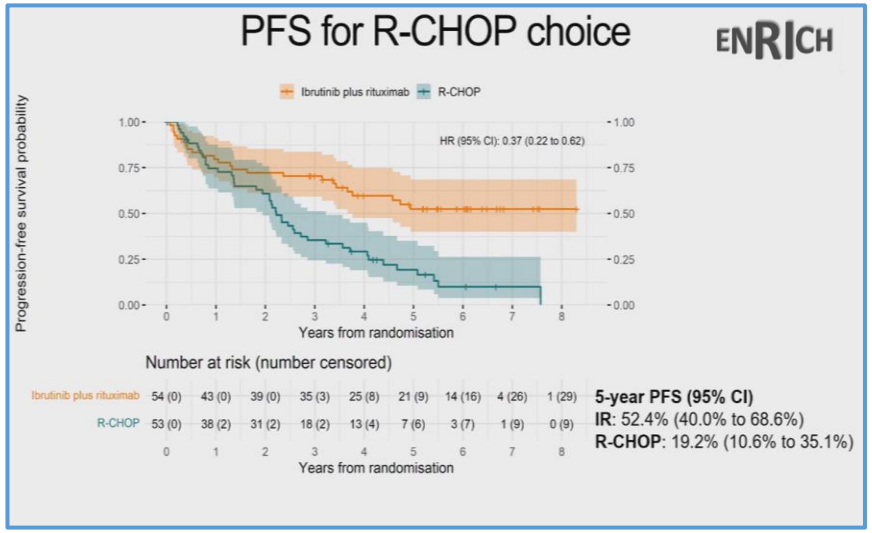
Patient characteristics

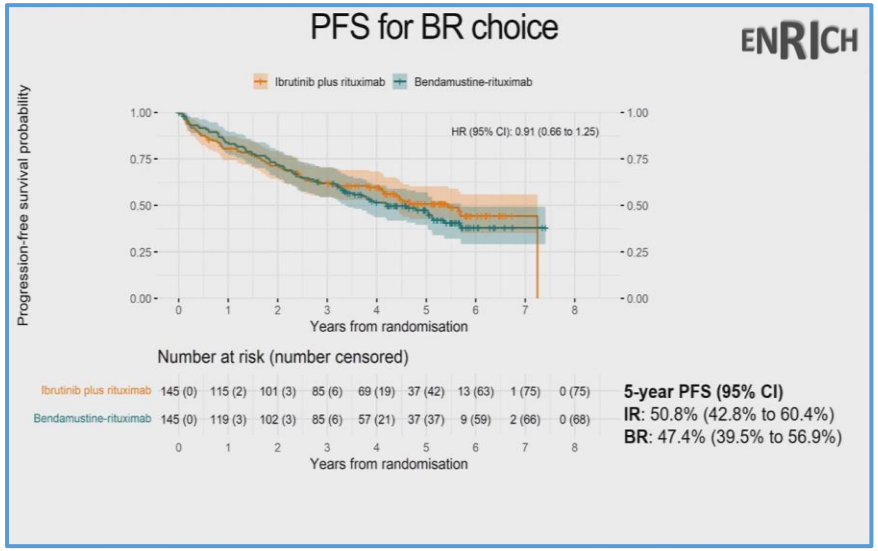
		Immunochemotherapy, N = 198	Ibrutinib plus rituximab, N = 199
Age (median, IQR)		74 (70, 78)	74 (70, 77)
Male		146 / 198 (73.7%)	150 / 199 (75.4%)
ECOG	0	107 / 198 (54.0%)	124 / 199 (62.3%)
	1	80 / 198 (40.4%)	64 / 199 (32.2%)
	2	11 / 198 (5.6%)	11 / 199 (5.5%)
Stage IV		183 / 198 (92.4%)	175 / 199 (87.9%)
Blastoid		15 / 192 (7.8%)	10 / 178 (5.6%)
Ki67 ≥ 30%		71 / 157 (45.2%)	55 / 142 (38.7%)
MIPI	Low	23 / 195 (11.8%)	23 / 198 (11.6%)
	Intermediate	61 / 195 (31.3%)	64 / 198 (32.3%)
	High	111 / 195 (56.9%)	111 / 198 (56.1%)
TP53 mutation		18 / 75 (24.0%)	22 / 80 (27.5%)

Chemo, chemotherapy; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; CI, confidence interval; CNS, central nervous system; D, Day; ECOG, Eastern Cooperative Oncology Group; HBC, Hepatitis B virus core protein; HCV, Hepatitis C virus; HIV, human immunodeficiency virus; I, ibrutinib; IQR, interquartile range; MCL, mantle cell lymphoma;
MIPI, Mantle Cell Lymphoma International Prognostic Index; od, once daily; R, rituximab; sc, subcutaneous.
Lewis DR, et al. ASH 2024. Oral presentation 235.

Results from the international randomized controlled trial, Enrich (cont'd)

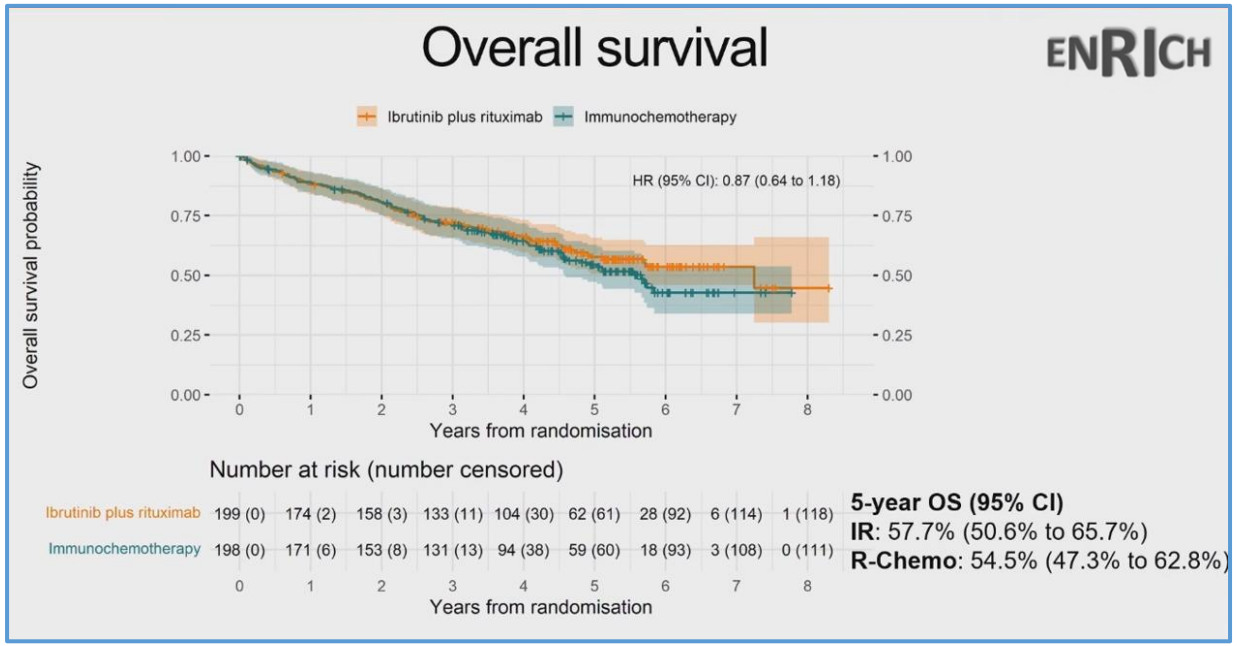


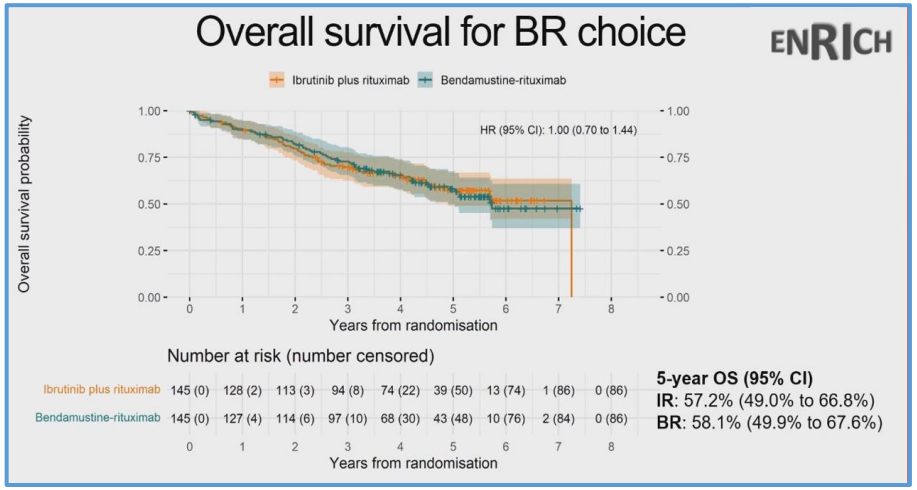


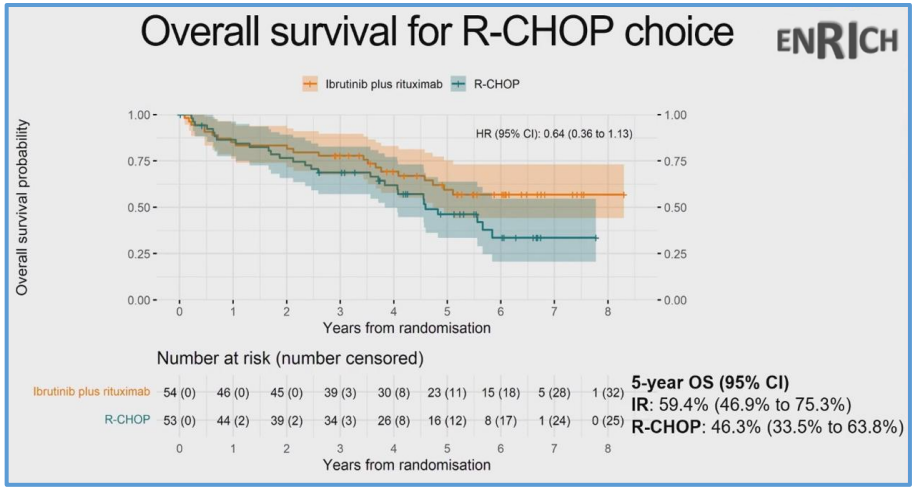


B, bendamustine; chemo, chemotherapy; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; CI, confidence interval; HR, hazard ratio; I, ibrutinib; mo, months; PFS, progression-free survival; R, rituximab.
Lewis DR, et al. ASH 2024. Oral presentation 235.

Results from the international randomized controlled trial, Enrich (cont'd)







B, bendamustine; chemo, chemotherapy; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; CI, confidence interval; HR, hazard ratio; I, ibrutinib; OS, overall survival; R, rituximab.
Lewis DR, et al. ASH 2024. Oral presentation 235.

Results from the international randomized controlled trial, Enrich (cont'd)

Grade 3-4 Adverse events

ENRICH

N participants (% of safety population)	Ibrutinib plus rituximab, N=198	Bendamustine-rituximab, N=143	R-CHOP, N=52
Total	125 (63.1%)	97 (67.8%)	36 (69.2%)
All Cardiac AEs	44 (22.2%)	7 (4.9%)	7 (13.5%)
All bleeding AEs	10 (5.1%)	3 (2.1%)	3 (5.8%)
Atrial Fibrillation	12 (6.1%)	1 (0.7%)	0
Neutropenia	18 (9.1%)	27 (18.9%)	11 (21.2%)
Neutropenic sepsis	6 (3.0%)	2 (1.4%)	8 (15.4%)
Corona virus infection	10 (5.1%)	10 (7.0%)	0

Grade 3 and 4 adverse events during induction treatment and maintenance

Safety population - patients who had at least one cycle of treatment

Conclusions

ENRICH

- This is the first randomised study to demonstrate an improved PFS for IR versus immunochemotherapy in previously untreated MCL
  - Primarily driven by improved PFS for IR versus RCHOP
  - PFS for IR versus BR broadly similar, despite more COVID-19 PFS events in IR arm
- Adverse event profile in keeping with known AE profile of ibrutinib
  - Less haematological toxicity versus chemoimmunotherapy
  - Earlier improvement in QOL scores in those treated with IR
- Subgroup analysis suggests IR has particular benefit in those with Ki67 <30%
- Ibrutinib-rituximab can be considered a standard of care in previously untreated MCL

AE, adverse event; B, bendamustine; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; COVID-19, coronavirus disease 2019; I, ibrutinib; MCL, mantle cell lymphoma; PFS, progression-free survival; QOL, quality of life; R, rituximab.

Lewis DR, et al. ASH 2024. Oral presentation 235.

Summary

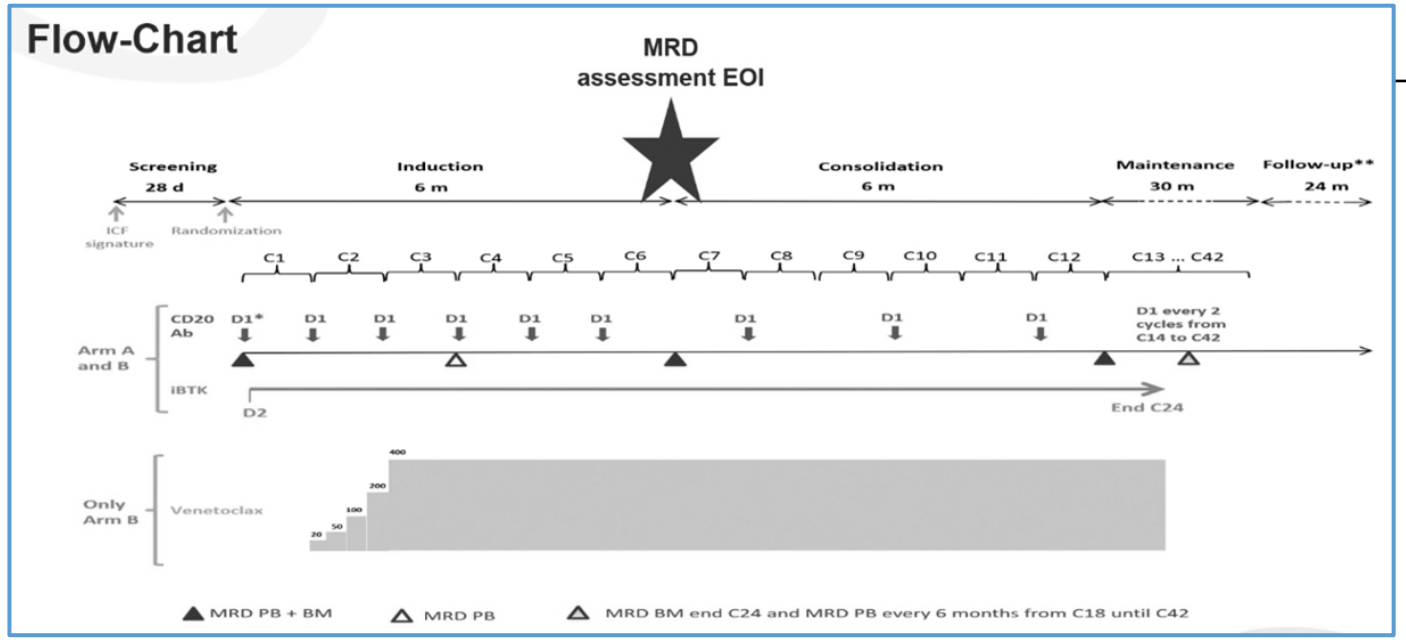
- Enrich is the first trial to demonstrate equivalence of IR to chemotherapy based treatment.

- However, again the design of the trials does not any longer reflect the urge for time limited treatments

- → Multidrug-combinations

The future: multidrug combinations

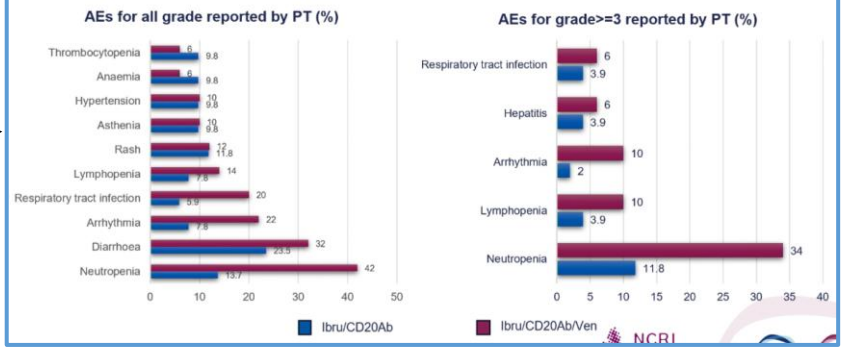
Initial results of OASIS II, a randomized Phase 2 trial



Patient's and disease characteristics at baseline (1)

MRD status	Safety set		informative MRD set	
Treatment arm	Ibru/CD20 N=51	Ibru/CD20/Ven N=50	Ibru/CD20 N=39	Ibru/CD20/Ven N=39
Median age (years)	65	66	67	63
Sex: Male	41 (80.4%)	37 (74.0%)	31 (79.5%)	28 (71.8%)
Ann Arbor stage				
III	4 (7.8%)	5 (10.0%)	2 (5.1%)	4 (10.3%)
IV	45 (88.2%)	44 (88.0%)	37 (94.9%)	35 (89.7%)
MIPI risk group				
Low	14 (27.5%)	13 (26.0%)	9 (23.1%)	10 (25.6%)
Intermediate	22 (43.1%)	23 (46.0%)	15 (38.5%)	17 (43.6%)
High	15 (29.4%)	14 (28.0%)	15 (38.5%)	12 (30.8%)
Blastoid Variant	1 (2.0%)	3 (6.1%)	1 (2.6%)	3 (7.9%)
>30% of Ki67 positivity cells	12/35 (34.3%)	20/42 (47.6%)	9/26 (34.6%)	16/32 (50%)
≤10% of P53 group at diagnosis	32/42 (76.2%)	33/38 (86.8%)	25/32 (78.1%)	24/28 (85.7%)

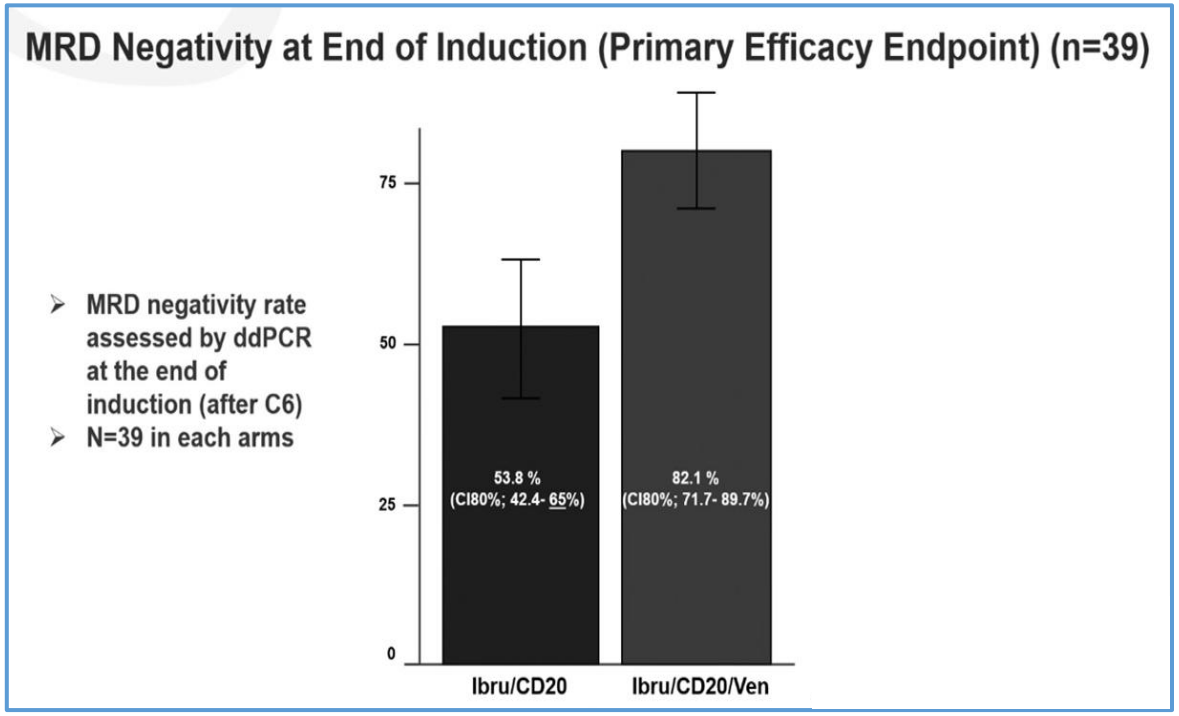
Safety evaluation – Most frequent AE (n=101)



Ab, antibody; AE, adverse event; BM, bone marrow; C, Cycle; CD, cluster of differentiation; d/D, Day; Ibru, ibrutinib; IBTK, Bruton tyrosine kinase inhibitor; ICF, informed consent form; m, months; MCL, mantle cell lymphoma; MIPI, Mantle Cell Lymphoma International Prognostic Index; MRD, minimal residual disease; PB, peripheral blood; PT, patient; Ven, venetoclax.

Le Gouill S, et al. ASH 2024. Oral presentation 745.

Initial results of OASIS II, a randomized Phase 2 trial (cont'd)



Treatment arm	Ibru/CD20Ab (n=51)	Ibru/CD20Ab/Ven (n=50)	Total (n=101)
CR	29 (56.9%)	32 (64 %)	61 (60.4%)
PR	11 (21.6%)	8 (16 %)	19 (18.8%)
ORR	40 (78.5%)	40 (80%)	80 (79,2%)
SD	2 (3.9%)	0	2 (2%)
PD	1 (2%)	0	1 (1%)
NE	8 (15.7%)	10 (20%)	18 (17.8%)

Ab, antibody; AE, adverse event; CD, cluster of differentiation; CI, confidence interval; CR, complete response; ddPCR, droplet digital polymerase chain reaction; Ibru, ibrutinib; mAb, monoclonal antibody; MCL, mantle cell lymphoma; MRD, minimal residual disease; NE, not estimable; ORR, overall response rate; OS, overall survival; PD, progressive disease;
PFS, progression-free survival; PR, partial response; SD, stable disease; Ven, venetoclax.
Le Gouill S, et al. ASH 2024. Oral presentation 745.

BOVEN: Zanubrutinib/Obinutuzumab/Venetoclax in TP53 mutated MCL

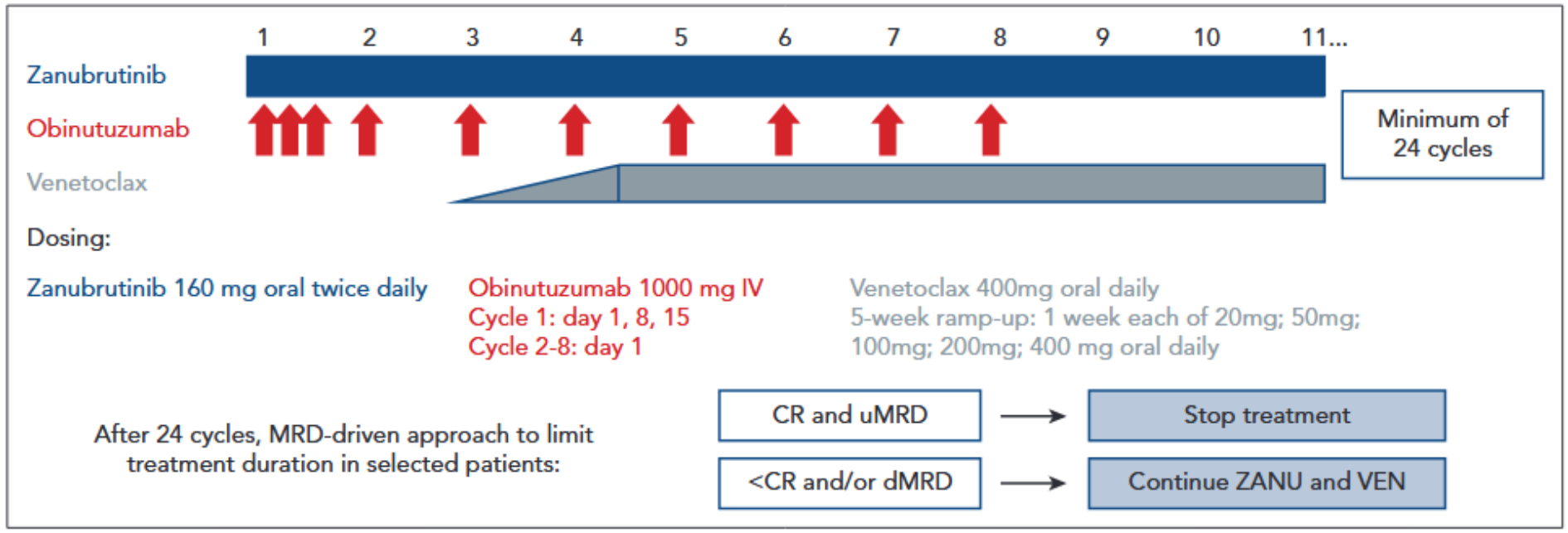
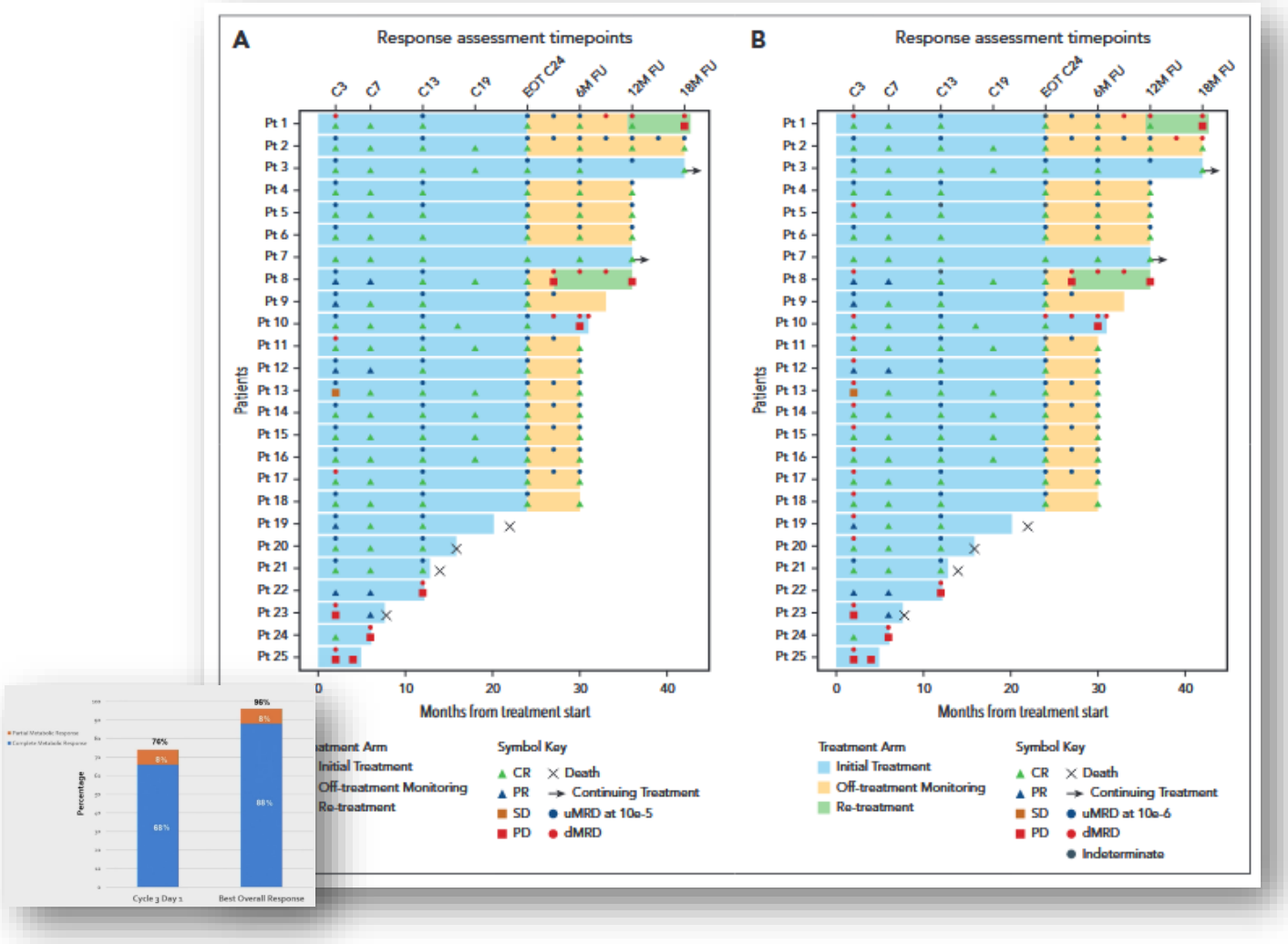
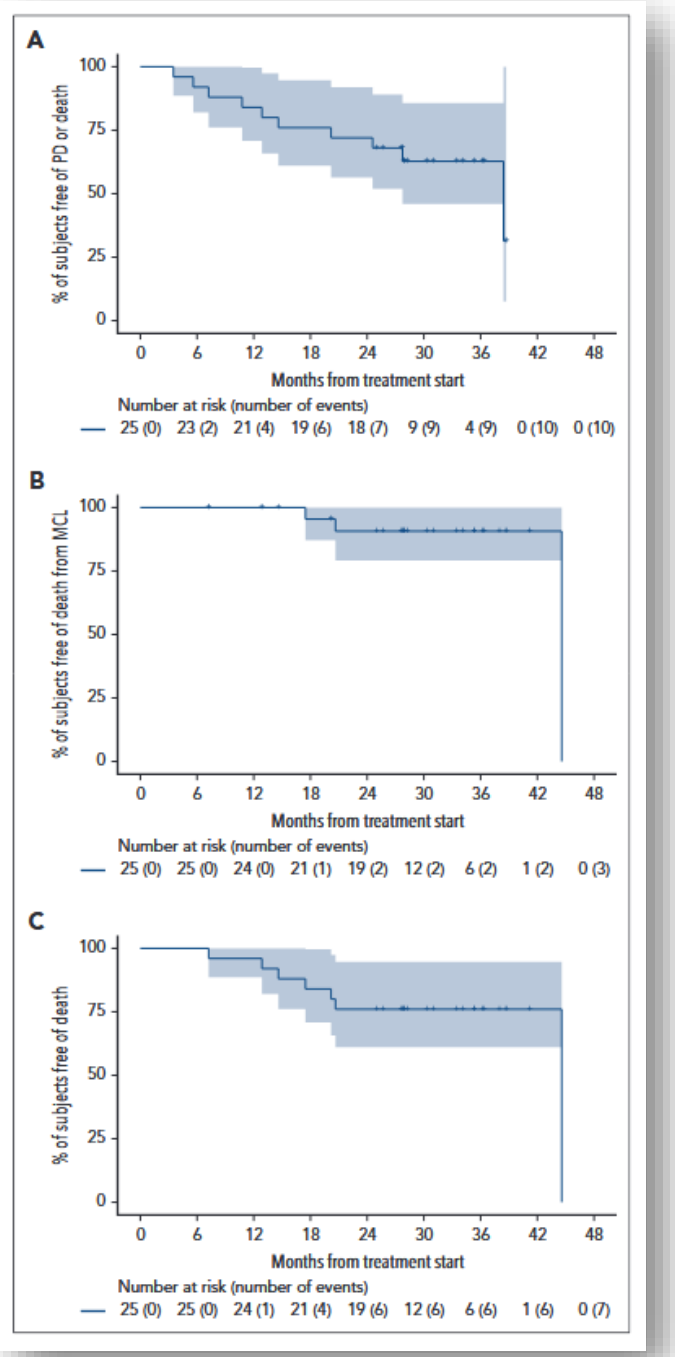


Figure 1. Study schema. Patients received obinutuzumab on C1 day 1, 8, and 15 and monthly on day 1 of C2 to C8. Patients received zanubrutinib (ZANU) at a dose of 160 mg by mouth twice daily for 2 28-day cycles before the weekly dose escalation of venetoclax (VEN) to a target dose of 400 mg/d began. ZANU and VEN were continued until disease progression or intolerance. After 24 cycles, if patients were in complete response (CR) and had uMRD status, ZANU and VEN were discontinued. dMRD, detectable MRD; uMRD, undetectable MRD; IV, intravenous.

Boven et al., JCO, 2025

Boven - results





Kumar et al., JCO, 2025

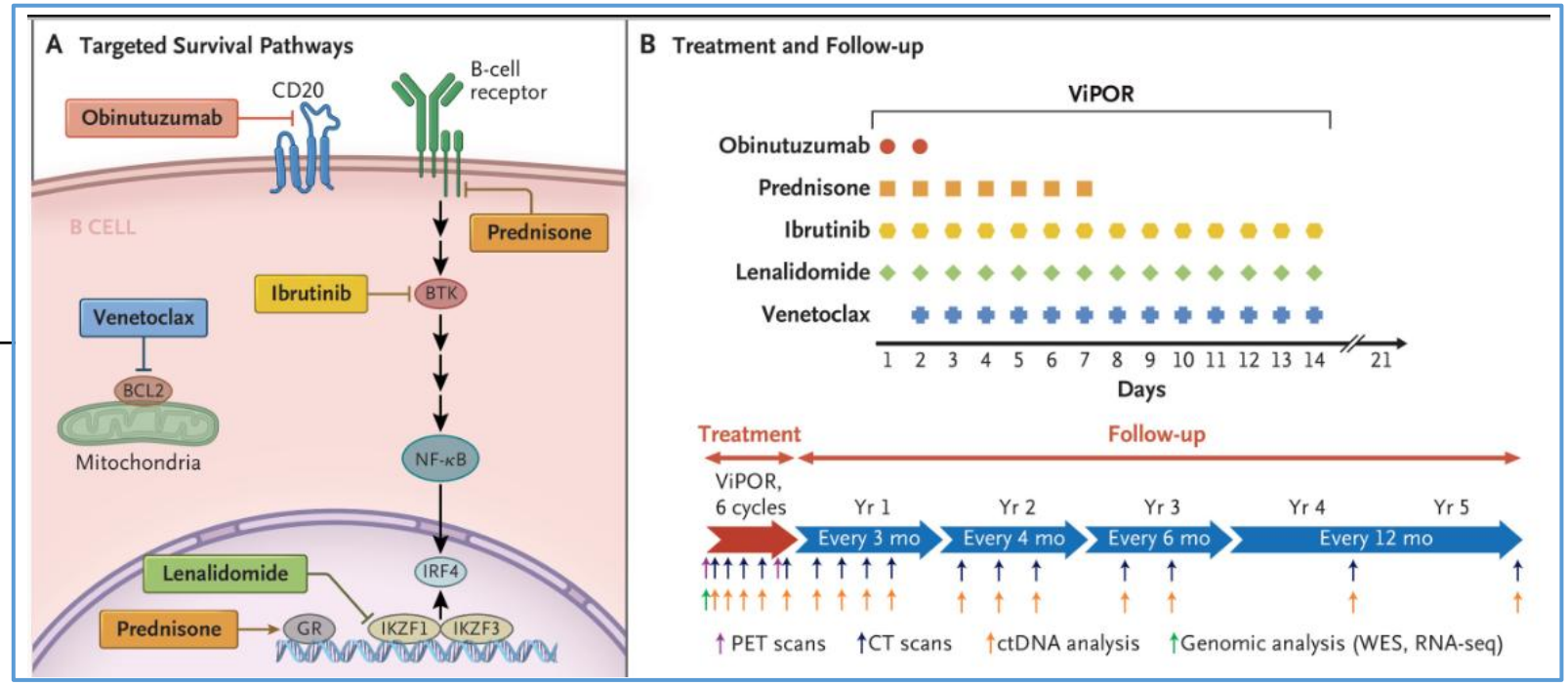
Phase 1b/2 study of venetoclax, ibrutinib, prednisone, obinutuzumab, and lenalidomide (ViPOR) in relapsed/refractory and treatment-naive mantle cell lymphoma: Preliminary analysis of safety, efficacy, and MRD

Aim

To investigate the potential for an all in chemotherapy-free combination

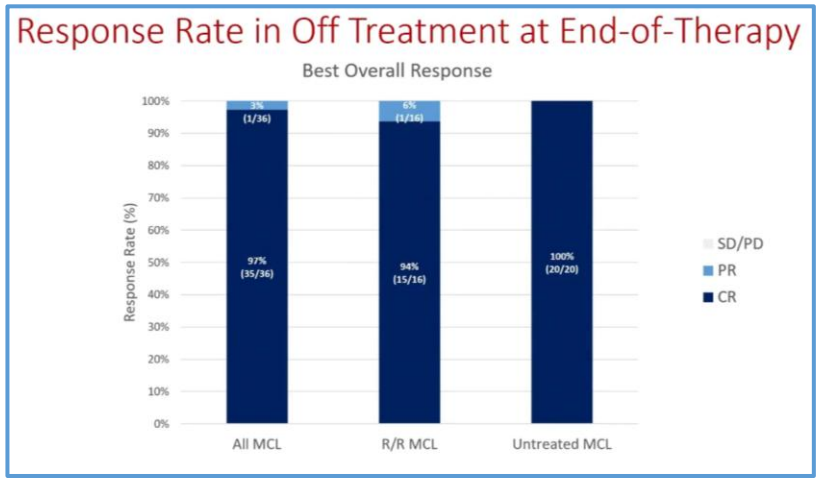
Design

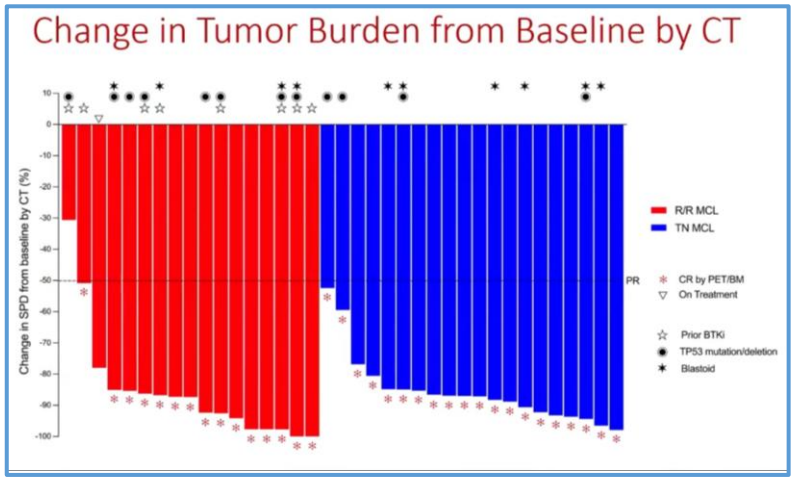
Single center, Phase 1/2

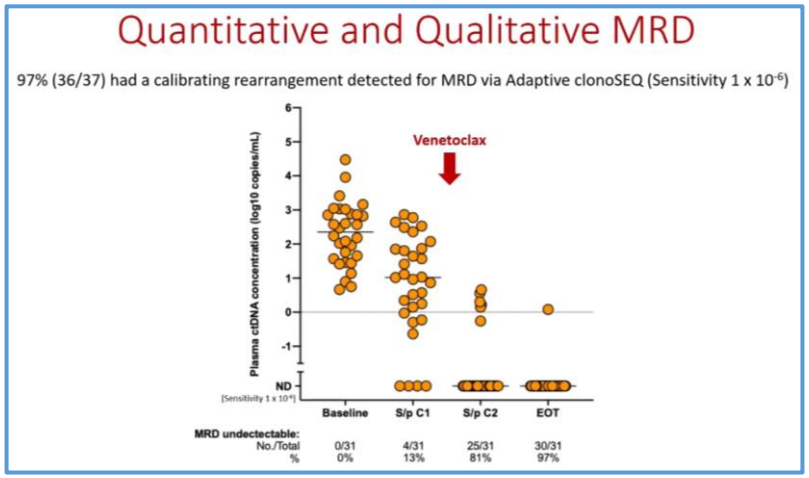


BCL2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; CD, cluster of differentiation; CT, computed tomography; ctDNA, circulating tumor deoxyribonucleic acid; GR, glucocorticoid receptor; IKZF, Ikaros family zinc finger protein; IRF4, interferon regulatory factor 4; mo, months; MRD, minimal residual disease; NF-KB, nuclear factor-kappa B;
PET, positron emission tomography; RNA-seq, ribonucleic acid sequencing; WES, whole exome sequencing; Yr, year.
Melani C, et al. ASH 2024. Oral presentation 750.

ViPOR: Preliminary analysis of safety, efficacy, and MRD (cont'd)



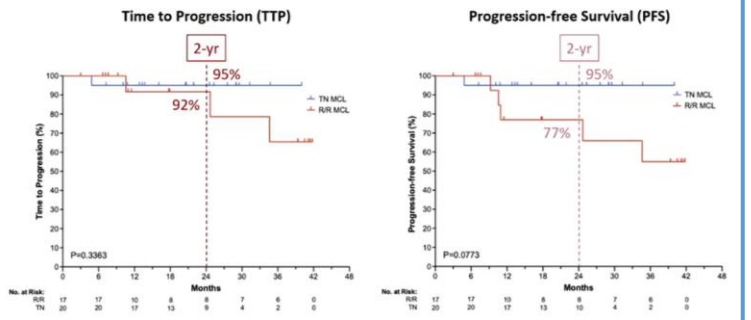




BM, bone marrow; BTKi, Bruton tyrosine kinase inhibitor; C, Cycle; CR, complete response; ctDNA, circulating tumor deoxyribonucleic acid; CT, computed tomography; EOT, end of treatment; MCL, mantle cell lymphoma; MRD, minimal residual disease; ND, not detected; PD, progressive disease; PET, positron emission tomography; PR, partial response;
R/R, relapsed/refractory; S/p, status post; SPD, sum of the product of diameters; SD, stable disease; TN, treatment-naïve.
Melani C, et al. ASH 2024. Oral presentation 750.

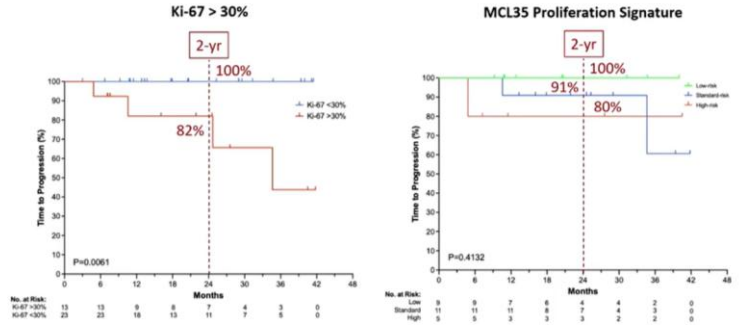
ViPOR: Preliminary analysis of safety, efficacy, and MRD (cont'd)

Survival Outcome in R/R vs TN MCL



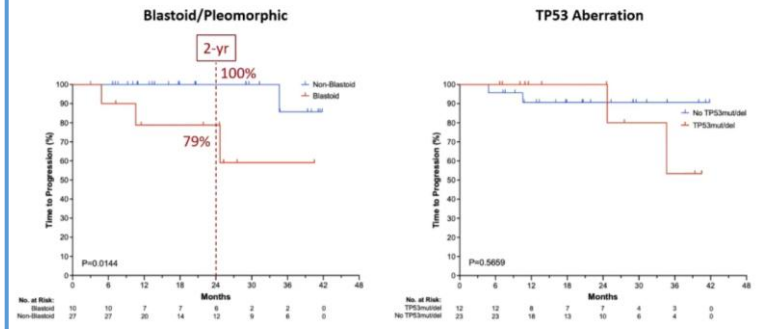
Median (range) follow-up = 27.6 (3.1-57.5) mo.

Time to Progression (TTP) in All MCL by Proliferation



Median (range) follow-up = 27.6 (3.1-57.5) mo.

Time to Progression (TTP) in All High-Risk MCL



Median (range) follow-up = 27.6 (3.1-57.5) mo.

MCL, mantle cell lymphoma; mo, months; R/R, relapsed/refractory; TN, treatment-naïve; yr, year.
Melani C, et al. ASH 2024. Oral presentation 750.

Summary

- Multi-drug combinations demonstrate high effiacy and acceptable tolerability
- Even/especially in high risk populations they might be of great potential to overcome intrinsic chemoresistance

- Time limited / risk & response tailored treatments can be of special merit for patients → to be tested prospectively in upcoming trials

EMCL-elderly 2023: VIRAL – Phase II

R

Ibrutinib induction and post induction

Bendamustin

Rituximab

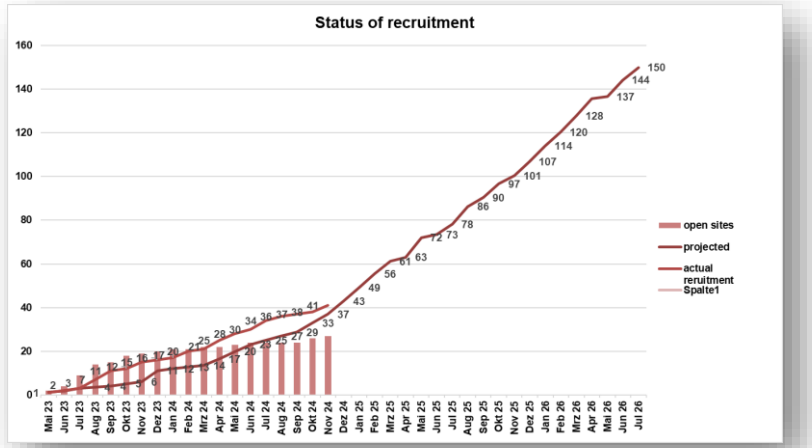
Rituximab maintenance

Rituximab

Rituximab maintenance

Venetoclax

Ibrutinib induction and post induction



EUROPEAN MCL NETWORK

In competitive matches, the teams have faced each other 12 times: Germany has won 2, Italy 4, and 6 matches ended in a draw. (weltfussball.de)

Thank you

German Lymphoma Alliance

UNIVERSITÄTSmedizin. MAINZ

Department of Haematology and Medical Oncology