Updates on CLL care in Asia

Singapore Lymphoma Scientific Symposium

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Singapore

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Disclosures

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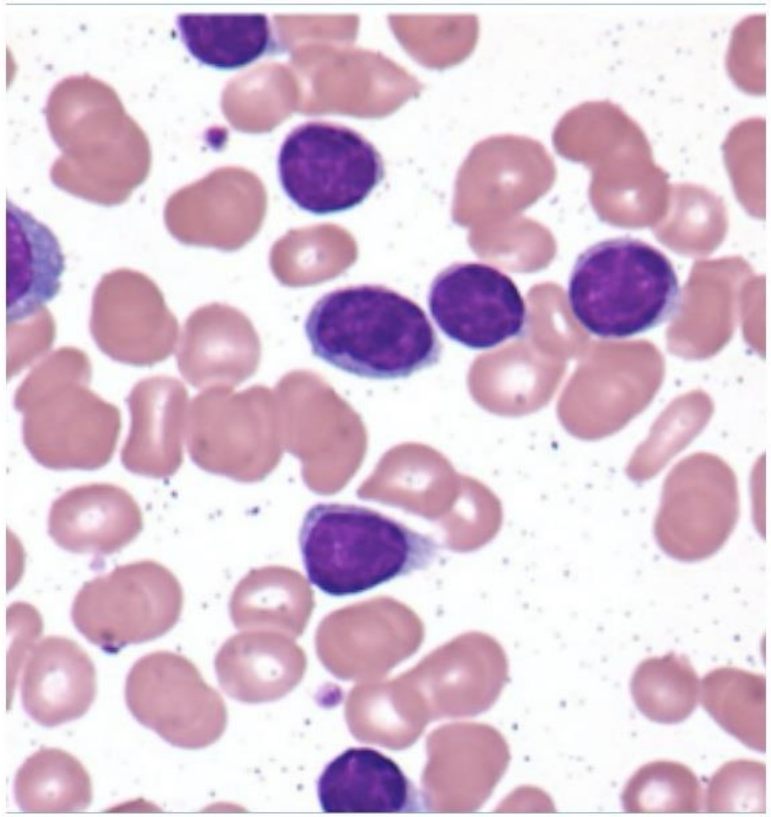
Diagnosis of CLL

- $\geq 5 \times 10^9$/L B-lymphocytes in blood for at least 3 months
- Clonality
- Typical morphology
- Typical immunophenotyping CD5+, CD23+, CD19+, CD20dim, FMC7-, CD79b-, weak surface Ig (IgM or IgD)

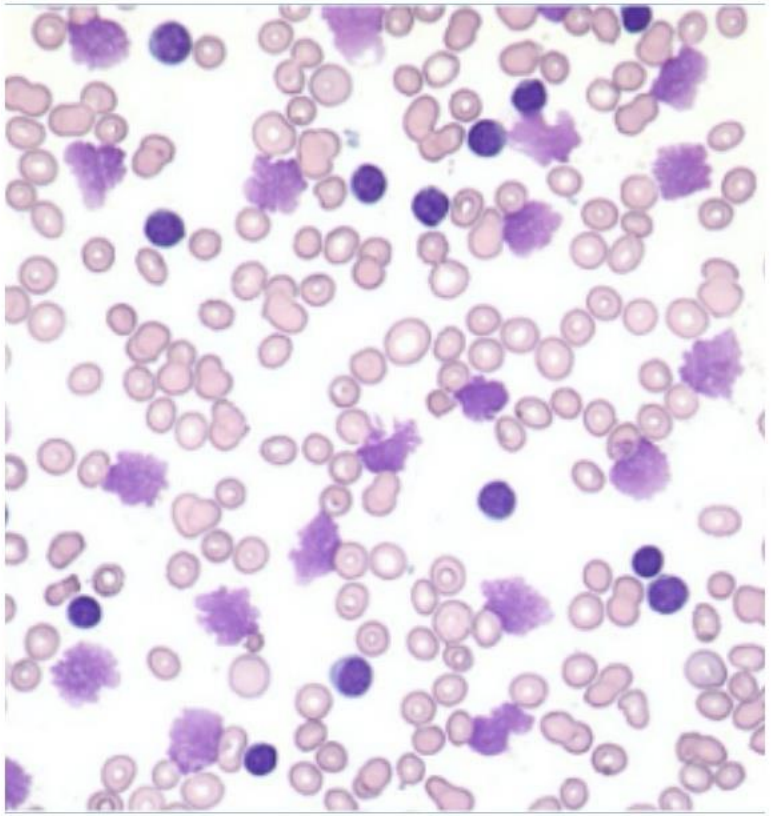
- Small lymphocytic lymphoma – same histology and immunophenotype but does not meet the lymphocytosis criteria

Peripheral blood smear



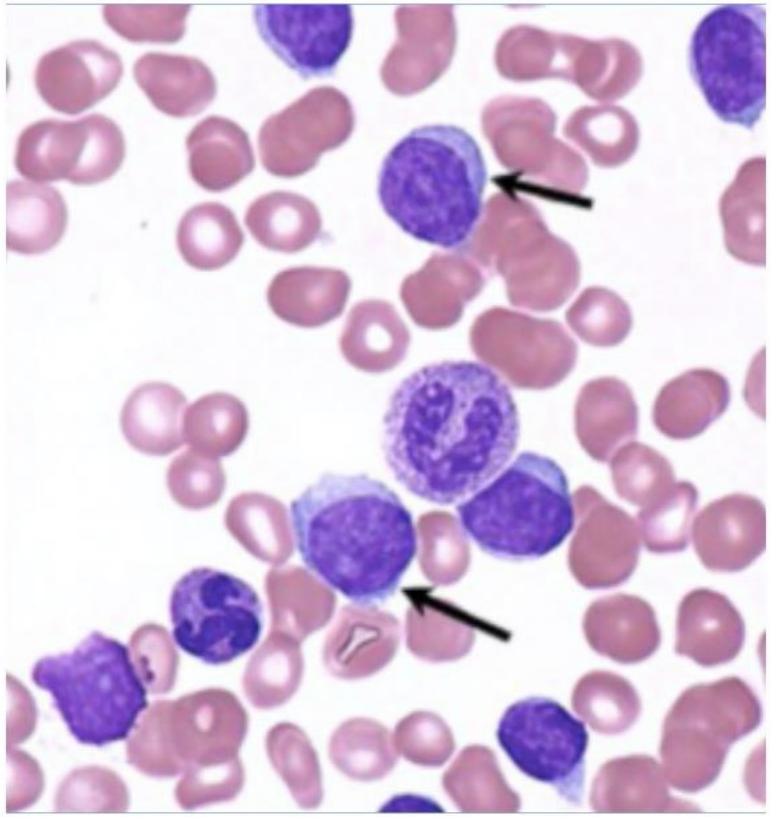
SMALL, MATURE LYMPHOCYTES

Dense nucleus, indiscernible nucleoli, clumped chromatin, scant cytoplasm



SMUDGE CELLS

Cell debris (damaged cells when preparing the blood smear)



OTHER LYMPHOID CELLS

E.g. larger or atypical cells, prolymphocytes

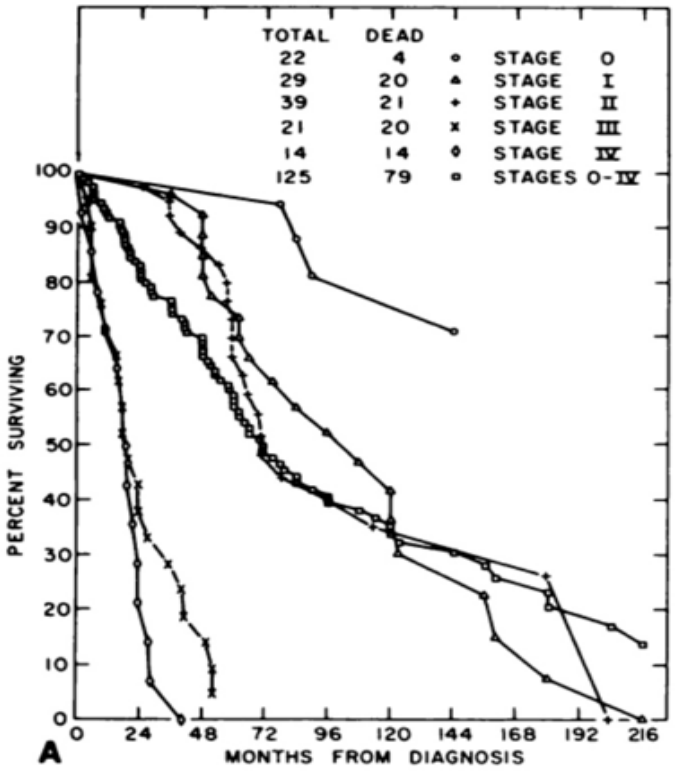
Peter Maslak, ASH Image Bank 2010.

CLL vs other lymphoproliferative diseases

	CLL	MCL	SMZL	B-PLL	LPL
CD19	+	+	+	+	+
CD20	dim	+	+	+	+
CD22	+			+	+
CD23	+	-	-	variable	-
CD5	+	+	-	-	-
CD10	-	-	-	-	-
FMC7	- or weak	+		+	
CD79b	dim			+	
sIg	dim	strong	strong	strong	strong

WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues 4th ed

Rai staging



Median survival

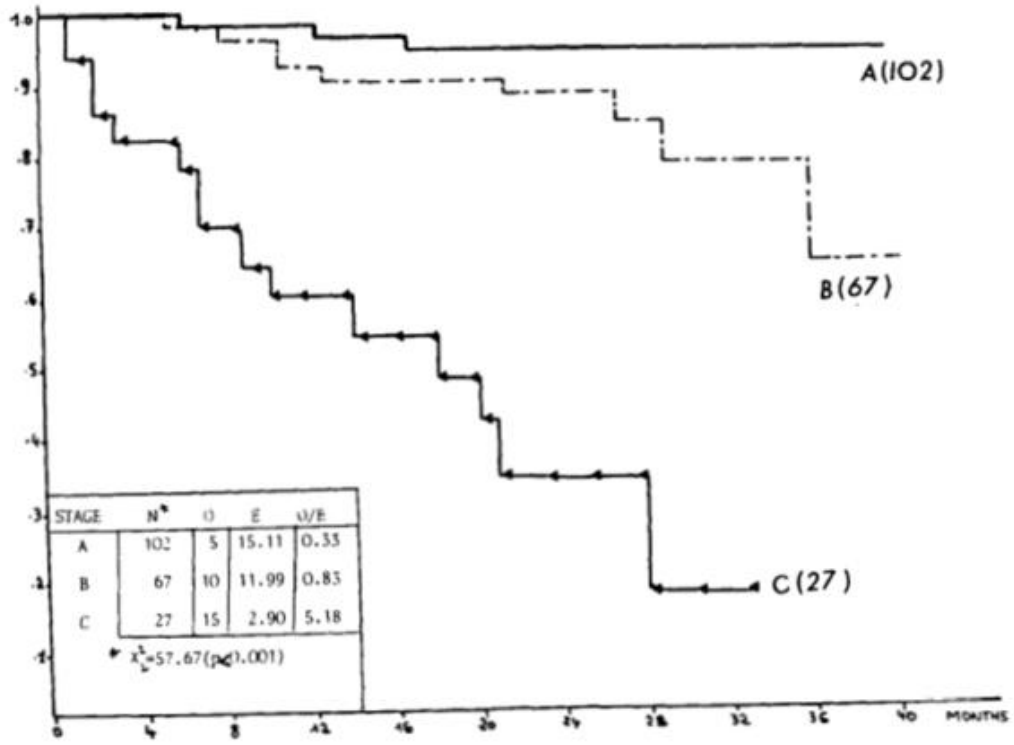
Stage 0: 150 months
Stage I: 101 months
Stage II: 71 months
Stage III: 19 months
Stage IV: 19 months

Original	Modified	Features	Median survival (months)
0	Low risk	Lymphocytosis	150
I	Intermediate risk	Lymphadenopathy	101
II	Intermediate risk	Splenomegaly +/- hepatomegaly	71
III IV	High risk	Anaemia (Hb < 11 g/dL) Thrombocytopenia (Plt < 100 x 10^9/L)	19

Blood (1975) 46 (2): 219-234.

Binet Staging

***Nodal regions and organ enlargement*
1 Head and neck
2. Axilla
3. Groins
4. Splenomegaly
5. Hepatomegaly



Stage	Features	Median survival (months)
A	Up to 2 involved nodal areas No anaemia or thrombocytopenia	Comparable to age-matched controls
B	3 or more involved nodal areas No anaemia or thrombocytopenia	84
C	Anaemia (Hb < 10 g/dL) and/or Thrombocytopenia (Platelet < 100 x 10^9/L)	24

Cancer. 1977:40(2):855.

Evaluation of CLL patients

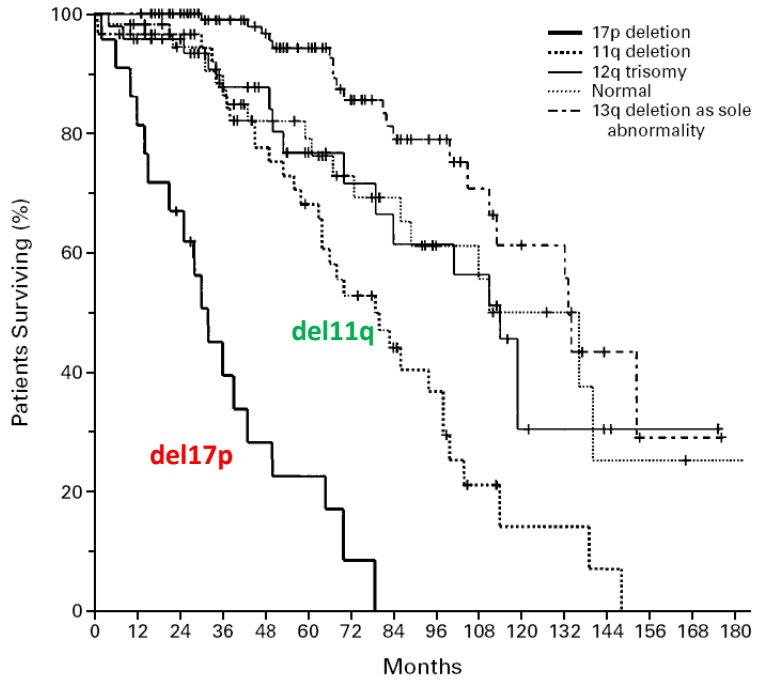
Diagnostic test	General practice	Clinical trial
Test to establish the diagnosis		
CBC, differential count	Always	Always
Immunophenotyping of peripheral blood lymphocytes	Always	Always
Assessment before treatment		
History, physical exam, performance status	Always	Always
CBC, differential count	Always	Always
Marrow aspirate and biopsy	When clinically indicated (unclear cytopenia)	Desirable
Serum chemistry, serum immunoglobulin, direct antiglobulin test	Always	Always
Chest radiograph	Always	Always
Infectious disease status	Always	Always

Blood. 2018;131:2745-2760.

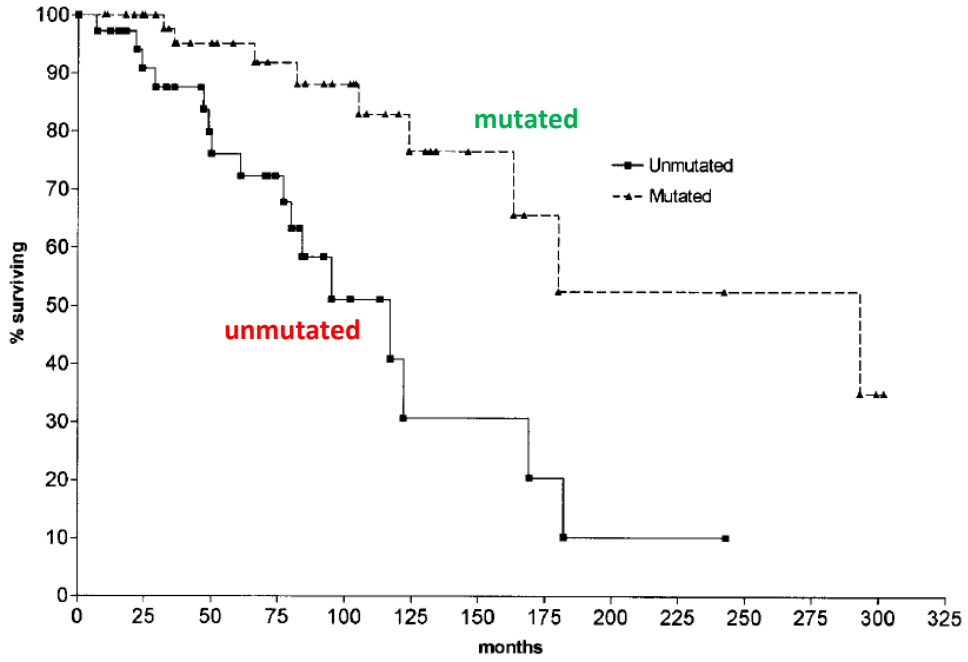
Poor genomic prognostic factors for CLL

- Del(17p) and/or TP53 gene mutations

- Unmutated IGVH



Döhner et al NEJM 2000



Hamblin et al. Blood 1999

Management of CLL

iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL

Blood 2018

Michael Hallek,[1,2] Bruce D. Cheson,[3] Daniel Catovsky,[4] Federico Caligaris-Cappio,[5] Guillermo Dighiero,[6] Hartmut Döhner,[7] Peter Hillmen,[8] Michael Keating,[9] Emili Montserrat,[10] Nicholas Chiorazzi,[11] Stephan Stilgenbauer,[7] Kanti R. Rai,[11] John C. Byrd,[12] Barbara Eichhorst,[1] Susan O'Brien,[13] Tadeusz Robak,[14] John F. Seymour,[15] and Thomas J. Kipps[16]

ESMO Clinical Practice Guideline interim update on new targeted therapies in the first line and at relapse of chronic lymphocytic leukaemia☆

Ann Oncol 2024

B. Eichhorst[1†], P. Ghia[2,3†], C. U. Niemann[4], A. P. Kater[5], M. Gregor[6], M. Hallek[1,7], M. Jerkeman[8] & C. Buske[9], on behalf of the ESMO Guidelines Committee*

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma

Version 3.2025 — April 2, 2025

NCCN.org

Management of CLL in Asia

Clinical and Experimental Medicine (2023) 23:2895–2907
https://doi.org/10.1007/s10238-023-01007-2

CORRESPONDENCE

Expert consensus on the management of chronic lymphocytic leukaemia in Asia

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Ann Acad Med Singap 2025;54:36-52
https://doi.org/10.47102/annals-acadmedsg.2024174

REVIEW ARTICLE

Consensus guidelines for the management of treatment-naïve chronic lymphocytic leukaemia in Singapore (2024)

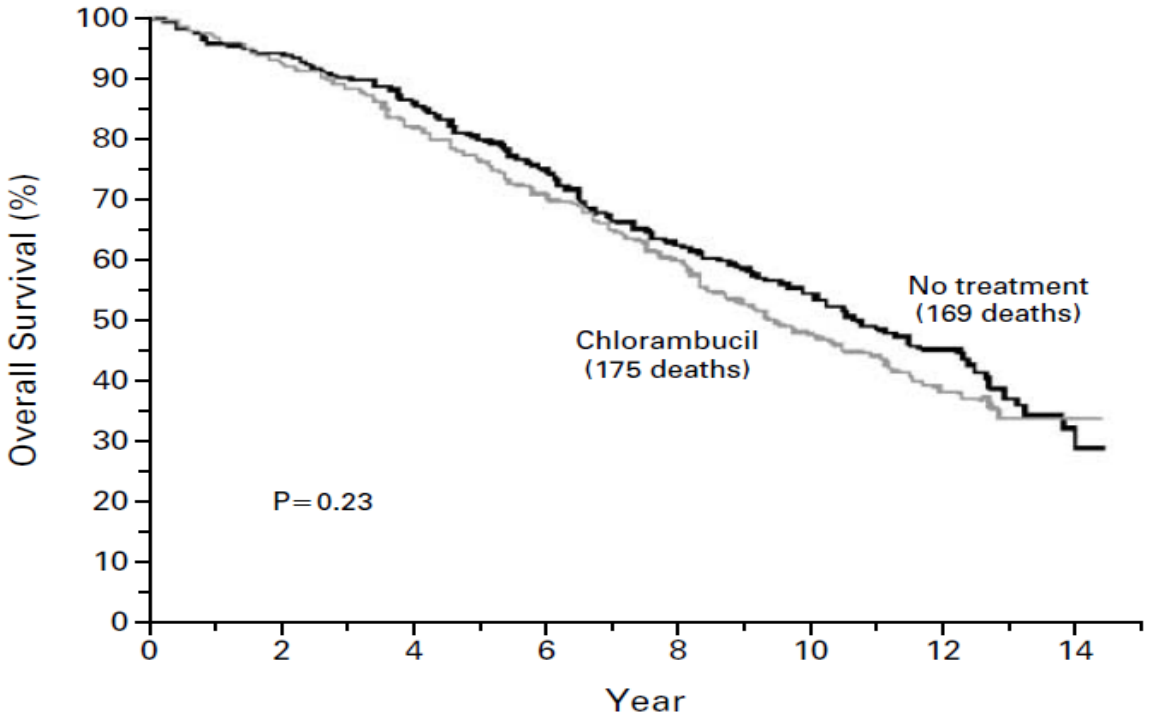
Yeow Tee Goh[1,2] *MMed*, Yvonne Loh[3] *FAMS*, Esther Chan[4] *FRCPath*, Yuh Shan Lee[5] *FRCPath*, Venkata Sreekanth Sampath[6] *FRCPath*, Daryl Tan[7] *FAMS*, Shin Yeu Ong[1,2*] *FRCPath*, Chandramouli Nagarajan[1,2*] *FRCPath*

- The International Workshop on CLL (iwCLL) guidelines should be used for both the indication for treatment and evaluation of therapy.

- Asymptomatic patients with early stage disease (Rai 0, Binet A) should be monitored without therapy unless there is evidence of disease development or disease related symptoms

Managing asymptomatic CLL

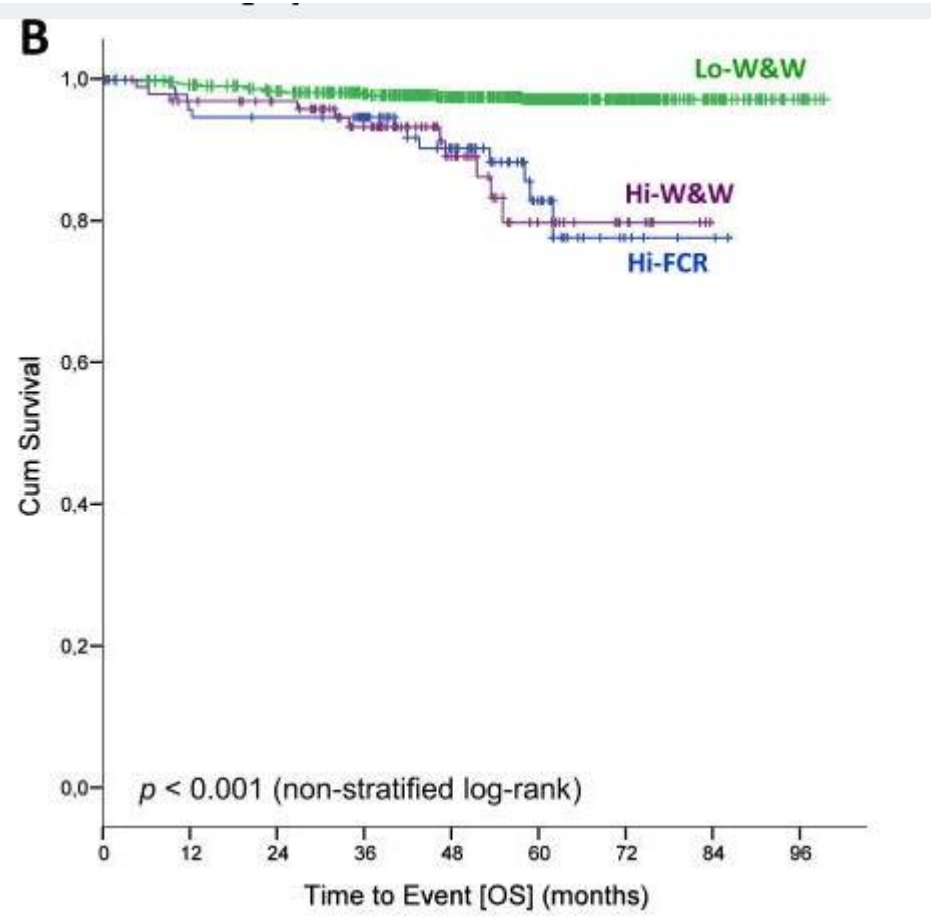
W&W *vs* Chemo or CIT



Dighiero G et al., N Engl J Med. 1998;338(21):1506-14.

High risk: any TWO of the followings

1. **TK >10U/L**
2. **LDT <12m**
3. **Unmutated IGHV**
4. **del(11q) or del(17p) or trisomy 12**

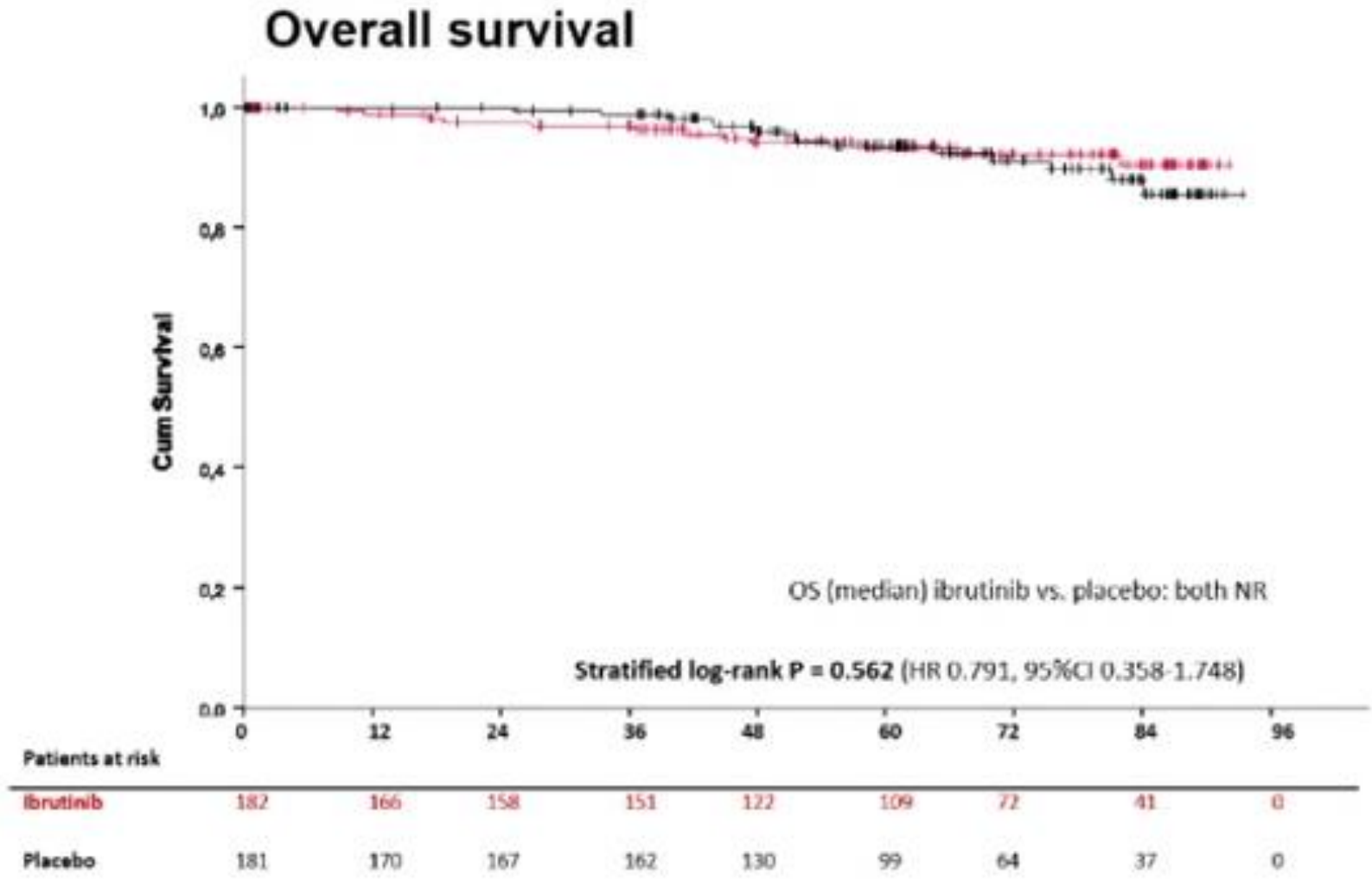


Herling CD et al., Leukemia. 2020;34(8):2038-50.

Ibrutinib in asymptomatic early stage CLL (CLL12)

No survival advantage with new agent treatment in early stage CLL

W&W is still the standard for asymptomatic early stage CLL



HemaSphere 7(S3):p e9488123, August 2023.

Factors that affect treatment decision

Patient factors

- Age
- Fitness / performance status
- Other co-morbidities

Leukaemia factors

- *TP53* gene aberrations (del17p or *TP53* gene mutations)
- *IGHV* gene mutation

Currently approved targeted agents for the treatment of CLL

- **BTK inhibitors (continuous as single agent)**

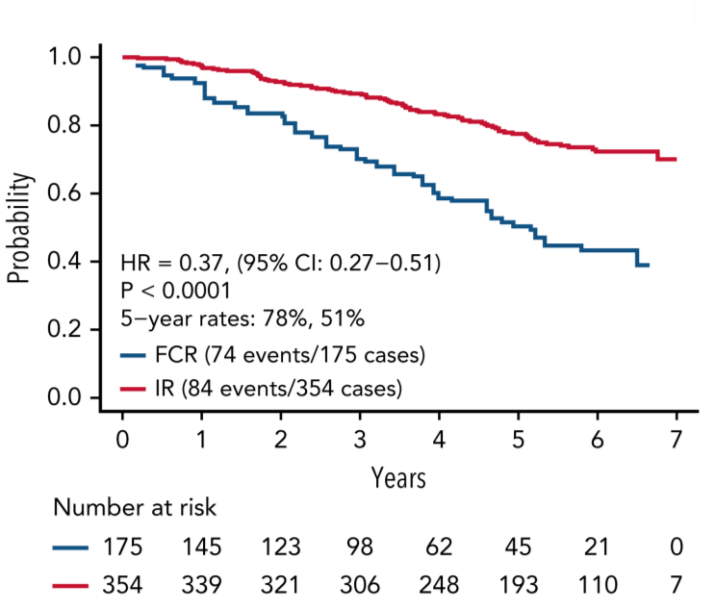
Ibrutinib, Acalabrutinib, Zanubrutinib

- **BH3 mimetics (time limited)**

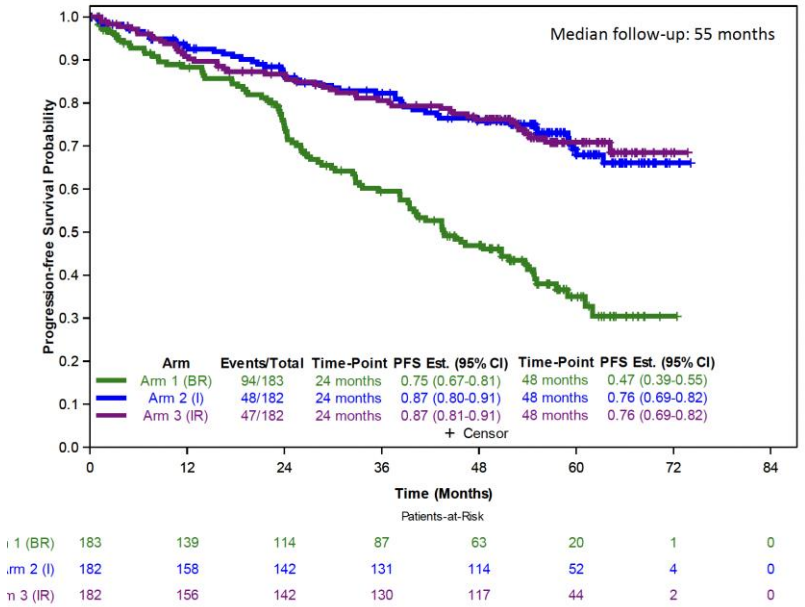
Venetoclax – typically in combination with anti-CD20 and/or BTKi

Ibrutinib (+ anti-CD20) vs CIT

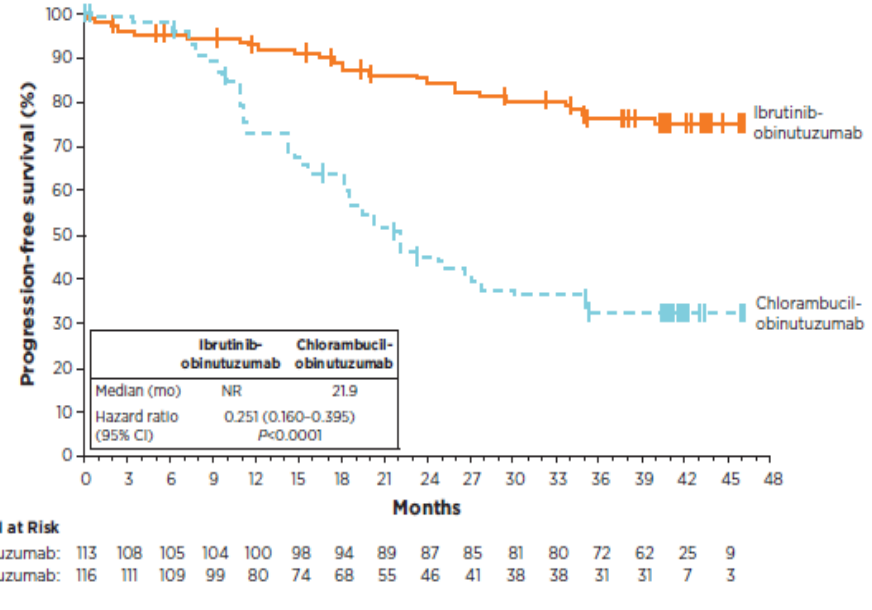
ECOG1912: Young/fit patients



A041202: Elderly/fit patients

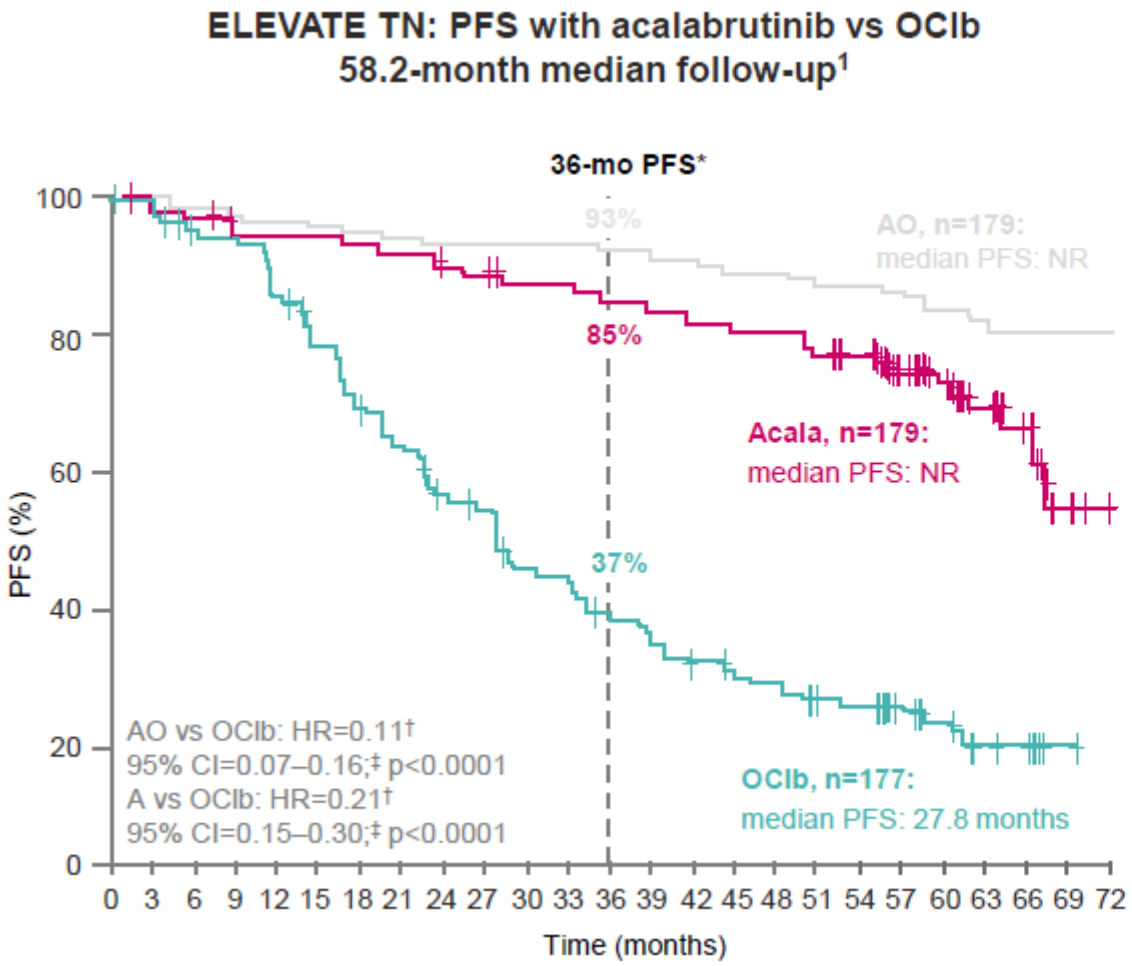


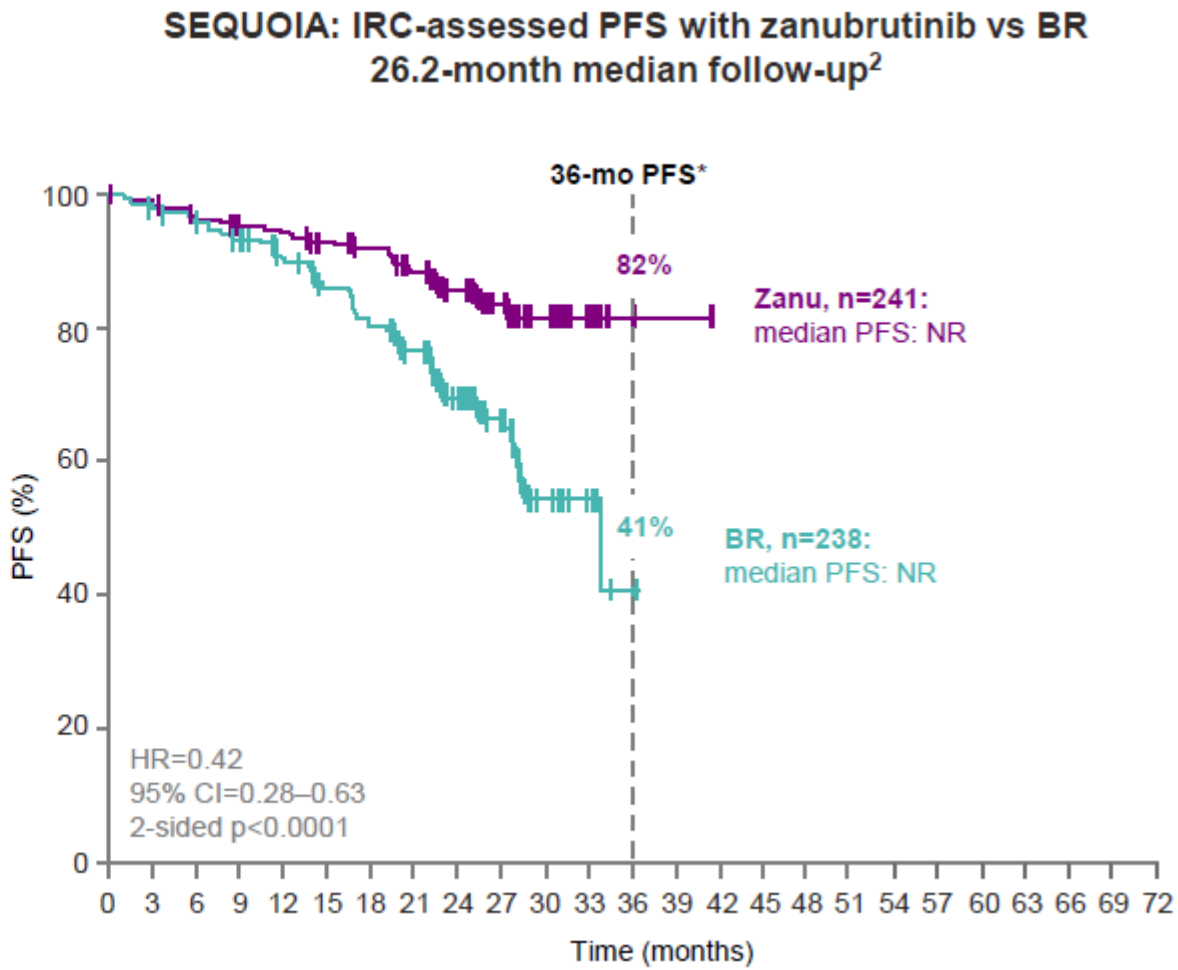
iLLUMINATE: Elderly/unfit patients



High efficacy of ibrutinib confirmed in randomized studies vs CIT

Acalabrutinib and Zanubrutinib in treatment-naïve CLL



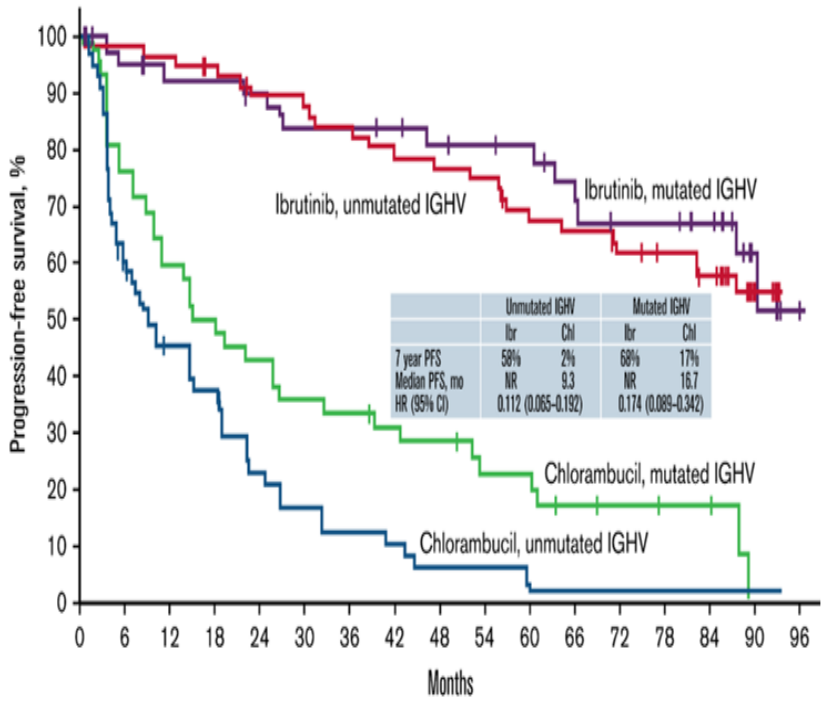


1. Sharman JP, et al. HemaSphere 2022; 6(Suppl 3):1082–1083 (Poster); 2. Tam CS, et al. Lancet Oncol 2022; 23:1031–1043

Adapted from ECHO 2023

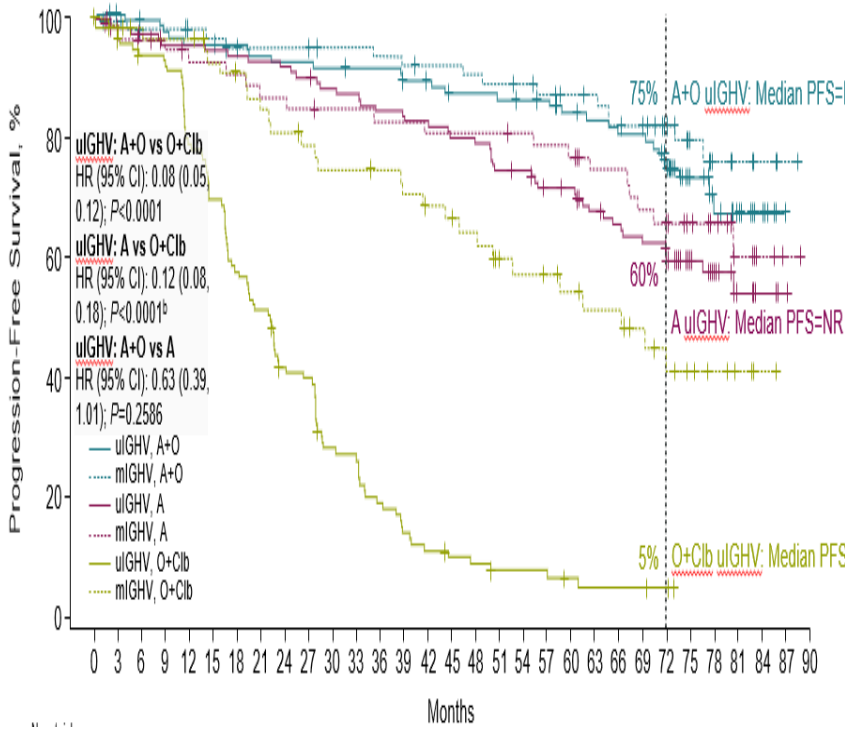
Continuous BTKi in CLL with unmutated IGHV

Resonate 2



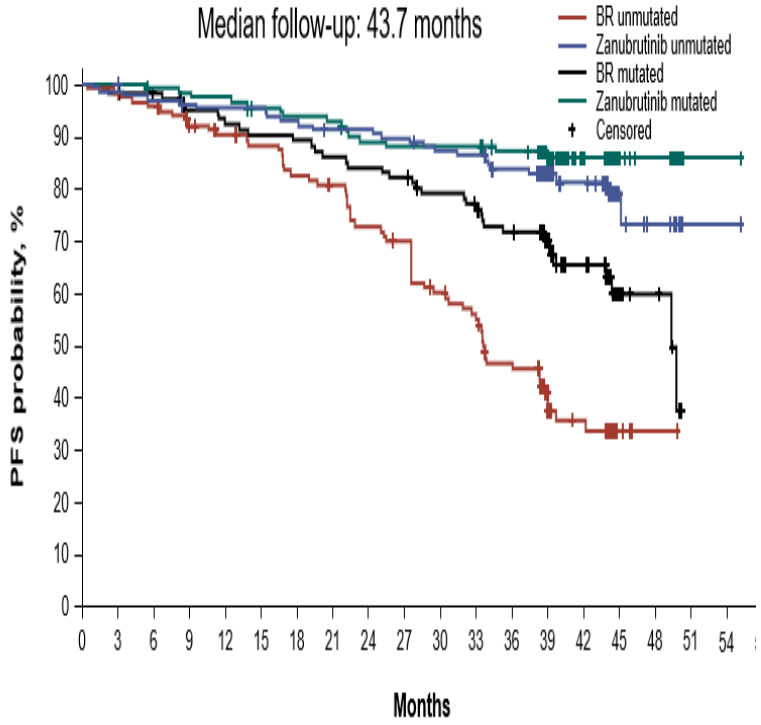
Barr et al, Blood Adv, 2022

ELEVATE TN



Sharman et al, ASH 2023

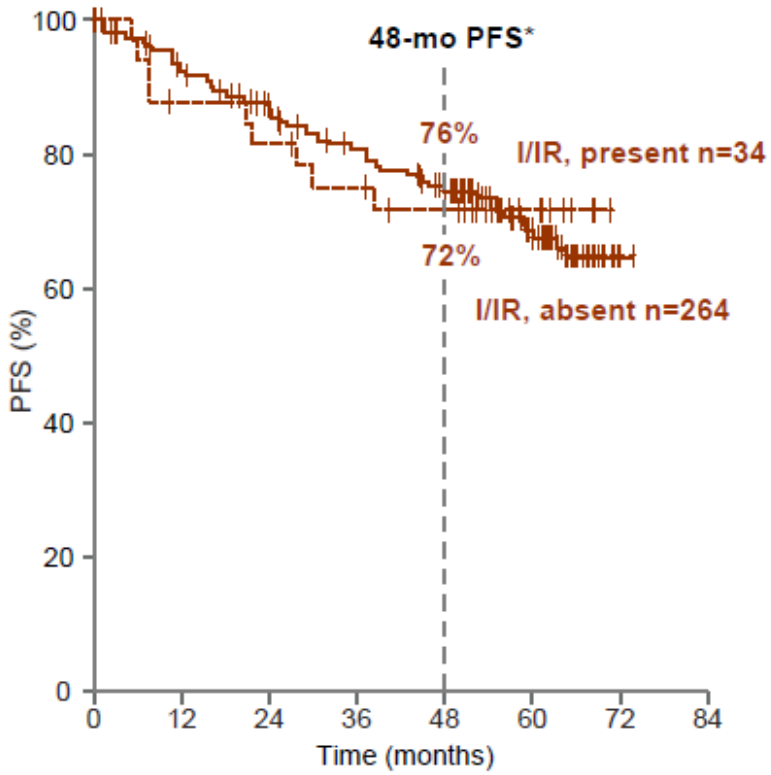
SEQUOIA



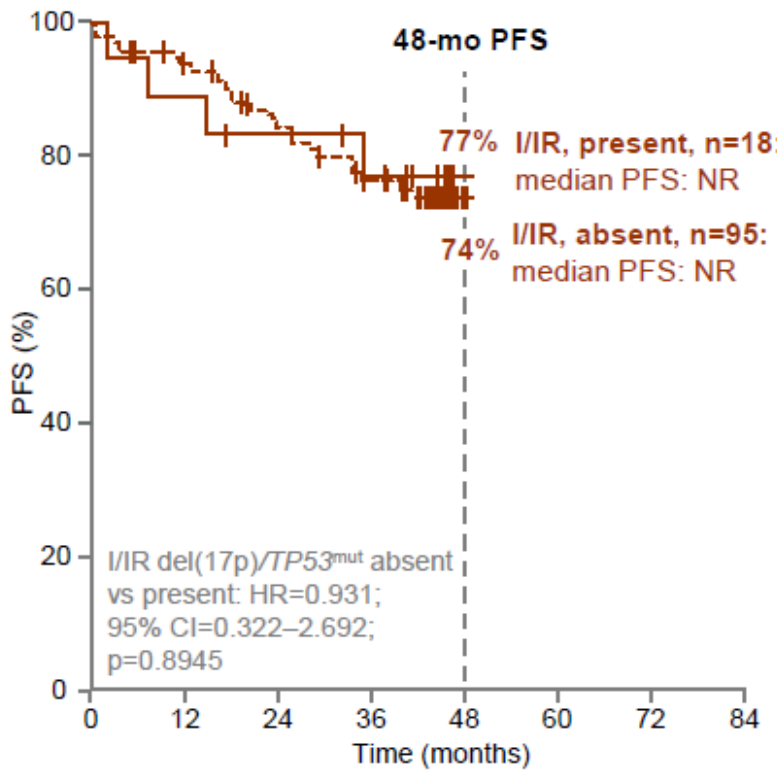
Shadman et al, ICML 2023

Continuous BTKi in CLL with TP53 aberrations (del17p and/or TP53 mutations)

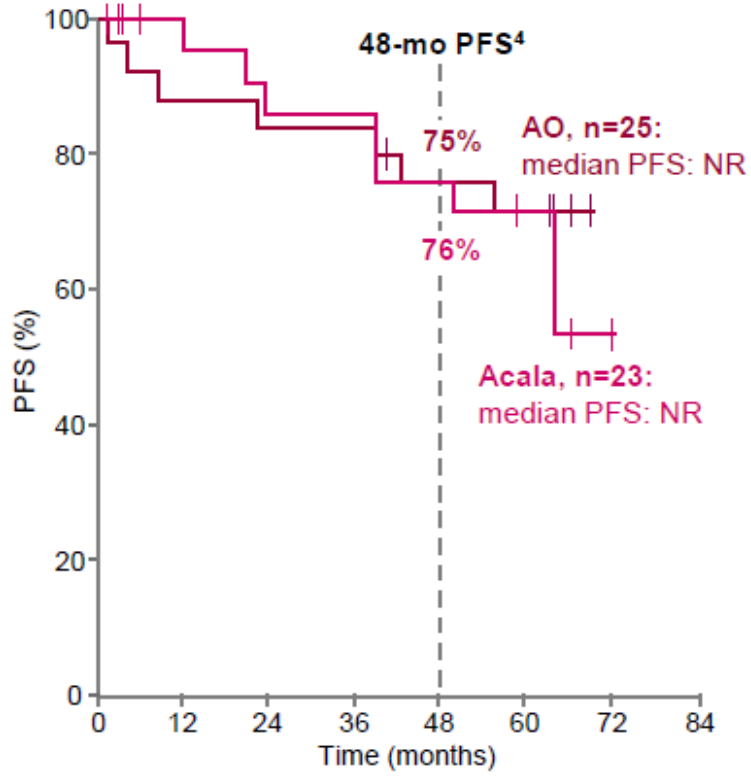
Alliance A041202: PFS with ibrutinib/IR by del(17p)/*TP53*^{mut} status 55-month median follow-up[1]



iLLUMINATE: PFS with IO by del(17p)/*TP53*^{mut} status 45-month median follow-up[2]



ELEVATE TN: PFS with acalabrutinib/AO in patients with del(17p)/*TP53*^{mut} 58.2-month median follow-up[3]



1. Woyach J, et al. Blood 2021; 138(Suppl 1):639 (Oral); 2. Moreno C, et al. Haematologica 2022; doi: 10.3324/haematol.2021.279012; 3. Sharman JP, et al. HemaSphere 2022; 6(Suppl 3):1082–1083 (Poster); 4. Sharman JP, et al. Leukemia 2022; 36:1171–1175

Adverse events with BTKi

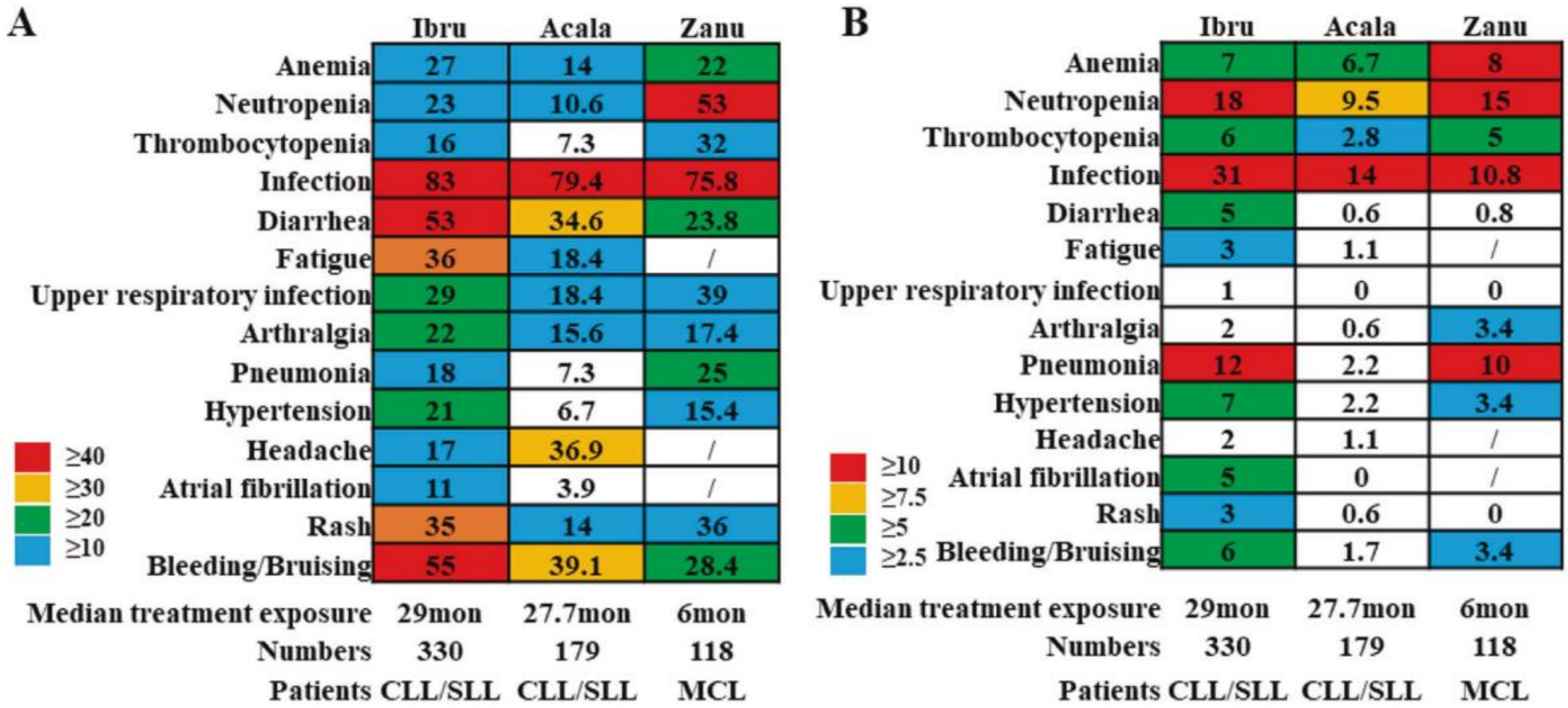
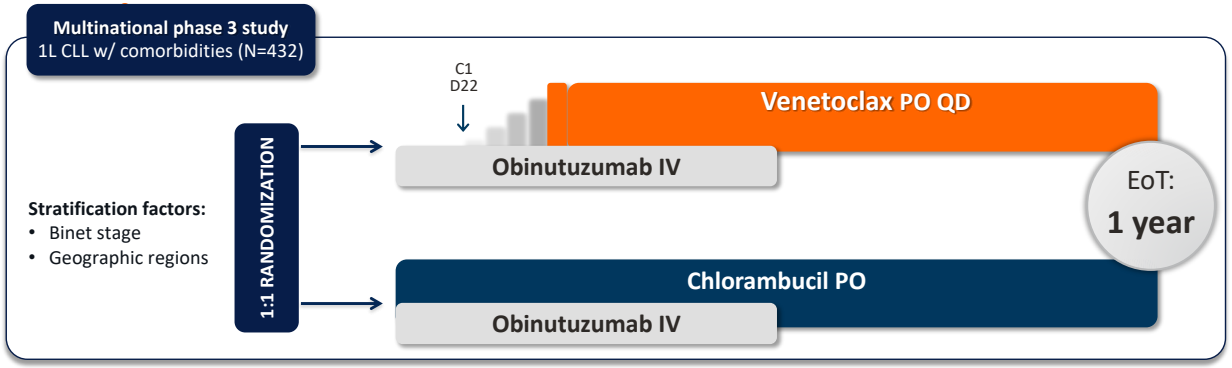


Fig. 4 Frequency of adverse events with ibrutinib, acalabrutinib, and zanubrutinib. A The comparison of any grade adverse events in ibrutinib, acalabrutinib, and zanubrutinib. **B** The comparison of grade 3-5 adverse events in ibrutinib, acalabrutinib, and zanubrutinib.

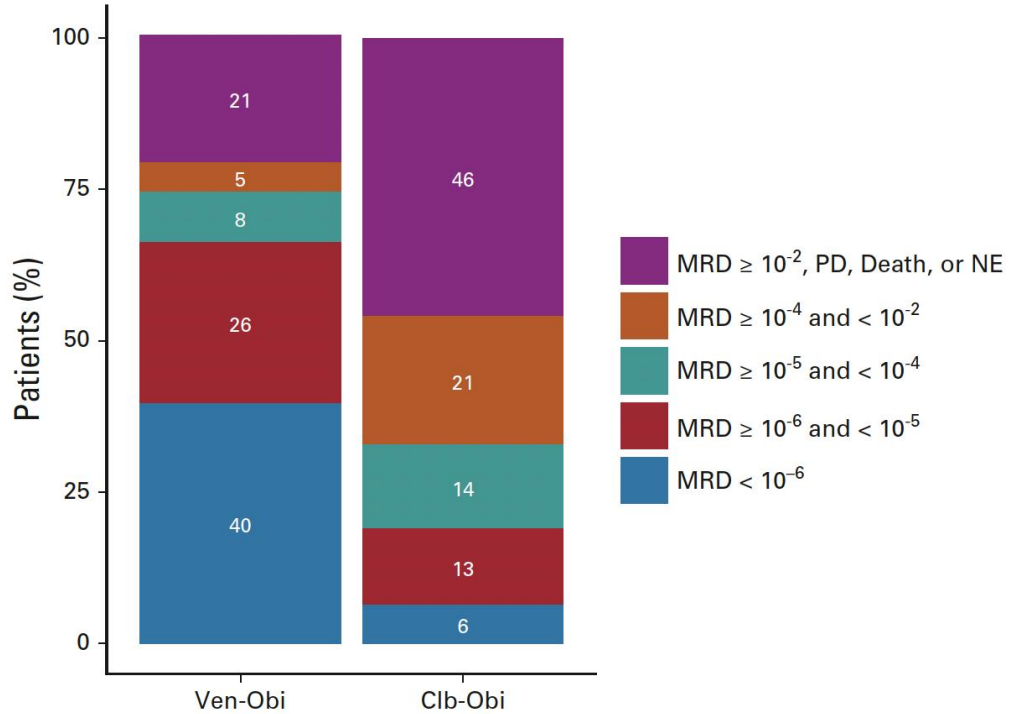
Wen T et al. Leukemia 2020

Fixed duration therapy
Venetoclax + obinutuzumab in first line CLL

CLL14

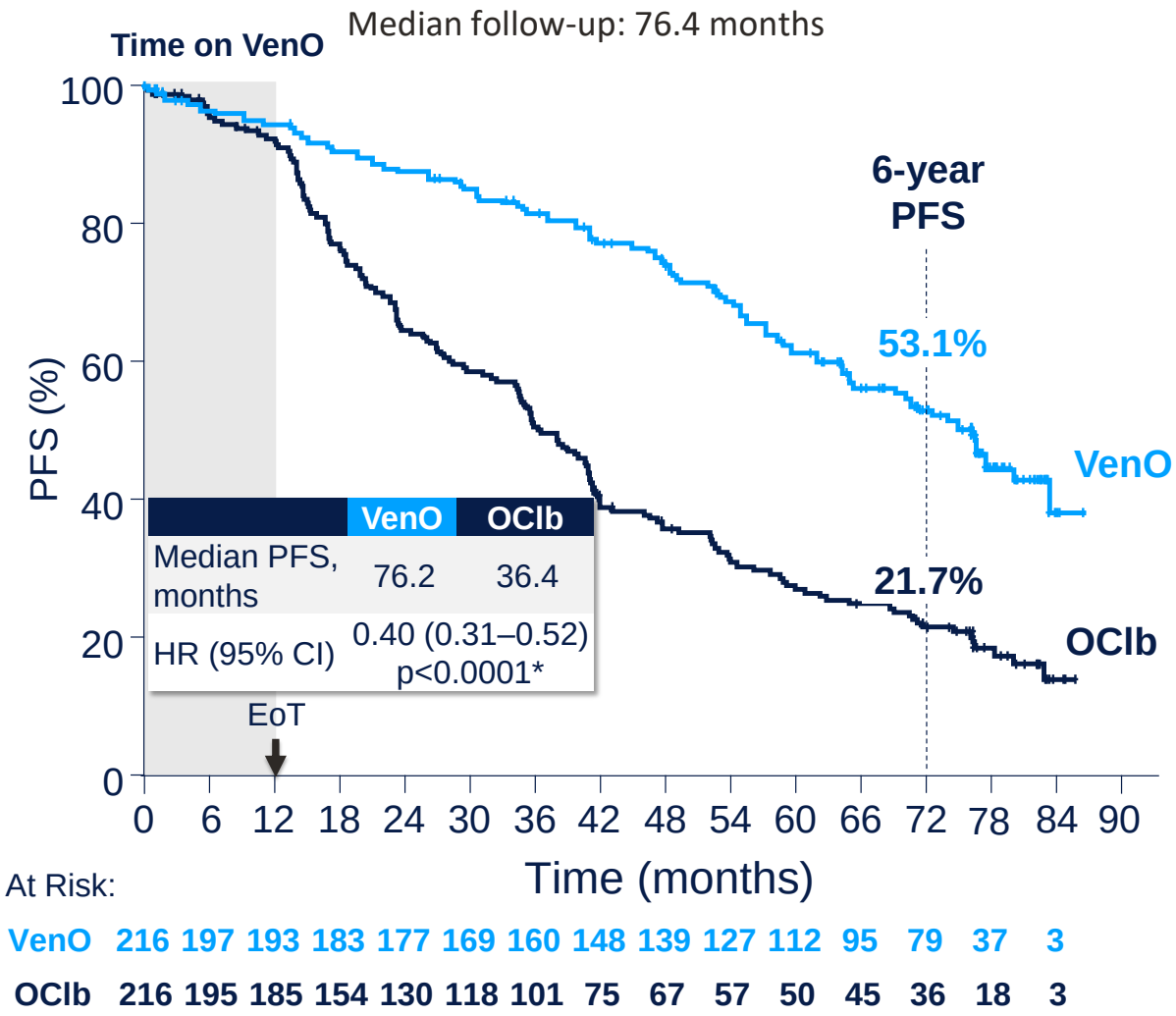


Peripheral blood MRD response by NGS 3 months after EoT



uMRD rates (<10^{-4}), as measured by NGS* in PB in the ITT population, were higher with VenO vs OClb; 40% of patients in the VenO arm achieved MRD <10^{-6} vs 6% in the OClb arm

PFS benefit was sustained 5 years after completing VenO, with a 60% reduction in risk of PD or death

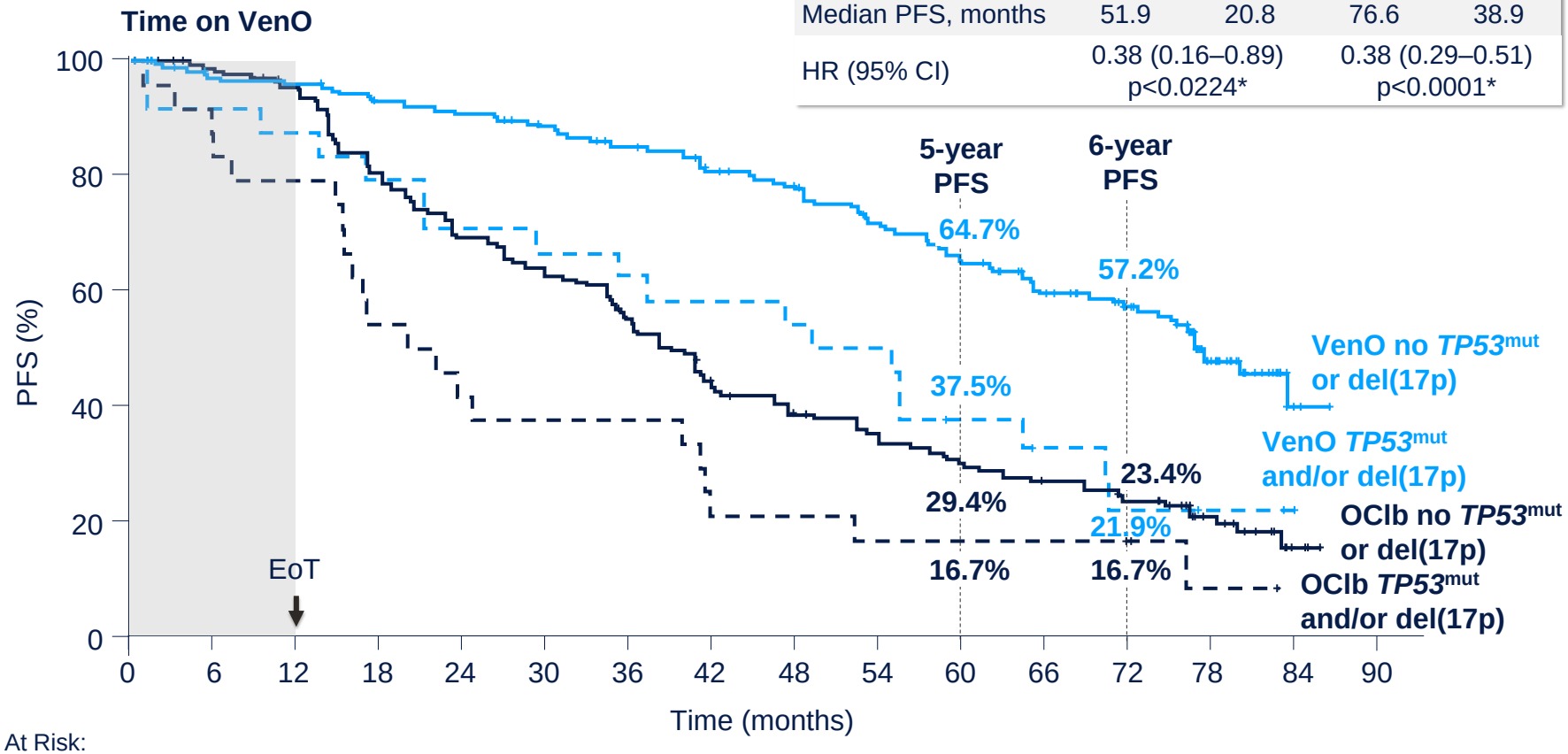


Al-Sawaf et al, EHA 2023

PFS in *TP53* mut / del(17p) patients treated with O-Ven in CLL14 (N =25)

Median follow-up: 76.4 months

	TP53^{mut} and/or del(17p)		No *TP53*^{mut} or del(17p)	
	VenO	OClb	VenO	OClb
Median PFS, months	51.9	20.8	76.6	38.9
HR (95% CI)	0.38 (0.16–0.89) p<0.0224*		0.38 (0.29–0.51) p<0.0001*	



At Risk:

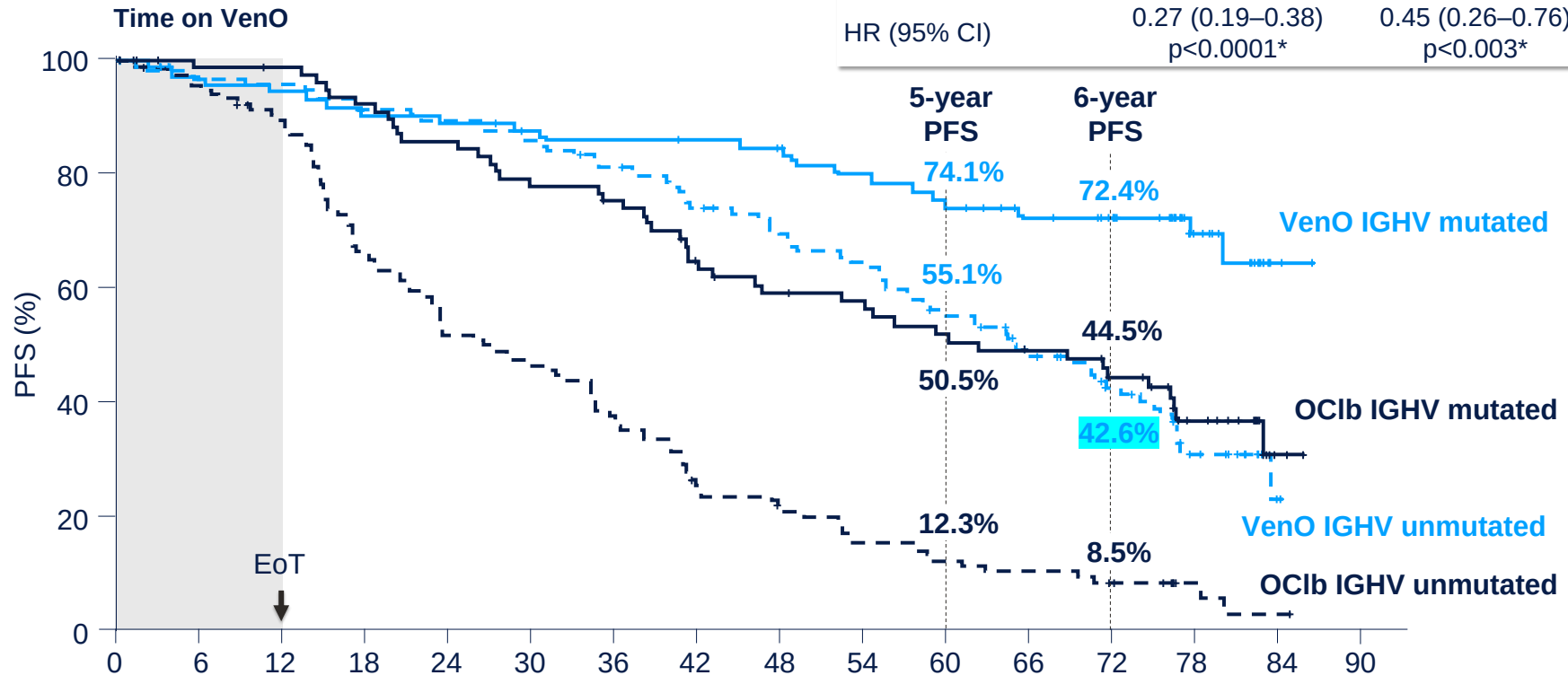
OClb *TP53*^{mut} and/or del(17p)	24	20	19	13	10	9	9	5	5	4	4	4	3	1	
VenO *TP53*^{mut} and/or del(17p)	25	22	21	19	17	16	15	14	13	12	8	6	4	2	
OClb no *TP53*^{mut} or del(17p)	184	169	160	135	117	106	90	68	60	51	45	40	33	17	3
VenO no *TP53*^{mut} or del(17p)	184	170	168	161	157	150	142	131	123	112	101	87	73	34	3

Al-Sawaf et al, EHA 2023

PFS according to **IGHV status** treated with O-Ven in CLL14

Median follow-up: 76.4 months

	IGHV unmutated		IGHV mutated	
	VenO	OClb	VenO	OClb
Median PFS, months	64.8	26.9	NE	62.2
HR (95% CI)	0.27 (0.19–0.38) p<0.0001*		0.45 (0.26–0.76) p<0.003*	

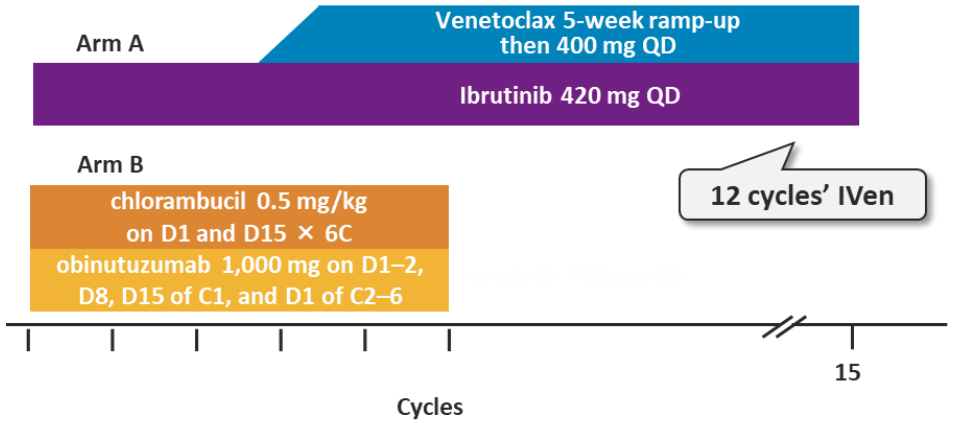


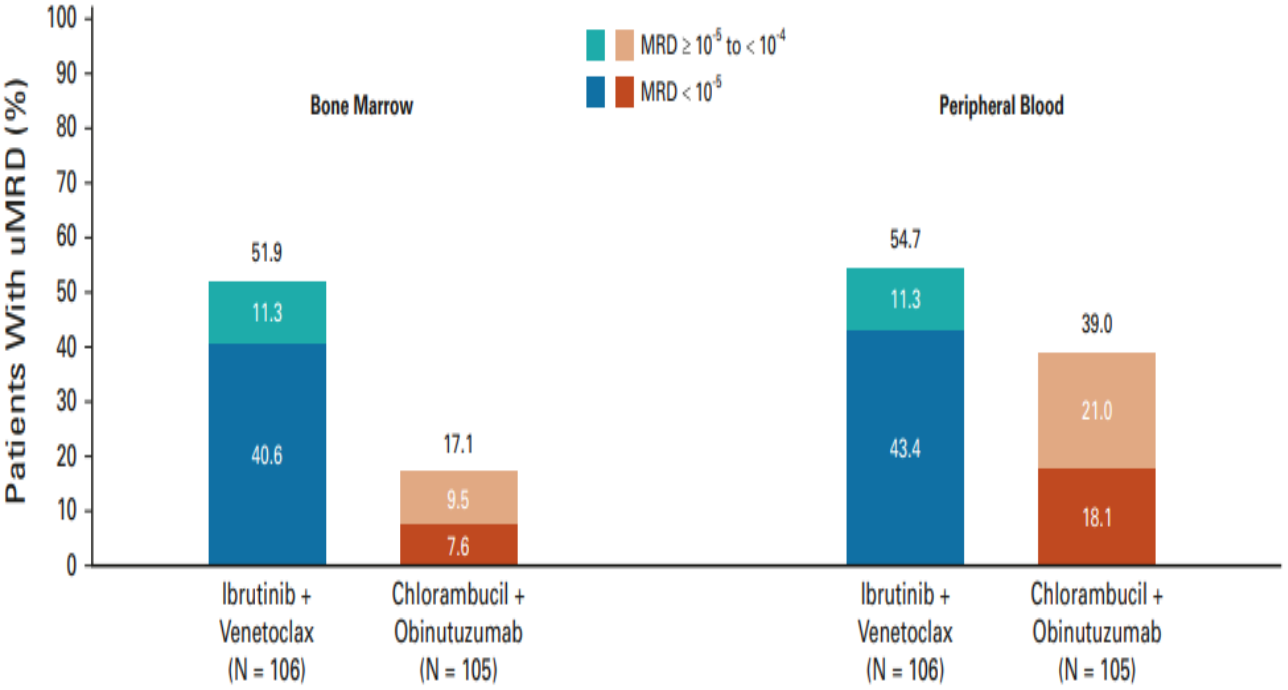
At Risk:															
OClb IGHV mutated	83	77	76	71	66	60	57	46	42	39	35	33	28	15	2
VenO IGHV mutated	76	70	68	65	64	61	60	59	57	53	49	44	39	19	2
OClb IGHV unmutated	123	110	101	75	59	53	41	26	22	16	13	11	8	3	1
VenO IGHV unmutated	121	111	110	103	101	96	90	80	73	68	57	47	37	17	1

Al-Sawaf et al, EHA 2023

Venetoclax + BTKi in first line CLL

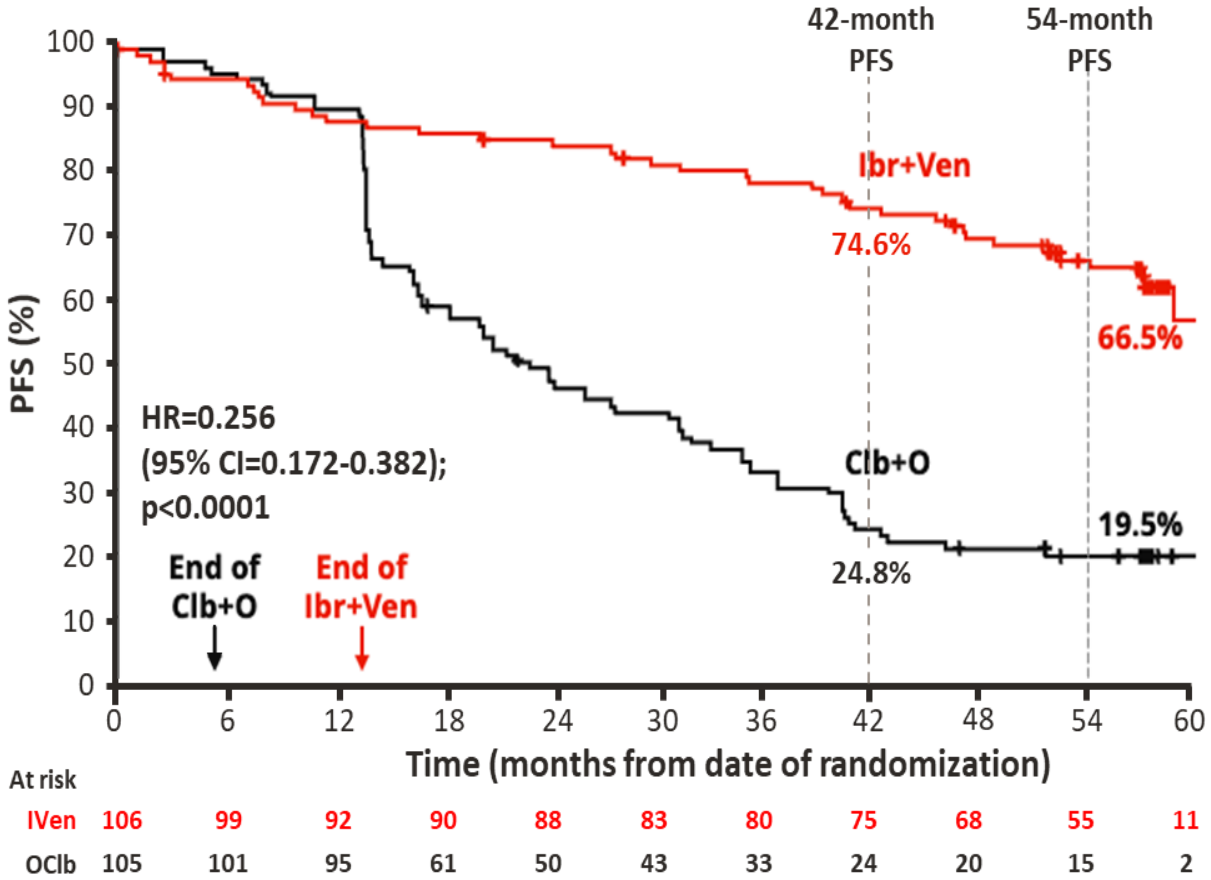
GLOW





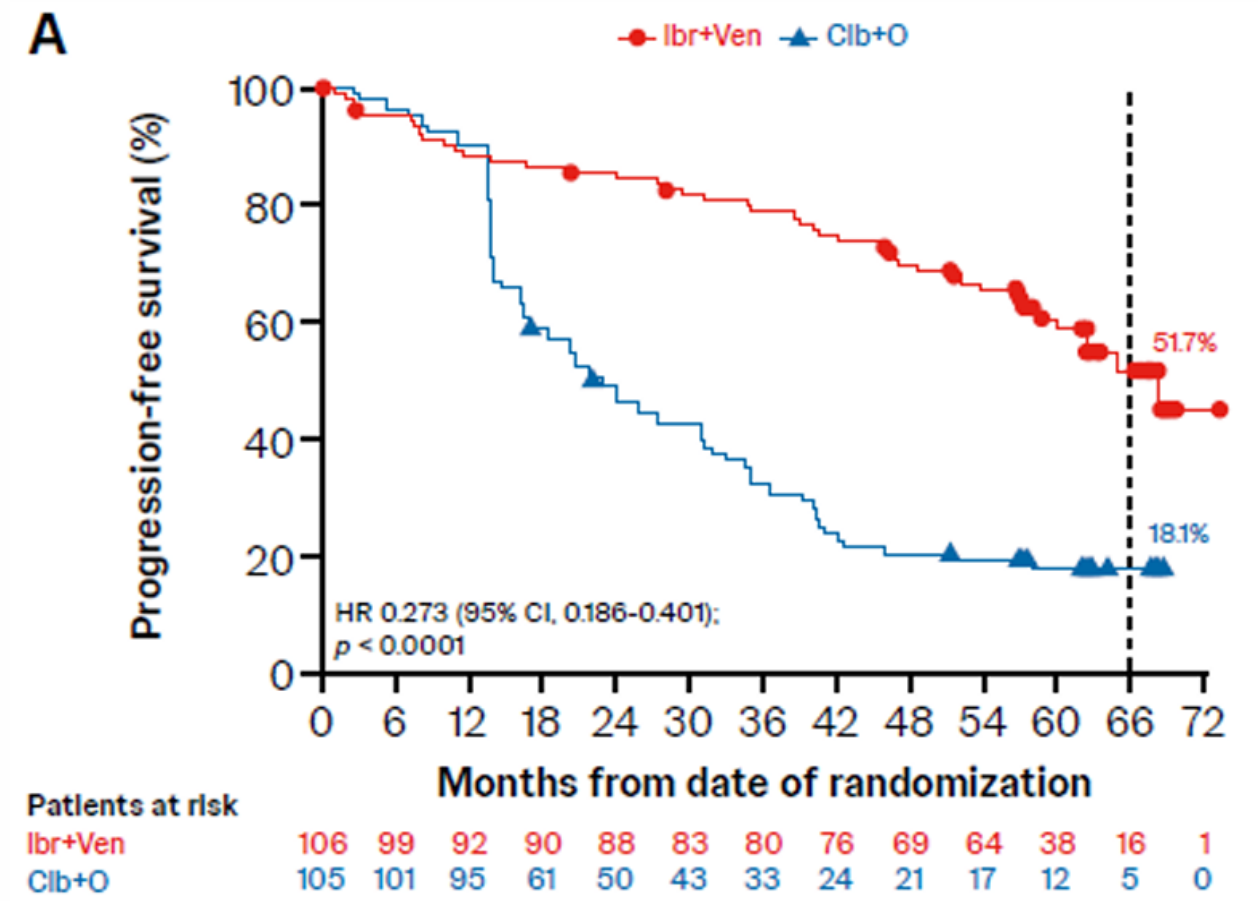
MRD by NGS at 3m after EOT

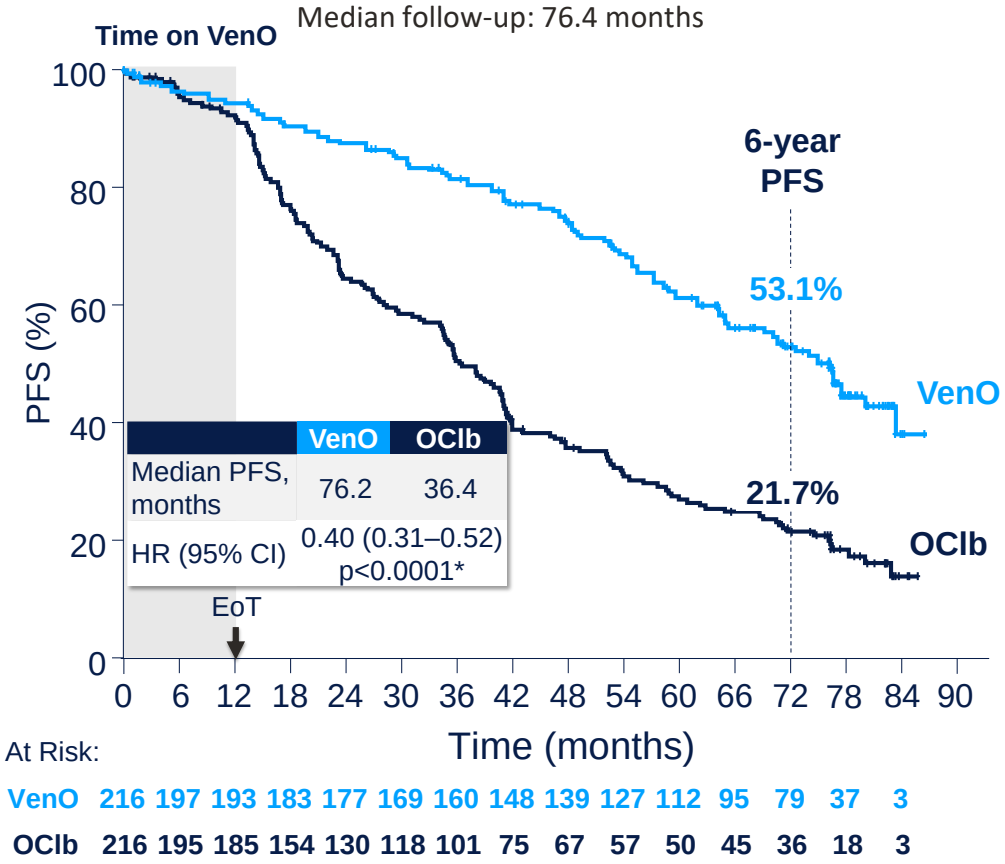
Median follow-up: 57.3 months



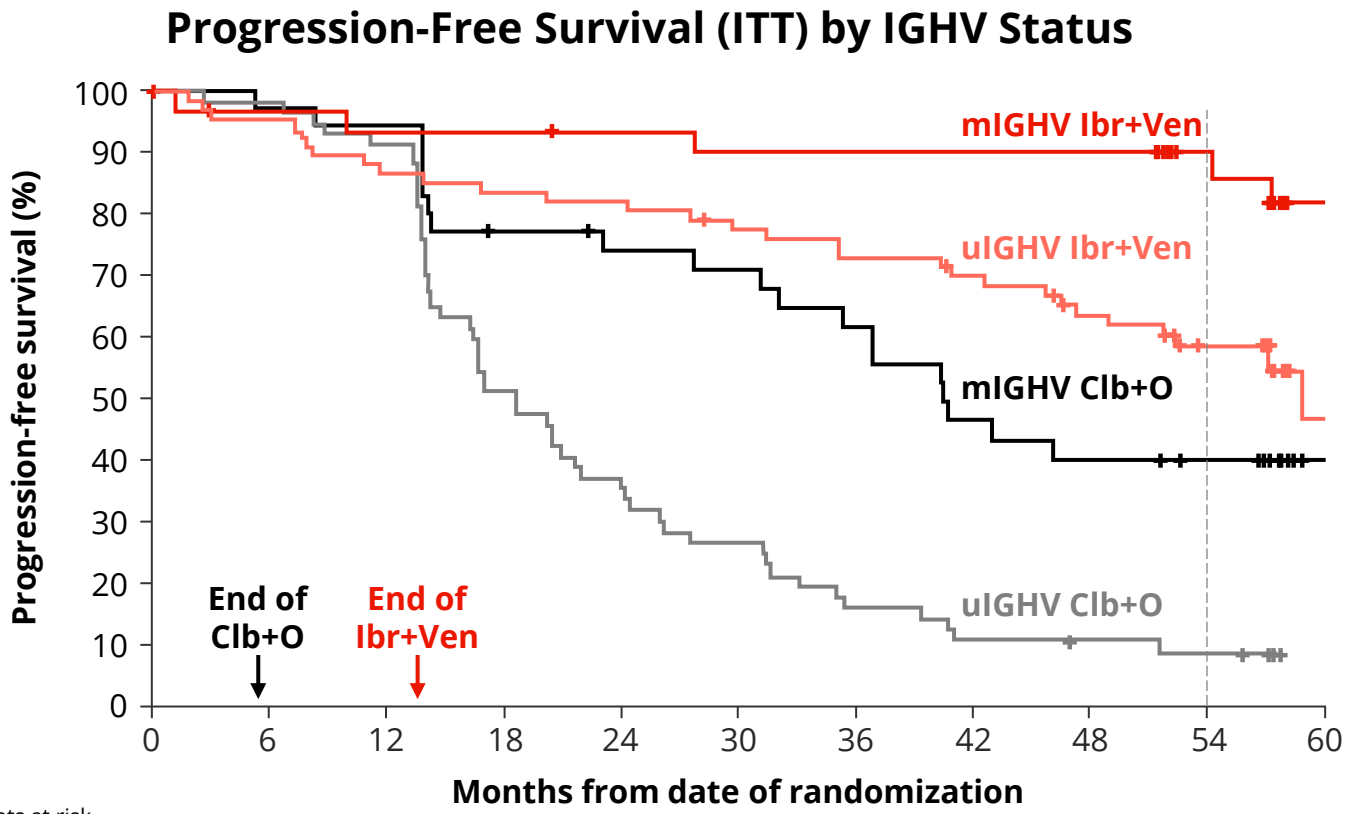
Moreno C, et al. ASH 2023. Abstract 634 (Oral)
Niemann CU, et al. ASH 2022. Abstract 93 (Oral)
Munir T, et al. J Clin Oncol, 2023

Ven + ibrutinib *vs* Ven + O





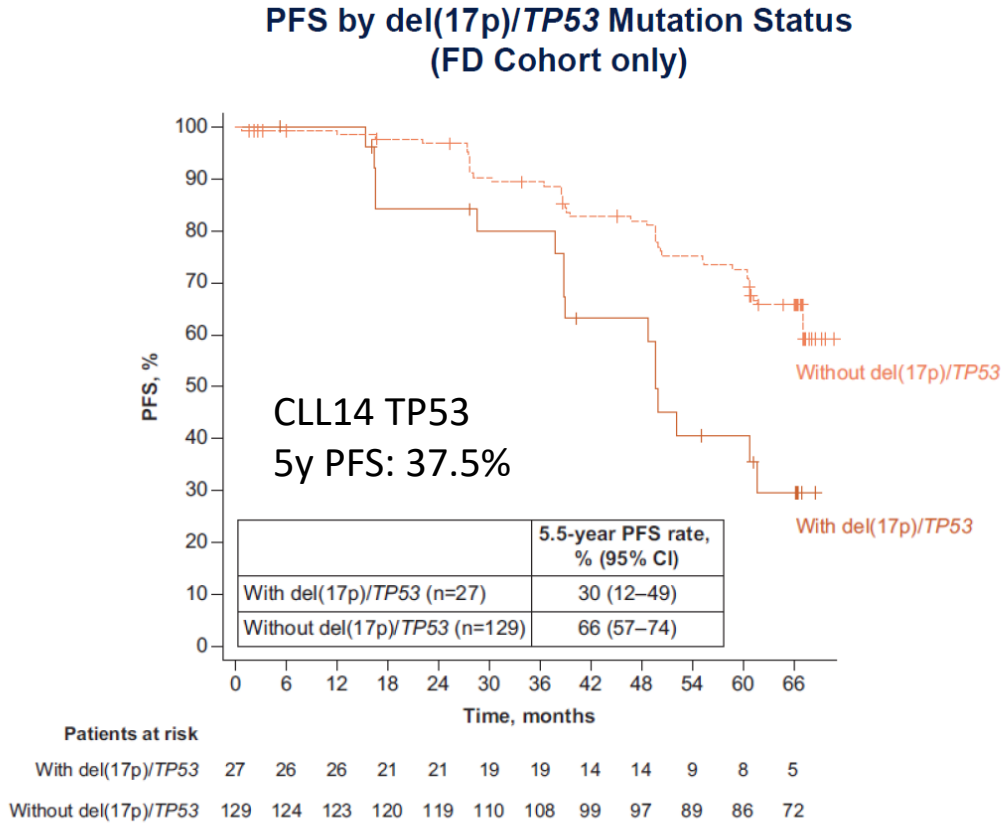
PFS according to IGHV status with Ven-Ibru in GLOW study

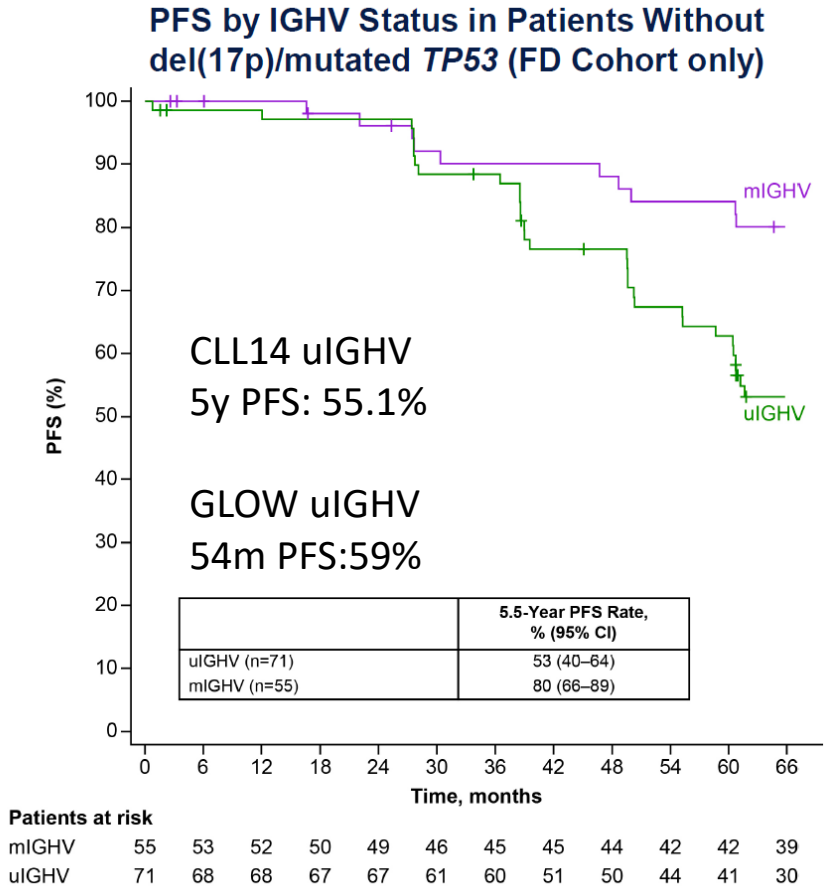


- Estimated 54-month PFS rates:
  - **Ibr+Ven:**
    - 90% for patients with mIGHV
    - 59% for patients with uIGHV
  - **Clb+O:**
    - 40% for patients with mIGHV
    - 8% for patients with uIGHV

Follows et al, ASH 2023

Impact of del(17p)/mutated *TP53*, and IGHV Status on Long-term PFS (CAPTIVATE FD Cohort)





mIGHV, mutated IGHV; PFS, progression-free survival; uIGHV, unmutated IGHV.

Venetoclax + Ibrutinib in 1st line CLL treatment

Clinical trial	Cohort	Combination regimen duration	CR/CRi response rate	MRD rate	PFS rate
MD Anderson[60-62]	TN high-risk CLL, N = 120; del 17p/*TP53* mutation, n = 27	IBR, 3 cycles; IBR + VEN, 24 cycles ± additional 12 cycles	59% at cycle 12 69% at cycle 24	52% (BM) at cycle 12 64% (BM) at cycle 24	90.1% at 5 y
CAPTIVATE[66,78]	TN FD, N = 159; MRD, N = 164; del 17p/*TP53* mutation, n = 23	IBR, 3 cycles; IBR + VEN, 12 cycles	FD cohort: 56% MRD cohort: 46%	FD cohort: 68% (PB) and 75% (PB) at cycle 12 MRD cohort: 75% (PB) and 68% (BM) at cycle 12	FD cohort: 70% at 5 y uMRD cohort: 95% placebo vs 100% ibrutinib at 1 y
FLAIR[75]	TN, N = 260; no del17p	IBR, 2 cycles; IBR + VEN, up to 72 cycles, defined by MRD	59.2%	52.4% (BM) at cycle 24 49.8% (BM) at 5 y	97.2% at 3 y
GLOW[76]	TN patients, >65 y or with comorbidities, N = 106; no del17p	IBR 3, cycles; IBR + VEN, 12 cycles	45%	55% (PB) at cycle 12	74.6% at 3.5 y

Adapted from Timofeeva N et al. Blood Neoplasia. 2024

Venetoclax + **BTKi** + **Obinutuzumab** in first line CLL

AMPLIFY Study [1]

AMPLIFY: randomized, multicenter, open-label, Phase III trial

TN CLL (N=867)

Key inclusion criteria
- Age ≥18 years
- TN CLL requiring treatment per iwCLL 2018 criteria[2]
- Without del(17p) or *TP53*[a]
- ECOG PS ≤2

Key exclusion criteria
- CIRS-Geriatric >6
- Significant cardiovascular disease

Stratification
- Age (>65 vs ≤65 years)
- *IGHV* mutational status
- Rai stage (≥3 vs <3)
- Geographic region

RANDOMIZE 1:1:1

- AV (14 cycles)
- AVO (14 cycles)
- FCR/BR (6 cycles)

***Crossover** not built into protocol*

Primary endpoint

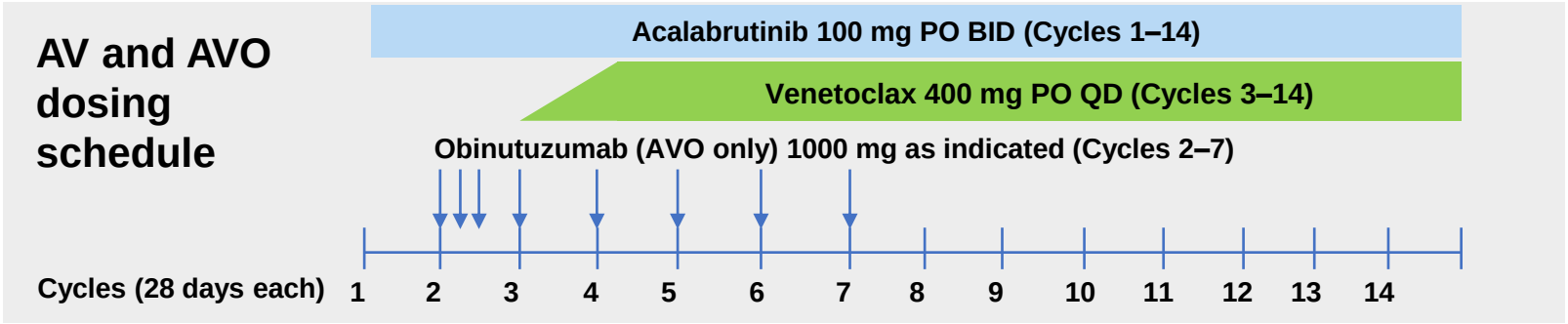
IRC-assessed PFS (AV vs FCR/BR)

If primary endpoint met, the following were

Secondary endpoints (tested in fixed sequential hierarchy)

1) IRC-PFS (AVO vs FCR/BR)
2) uMRD (AV vs FCR/BR) in PB by FC
3) uMRD (AVO vs FCR/BR) in PB by FC
4) OS (AV vs FCR/BR)
5) OS (AVO vs FCR/BR)

AV and AVO dosing schedule



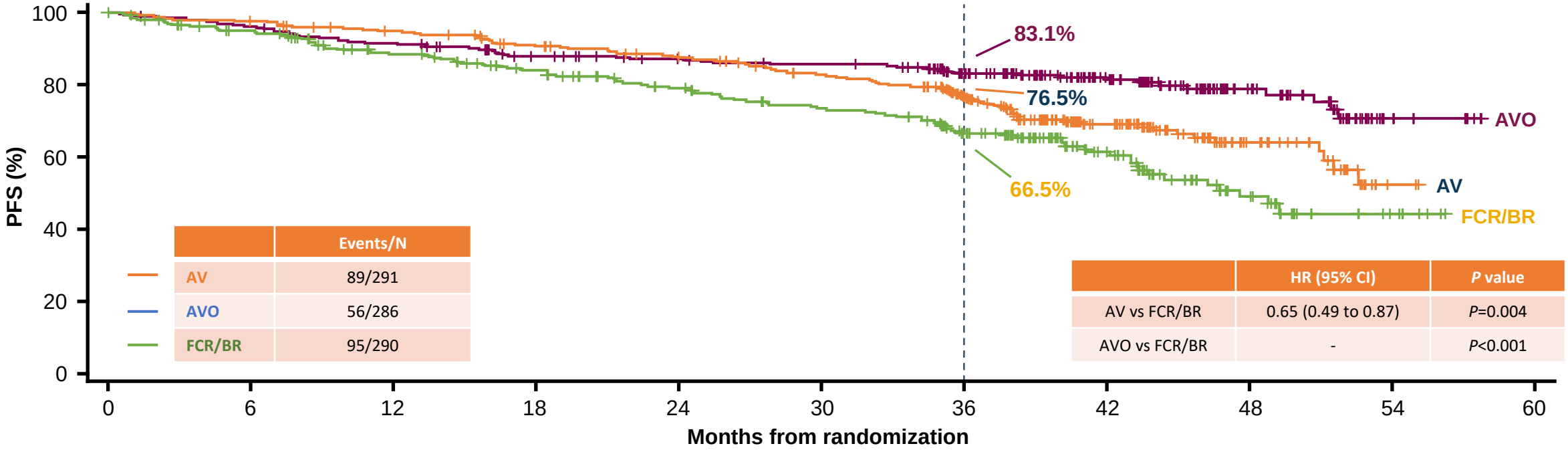
NCT03836261. Data cutoff: April 30, 2024.

[a]Performed by central laboratory.

AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BID, twice a day; BR, bendamustine-rituximab; CIRS-Geriatric, Cumulative Illness Rating Scale-Geriatric; CLL, chronic lymphocytic leukemia; ECOG PS, Eastern Cooperative Oncology Group performance status; FC, flow cytometry; FCR, fludarabine-cyclophosphamide-rituximab; IGHV, immunoglobulin heavy-chain variable region gene; IRC, independent review committee; iwCLL, International Working Group on CLL; OS, overall survival; PB, peripheral blood; PFS, progression-free survival; QD, daily; TN, treatment-naive; uMRD, undetectable measurable residual disease.

1. Brown JR, et al. *N Engl J Med*. 2025. 2. Hallek M, et al. *Blood*. 2018;131:2745-60.

IRC-assessed PFS



Patients at risk

AV	291	282	269	251	237	219	177	102	35	3	0
AVO	286	272	258	237	225	219	191	116	51	7	0
FCR/BR	290	236	208	189	170	154	127	66	28	6	0

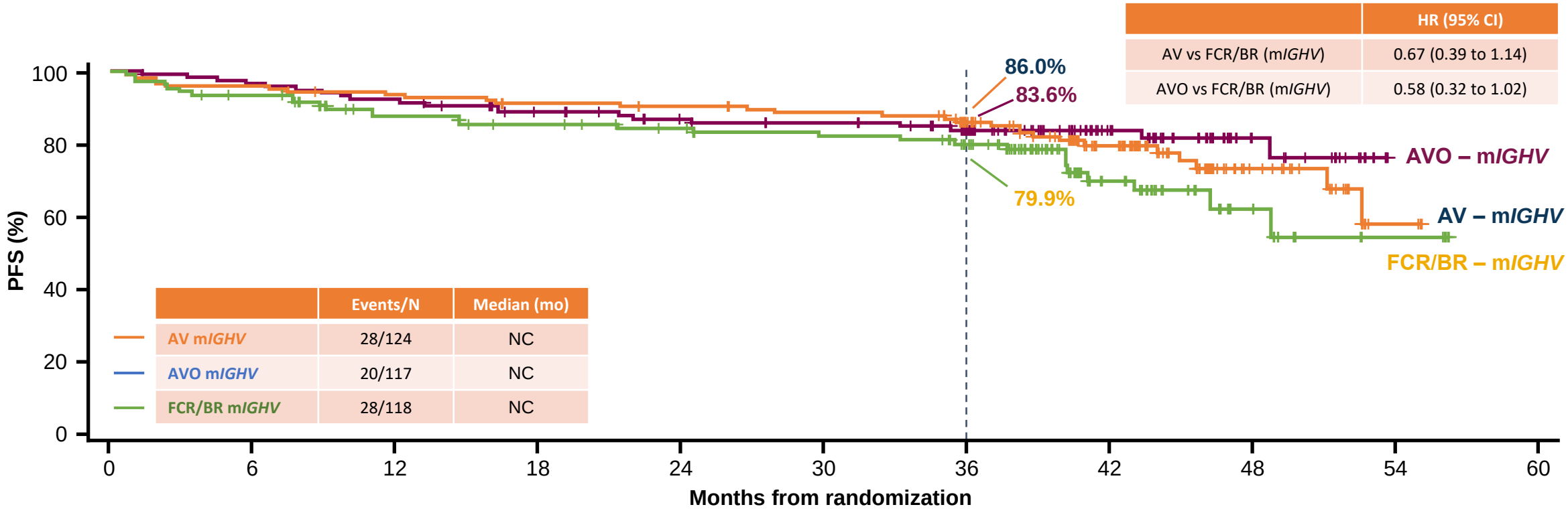
Median PFS was NC for AV and AVO, and was 47.6 mo for FCR/BR

PFS assessed by blinded independent central review. ITT population. Median follow-up from randomization: 40.8 months (range, 0–59 months). Hazard ratio (95% CI) computed using an unstratified Cox proportional-hazards model.

AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CI, confidence interval; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; IRC, independent review committee; ITT, intent-to-treat; mo, months; N, number; NC, not calculable; PFS, progression-free survival.

1. Brown JR, et al. *N Engl J Med*. 2025.

PFS in the m*IGHV* Subgroup



Patients at risk

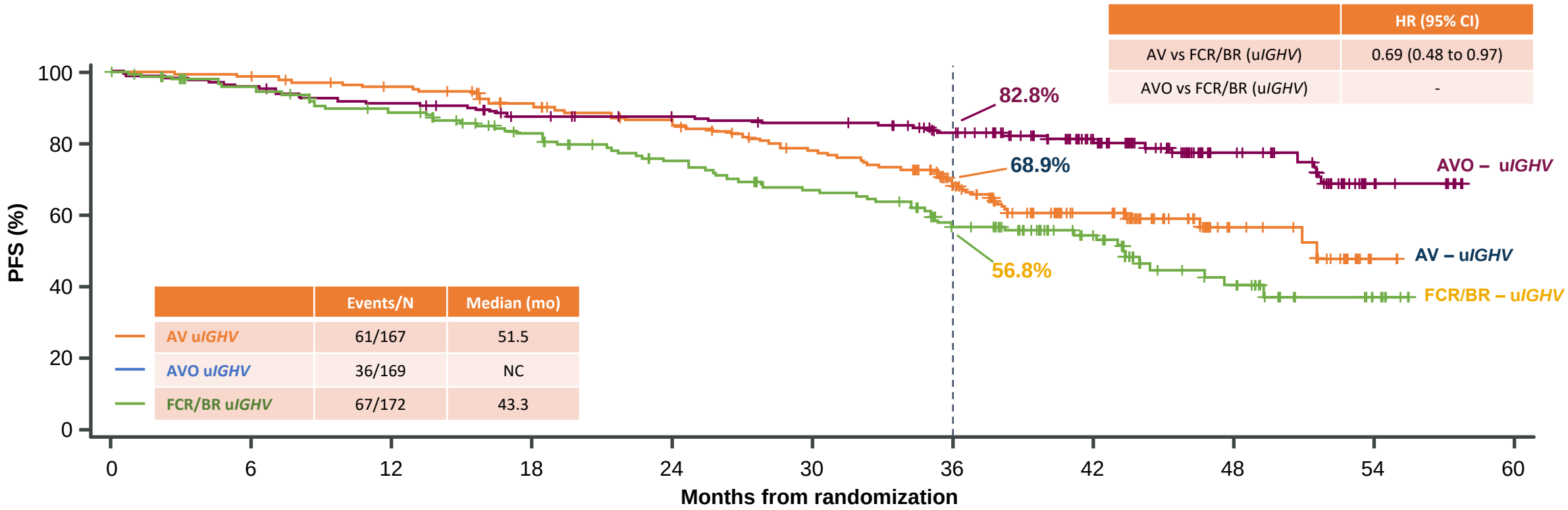
AV m*IGHV*	124	119	114	110	108	105	91	54	18	2	0
AVO m*IGHV*	117	111	106	96	89	86	73	41	15	0	
FCR/BR m*IGHV*	118	99	86	81	76	72	65	28	9	2	0

PFS assessed by IRC; PFS by *IGHV* status was a prespecified analysis (ITT population). Hazard ratio (95% CI) computed using an unstratified Cox proportional-hazards model.

AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CI, confidence interval; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; IRC, independent review committee; ITT, intent-to-treat; mIGHV, mutated immunoglobulin heavy-chain variable region gene; N, number; NC, not calculable; PFS, progression-free survival.

1. Brown JR, et al. *N Engl J Med*. 2025.

PFS in the u*IGHV* Subgroup



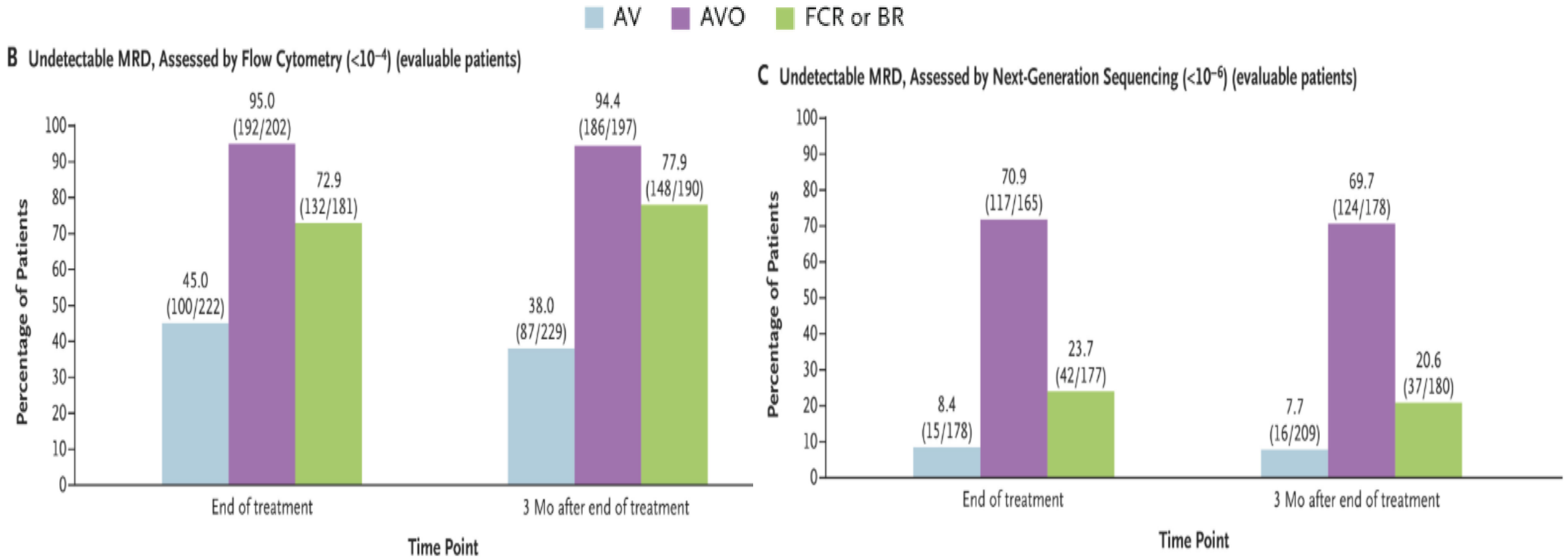
Patients at risk

AV u*IGHV*	167	163	155	141	129	114	86	48	17	1	0
AVO u*IGHV*	169	161	152	141	136	133	118	75	36	7	0
FCR/BR u*IGHV*	172	137	122	108	94	82	62	38	19	4	0

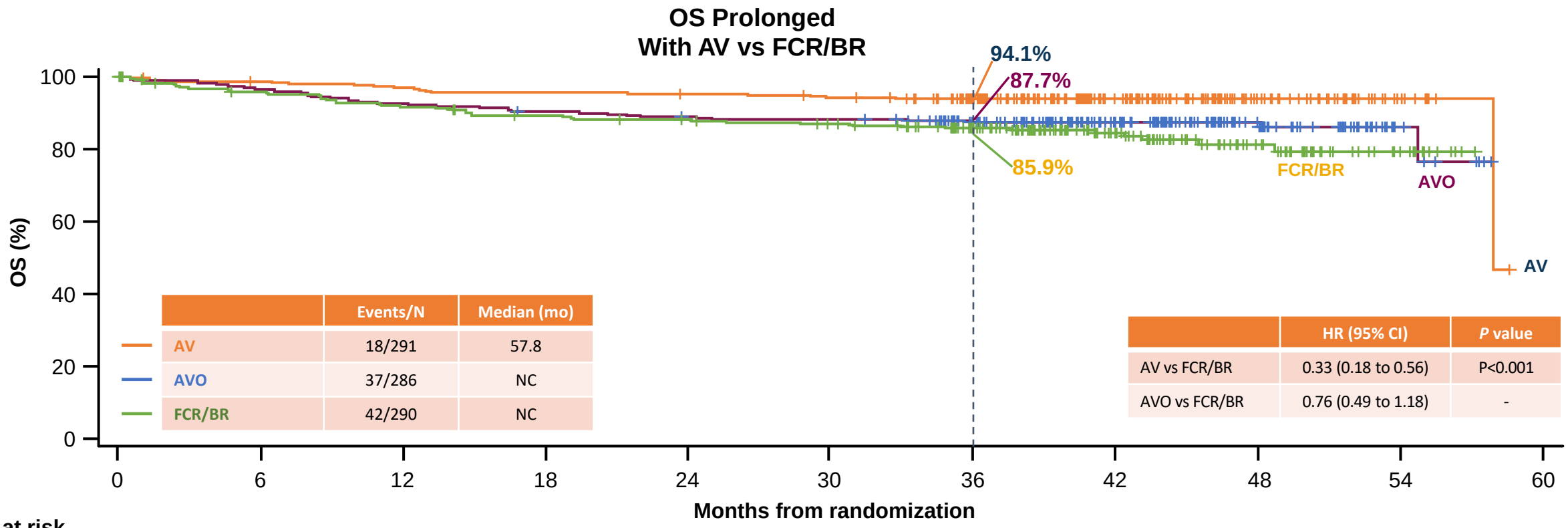
PFS by *IGHV* mutation status assessed by blinded independent central review was a prespecified analysis (ITT population). Hazard ratio (95% CI) computed using an unstratified Cox proportional-hazards model.

AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CI, confidence interval; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; IGHV, immunoglobulin heavy-chain variable region gene; IRC, independent review committee; ITT, intent-to-treat; mo, months; N, number; NC, not calculable; PFS, progression-free survival; uIGHV, unmutated immunoglobulin heavy-chain variable region gene.

1. Brown JR, et al. *N Engl J Med*. 2025.


AV
AVO
FCR or BR
B Undetectable MRD, Assessed by Flow Cytometry (<10⁻⁴) (evaluable patients)
Percentage of Patients
100
90
80
70
60
50
40
30
20
10
0
45.0
(100/222)
95.0
(192/202)
72.9
(132/181)
38.0
(87/229)
94.4
(186/197)
77.9
(148/190)
End of treatment
3 Mo after end of treatment
Time Point
C Undetectable MRD, Assessed by Next-Generation Sequencing (<10⁻⁶) (evaluable patients)
Percentage of Patients
8.4
(15/178)
70.9
(117/165)
23.7
(42/177)
7.7
(16/209)
69.7
(124/178)
20.6
(37/180)
End of treatment
3 Mo after end of treatment
Time Point

Overall Survival[a]



	Events/N	Median (mo)
AV	18/291	57.8
AVO	37/286	NC
FCR/BR	42/290	NC

	HR (95% CI)	*P* value
AV vs FCR/BR	0.33 (0.18 to 0.56)	P<0.001
AVO vs FCR/BR	0.76 (0.49 to 1.18)	-

Patients at risk

AV	291	286	281	277	275	270	233	142	58	10	0
AVO	286	276	265	257	252	250	223	143	64	10	0
FCR/BR	290	247	236	228	223	217	182	98	45	13	0

ITT population.

Hazard ratio (95% CI) computed using a Cox proportional-hazards model stratified by the randomization strata. *P*-value based on two-sided stratified log-rank test.

[a]OS results were immature at the time of this analysis.

AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CI, confidence interval; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; ITT, intent-to-treat; mo, months; N, number; OS, overall survival.

1. Brown JR, et al. *N Engl J Med*. 2025.

Events of Clinical Interest

	AV (n=291)		AVO (n=284)		FCR/BR (n=259)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any ECI	222 (76.3)	136 (46.7)	242 (85.2)	188 (66.2)	185 (71.4)	141 (54.4)
Cardiac events	27 (9.3)	5 (1.7)	34 (12.0)	7 (2.5)	9 (3.5)	3 (1.2)
Atrial fibrillation/flutter	2 (0.7)	1 (0.3)	6 (2.1)	2 (0.7)	2 (0.8)	2 (0.8)
Ventricular tachyarrhythmias[a]	2 (0.7)	0	3 (1.1)	0	0	0
Hypertension	12 (4.1)	8 (2.7)	11 (3.9)	6 (2.1)	7 (2.7)	2 (0.8)
Hemorrhage	94 (32.3)	3 (1.0)	86 (30.3)	6 (2.1)	11 (4.2)	1 (0.4)
Major hemorrhage	3 (1.0)	3 (1.0)	8 (2.8)	6 (2.1)	2 (0.8)	1 (0.4)
Neutropenia (any)[b]	108 (37.1)	94 (32.3)	143 (50.4)	131 (46.1)	132 (51.0)	112 (43.2)
Infections (any)	148 (50.9)	36 (12.4)	153 (53.9)	67 (23.6)	82 (31.7)	26 (10.0)
Second primary malignancies	15 (5.2)	5 (1.7)	12 (4.2)	5 (1.8)	2 (0.8)	0
Excluding NMSC	8 (2.7)	5 (1.7)	7 (2.5)	4 (1.4)	1 (0.4)	0
Tumor lysis syndrome	1 (0.3)	1 (0.3)	1 (0.4)	1 (0.4)	8 (3.1)	8 (3.1)

Data are n (%). ECIs listed by category and sub-category. Patients with multiple occurrences in the same category were counted once per category regardless of the number of occurrences.

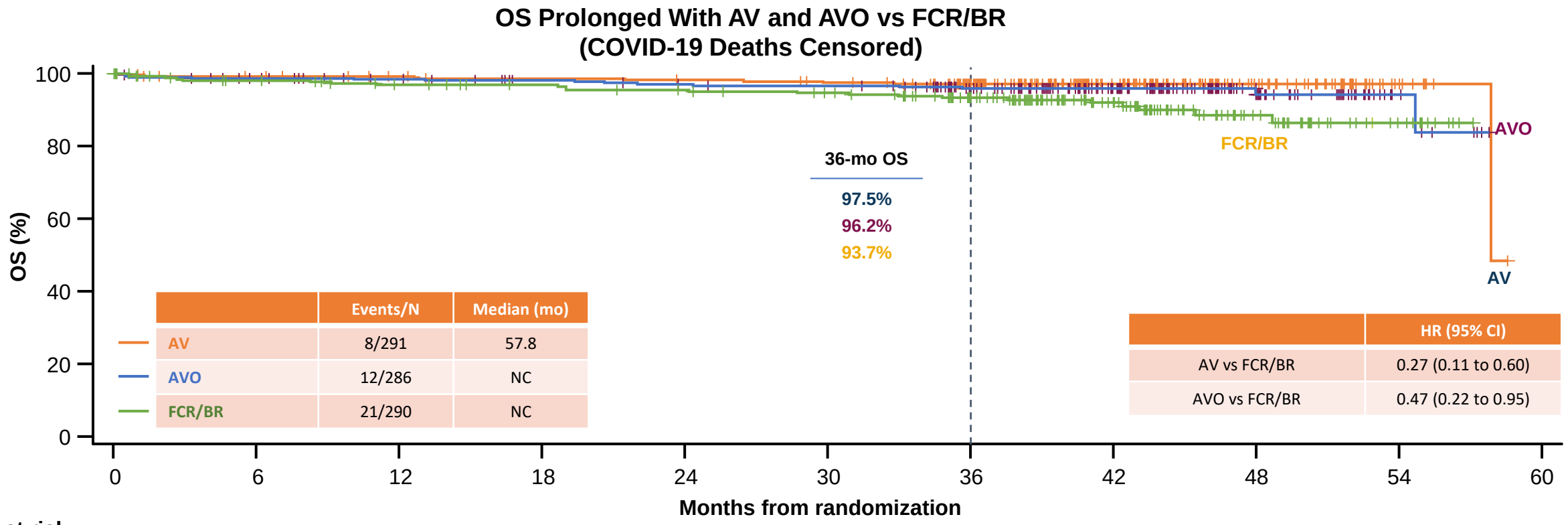
AEs with an onset date or that worsen on or after the date of first dose and up to and including 30 days following the date of last dose of treatment or up to the day prior to start of subsequent anti-CLL therapy, whichever comes first.

[a]Ventricular tachyarrhythmias consisted of ventricular extrasystoles (n=1 in AV arm; n=2 in AVO arm) and ventricular tachycardia (n=1 each in AV and AVO arms). [b]Includes neutropenia, neutrophil count decreased, and febrile neutropenia.

AE, adverse event; AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; ECI, event of clinical interest; FCR, fludarabine-cyclophosphamide-rituximab; n, number; NMSC, non-melanoma skin cancer.

1. Brown JR, et al. *N Engl J Med*. 2025.

Overall Survival Censoring COVID-19 Deaths[a,b]



Patients at risk

AV	291	286	281	277	275	270	233	142	58	10	0
AVO	286	276	265	257	252	250	223	143	64	10	0
FCR/BR	290	247	236	228	223	217	182	98	45	13	0

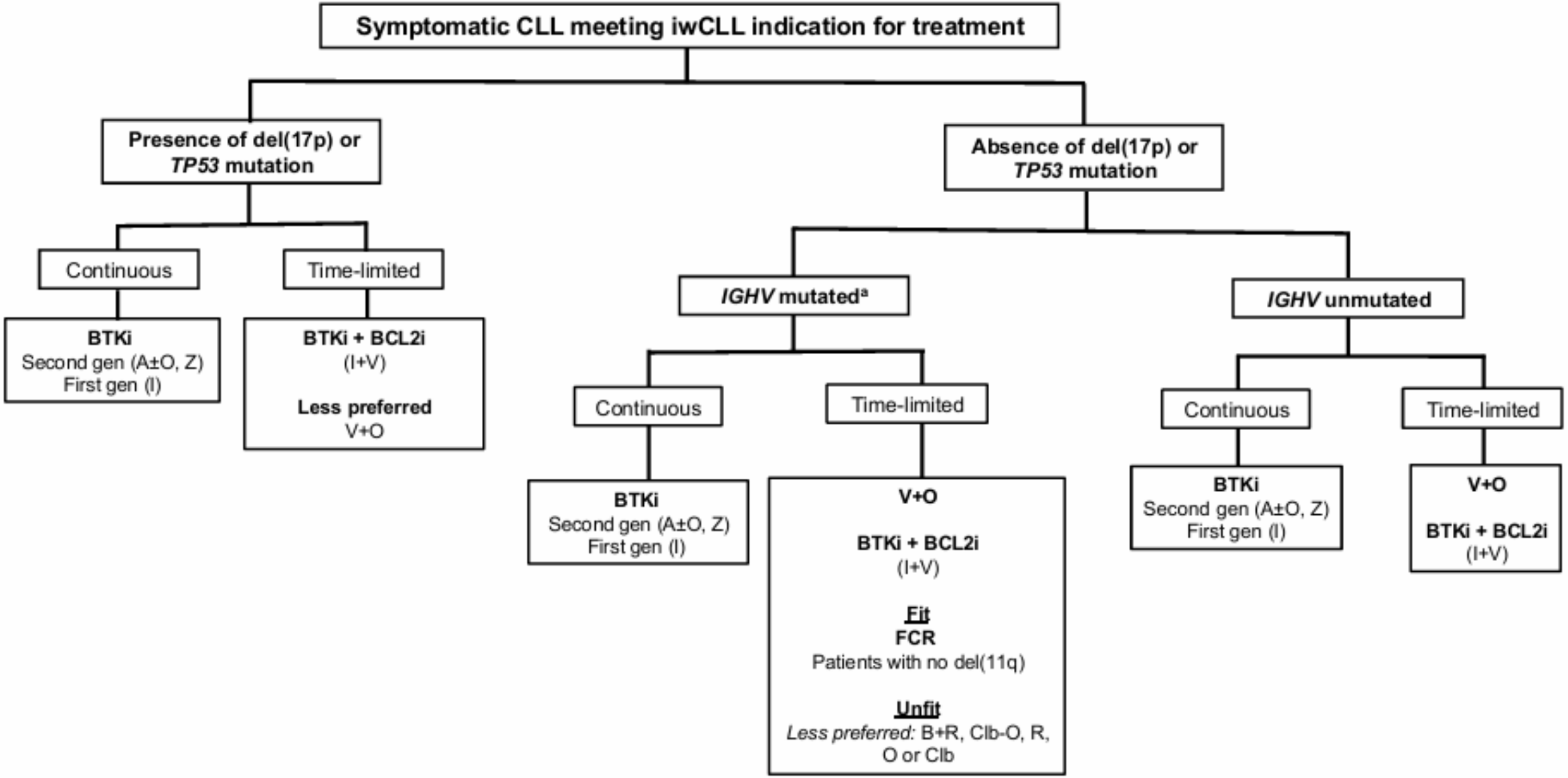
ITT population.

Hazard ratio (95% CI) computed using a Cox proportional-hazards model stratified by the randomization strata. *P*-value based on two-sided stratified log-rank test.

[a]OS results were immature at the time of this analysis. [b]Confidence interval widths have not been adjusted for multiplicity and may not be used in place of hypothesis testing.
AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CI, confidence interval; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; ITT, intent-to-treat; mo, months; N, number; OS, overall survival.

1. Brown JR, et al. *N Engl J Med*. 2025.

Algorithm for treatment-naïve CLL



Goh YT et al. Ann Acad Med Singap. 2025

THANK YOU