Kronik Lenfositik Lösemi

DR FATİH DEMİRKAN
DOKUZ EYLÜL ÜNİVERSİTESİ HEMATOLOJİ BD

LENFOPROLİFERATİF HASTALIKLAR GÜNCELLEMESİ

8.1. 2022

Sunum Planı

- KLL 1. sıra tedaviler
- KLL R/R hastalıkta tedaviler
- KLL ve COVID-19

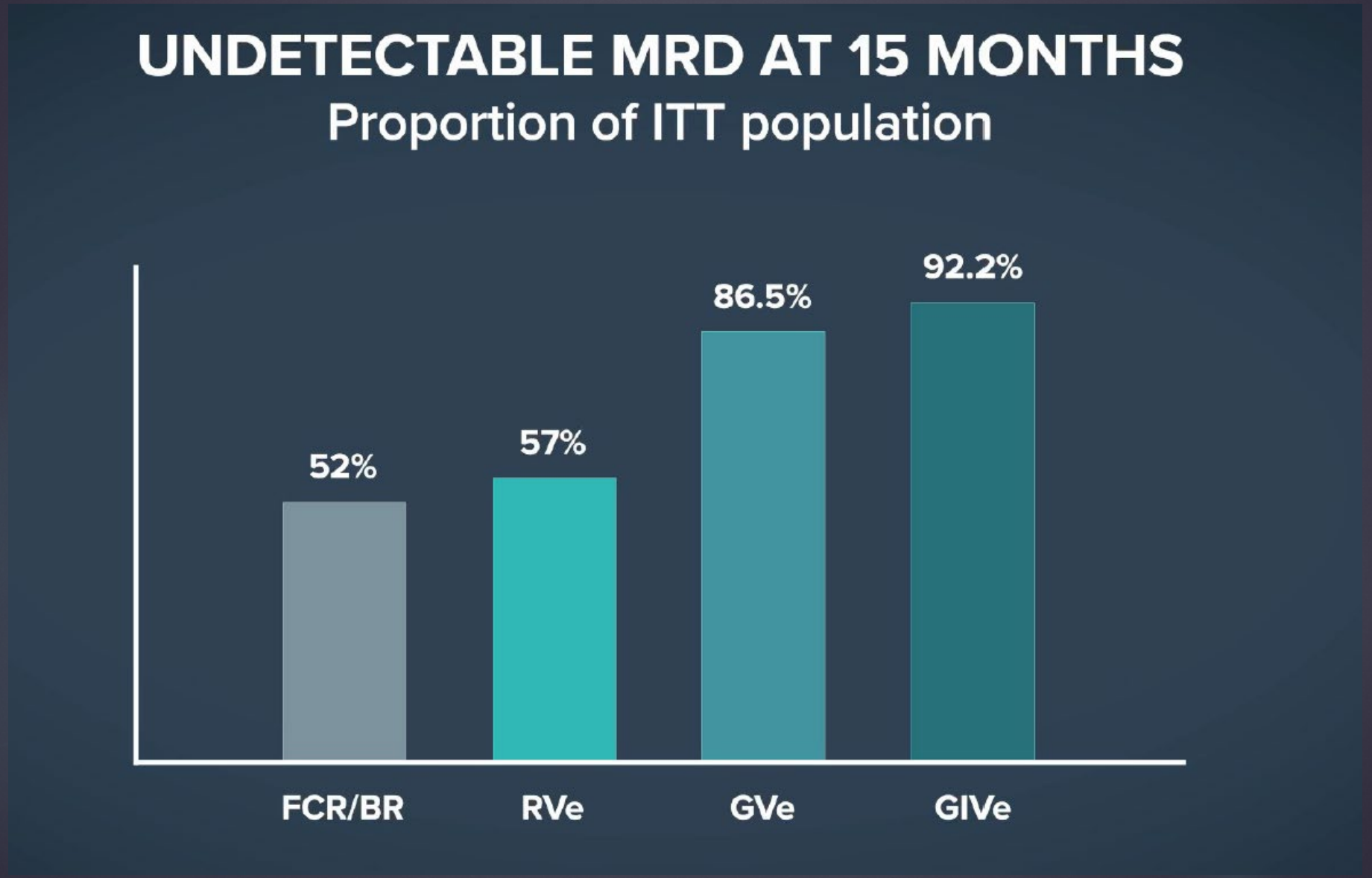
ASH 2021 #71

A Randomized Phase III Study of Venetoclax-Based Time-Limited Combination Treatments (RVe, GVe, GIVe) Vs Standard Chemoimmunotherapy (CIT: FCR/BR) in Frontline Chronic Lymphocytic Leukemia (CLL) of Fit Patients: First Co-Primary Endpoint Analysis of the International Intergroup GAIA (CLL13) Trial

Barbara Eichhorst, Carsten Niemann, Arnon P. Kater, Moritz Fürstenau, Julia Von Tresckow, Can Zhang, Sandra Robrecht, Michael Gregor, Gunnar Juliusson, Patrick Thornton, Philipp B. Staber, Tamar Tadmor, Vesa Lindström, Caspar Da Cunha-Bang, Christof Schneider, Christian Bjørn Poulsen, Thomas Illmer, Björn Schöttker, Ann Janssens, Ilse Christiansen, Thomas Noesslinger, Michael Baumann, Marjolein van der Klift, Ulrich Jaeger, Henrik Frederiksen, Maria B.L. Leijs, Mels Hoogendoorn, Kourosh Lotfi, Holger Hebart, Tobias Gaska, Harry R. Koene, Florian Simon, Nisha De Silva, Anna-Maria Fink, Kirsten Fischer, Clemens-Martin Wendtner, Karl-Anton Kreuzer, Matthias Ritgen, Monika Brüggemann, Eugen Tausch, Mark-David Levin, Marinus H.J. Van Oers, Christian H. Geisler, Stephan Stilgenbauer, and Michael Hallek

CLL 13

- A total of 926 pts (CIT: 229 (150 FCR, 79 BR), RVe: 237, GVe: 229, GIVe: 231) with a median age of 61 years (range 27-84) were accrued between 12/2016 and 09/2019
- six courses of **CIT** (FCR for pt ≤65 years: fludarabine 25 mg/m² d1-3, cyclophosphamide 250 mg/m² d1-3, rituximab 375 mg/m² d1 cycle 1 and 500 mg/m² d1 cycle 2-6; BR for pt >65 years: bendamustine 90mg/m² d1-2, rituximab)
- (standard ramp-up from cycle 1 d22, 400 mg/d cycle 2-12): V and rituximab (375/500mg/m² d1 cycle 1-6) [**RVe**],
- V and obinutuzumab (1000 mg d1, 8, 15 cycle 1 and d1 cycle 2-6) [**GVe**],
- V, obinutuzumab and ibrutinib (420 mg/d cycle 1-12, if MRD-detectable continued until cycle 36) [**GIVe**]


UNDETECTABLE MRD AT 15 MONTHS
Proportion of ITT population
52%
57%
86.5%
92.2%
FCR/BR
RVe
GVe
GIVe

ASH 2021 #642

Ibrutinib Plus Rituximab Is Superior to FCR in Previously Untreated CLL: Results of the Phase III NCRI FLAIR Trial

...

Peter Hillmen, Alexandra Pitchford, Adrian Bloor, Angus Broom, Moya Young, Ben Kennedy, Renata Walewska, Michelle Furtado, Gavin Preston, Jeffrey R. Neilson, Nicholas Pemberton, Gamal Sidra, Nicholas Morley, Kate Cwynarski, Anna Schuh, Francesco Forconi, Nagah Elmusharaf, Shankara Paneesha, Christopher P. Fox, Dena Howard, Anna Hockaday, David Cairns, Sharon Jackson, Natasha Greatorex, Piers E.M. Patten, David Allsup and Talha Munir

PROGRESSION-FREE SURVIVAL

Not reached with ibrutinib + rituximab vs 66.5 months with FCR

High-risk Subgroups

	IGHV unmutated	IGHV mutated	11q deletion	Normal karyotype	13q deletion	Trisomy 12
HR for PFS or death	0.41	0.66	0.29	0.37	0.62	0.41
	$p<0.001$	$p<0.179$	$p<0.001$	$p<0.001$	$p<0.093$	$p<0.129$

SAFETY

Causes of Death	FCR	IR
CLL	4	3
Non-hematologic malignancy	4	7
AML/MDS	3	0
ALL	1	0
Richters transformation	3	1

Causes of Death	FCR	IR
Infections (non-COVID)	6	4
COVID-19	3	3
Hemorrhage	1	2
Cardiac	2	9
Other	2	1

ASH 2021 #396

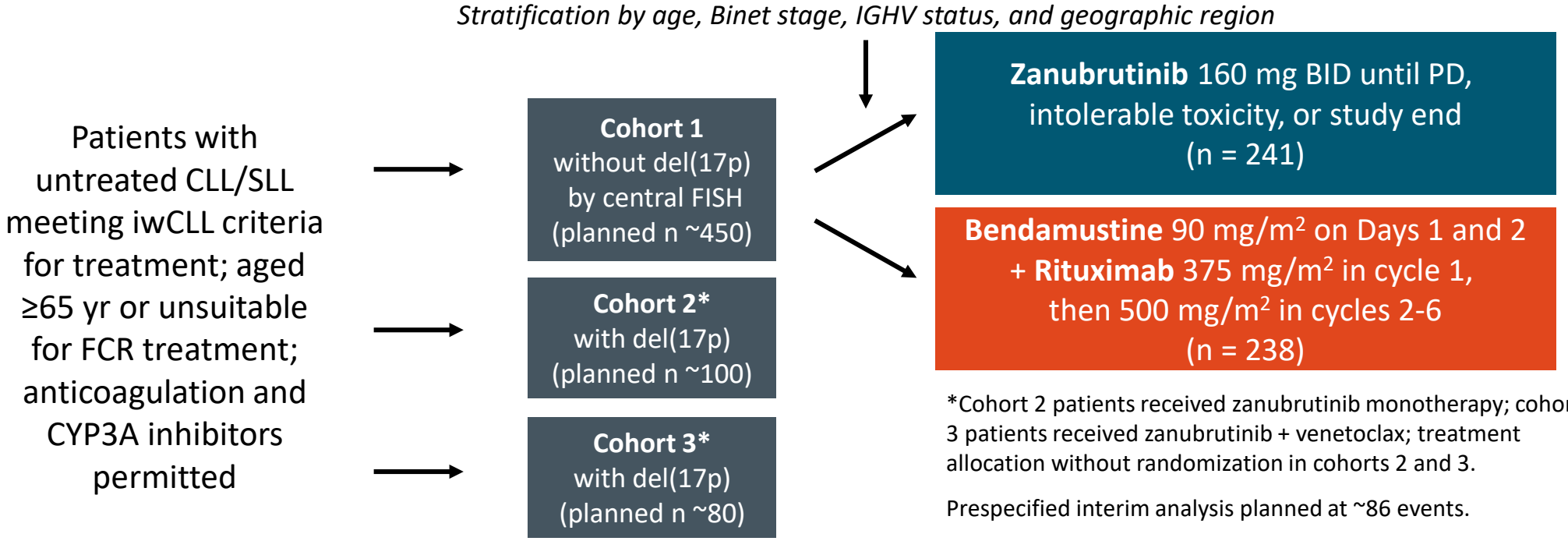
SEQUOIA: Results of a Phase 3 Randomized Study of Zanubrutinib versus Bendamustine + Rituximab (BR) in Patients with Treatment-Naïve (TN) Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

...

Constantine S. Tam, Krzysztof Giannopoulos, Wojciech Jurczak, Martin Šimkovič, Mazyar Shadman, Anders Österborg, Luca Laurenti, Patricia Walker, Stephen Opat, Henry Chan, Hanna Ciepluch, Richard Greil, Monica Tani, Marek Trněný, Danielle M. Brander, Ian W. Flinn, Sebastian Grosicki, Emma Verner, Jennifer R. Brown, Brad S. Kahl, Paolo Ghia, Tian Tian, Carol Marimpietri, Jason C. Paik, Aileen Cohen, Jane Huang, Tadeusz Robak, and Peter Hillmen

SEQUOIA: Study Design

- Multicenter, multicohort, open-label, part-randomized phase III trial



*Cohort 2 patients received zanubrutinib monotherapy; cohort 3 patients received zanubrutinib + venetoclax; treatment allocation without randomization in cohorts 2 and 3.

Prespecified interim analysis planned at ~86 events.

- Primary endpoint (cohort 1): IRC-assessed PFS
- Secondary endpoints (cohort 1): investigator-assessed PFS, ORR, OS, safety

Tam. ASH 2021. Abstr 396.

SEQUOIA (Cohort 1): Baseline Characteristics

Characteristic	Zanubrutinib (n = 241)	Bendamustine + Rituximab (n = 238)
Median age, yr (IQR)	70 (66-75)	70 (66-74)
Aged ≥65 yr, n (%)	196 (81.3)	192 (80.7)
Male, n (%)	154 (63.9)	144 (60.5)
ECOG PS 2, n (%)	15 (6.2)	20 (8.4)
Region, n (%)		
▪ North America	34 (14.1)	28 (11.8)
▪ Europe	174 (72.2)	172 (72.3)
▪ Asia/Pacific	33 (13.7)	38 (16.0)

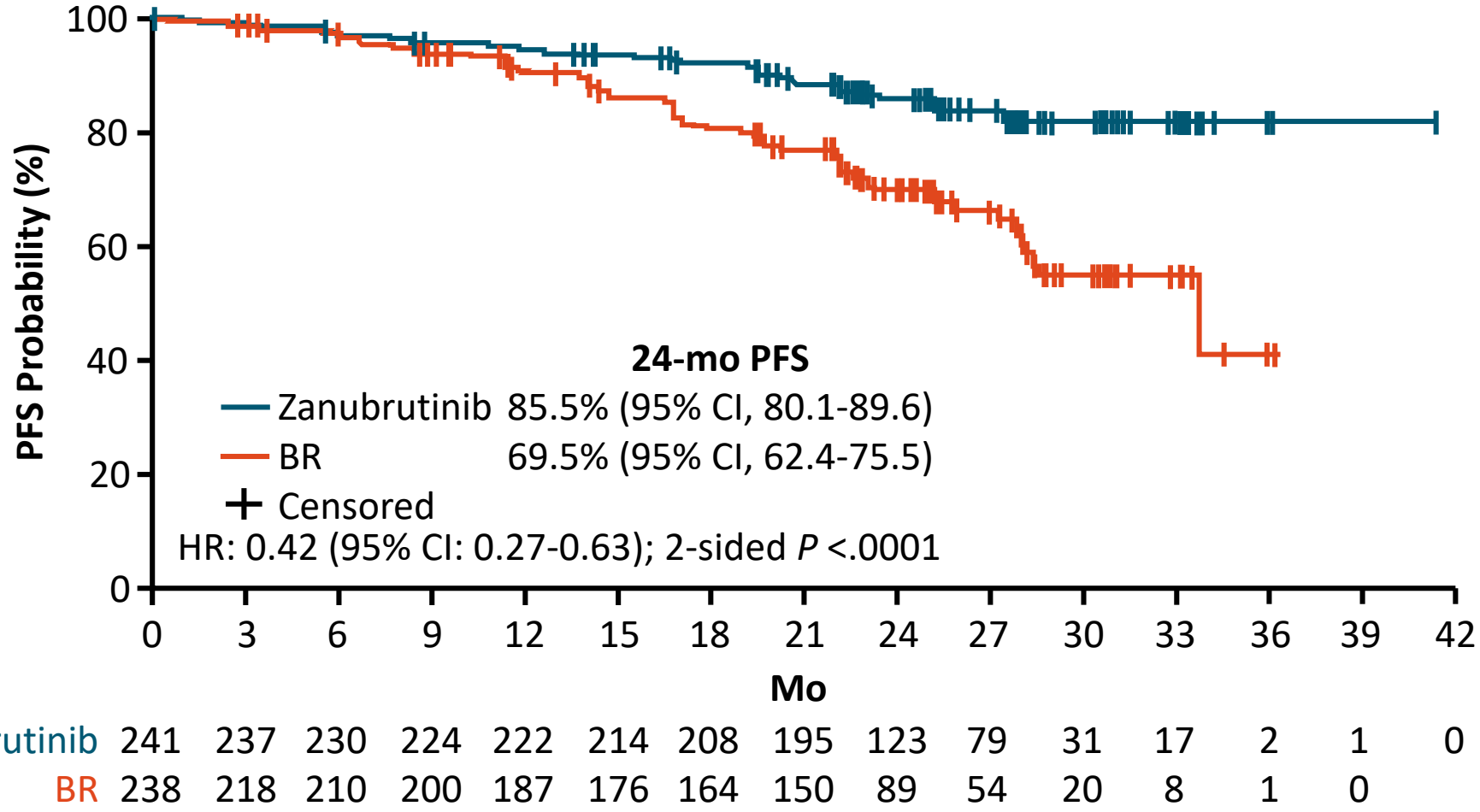
Characteristic, n (%)	Zanubrutinib (n = 241)	Bendamustine + Rituximab (n = 238)
Binet stage C*	70 (29.0)	70 (29.4)
Bulky disease ≥5 cm	69 (28.6)	73 (30.7)
Cytopenia†	102 (42.3)	109 (45.8)
del(11q)	43 (17.8)	46 (19.3)

Characteristic, n/N (%)	Zanubrutinib	Bendamustine + Rituximab
TP53 mutation	15/232 (6.5)	13/223 (5.8)
Unmutated *IGHV* gene	125/234 (53.4)	121/231 (52.4)

*Patients with SLL had Binet stage calculated as if they had CLL.
†Defined as anemia (hemoglobin ≤110 g/L), thrombocytopenia (platelets ≤100 x 10^9/L), or neutropenia (absolute neutrophil count ≤1.5 x 10^9/L).

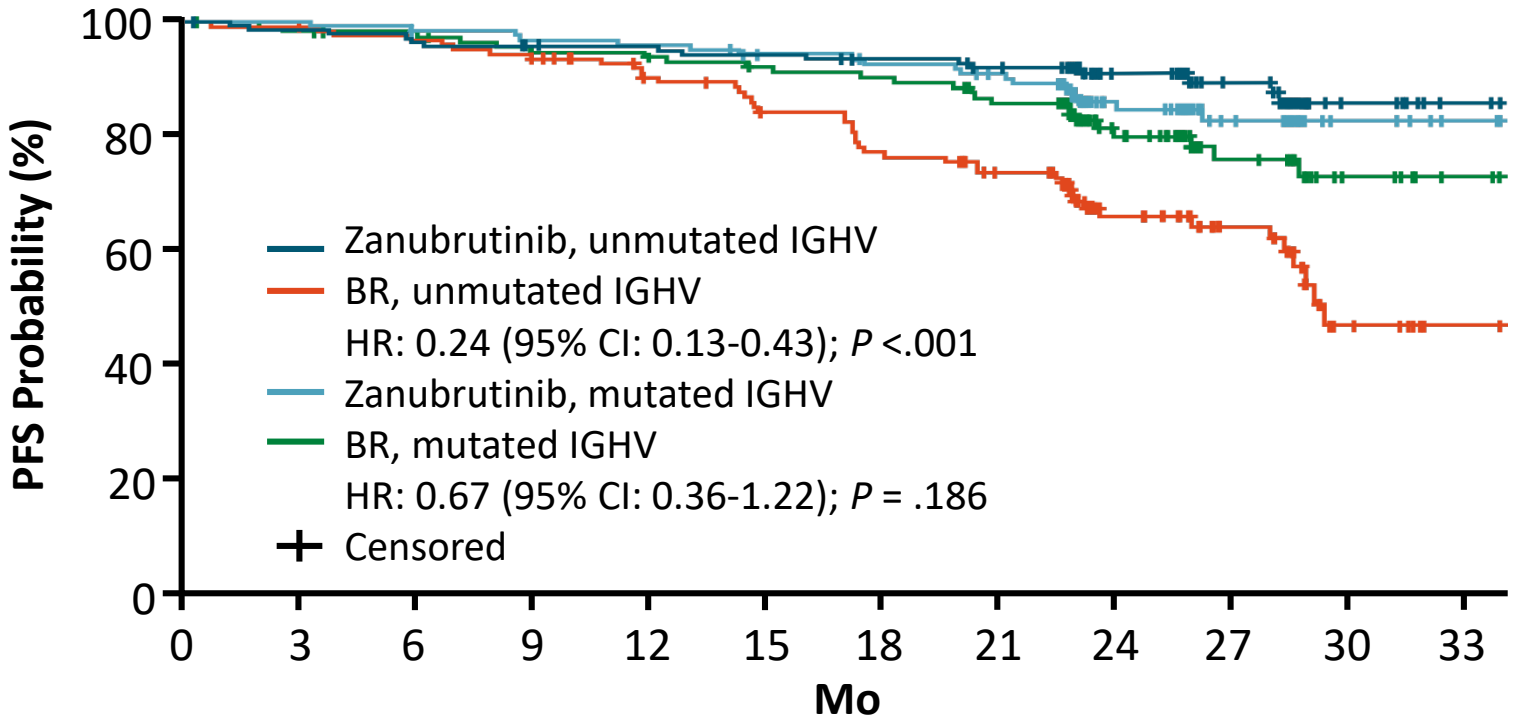
Tam. ASH 2021. Abstr 396.

SEQUOIA (Cohort 1): IRC-Assessed PFS (Primary Endpoint)



Tam. ASH 2021. Abstr 396.

SEQUOIA (Cohort 1): IRC-Assessed PFS by IGHV Status



Zanubrutinib - Unmutated	125	121	117	114	113	112	109	104	68	44	14	6
BR - Unmutated	121	110	106	100	90	82	73	65	39	25	6	1
Zanubrutinib - Mutated	109	109	106	104	103	97	94	88	53	33	15	10
BR - Mutated	110	101	98	94	91	88	86	80	47	27	14	7

Tam. ASH 2021. Abstr 396.

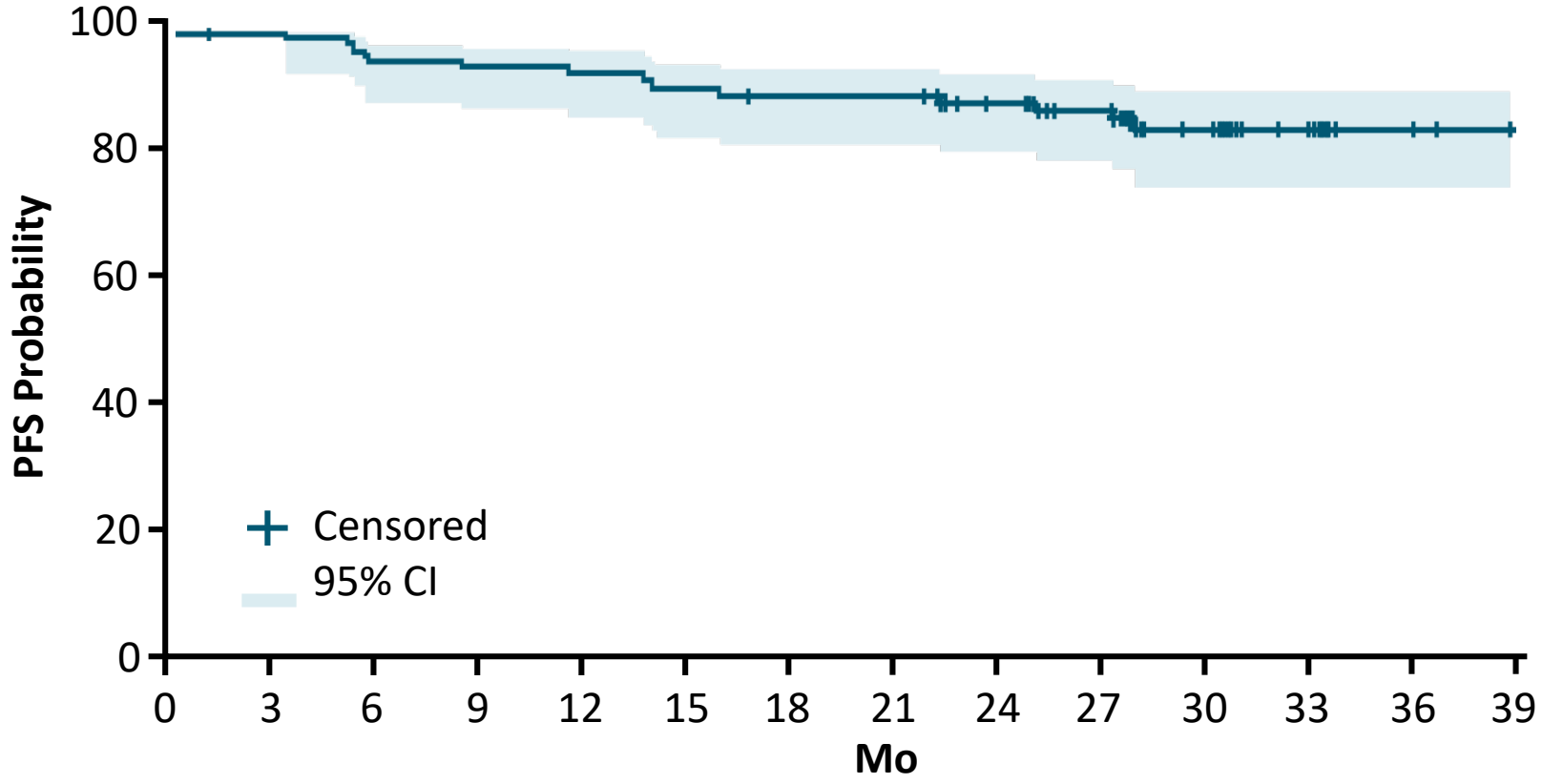
SEQUOIA (Cohort 1): AEs of Interest

AEs, n (%)	Zanubrutinib (n = 240)*		Bendamustine + Rituximab (n = 227)*	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Anemia	11 (4.6)	1 (0.4)	44 (19.4)	4 (1.8)
Neutropenia	38 (15.8)	28 (11.7)	129 (56.8)	116 (51.1)
Thrombocytopenia	11 (4.6)	5 (2.1)	40 (17.6)	18 (7.9)
Arthralgia	32 (13.3)	2 (0.8)	20 (8.8)	1 (0.4)
Atrial fibrillation	8 (3.3)	1 (0.4)	6 (2.6)	3 (1.3)
Bleeding	108 (45.0)	9 (3.8)	25 (11.0)	4 (1.8)
▪ Major bleeding	12 (5.0)	9 (3.8)	4 (1.8)	4 (1.8)
Diarrhea	33 (13.8)	2 (0.8)	31 (13.7)	5 (2.2)
Hypertension	34 (14.2)	15 (6.3)	24 (10.6)	11 (4.8)
Infections	149 (62.1)	39 (16.3)	127 (55.9)	43 (18.9)
Myalgia	9 (3.8)	0 (0.0)	3 (1.3)	0 (0.0)
Other cancers	31 (12.9)	17 (7.1)	20 (8.8)	7 (3.1)
▪ Dermatologic	16 (6.7)	2 (0.8)	10 (4.4)	2 (0.9)

*Safety was assessed in patients who received ≥1 treatment dose; 1 patient in the zanubrutinib arm and 11 patients in the combination arm did not receive treatment.

Tam. ASH 2021. Abstr 396.

SEQUOIA (Cohort 2): IRC-Assessed PFS in Patients With del(17p)



Zanubrutinib	110	109	104	103	102	98	96	96	86	74	37	19	2	0

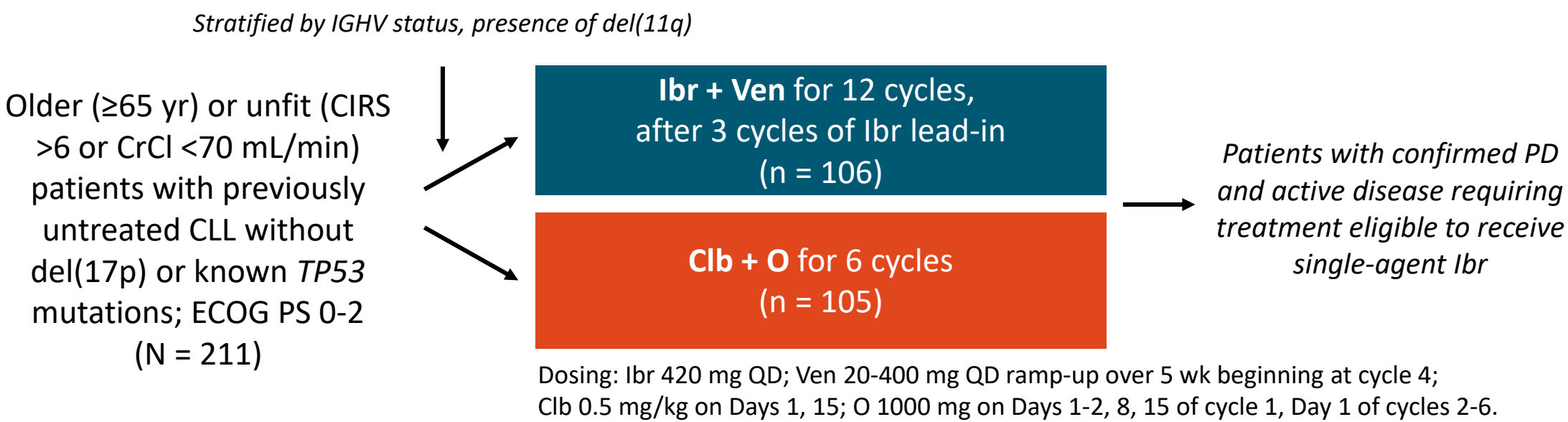
Tam. ASH 2021. Abstr 396.

GLOW: MRD Outcomes After First-line Fixed-Duration Ibrutinib + Venetoclax vs Chlorambucil + Obinutuzumab for Older/Unfit Patients With CLL

Munir. ASH 2021. Abstr 70

GLOW: Study Design

- Randomized phase III trial



Dosing: Ibr 420 mg QD; Ven 20-400 mg QD ramp-up over 5 wk beginning at cycle 4;
Clb 0.5 mg/kg on Days 1, 15; O 1000 mg on Days 1-2, 8, 15 of cycle 1, Day 1 of cycles 2-6.

- Primary endpoint: PFS by IRC
- Median follow-up: 34.1 mo
- Current MRD analysis: uMRD at $<10^{-4}$ and $<10^{-5}$ by NGS
  - PB/BM concordance calculated for patients with evaluable data at EOT+3

Munir. ASH 2021. Abstr 70.

GLOW: uMRD Rates

uMRD at EOT+3, %	Ibr + Ven (n = 106)	Clb + O (n = 105)	*P* Value
$<10^{-4}$			
▪ BM	51.9	17.1	<.0001
▪ PB	54.7	39.0	.0259
▪ BM/PB concordance	92.9	43.6	
$<10^{-5}$			
▪ BM	40.6	7.6	NR
▪ PB	43.4	18.1	NR
▪ BM/PB concordance	90.9	36.8	

Munir. ASH 2021. Abstr 70.

GLOW: MRD Dynamics Posttreatment

- uMRD in PB better sustained with Ibr + Ven vs Clb + O from EOT+3 to EOT+12

uMRD Dynamics From EOT+3 to EOT+12	Ibr + Ven	Clb + O
Sustained uMRD $<10^{-4}$, % (n/N)	84.5 (49/58)	29.3 (12/41)
Sustained uMRD $<10^{-5}$, % (n/N)	80.4 (37/46)	26.3 (5/19)
Decrease in uMRD $<10^{-4}$ rate, %	6	27

- Patients treated with Ibr + Ven with detectable MRD $\geq 10^{-4}$ at EOT+3 less likely to:
  - Convert to PD at EOT+12 vs patients treated with Clb + O
  - Have increasing levels of detectable MRD at EOD+12 vs patients treated with Clb + O

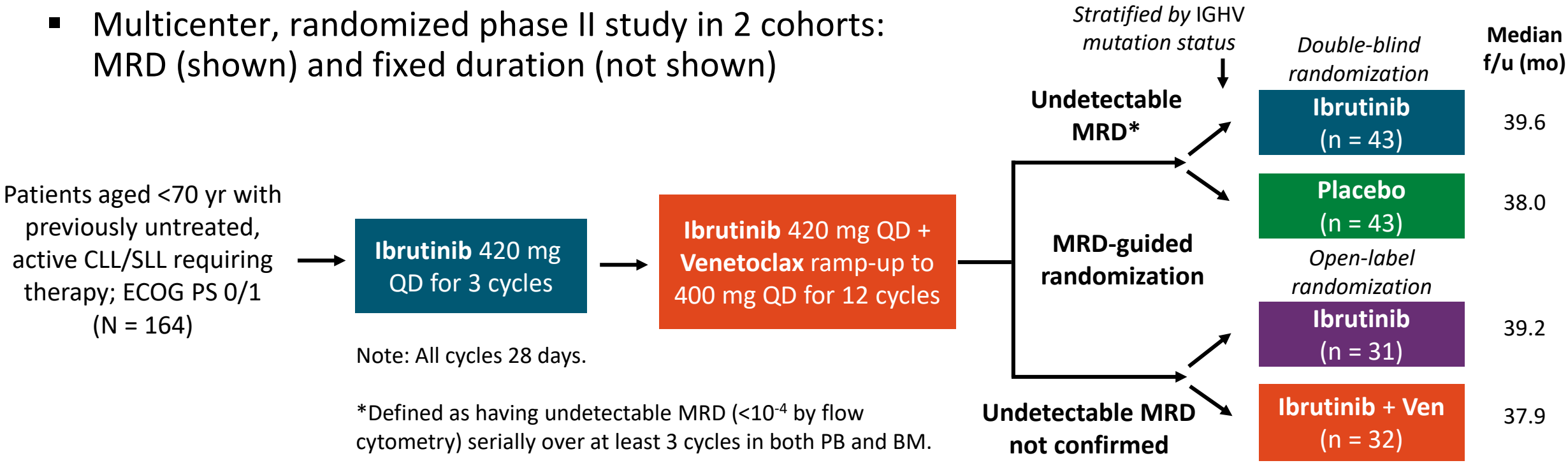
Munir. ASH 2021. Abstr 70.

CAPTIVATE MRD Cohort: 2-Yr Postrandomization Efficacy and Safety With First-Line Ibrutinib + Venetoclax in CLL

Ghia. ASH 2021. Abstr 68

CAPTIVATE (MRD Cohort): Study Design

- Multicenter, randomized phase II study in 2 cohorts: MRD (shown) and fixed duration (not shown)



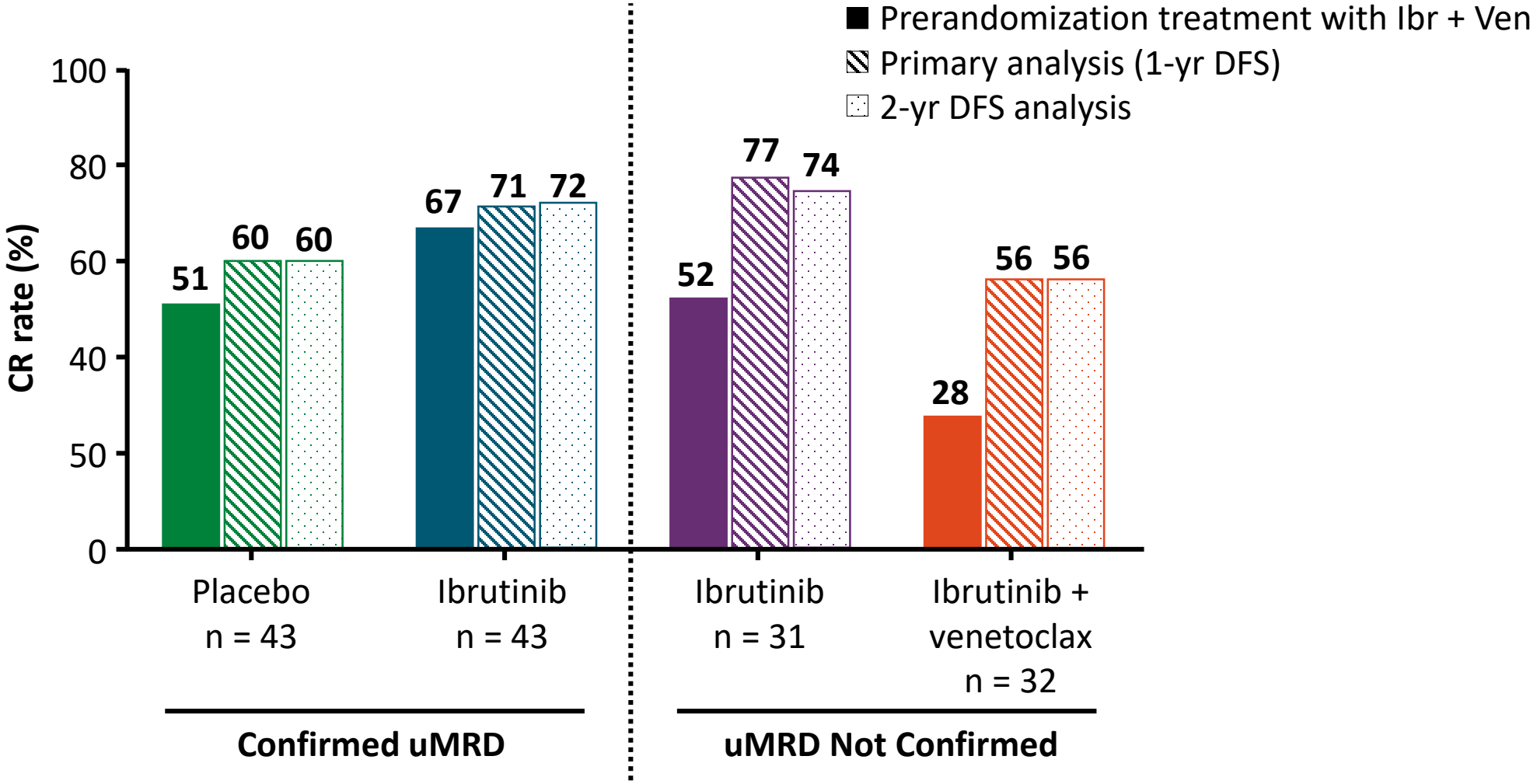
Note: All cycles 28 days.

*Defined as having undetectable MRD ($<10^{-4}$ by flow cytometry) serially over at least 3 cycles in both PB and BM.

- Primary endpoint analysis: 95% to 100% 1-yr DFS rate in patients with confirmed undetectable MRD[1]
- Secondary endpoints: undetectable MRD, response, PFS, safety[2]

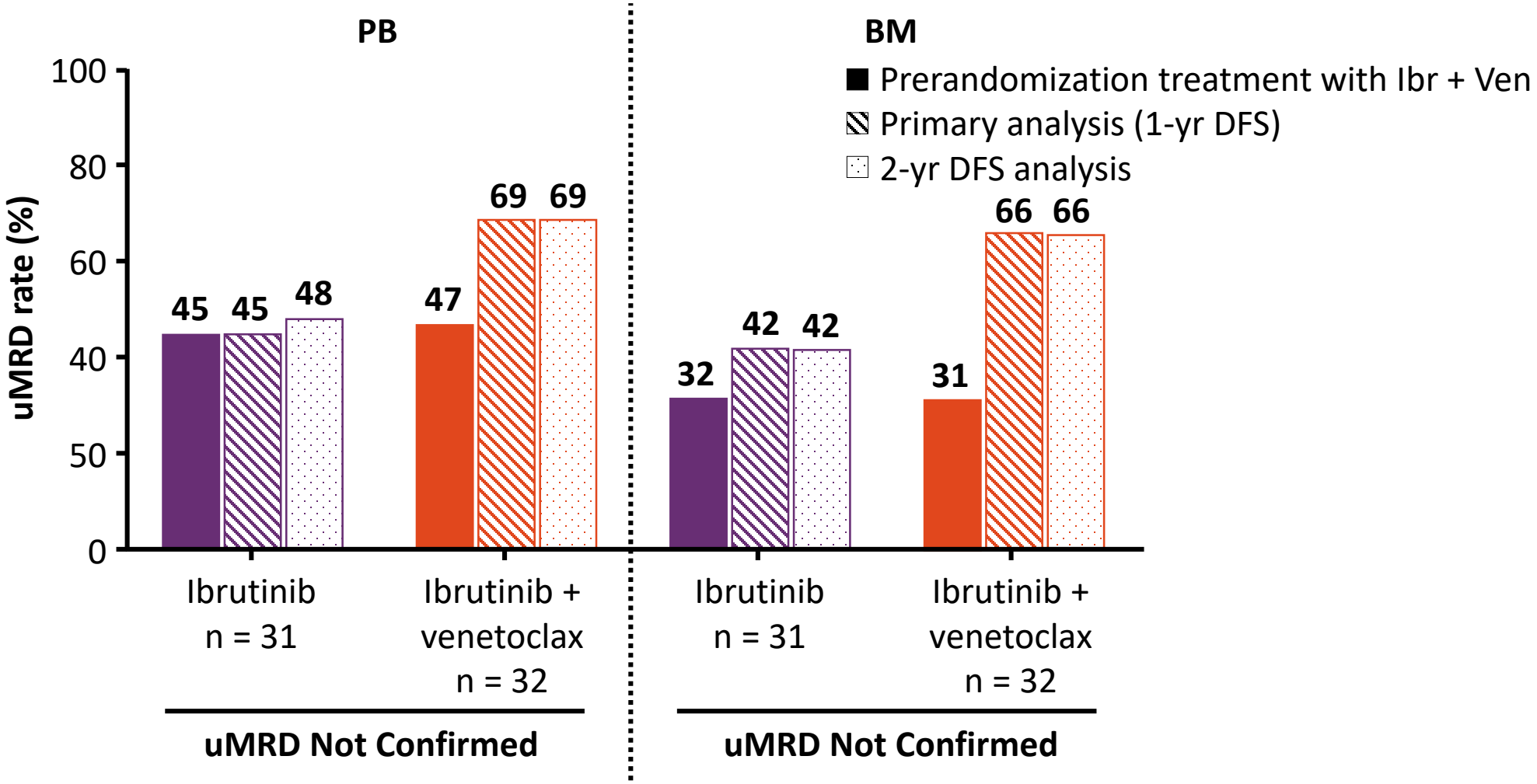
1. Wierda. ASH 2020. Abstr 123. 2. Ghia. ASH 2021. Abstr 68.

CAPTIVATE (MRD Cohort): CR Rates With 24-Mo Follow-up After Randomization



Ghia. ASH 2021. Abstr 68. Reproduced with permission.

CAPTIVATE (MRD Cohort): uMRD Rates in Population With No Confirmed uMRD



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CAPTIVATE (MRD Cohort): Investigators' Conclusions

- MRD-guided treatment following first-line ibrutinib + venetoclax showed continued efficacy in patients with CLL/SLL
  - No additional DFS events in patients with confirmed uMRD who received either ibrutinib or placebo
  - 2-yr DFS rate: 95% to 100% in patients with confirmed uMRD
  - All treatment arms with MRD-guided randomization had 3-yr PFS rates ≥95%
  - Retreatment with single-agent ibrutinib may be effective after progression on fixed-dose ibrutinib + venetoclax
- No new safety signals observed (median study follow-up: 38 mo)

Ghia. ASH 2021. Abstr 68.

ASH 2021 #392

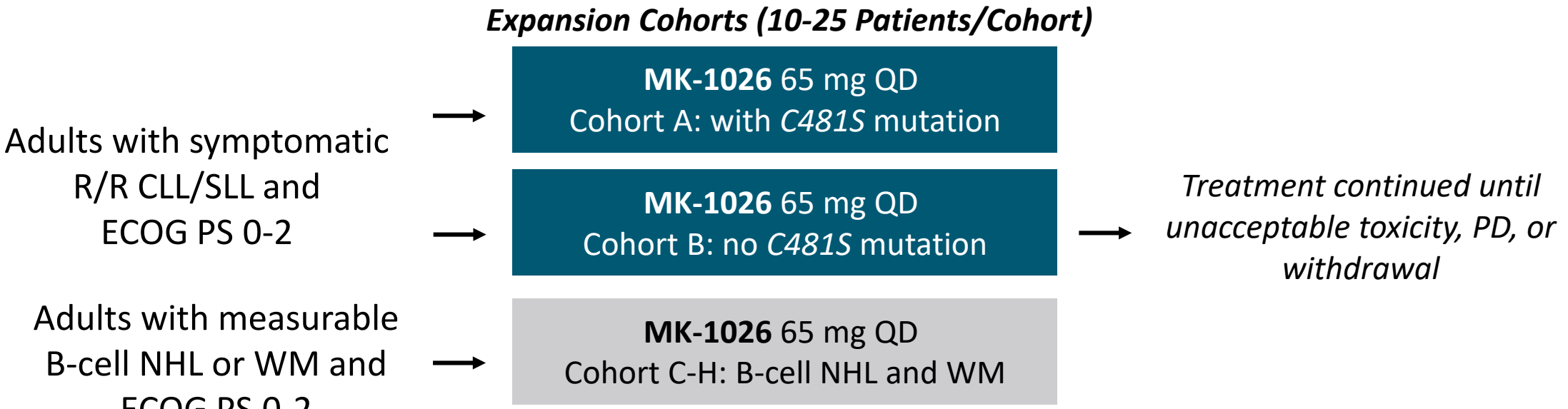
Preliminary Efficacy and Safety of MK-1026, a Non-Covalent Inhibitor of Wild-Type and C481S Mutated Bruton Tyrosine Kinase, in B-Cell Malignancies: A Phase 2 Dose Expansion Study

...

Jennifer A. Woyach, Ian W. Flinn, Farrukh T. Awan, Herbert Eradat, Danielle M. Brander, Michael Tees, Sameer A. Parikh, Tycel Phillips, Wayne Wang, Nishitha M. Reddy, Mohammed Z.H. Farooqui, John C. Byrd, Deborah M. Stephens

MK-1026-001: Study Design

- Multicenter, open-label, single-arm, dose-expansion phase II trial



Current analysis reports data from CLL/SLL cohorts only.
Cohort A: R/R CLL/SLL with ≥2 prior therapies, including covalent BTK inhibitor and documented *C481* mutation.
Cohort B: R/R CLL/SLL progressed on/intolerant to BTK inhibitor, with ≥2 prior therapies and no *C481* mutation.

- Primary endpoint: ORR per iwCLL criteria
- Secondary endpoints: DoR, safety, tolerability

Woyach. ASH 2021. Abstr 392.

MK-1026-001: Baseline Characteristics

Characteristic	Overall Population (N = 118)
Median age, yr (range)	66.6 (38-86)
Male, n (%)	91 (77.1)
White, n (%)	105 (89.0)
CLL/SLL, n (%)	68 (57.6)
WM, n (%)	4 (3.4)
B-cell NHL,* n (%)	44 (37.3)
MK-1026 65 mg QD, n (%)	94 (79.7)

*DLBCL, FL, high-grade BCL, MCL, MZL, RT.

Characteristic	CLL/SLL 65 mg QD (n = 51)
Median prior therapy lines, n (range)	4 (1-18)
Prior BTK inhibitor, n (%)	43 (84.3)
ECOG PS, n (%) ▪ 0/1/2	14 (27.5)/32 (62.7)/5 (9.8)
IGHV unmutated, n (%) ▪ Mutated ▪ Unknown	30 (58.8) 2 (3.9) 19 (37.3)
Del(17p) present, n (%) ▪ Absent ▪ Missing	12 (23.5) 33 (64.7) 6 (11.8)
BTK *C481S* present, n (%) ▪ Absent ▪ Missing	32 (62.7) 12 (23.5) 7 (13.7)

MK-1026-001: Response

Response, n (%) (95% CI)	CLL/SLL 65 mg QD (n = 38)
ORR	22 (57.9) (40.8-73.6)
CR	1 (2.6) (0.0-13.8)
PR	12 (31.6) (17.5-48.6)
PR-L	9 (23.7) (11.4-40.2)
SD	15 (39.5)

- Median DoR, mo: NE (95% CI: 8.3-NE)
- SPD decrease observed in 93.9%, ≥50% decrease in 69.7% (n = 33)

Woyach. ASH 2021. Abstr 392.

MK-1026-001: Treatment-Emergent Adverse Events

TEAEs, n (%)	All Patients (N = 118)
Any TEAE	114 (96.6)
Grade ≥3	80 (68.0)
MK-1026 related	78 (66.1)
Grade ≥3 related	31 (26.3)
Leading to d/c	9 (7.6)

Common TEAEs Occurring in ≥20%, %	All Patients (N = 118)	
	Any Grade	Grade ≥3
Fatigue	33.1	3.4
Constipation	31.4	0.8
Dysgeusia	28.0	0
Cough	24.6	0
Nausea	24.6	0.8
Pyrexia	24.6	0
Dizziness	22.9	0
Hypertension	22.9	9.3
Peripheral edema	22.0	0
Diarrhea	21.2	0.8
Arthralgia	20.3	0

Woyach. ASH 2021. Abstr 392.

ASH 2021 #391

Pirtobrutinib, A Next Generation, Highly Selective, Non-Covalent BTK Inhibitor in Previously Treated CLL/SLL: Updated Results from the Phase 1/2 BRUIN Study

...

Anthony R. Mato, John M. Pagel, Catherine C. Coombs, Nirav N. Shah, Nicole Lamanna, Tahla Munir, Ewa Lech-Marańda, Toby A. Eyre, Jennifer A. Woyach, William G. Wierda, Chan Yoon Cheah, Jonathon B. Cohen, Lindsey E. Roeker, Manish R. Patel, Bita Fakhri, Minal A. Barve, Constantine S. Tam, David John Lewis, James N. Gerson, Alvaro J. Alencar, Chaitra S. Ujjani, Ian W. Flinn, Suchitra Sundaram, Shuo Ma, Deepa Jagadeesh, Joanna M Rhodes, Justin Taylor, Omar Abdel-Wahab, Paolo Ghia, Stephen J. Schuster, Denise Wang, Binoj Nair, Edward Zhu, Donald Tsai, Matthew S. Davids, Jennifer R. Brown, and Wojciech Jurczak

EFFICACY IN BTK PRE-TREATED PATIENTS

Median 3 prior lines of therapy

Overall response rate	68%
Best response	
Complete response	1%
Partial response	54%
Complete response with lymphocytosis	13%
Stable disease	25%

SAFETY

Treatment-emergent adverse events

	Grade 1	Grade 2	Grade 3	Grade 4
Fatigue	13%	8%	1%	-
Diarrhea	15%	4%	<1%	<1%
Neutropenia	1%	2%	8%	6%
Confusion	15%	2%	-	-

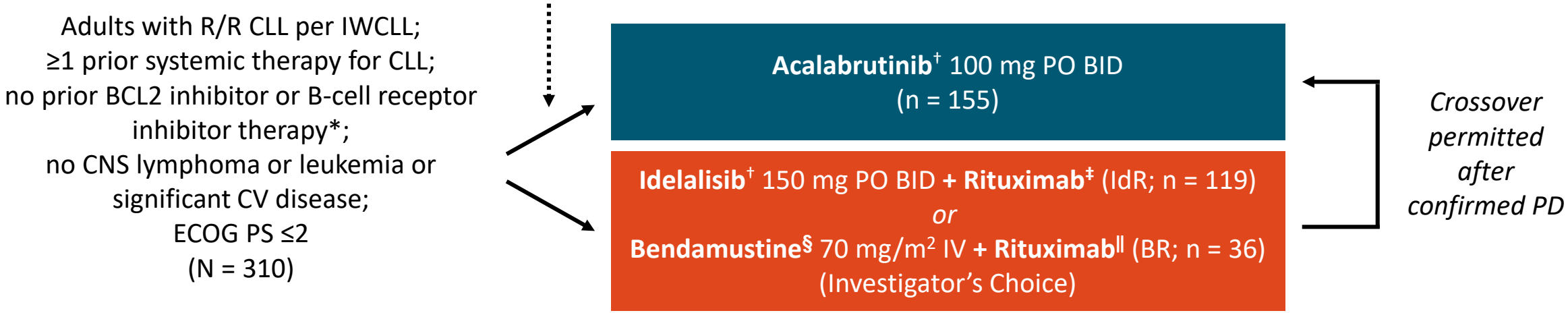
3-Yr Follow-up of ASCEND Phase III Trial: Acalabrutinib vs Idelalisib/Rituximab or Bendamustine/Rituximab in R/R CLL

Jurczak. ASH 2021. Abstr 393.

ASCEND: Study Design

- Global, multicenter, randomized, open-label phase III trial (data cutoff: October 26, 2020)

Stratification by presence of del(17p) (yes vs no); ECOG PS (0-1 vs 2); prior therapies (1-3 vs ≤4)

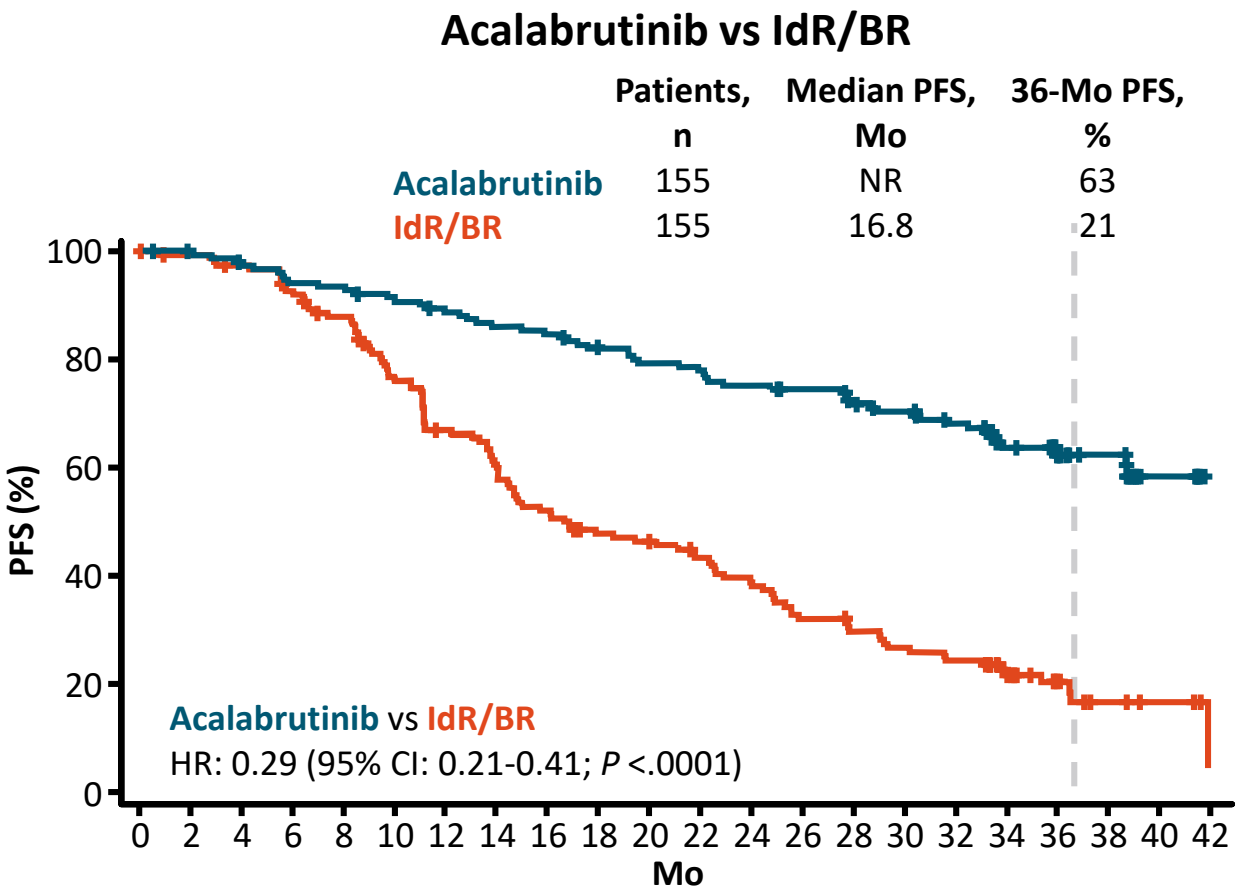


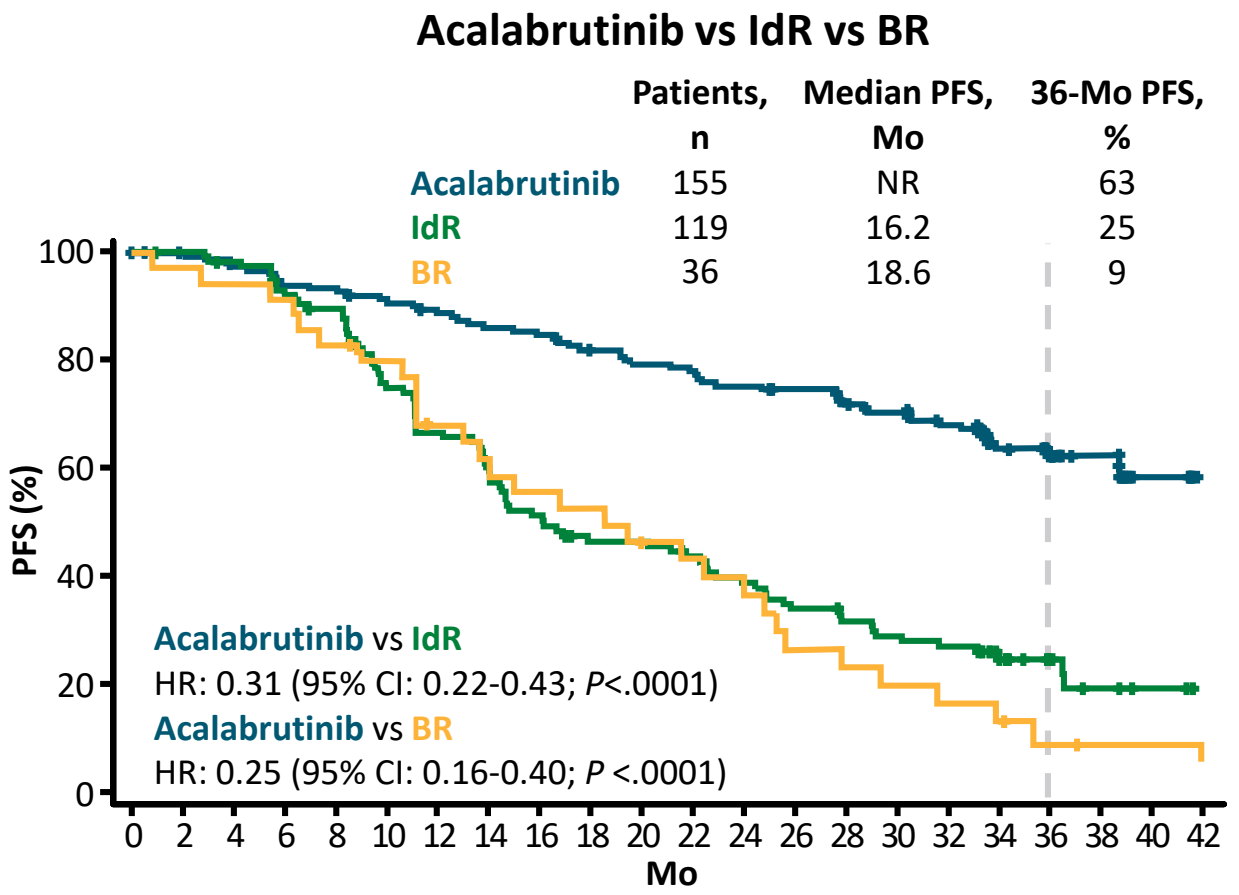
*Prior bendamustine allowed if investigator choice of control treatment was IdR, and if prior response to bendamustine was >24 mo. †Dosed until PD or unacceptable toxicity. ‡Rituximab 375 mg/m^2 IV on Day 1 of cycle 1, then 500 mg/m^2 every 2 wk for 4 infusions, followed by every 4 wk for 3 infusions. §Bendamustine on Days 1 and 2 of cycles 1-6. ‖Rituximab 375 mg/m^2 IV on Day 1 of cycle 1, then 500 mg/m^2 on Day 1 of cycles 2-6.

- Primary endpoint: PFS
- Secondary endpoints: ORR, OS, safety

Jurczak. ASH 2021. Abstr 393.

ASCEND 3-Yr Update: Investigator-Assessed PFS





- Median time on study: acalabrutinib, 36.0 mo; IdR/BR, 35.2 mo

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ASCEND 3-Yr Update: Safety Summary

AEs, n (%)	Acalabrutinib (n = 154)	IdR (n = 118)	BR (n = 35)
Any AEs (all grades)	148 (96)	117 (99)	28 (80)
▪ Grade ≥3	96 (62)	108 (92)	17 (49)
▪ Grade 5	14 (9)	8 (7)	2 (6)
Serious AEs*	59 (38)	74 (63)	9 (26)
Treatment-related AEs	111 (72)	113 (96)	24 (69)
AEs leading to dose reduction	7 (5)	15 (13)	5 (14)
AEs leading to dose withholding	64 (42)	79 (67)	7 (20)
AEs leading to dose d/c	32 (21)	77 (65)	6 (17)
Death within 30 days of last dose	13 (8)[†]	5 (4)[‡]	1 (3)[§]

*Serious AEs reported in ≥5% of patients in any group included: pneumonia (acalabrutinib, 8%; IdR, 9%; BR, 3%); diarrhea (acalabrutinib, 1%; IdR, 15%); pyrexia (acalabrutinib, 2%; IdR, 7%; BR, 3%). [†]Primary causes of death for acalabrutinib: n = 10, AE (n = 1 each, respiratory failure, brain neoplasm, cardiorespiratory arrest, cardiopulmonary failure, pneumonia, neuroendocrine carcinoma, sepsis, bronchitis, cachexia, and neutropenic sepsis); n = 1 each PD, Richter transformation, and unknown. [‡]Primary cause of death for IdR: n = 5, AE (n = 1 each, cardiopulmonary failure, myocardial infarction, pneumonitis, sepsis, and interstitial lung disease). [§]Primary cause of death for BR: n = 1, AE (acute cardiac failure).

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ASCEND 3-Yr Update: AEs of Clinical Interest

AEs of Clinical Interest, n (%)	Acalabrutinib (n = 154)		IdR (n = 118)		BR (n = 35)	
	Any	Grade ≥3	Any	Grade ≥3	Any	Grade ≥3
Atrial fibrillation	10 (7)	2 (1)	4 (3)	1 (1)	1 (3)	1 (3)
Hemorrhage	46 (30)	4 (3)	10 (9)	3 (3)	2 (6)	1 (3)
▪ Major hemorrhage*	5 (3)	4 (3)†	3 (3)‡	3 (3)‡	1 (3)	1 (3)
Hypertension	11 (7)	7 (5)	6 (5)	1 (1)	0	0
Infections	100 (65)	38 (25)	83 (70)	37 (31)	17 (49)	4 (11)
Second primary malignancies excluding non-melanoma skin carcinomas	11 (7)	8 (5)	2 (2)	1 (1)	2 (6)	2 (6)
Tumor lysis syndrome	1 (1)	1 (1)	1 (1)	1 (1)	0	0

*Major hemorrhage: any serious or grade ≥3 hemorrhage, or CNS hemorrhage of any grade. †Includes n = 1 each of grade 4 GI hemorrhage, grade 3 GI hemorrhage, grade 4 ITP , and grade 3 intestinal hemorrhage. ‡Includes n = 1 each of grade 3 GI hemorrhage, grade 3 and grade 4 ITP, and grade 3 hematuria.

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ASH 2021 #637

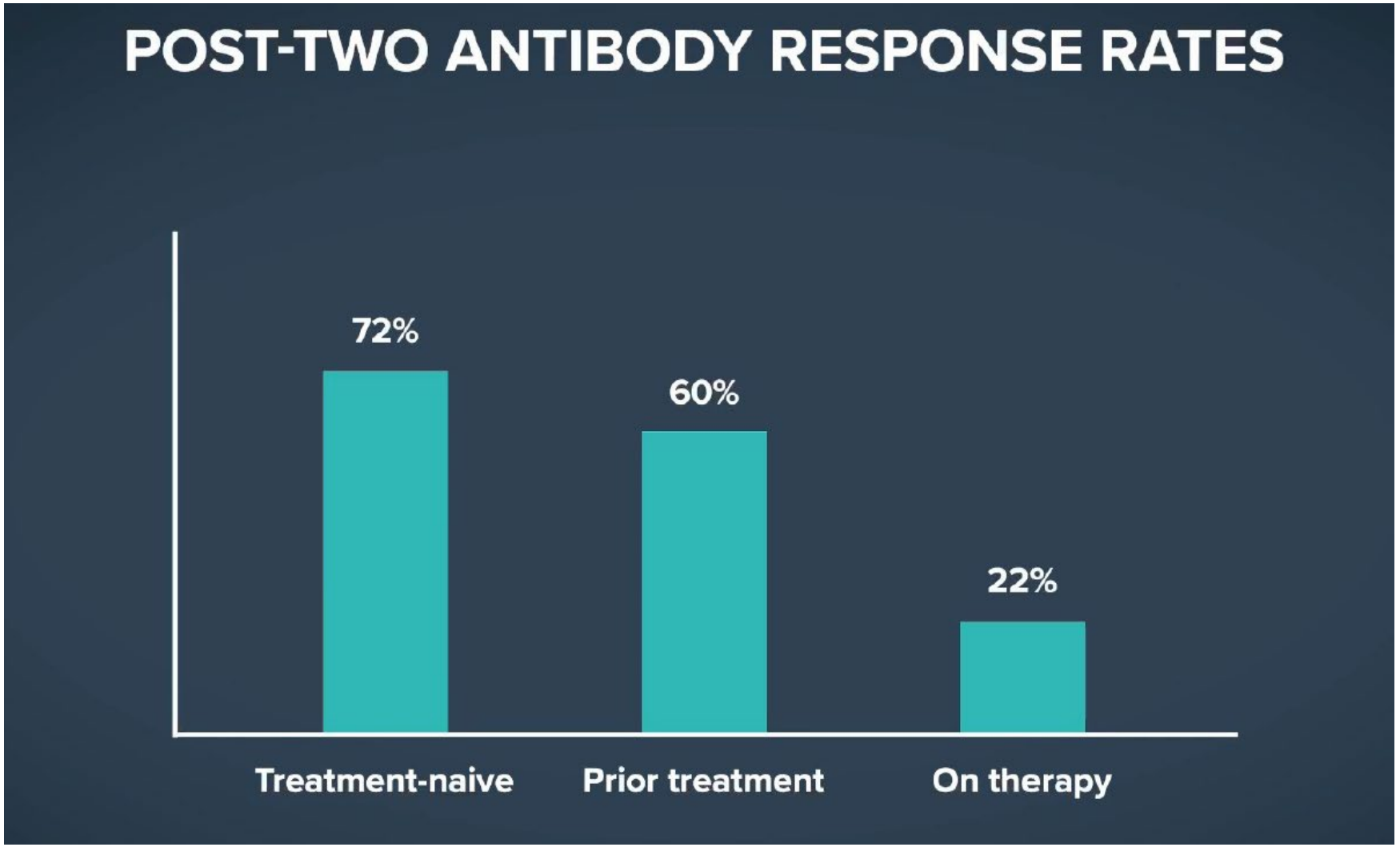
Humoral Response to mRNA Vaccines BNT162b2 and mRNA-1273 COVID-19 in Chronic Lymphocytic Leukemia Patients

...

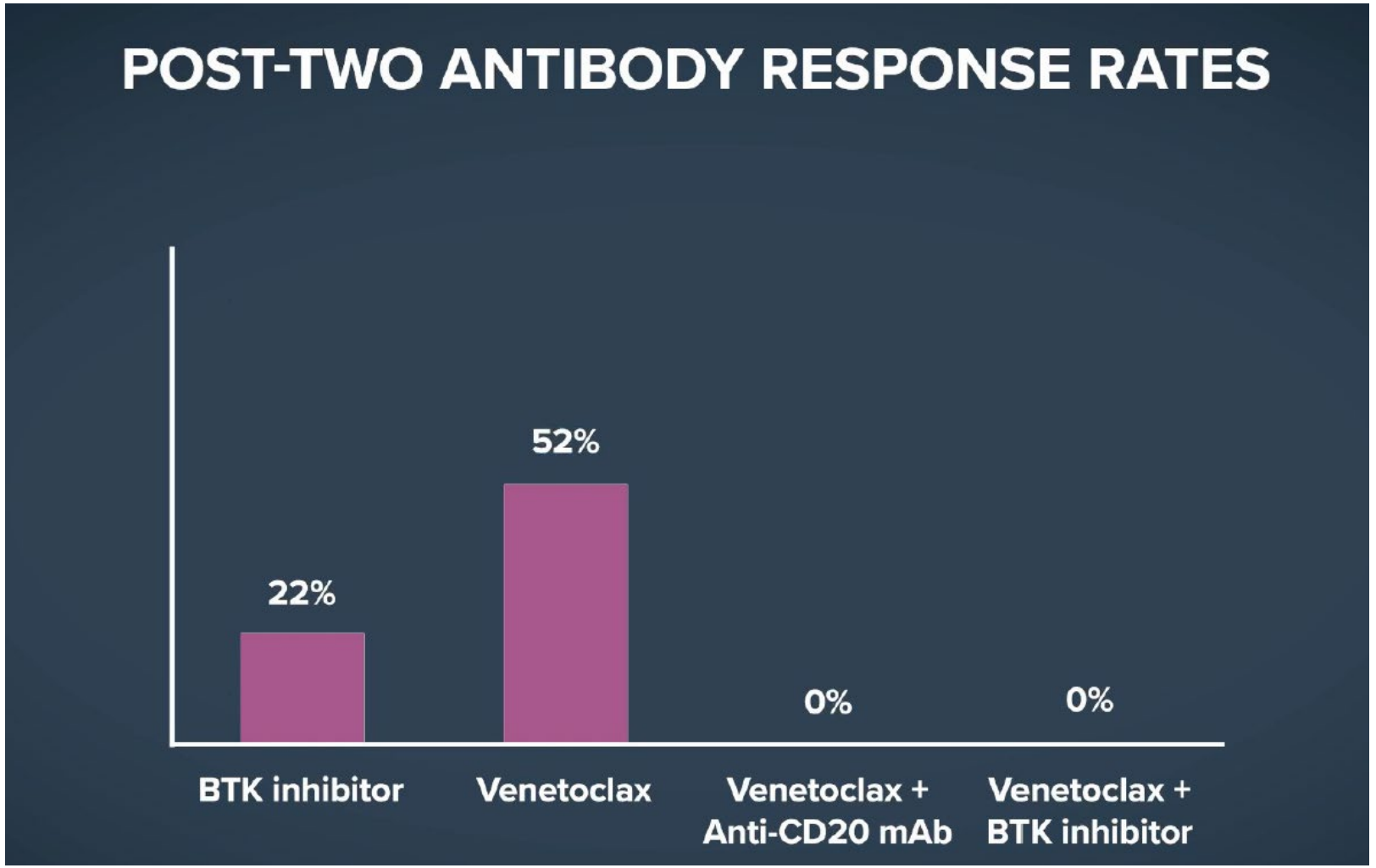
Cristina Bagacean, Rémi Letestu, Chadi Al Nawakil, Ségolène Brichler, Vincent Lévy, Nanthara Sritharan, Alain Delmer, Caroline Dartigeas, Véronique Leblond, Damien Roos-Weil, Marie C Béné, Aline Clavert, Driss Chaoui, Philippe Genet, Romain Guieze, Kamel Laribi, Yamina Touileb, Bernard Drenou, Lise Willems, Cécile Tomowiak, Fatiha Merabet, Christian Puppink, Hugo Legendre, Xavier Troussard, Stéphanie Malartre, Florence Cymbalista and Anne-Sophie Michallet

- A total of 530 patients and 14 controls were included in the study. Vaccine response was evaluated post-dose 1 for 158 CLL patients, post-dose 2, for 506 patients and post-dose 3 for 66 patients.
- Double-dose mRNA vaccination generated a humoral response in 52% of our CLL cohort

Bagacean C et al # 637



Bagacean C et al # 637



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- Post-dose 2 seronegative patients were proposed a third dose and to date, 66 have been tested for the antibody response 4-6 weeks post-dose 3. The post-dose 3 response rate was 42% (28/66).
- An additional cohort of 40 CLL patients who presented a SARS-CoV-2 infection prior to vaccination participated to the study and was analyzed independently. All patients achieved seroconversion after infection and a single dose of vaccine, even though 30% (n=12) had an ongoing CLL treatment

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ASH 2021 #638

Cellular Immune Responses to BNT162b2 mRNA COVID-19 Vaccine in Patients with Chronic Lymphocytic Leukemia

...

Gilad Itchaki, Lior Rokach, Ohad Benjamini, Osnat Bairey, Adi Sabag, Helly Vernitsky, Hila Cohen, Shahar Rotem, Uri Elia, Pia Raanani, Erez Bar-Haim, and Tamar Tadmor

- Aim of the study: To investigate T-cell response determined by interferon gamma (IFNγ) secretion in patients with CLL following BNT162b mRNA Covid-19 vaccine, in comparison with serologic response.
- Out of 83 patients, 68 were eligible for the analysis (with positive internal control)
- T cell immune response to the vaccine was evident in 22 (32%) patient

Itchaki G et al # 638

IgG spike ve T hücre Yanıtı Korelasyonu

Variable	T-cell response		Total	Odds ratio (95% CI)	p-value
	Present	Absent			
	n=20	n=46	n=68		
IgG Spike (during the T-cell test)					0.048
• Negative	12 (24%)	38 (76%)	50	1 (ref)	
• Positive	8 (50%)	8 (50%)	16	3.1667 (0.98-10.26)	

Table 2: IgG anti Spike and T-cell response to BNT162b2 mRNA COVID-19 vaccine in patie with chronic lymphocytic leukemia

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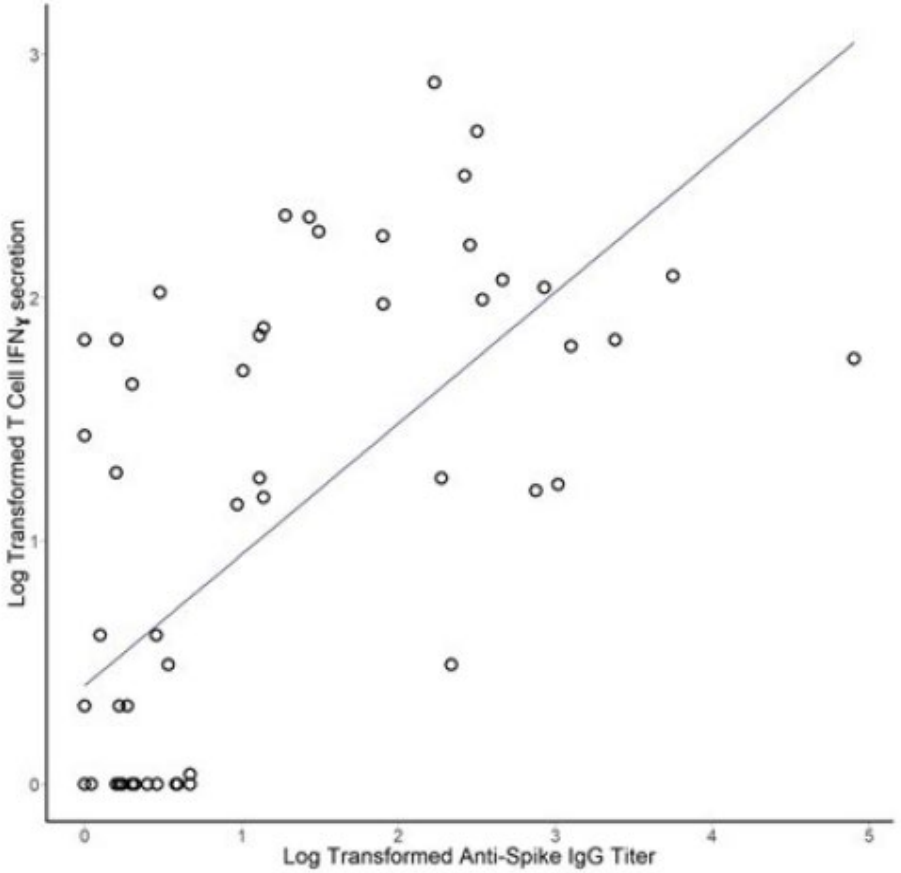

Figure 1: Correlation between IgG anti-Spike and T-cell response to BNT162b2 mRNA COVID-19 Vaccine in patients with chronic lymphocytic leukemia