THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

Current Evidence in Management of CLL & Future Direction

Nitin Jain, MD
Associate Professor
Department of Leukemia
MD Anderson Cancer Center
Houston, TX

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Pharmacyclics, AbbVie, Genentech, AstraZeneca, BMS, Pfizer, ADC Therapeutics, Incyte, Servier, Cellectis, Verastem, Adaptive Biotechnologies, Precision Biosciences

Advisory Board / Honoraria

Pharmacyclics, Janssen, AbbVie, Genentech, AstraZeneca, Verastem, Adaptive Biotechnologies, Servier, Precision Biosciences

Treatments for CLL

Treatment Evolution

1960s

Alkylating agents
- Chlorambucil
- Cyclophosphamide

1970s

Purine nucleosides
- Fludarabine
- Pentostatin
- Cladribine

1980s

1990s

Purine nucleosides and alkylators

2000s

Chemoimmunotherapy (FCR, BR)
Alemtuzumab
Lenalidomide

2014-

BTK inhibitors (Ibrutinib, Acalabrutinib)
PI3K inhibitors (Idelalisib, Duvelisib)
BCL-2 inhibitors (Venetoclax)
Novel CD20 mAb (Obinutuzumab)

Evolving Treatment Paradigm

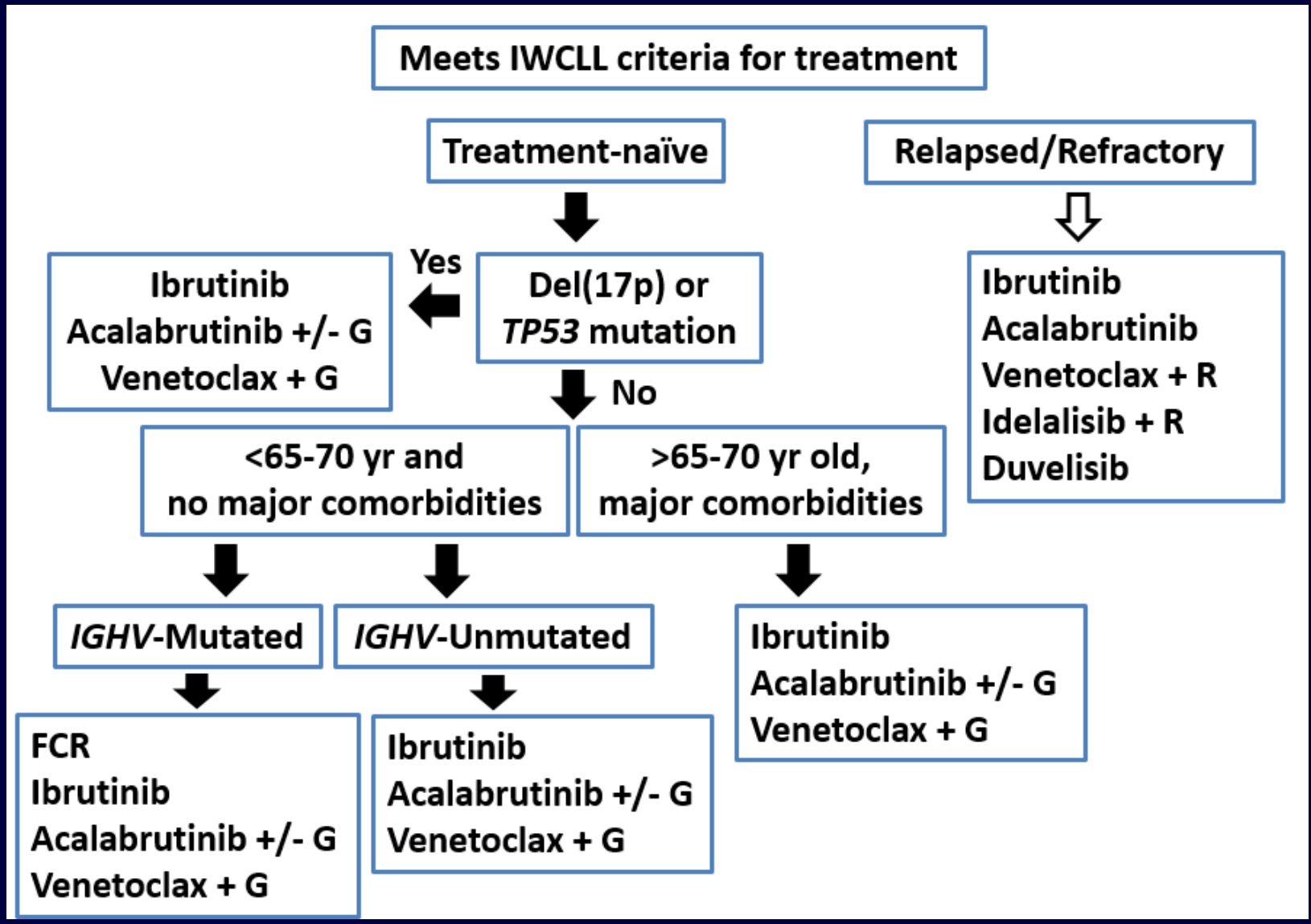
Chemoimmunotherapy era

- **FCR (young fit)**
- **BR / Chlorambucil-based (older adults)**

Targeted Therapies era

- **FCR (young fit *IGHV*-m)**
- **Targeted therapies (all others)**

Current Standard Rx of CLL



Adapted from Jain N, O'Brien S. Cancer J. 2019;25(6):374-377.

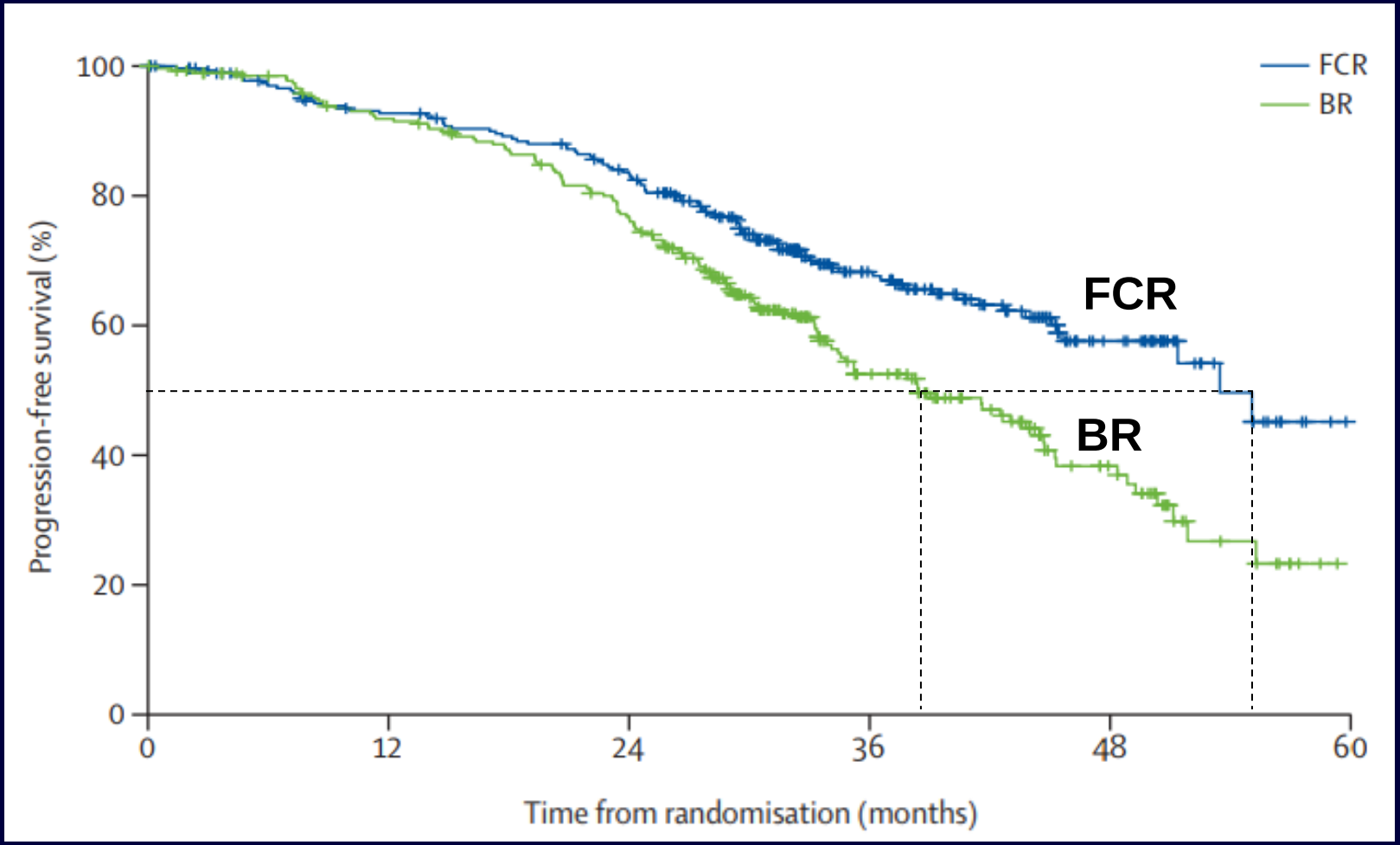
YOUNG ‘FIT’ PTS (FCR ELIGIBLE)

Firstline Treatment with FCR

Response	# Pts	%	
CR	217	(72)	95%
Nodular PR	31	(10)	
PR	37	(12)	
No Response	13	(4)	
Early Death	2	(1)	

Keating et al. J Clin Oncol. 2005;23(18):4079-88.

CLL10: PFS Better with FCR



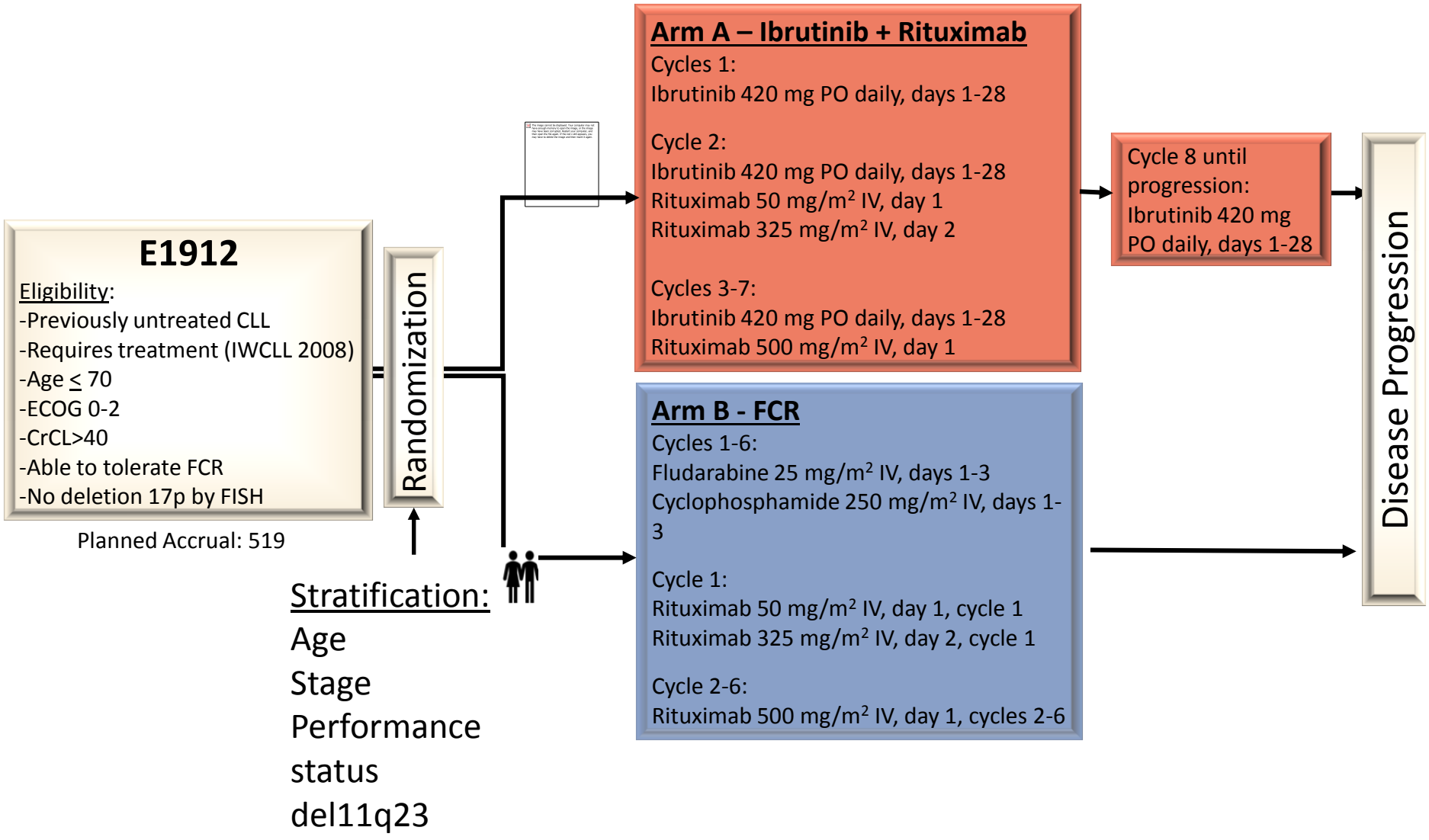
Median PFS FCR 55.2 months vs. BR 41.7 months p= 0.0003

Eichhorst et al. Lancet Oncol. 2016;17(7):928-942.

Update From the E1912 Trial Comparing Ibrutinib & Rituximab to FCR in Younger Patients with Previously Untreated Chronic Lymphocytic Leukemia (CLL)

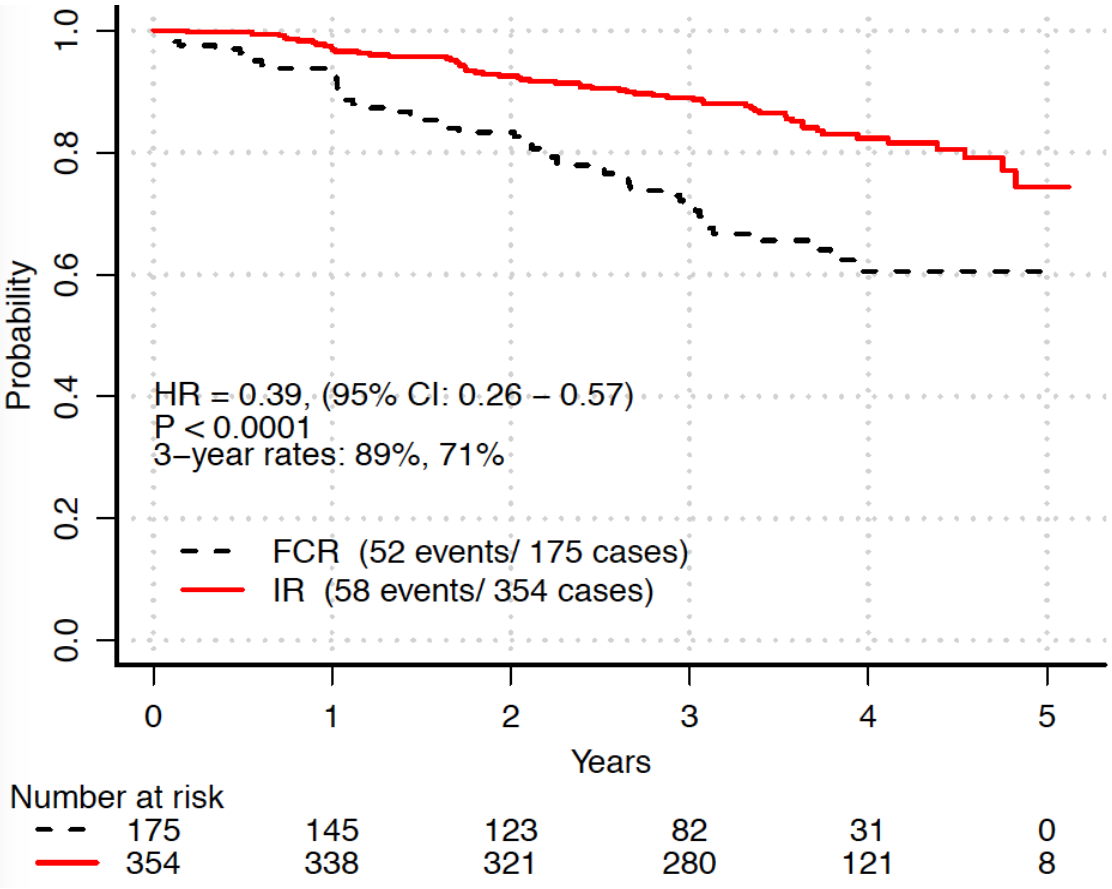
Tait Shanafelt, Xin Victoria Wang, Neil E. Kay, Susan O'Brien, Jacqueline Barrientos , Curt Hanson, Harry Erba, Rich Stone, Mark Litzow, Marty Tallman

Study design

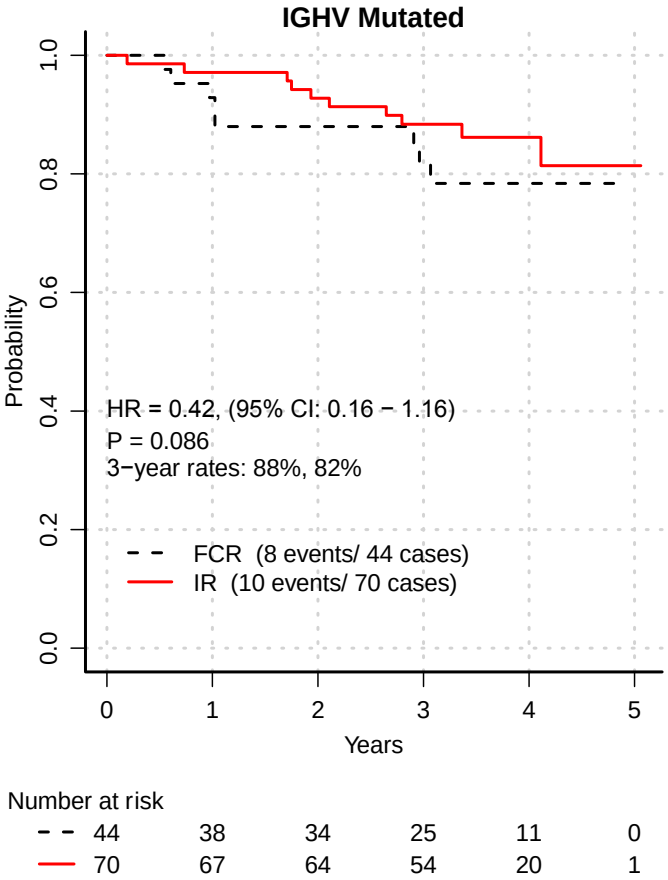


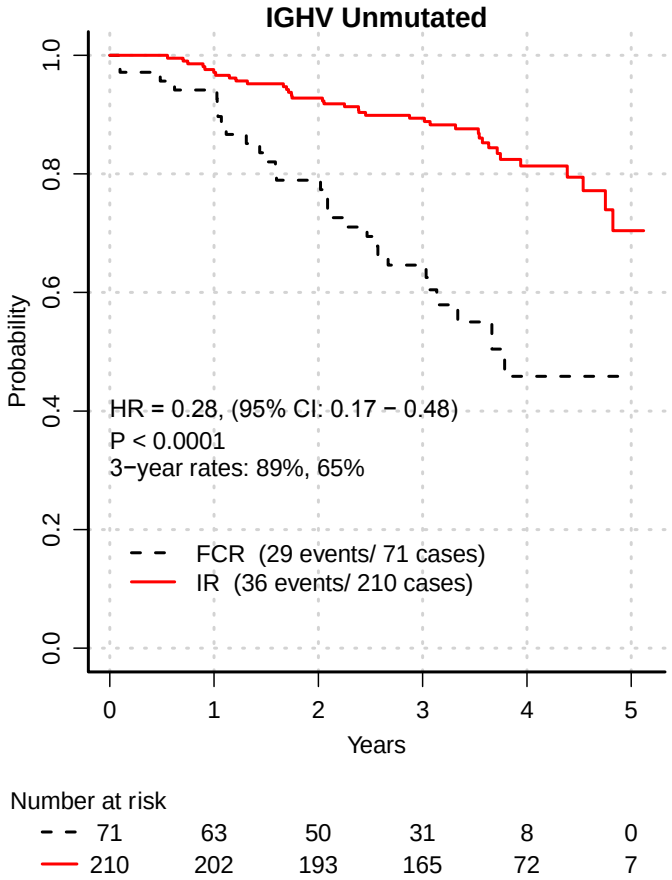
Median follow-up 48 months

Progression Free Survival

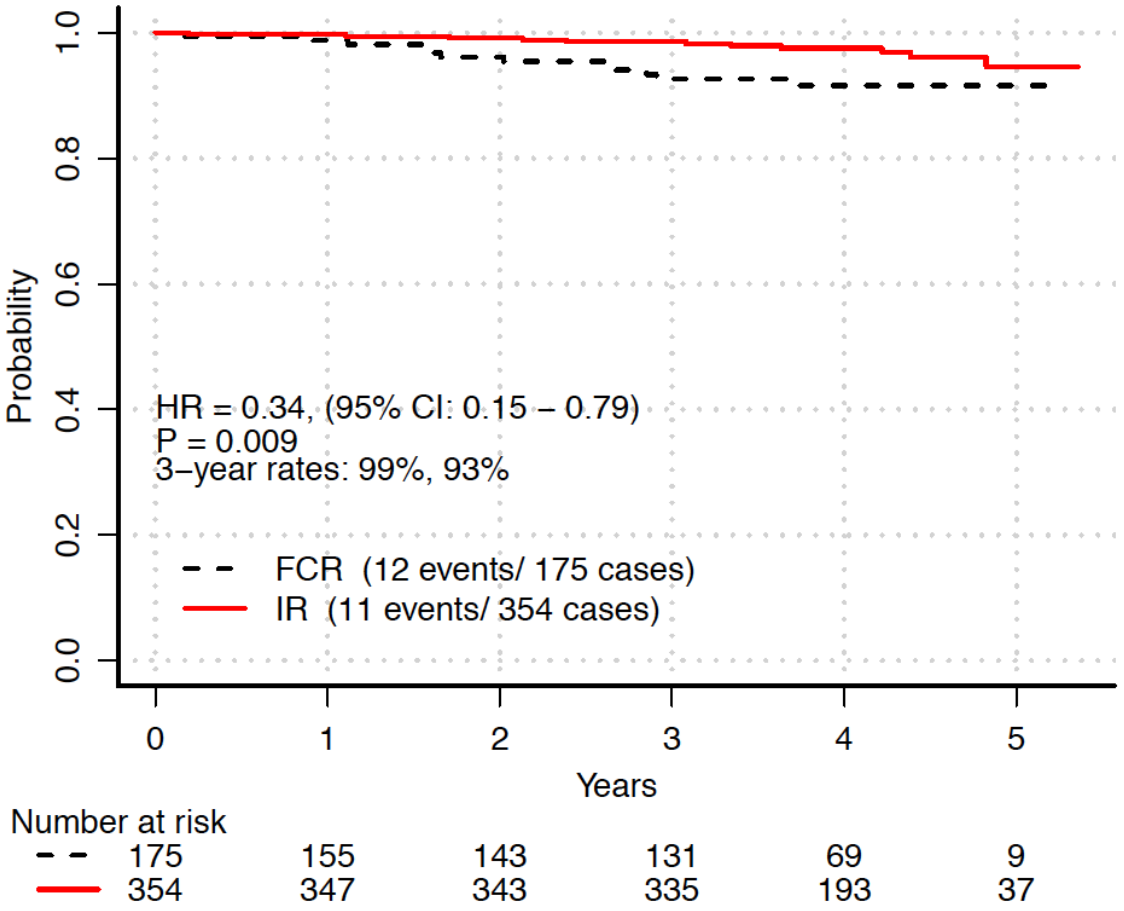


Progression Free Survival: IGHV Status

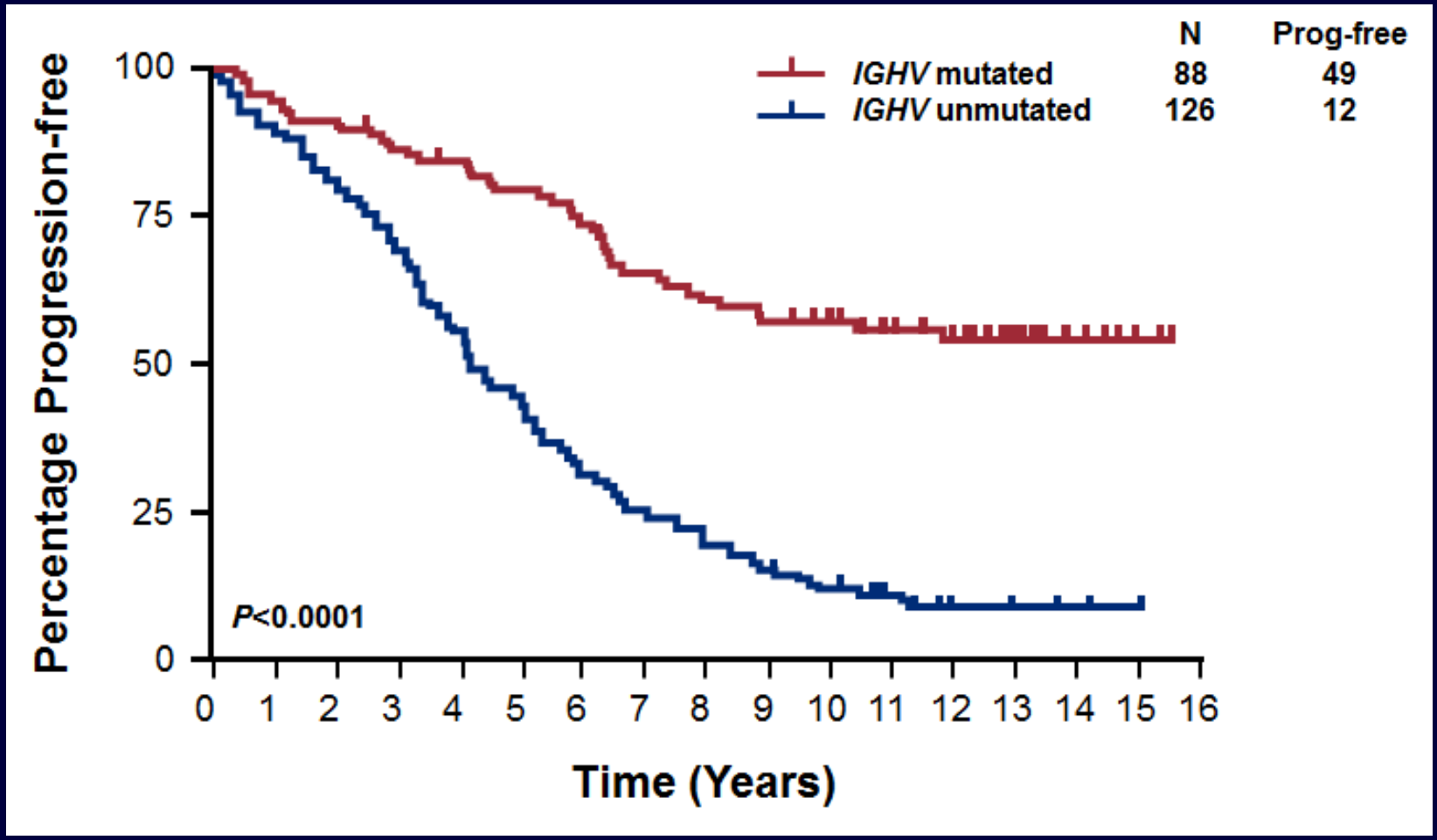




Overall Survival



Favorable Long-term PFS with First-line FCR in *IGHV*-M Subgroup



Thompson et al. Blood. 2016;127(3):303-9.

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Ibrutinib, Fludarabine, Cyclophosphamide, and Obinutuzumab (iFCG) for First-line Treatment of *IGHV*-mutated CLL without del(17p)/mutated *TP53*

Nitin Jain, Philip Thompson, Jan Burger, Alessandra Ferrajoli, Koichi Takahashi, Zeev Estrov, Gautam Borthakur, Prithviraj Bose, Tapan Kadia, Naveen Pemmaraju, Koji Sasaki, Naveen Garg, Xuemei Wang, Rashmi Kanagal-Shamanna, Keyur Patel, Jeffrey Jorgensen, Sa Wang, Wanda Lopez, Ana Ayala, William Plunkett, Varsha Gandhi, Hagop Kantarjian, Susan O'Brien, Michael Keating, William Wierda

Department of Leukemia, MDACC

ASH 2019, Abstract 357

iFCG Trial Rationale

- **Higher U-MRD will improve PFS and OS**
  - **Obinutuzumab: higher U-MRD than rituximab (CLL11)**
  - **Ibrutinib with CIT: higher U-MRD (HELIOS trial)**
- **Reducing chemo may lower t-MDS/AML**
  - **Number of FC cycles reduced from 6 to 3**

iFCG Phase II Clinical Trial

- Investigator-initiated phase II trial
- First-line treatment
- *IGHV*-M CLL
- No del(17p) or *TP53* mutation
- iFCG regimen
  - **I**brutinib
  - **F**ludarabine
  - **C**yclophosphamide
  - Obinutuzumab (**G**A101)

iFCG: Study Design

iFCG 3 courses

↓

Ibrutinib 9 courses (all pts)
+
Obinutuzumab 3 courses (CR/CRi with BM U-MRD4)
or
Obinutuzumab 9 courses (PR or BM MRD^{pos})

↓

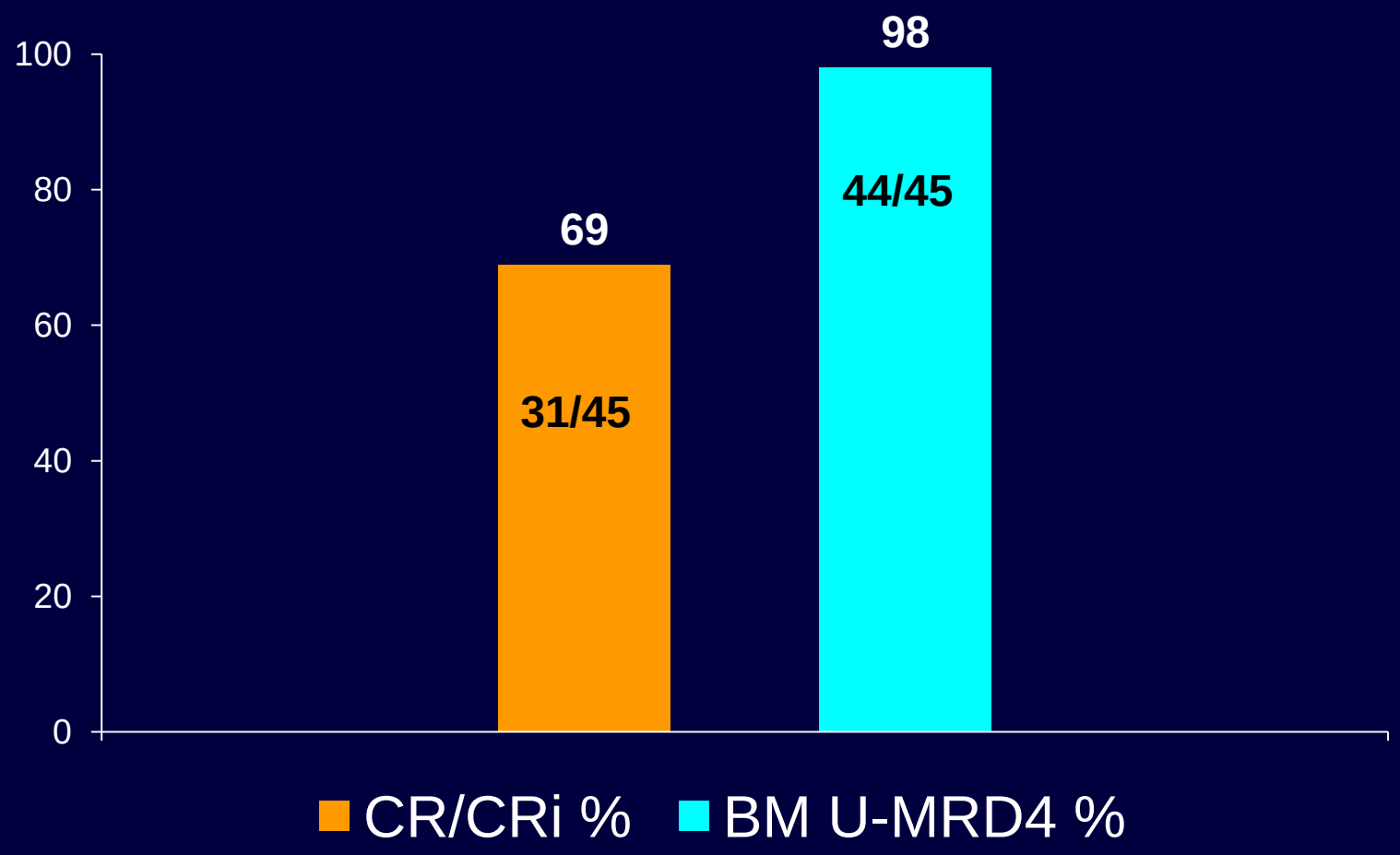
After 12 courses
BM U-MRD4 → stop ibrutinib
BM MRD^{pos} → continue ibrutinib

Baseline Characteristics (N=45)

		n (%) or median [range]
Age, yrs		60 [25-71]
Gender, M		35 (78)
Rai stage	0 I-II III-IV	1 (2) 22 (49) 22 (49)
ALC, K/μL PLT, K/μL HGB, g/dL		52.9 [1.5-208] 120 [62-292] 11.9 [8.5-15.6]
B2M, mg/L		2.7 [1.3-8.1]
FISH	Del(13q) Trisomy 12 Negative Del(11q)	31 (69) 7 (16) 6 (13) 1 (2)
Cytogenetics (n=39)	Diploid	27 (69)
Mutations (n=39)	MYD88 SF3B1 NOTCH1 BIRC3	5 (13) 3 (8) 1 (3) 1 (3)

* 1 pt was later reclassified as *IGHV*-UM

Best Response (N=45)
Intent to Treat

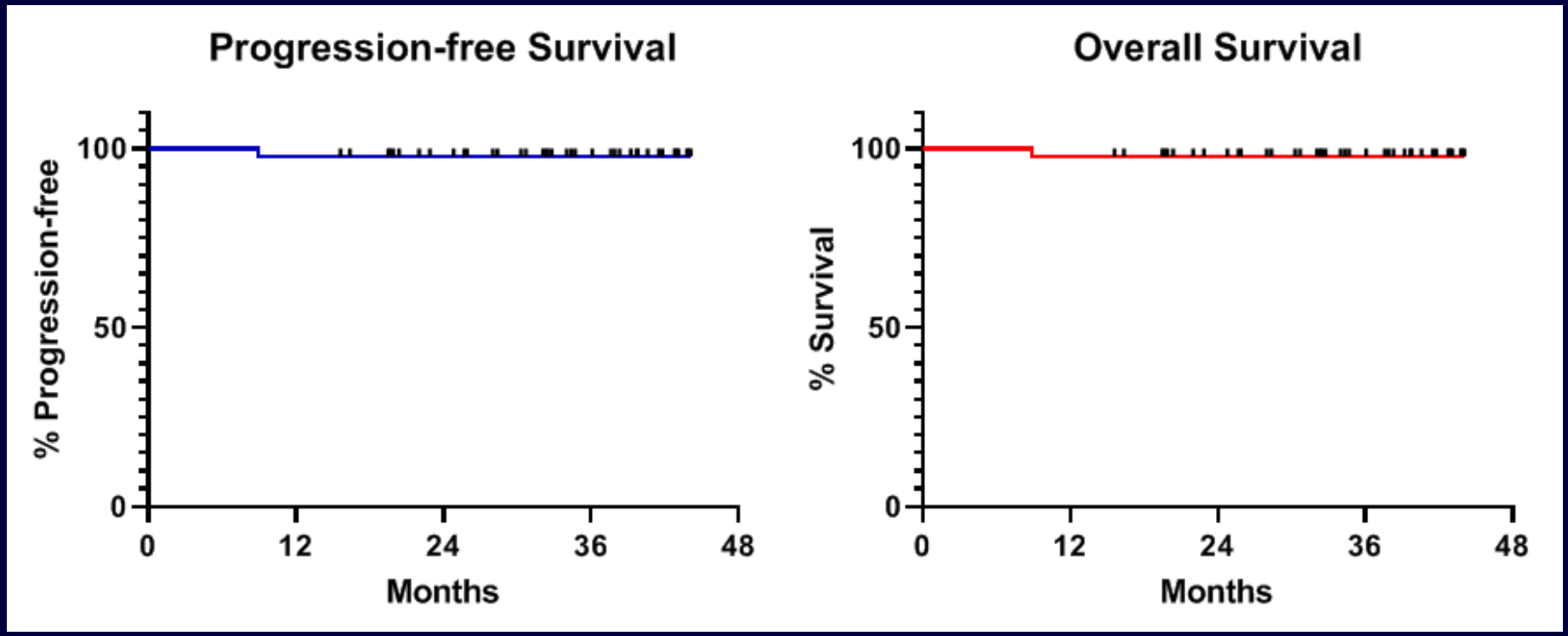


BM-UMRD4 in *IGHV*-M after C6

Trial	Regimen	N	BM U-MRD4 %	
			Evaluable	ITT
MDACC[1]	FCR x6	88	51	40
MDACC[2]	FCR x6	82	56	34
CLL8[3]	FCR x6	113	50	13
CLL10[4]	FCR x6	123	62	28
GREEN[5]	FCG x6	37	67	38
DFCI[6]	iFCR x6	33	79	79
MDACC	iFCG x3 → iG x3	45	95	89

[1]Keating, JCO 2005; [1]Tam, Blood 2008; [1]Thompson, Blood 2016; [2]Strati, Blood 2014; [3]Hallek, Lancet 2010; [3]Bottcher, JCO 2012, [4]Eichhorst, Lancet Onc 2016; [4]Personal communication Barbara Eichhorst, GCLLSG; [5]Bosch, Leukemia 2019; [6]Davids, Lancet Haematol 2019.

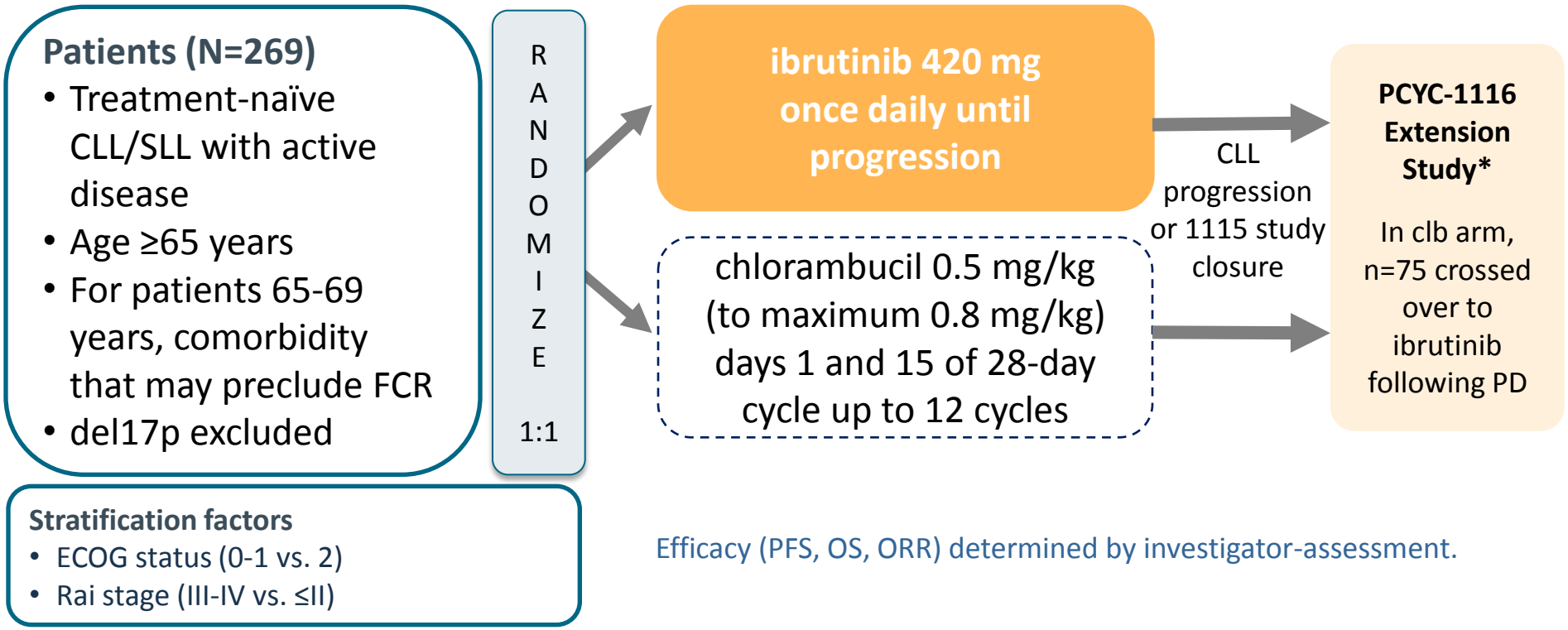
PFS and OS for all Pts (N=45)



No patient had disease progression
1 patient with MRD relapse

PATIENTS ≥65 YRS (FCR INELIGIBLE)

RESONATE-2 (PCYC-1115/1116) Study Design

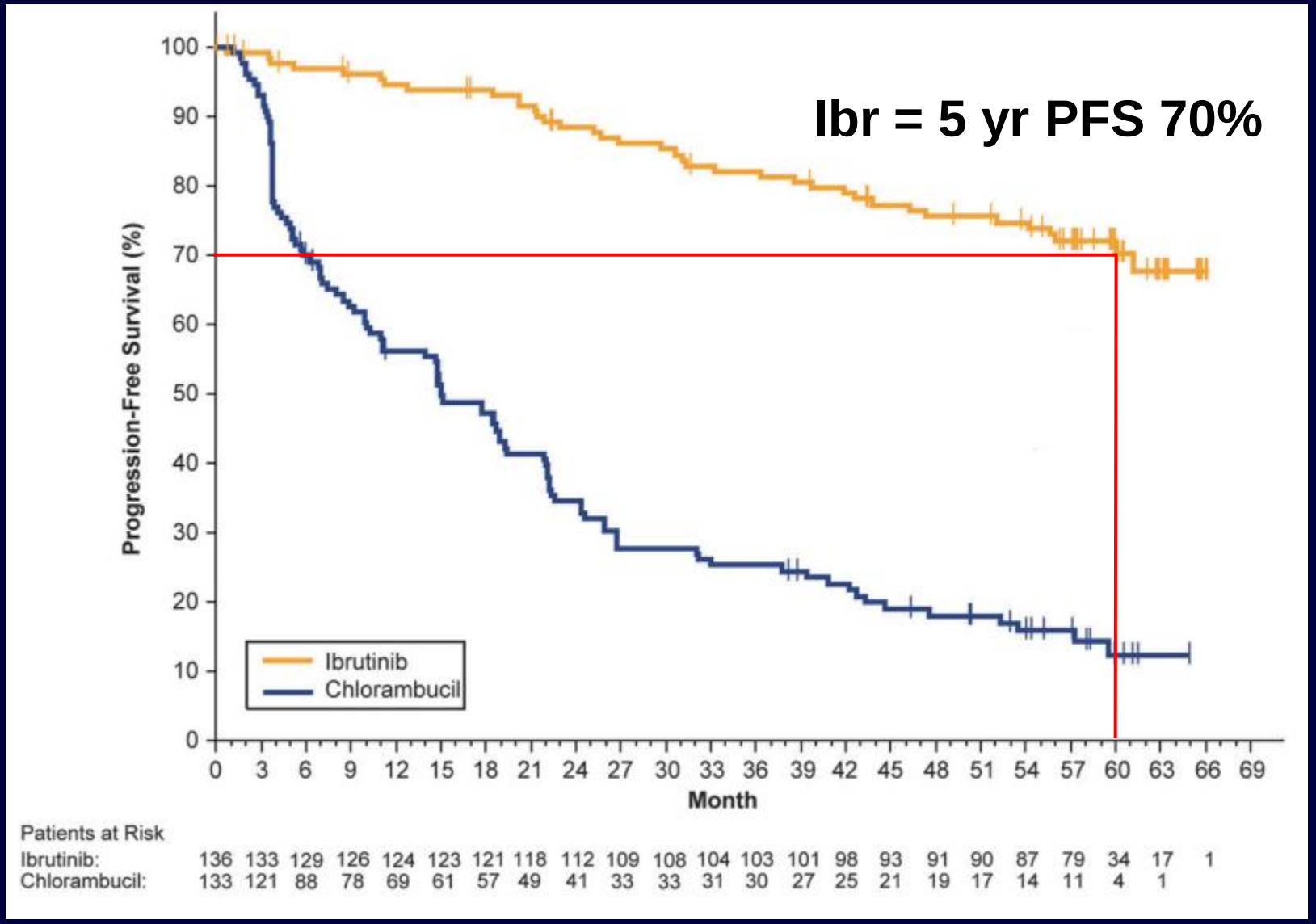


Efficacy (PFS, OS, ORR) determined by investigator-assessment.

*Patients could enroll in separate extension study PCYC-1116 after independent review committee-confirmed PD or at study PCYC-1115 closure for continuing treatment and follow-up.

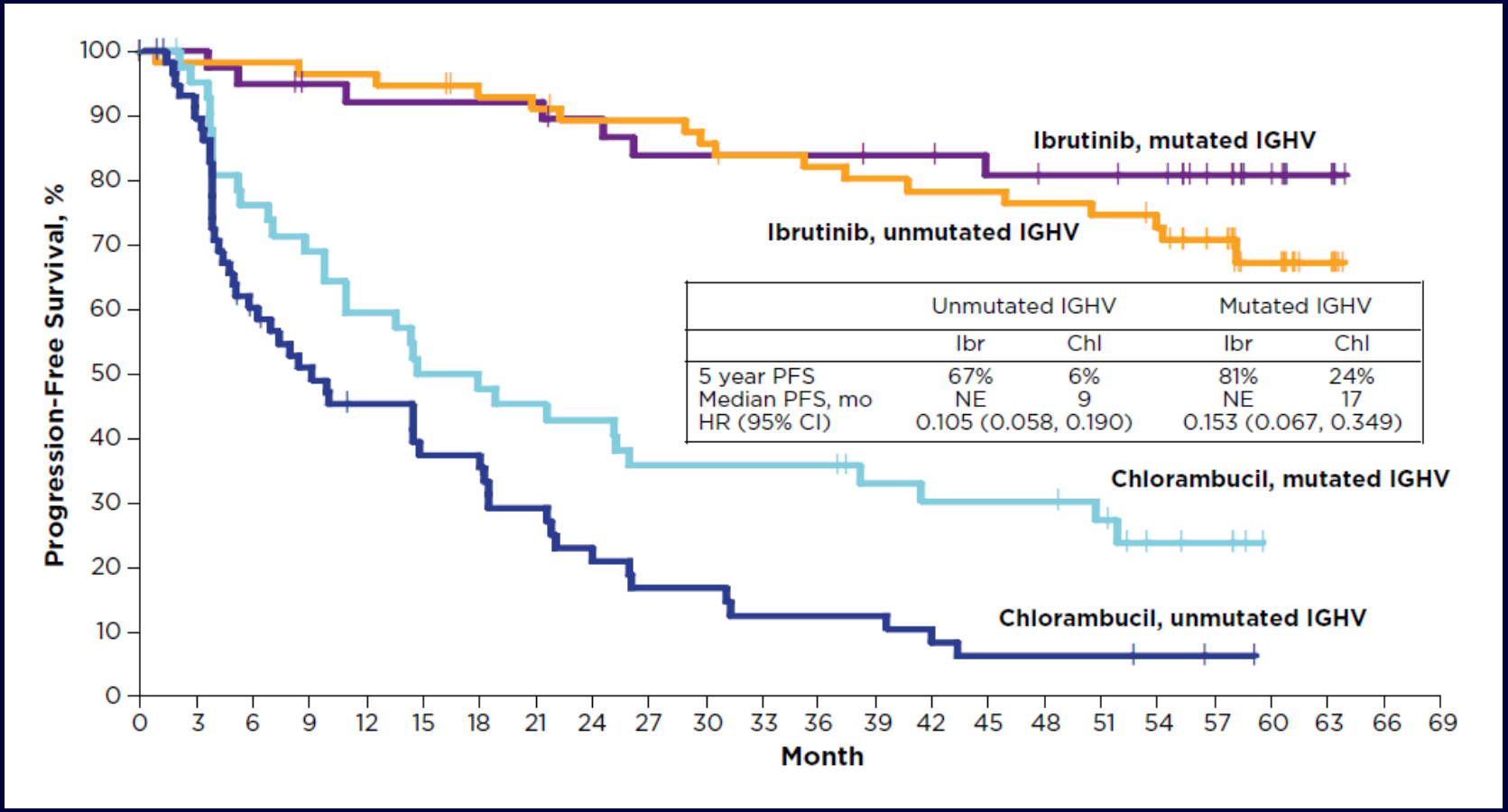
Burger et al. Leukemia. 2019 Oct 18

RESONATE 2, 5-yr Follow-up



Burger et al. Leukemia. 2019 Oct 18

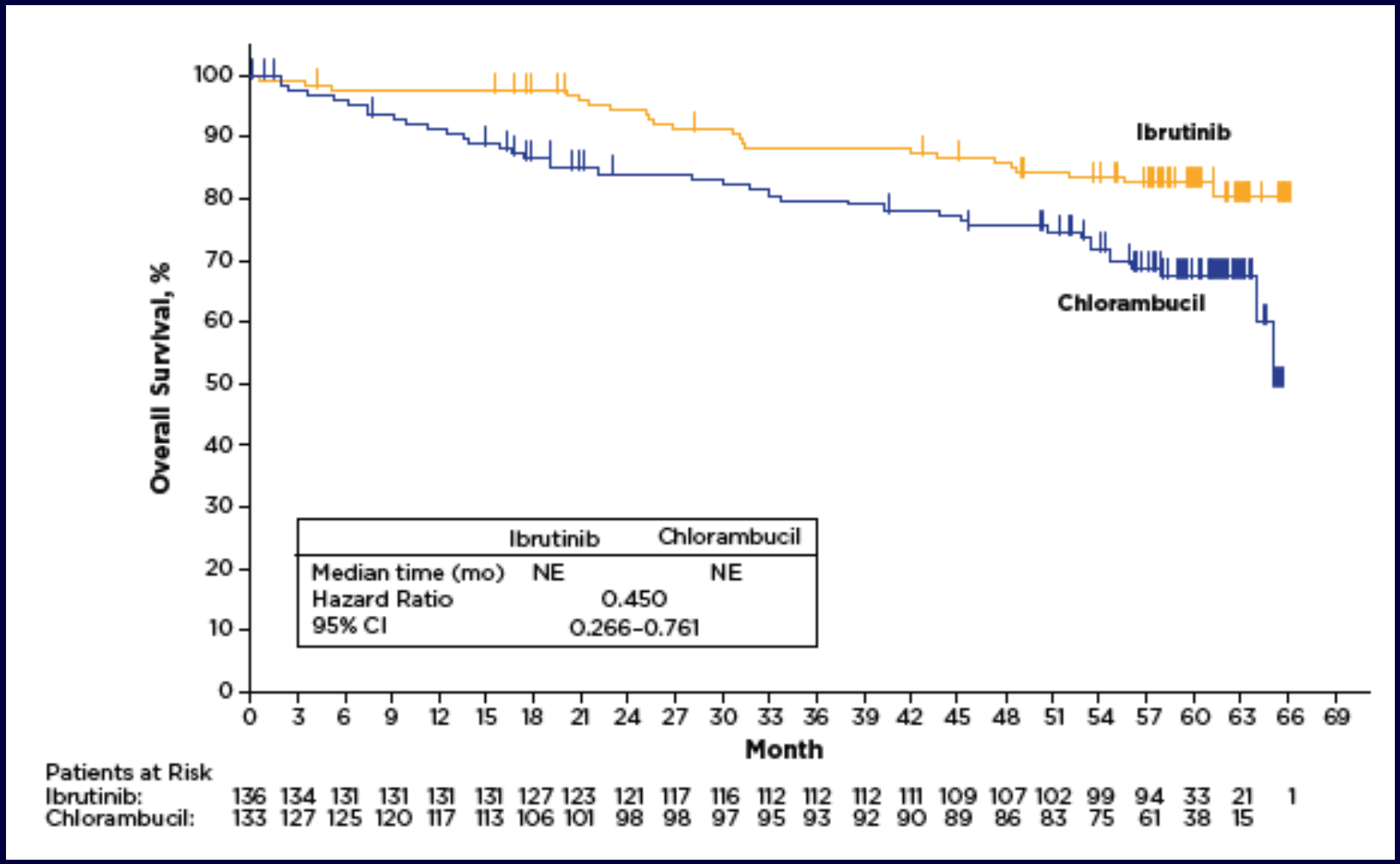
RESONATE 2, 5-yr Follow-up



	Unmutated IGHV		Mutated IGHV	
	Ibr	Chl	Ibr	Chl
5 year PFS	67%	6%	81%	24%
Median PFS, mo	NE	9	NE	17
HR (95% CI)	0.105 (0.058, 0.190)		0.153 (0.067, 0.349)	

Burger et al. Leukemia. 2019 Oct 18

RESONATE 2, 5-yr Follow-up



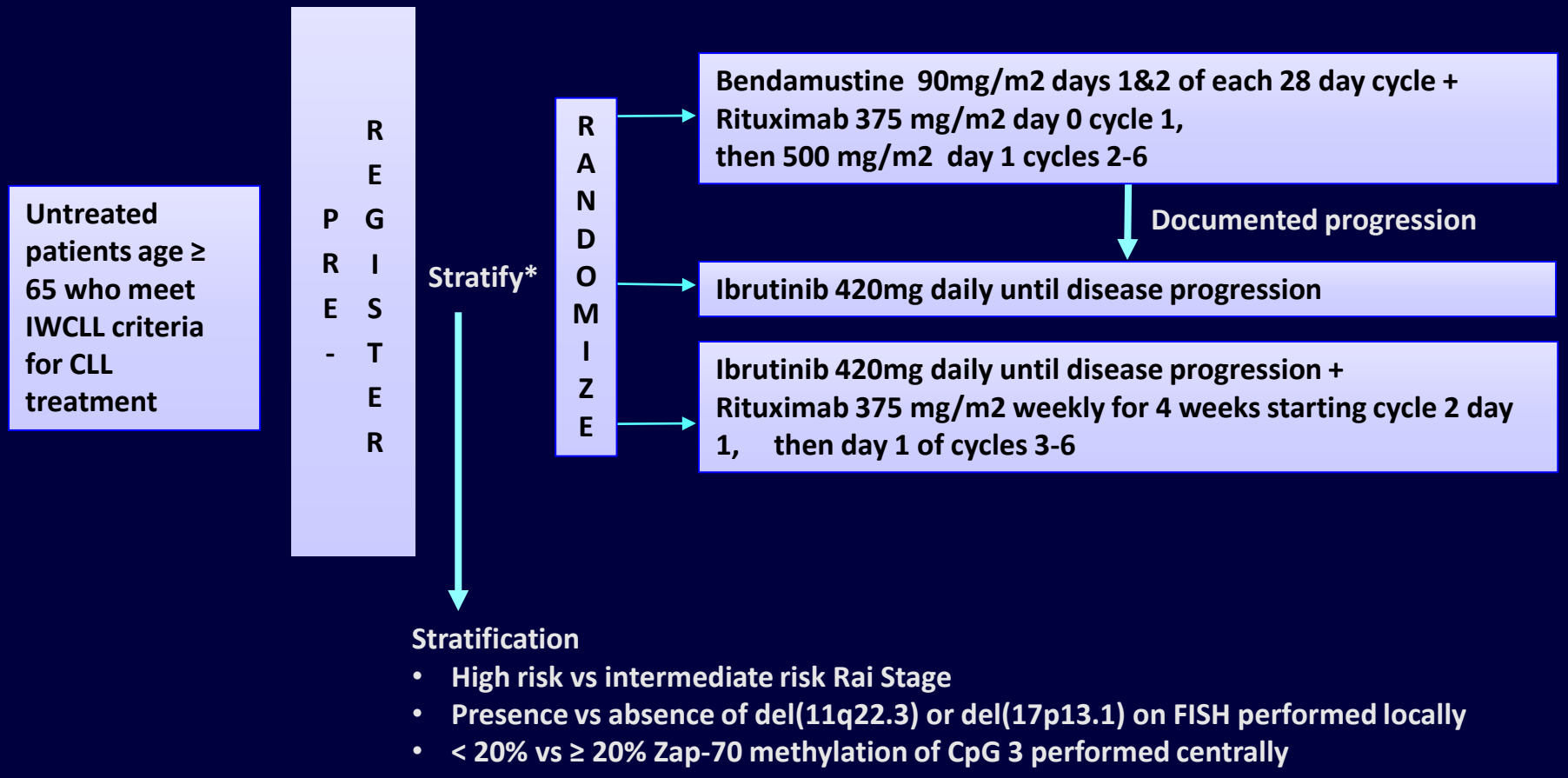
Burger et al. SOHO Annual Meeting, 2019

Ibrutinib alone or in combination with rituximab produces superior progression free survival (PFS) compared with bendamustine plus rituximab in untreated older patients with chronic lymphocytic leukemia (CLL): Results of Alliance North American Intergroup Study A041202

Jennifer A. Woyach, Amy S. Ruppert, Nyla Heerema, Weiqiang Zhao, Allison M Booth, Wei Ding, Nancy L. Bartlett, Danielle M Brander, Paul M Barr, Kerry A Rogers, Sameer Parikh, Steven Coutre, Arti Hurria, Gerard Lozanski, Sreenivasa Nattam, Richard A. Larson, Harry Erba, Mark Litzow, Carolyn Owen, James Atkins, Jeremy Abramson, Rich Little, Scott E. Smith, Richard M. Stone, Sumithra Mandrekar, John C. Byrd

ASH 2018 Plenary Abstract
Woyach et al. N Engl J Med. 2018 Dec 27;379(26):2517-2528.

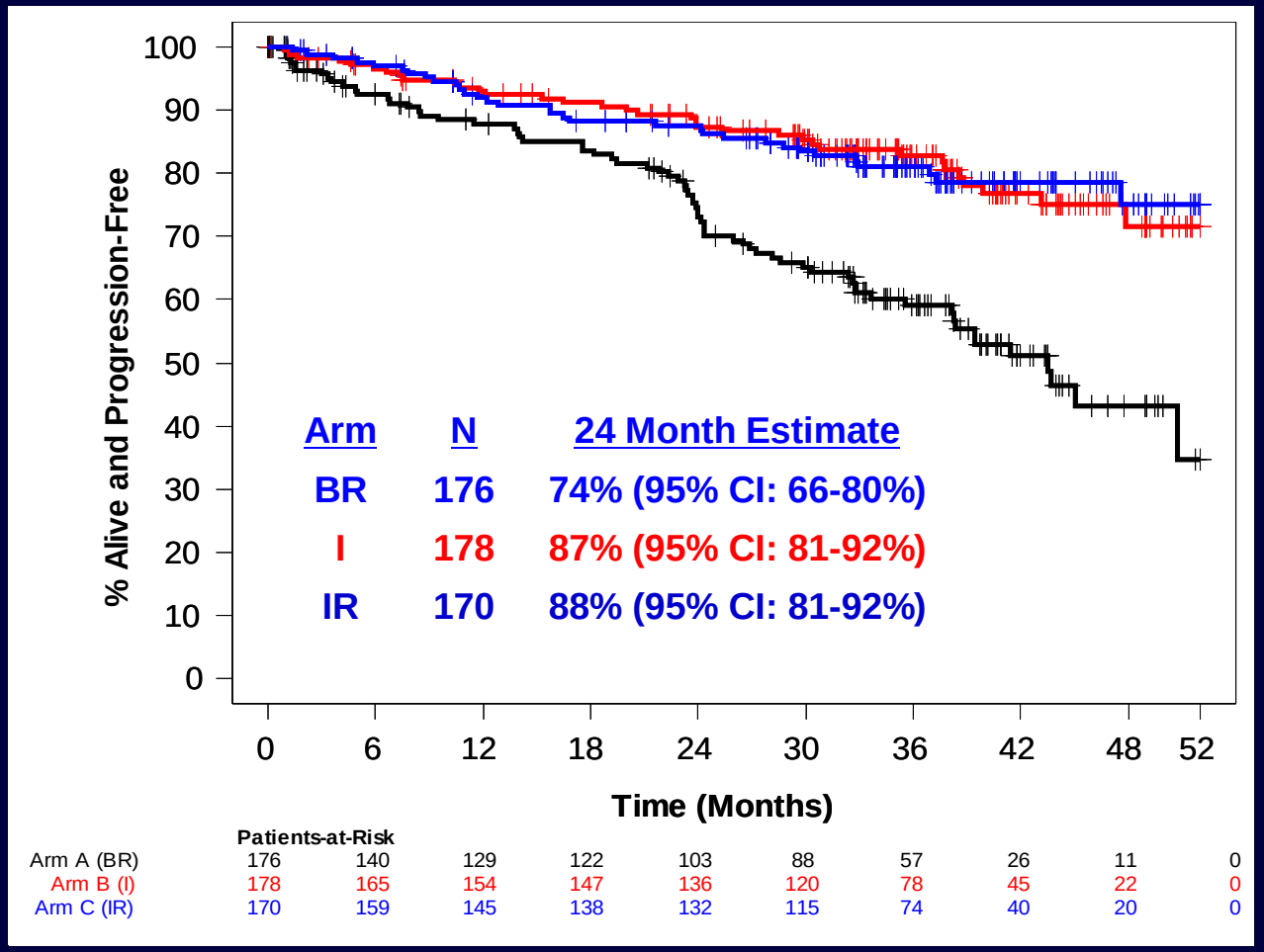
Treatment Schema



Woyach et al. N Engl J Med. 2018 Dec 27;379(26):2517-2528.

Primary Endpoint: Progression Free Survival

Eligible Patient Population



I vs BR:
Hazard Ratio 0.39
95% CI: 0.26-0.58
(1-sided P-value <0.001)

IR vs BR:
Hazard Ratio 0.38
95% CI: 0.25-0.59
(1-sided P-value <0.001)

IR vs I:
Hazard Ratio 1.00
95% CI: 0.62-1.62
(1-sided P-value 0.49)

Woyach et al. N Engl J Med. 2018 Dec 27;379(26):2517-2528.

Abstract 31

Phase 3 Study of Acalabrutinib Combined With Obinutuzumab or Alone vs Obinutuzumab Plus Chlorambucil in Patients With Treatment-Naive Chronic Lymphocytic Leukemia: Results From ELEVATE TN

Jeff P. Sharman, Versha Banerji, Laura Maria Fogliatto, Yair Herishanu, Talha Munir, Renata Walewska, George Follows, Karin Karlsson, Paolo Ghia, Gillian Corbett, Patricia Walker, Miklos Egyed, Wojciech Jurczak, Gilles Salles, Ann Janssens, Florence Cymbalista, William Wierda, Steven Coutre, John M. Pagel, Alan P. Skarbnik, Manali Kamdar, Jennifer A. Woyach, Raquel Izumi, Veerendra Munugalavadla, Priti Patel, Min Hui Wang, Sofia Wong, and John C. Byrd

ClinicalTrials.gov identifier: NCT02475681. This study was sponsored by Acerta Pharma, a member of the AstraZeneca group

ELEVATE TN Study Design (ACE-CL-007)

Treatment-naive CLL (N=535)

Age ≥65 or

<65 years with coexisting conditions:

- CIRS score >6, or
- creatinine clearance <70 mL/min

Stratification

- del(17p), y vs n
- ECOG PS 0-1 vs 2
- Geographic region (N America, W Europe, or other)

RANDOMIZE 1:1:1

Acalabrutinib[a] + Obinutuzumab (G)[b]

[a]100 mg PO BID

[b]1000 mg IV on D1, 2, 8, and 15 of Cycle 2, + D1 of subsequent 28-day cycles for a total of 6 cycles

Acalabrutinib

100 mg PO BID

Obinutuzumab (G)[c] + Chlorambucil[d]

[c]1000 mg IV on D1, 2, 8, and 15 of Cycle 1, + D1 of subsequent 28-day cycles for a total of 6 cycles

[d]0.5 mg/kg PO on D1 + 15 of each 28-day cycle for 6 cycles

Primary endpoint

- PFS (assessed by IRC) Acala-G vs G-Clb

Key secondary endpoints

- PFS acalabrutinib vs G-Clb
- ORR (assessed by IRC and investigator)
- Time to next treatment
- OS
- Safety

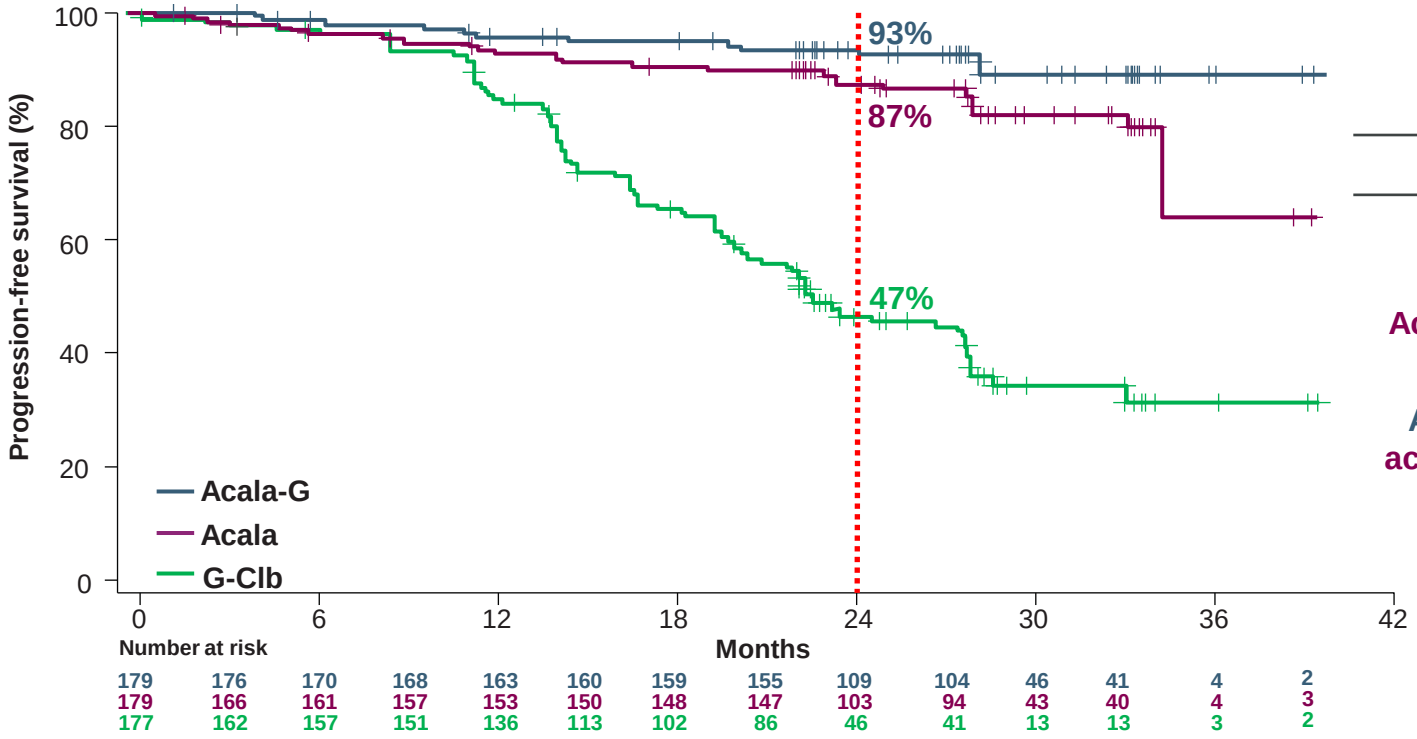
Crossover *from G-Clb to acalabrutinib was allowed after IRC-confirmed progression*

- Interim analysis was planned based on events (after occurrence of ~111 IRC-assessed PFS events in the combination therapy arms) or after 24 months if the required number of events was not met by this time

Acala, acalabrutinib; CIRS, Cumulative Illness Rating Scale; ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; IV, intravenously; OS, overall survival; PO, orally

IRC-Assessed Progression-Free Survival

Median follow-up 28.3 months



Hazard ratio (95% CI)	
Acala-G vs G-Clb	**0.10** (0.06, 0.17) p<0.0001
Acalabrutinib vs G-Clb	**0.20** (0.13, 0.30) p<0.0001
Acala-G vs acalabrutinib[a]	**0.49** (0.26, 0.95)

Kaplan-Meier estimates performed by IRC and all analyses for the intention-to-treat population. No. of events: Acala-G, 14 (7.8%); Acala, 26 (14.5%); G-Clb, 93 (52.5%)

[a]*Post hoc* analysis.

Richter's transformation occurred in: Acala-G n=1, Acala n=5, G-Clb n=1

Events of Clinical Interest for Acalabrutinib

AEs, n (%)	Acala-G N=178		Acalabrutinib N=179		G-Clb N=169	
	Any	Grade ≥3	Any	Grade ≥3	Any	Grade ≥3
Atrial fibrillation	6 (3.4)	1 (0.6)	7 (3.9)	0	1 (0.6)	0
Hypertension	13 (7.3)	5 (2.8)	8 (4.5)	4 (2.2)	6 (3.6)	5 (3.0)
Bleeding	76 (42.7)	3 (1.7)	70 (39.1)	3 (1.7)	20 (11.8)	0
Major bleeding[a]	5 (2.8)[b]	3 (1.7)	3 (1.7)[c]	3 (1.7)	2 (1.2)[d]	0
Infections	123 (69.1)	37 (20.8)	117 (65.4)	25 (14.0)	74 (43.8)	14 (8.3)
Second primary malignancies, excluding NMSC	10 (5.6)[e]	6 (3.4)	5 (2.8)[f]	2 (1.1)	3 (1.8)[g]	2 (1.2)

There were no reported events of ventricular tachyarrhythmias

[a]Defined as any serious or grade ≥3 hemorrhagic event, or any grade hemorrhagic event in the central nervous system. [b]Includes gastric ulcer hemorrhage, gastrointestinal hemorrhage, hematemesis, postprocedural hemorrhage, and subdural hemorrhage. [c]Includes hemarthrosis, postprocedural hematoma, and retinal hemorrhage. [d]Includes subdural hemorrhage and hemoptysis. [e]Includes non-small cell lung cancer (n=2), squamous cell carcinoma (n=2), basosquamous carcinoma, bladder transitional cell carcinoma, breast cancer, gastric cancer stage IV, metastases to bone, prostate cancer, and renal cell carcinoma (all n=1). [f]Includes prostate cancer (n=2), glioblastoma, malignant melanoma in situ, transitional cell carcinoma (all n=1). [g]Includes prostate cancer, acute myelomonocytic leukemia, and lung adenocarcinoma (all n=1)

NMSC, nonmelanoma skin cancer

Ibrutinib leads to impressive PFS in Firstline setting

Indefinite Therapy

Low CR (10% 1-yr, 30% 5-yr)

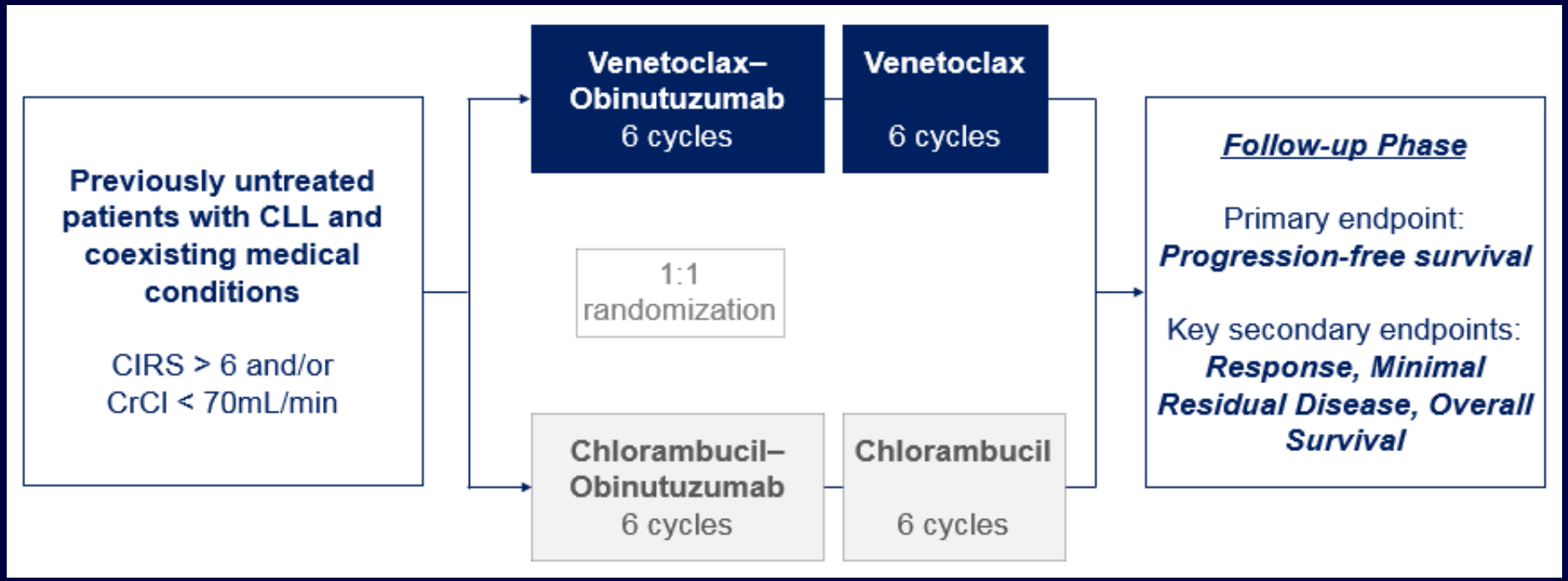
U-MRD Extremely Rare

What else is exciting in firstline therapy for CLL?

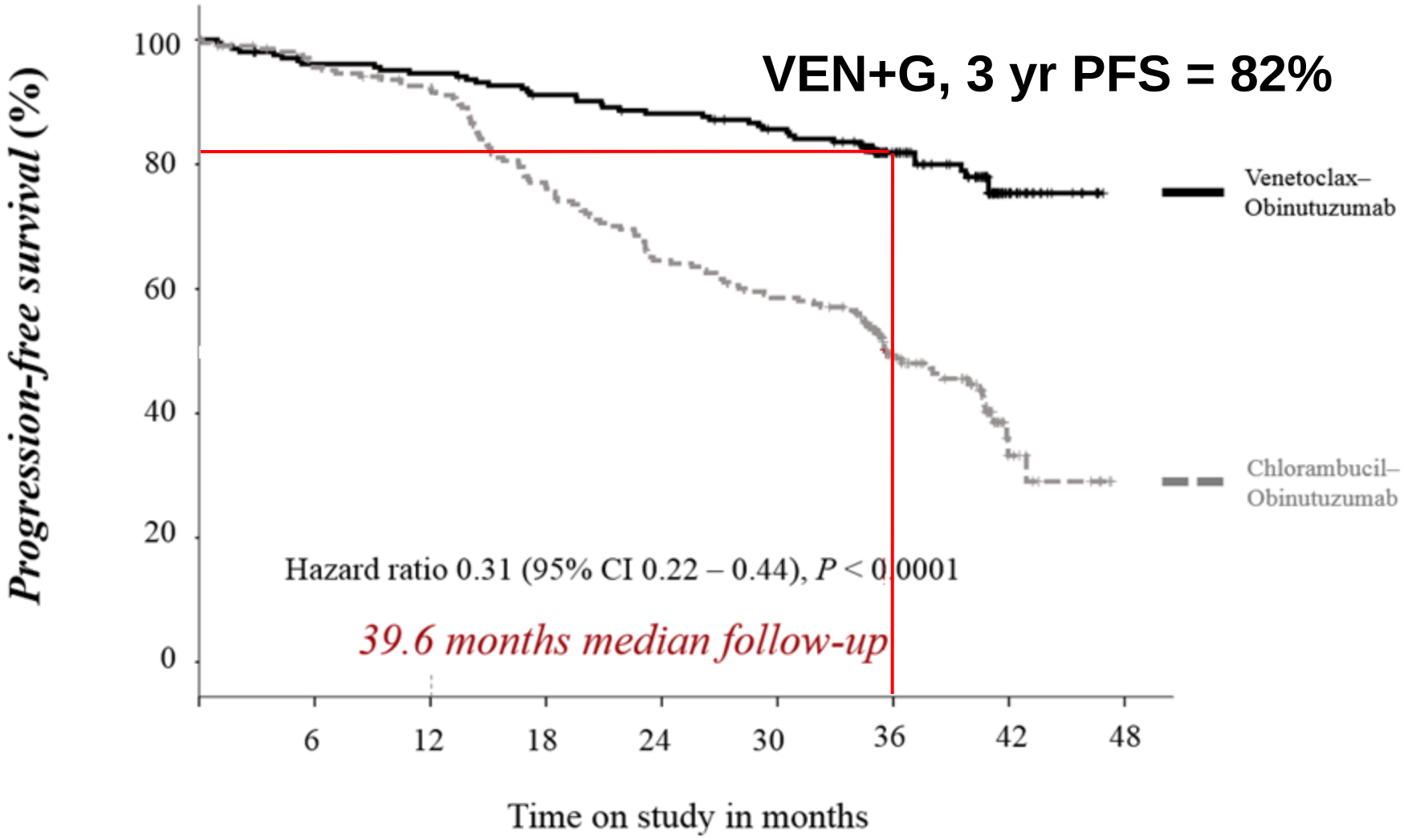
Time Limited Therapies (1-2 yr)

High CR rate / High U-MRD

CLL14: VEN + G vs. Chlorambucil + G



Fischer K et al. NEJM. 2019 Jun 6;380(23):2225-2236.



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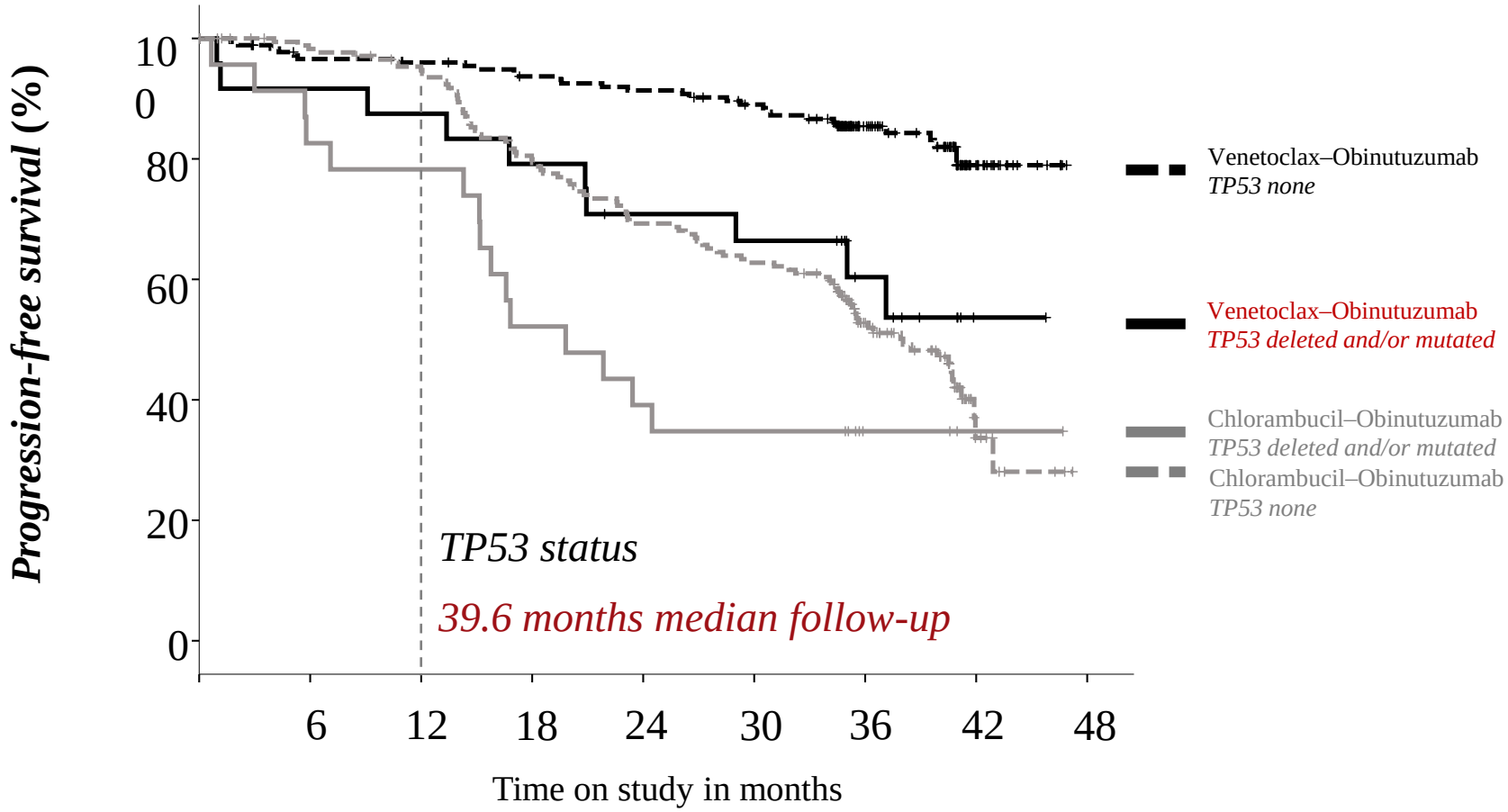


Fischer K et al. NEJM. 2019 Jun 6;380(23):2225-2236.

Undetectable MRD by ASO-PCR	**Venetoclax-Obinutuzumab**	**Chlorambucil-Obinutuzumab**	*P* value
Number of patients, N	**216**	**216**	
Peripheral blood			
Undetectable (<10-4)	**76 %**	**35 %**	**< 0.001**
Undetectable ($<10^{-4}$) in complete response	42 %	14 %	< 0.001
Bone marrow			
Undetectable ($<10^{-4}$)	**57 %**	**17 %**	**< 0.001**
Undetectable ($<10^{-4}$) in complete response	34 %	11 %	< 0.001

By ASO-PCR 3 months after completion of treatment
Concordance BM vs. Blood: 86.8% for both treatment groups

Fischer K et al. NEJM. 2019 Jun 6;380(23):2225-2236.

GRADE 3 OR 4 ADVERSE EVENTS

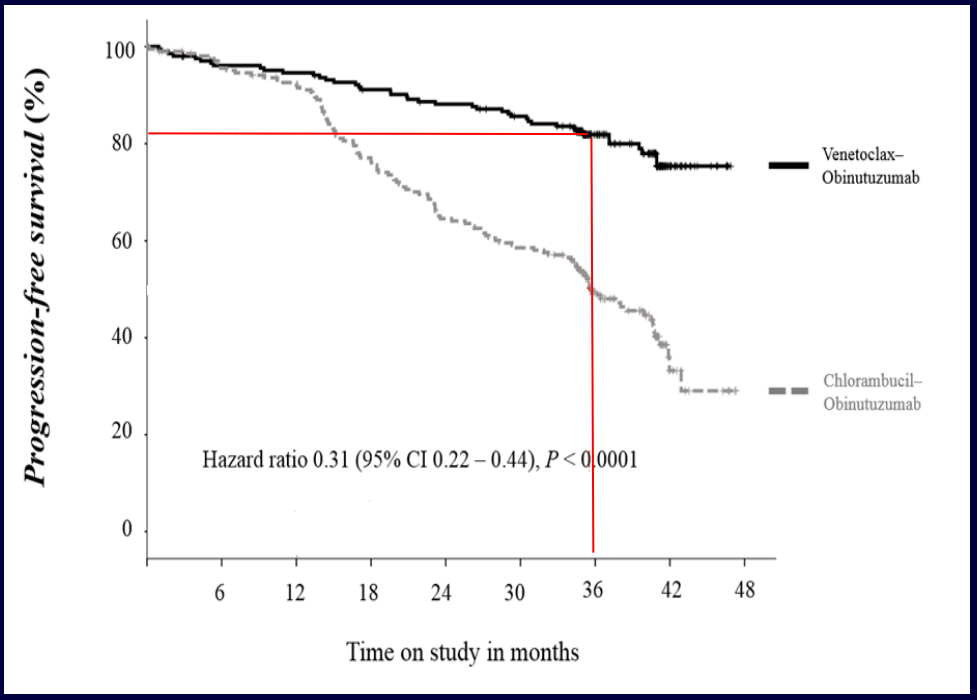
	Venetoclax-Obinutuzumab	Chlorambucil-Obinutuzumab
Number of patients, N	212*	214
Blood and lymphatic system disorders	**60 %**	**55 %**
Neutropenia	**53 %**	48 %
Thrombocytopenia	14 %	15 %
Anemia	8 %	7 %
Febrile neutropenia	5 %	4 %
Injury, poisoning and procedural comp.	12 %	14 %
Infusion-related reaction	9 %	10 %
Infections and infestations	18 %	15 %
Pneumonia	4 %	4 %
Investigations	15 %	11 %
Neutrophil counts decreased	4 %	5 %
Metabolism and nutrition disorders**	12 %	6 %

* Nine patients received obinutuzumab only; ** Two-sided *P* value was 0.02

CLL·14

Fischer K et al. NEJM. 2019 Jun 6;380(23):2225-2236.

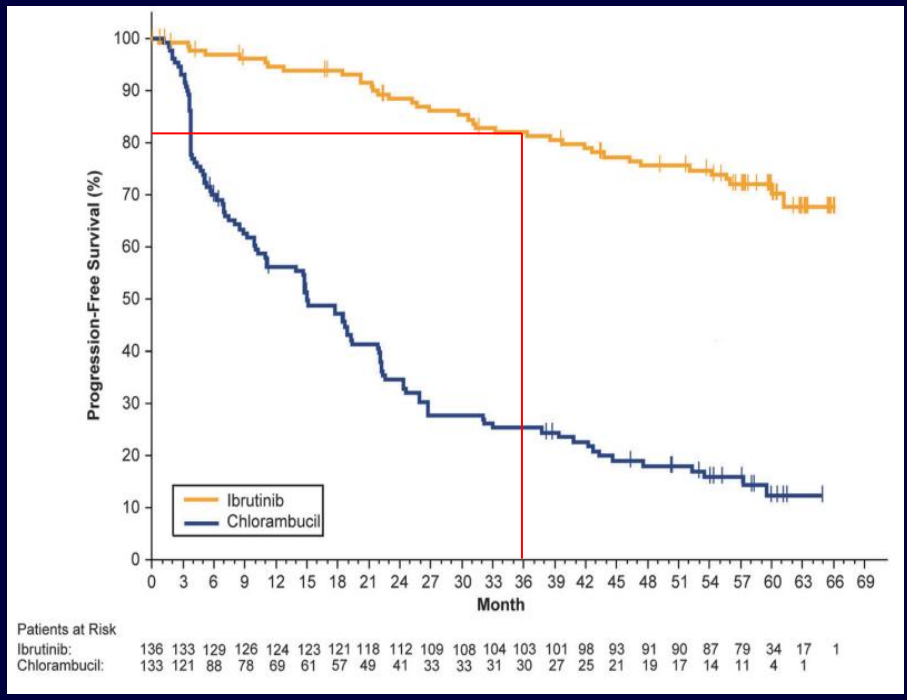
CLL14, VEN + G



Median age 72
IGHV-UM 61%
Del(17p) 9%
CIRS >6 86%

3 yr PFS = 82%

RESONATE-2, Ibr



Median age 73
IGHV-UM 48%
Del(17p) 0%
CIRS >6 31%

3 yr PFS ≈ 82%

Pros and Cons of Available Treatment Approaches

Ibrutinib

- **Pro**
  - Longer follow-up
- **Con**
  - Indefinite duration
  - Low CR/uMRD
  - Atrial fibrillation, bleeding

Acalabrutinib

- **Pro**
  - Reduced off-target effects
- **Con**
  - Shorter follow-up
  - Indefinite duration
  - Low CR/uMRD

Venetoclax + Obinutuzumab

- **Pro**
  - Time-limited duration
  - Higher CR/uMRD
- **Con**
  - Shorter follow-up
  - TLS logistics
  - IV administration of obinutuzumab
  - Neutropenia

BCR vs. BCL2 Inhibitors

	BCR Inhibitor (Ibrutinib)	BCL2 Inhibitor (Venetoclax)
Response	Blood ++ LN +++ Marrow +	Blood +++ LN ++ Marrow +++
Lymphocytosis	+++	-
CR in R/R CLL	10%	20-25%
AE profile	Atrial fibrillation, neutropenia, bleeding	TLS, neutropenia

THE UNIVERSITY OF TEXAS
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CANCER CENTER

Combined Ibrutinib and Venetoclax for First-Line Treatment for Patients with Chronic Lymphocytic Leukemia (CLL)

Nitin Jain, Michael Keating, Philip Thompson, Alessandra Ferrajoli, Jan Burger, Gautam Borthakur, Koichi Takahashi, Zeev Estrov, Nathan Fowler, Tapan Kadia, Marina Konopleva, Yesid Alvarado, Musa Yilmaz, Courtney DiNardo, Prithviraj Bose, Maro Ohanian, Naveen Pemmaraju, Elias Jabbour, Koji Sasaki, Rashmi Kanagal-Shamanna, Keyur Patel, Jeffrey Jorgensen, Sa Wang, Naveen Garg, Xuemei Wang, Katrina Sondermann, Nichole Cruz, Chongjuan Wei, Ana Ayala, William Plunkett, Hagop Kantarjian, Varsha Gandhi, William Wierda

Department of Leukemia, MDACC

ASH 2019, Abstract 34

Ibrutinib and Venetoclax

- Investigator-initiated phase II trial

- Patients with treatment-naïve CLL/SLL with at least one feature:
  - Del(17p) or mutated *TP53*
  - Del(11q)
  - Unmutated *IGHV*
  - Age ≥65 yrs

Treatment Schema

	C1	C2	C3	C4-->27
Ibrutinib	420mg daily	420mg daily	420mg daily	420mg daily
Venetoclax	-	-	-	20mg daily 1 week; 50mg daily 1 week; 100mg daily 1 week; 200mg daily 1 week; 400mg daily continuous

Duration of therapy: <u>24 cycles</u> of combination treatment

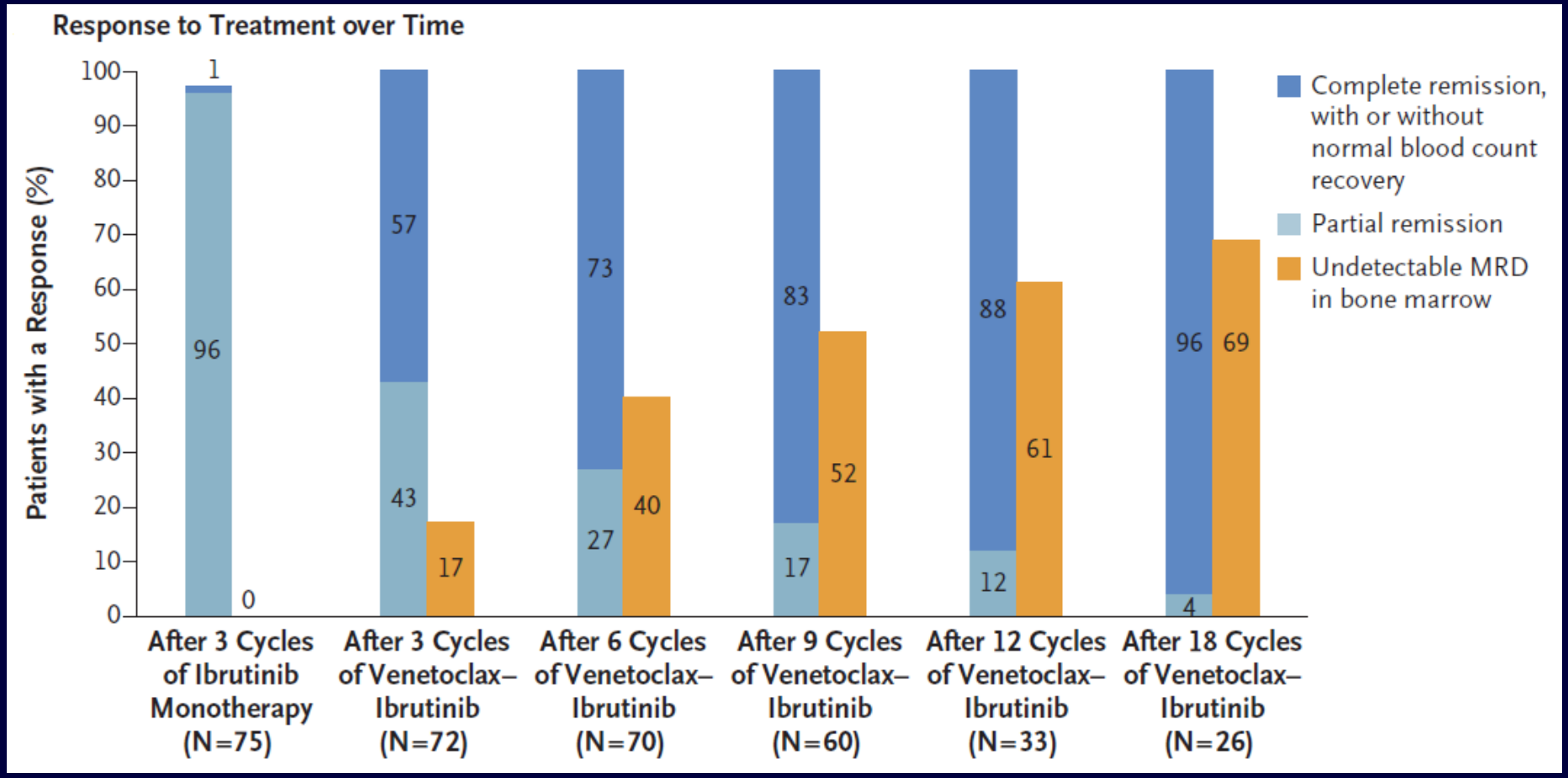
- **If BM MRD+ at 24 cycles, ibrutinib alone continues until PD**

Baseline Characteristics (N=80)

		n (%) or median [range]
Age, years		65 [26-83]
	≥65	43 (54)
	≥70	24 (30)
Gender, M		57 (71)
ALC, K/μL		75.6 [1.14-338]
PLT, K/μL		130 [28-334]
HGB, g/dL		11.6 [7.7-15.8]
B2M, mg/L		3.5 [1.7-13.7]
FISH	Del(17p)	14 (18)
	Del(11q)	20 (25)
	Trisomy 12	17 (21)
	Negative	10 (12)
	Del(13q)	19 (24)
IGHV status (n=76)	Unmutated	63 (83)
Cytogenetics (n=78)	Complex	12 (15)
	Diploid	32 (41)
Mutations (n=79)	*TP53*	11 (14)
	NOTCH1	22 (28)
	SF3B1	18 (23)
	BIRC3	5 (6)

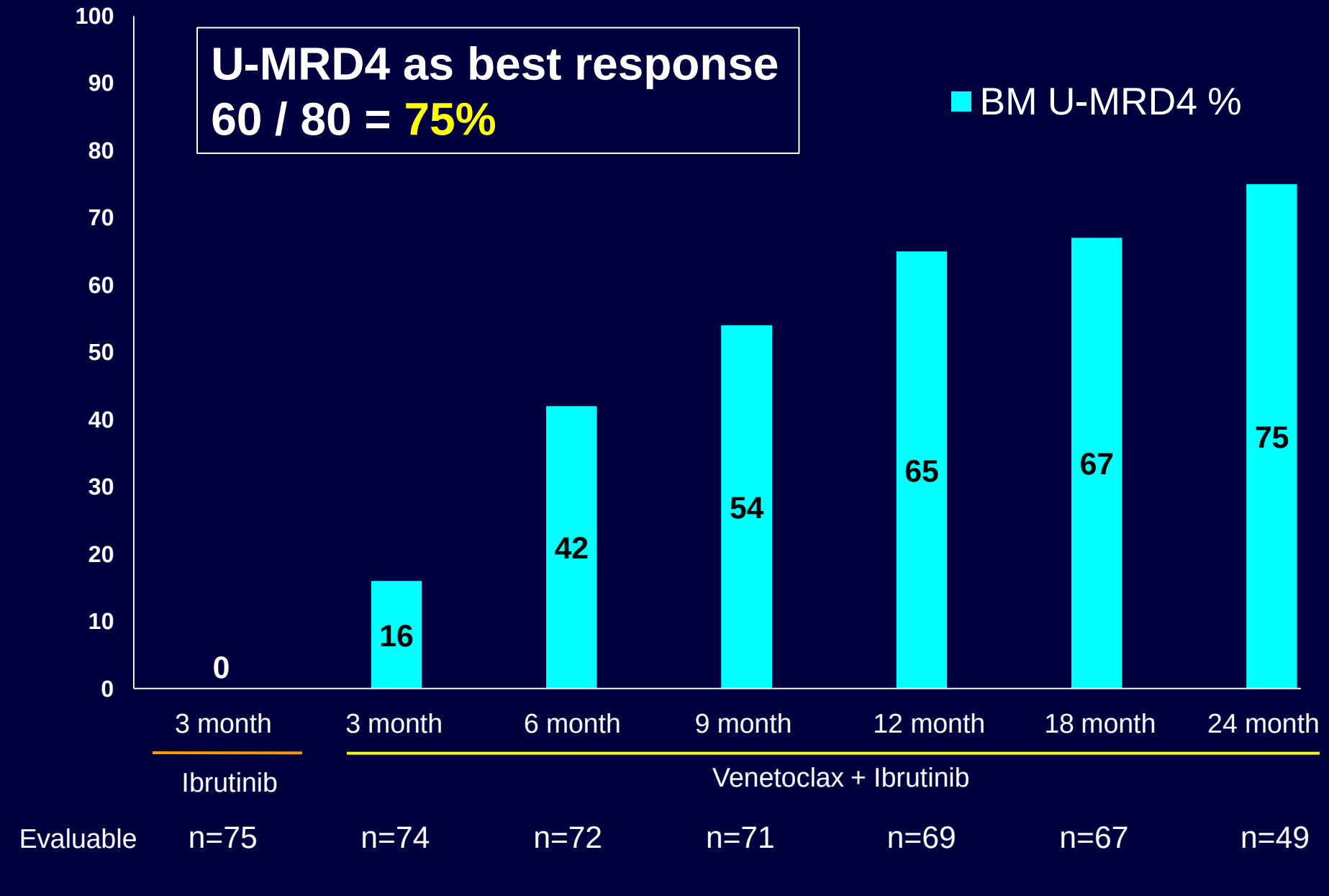
92% pts had either unmutated *IGHV*, *TP53* aberration or del(11q)

VEN +IBR, Responses Improve with Ongoing Therapy



Jain N et al. NEJM. 2019 May 30;380(22):2095-2103.

BM MRD4 Responses at Serial Time-Points

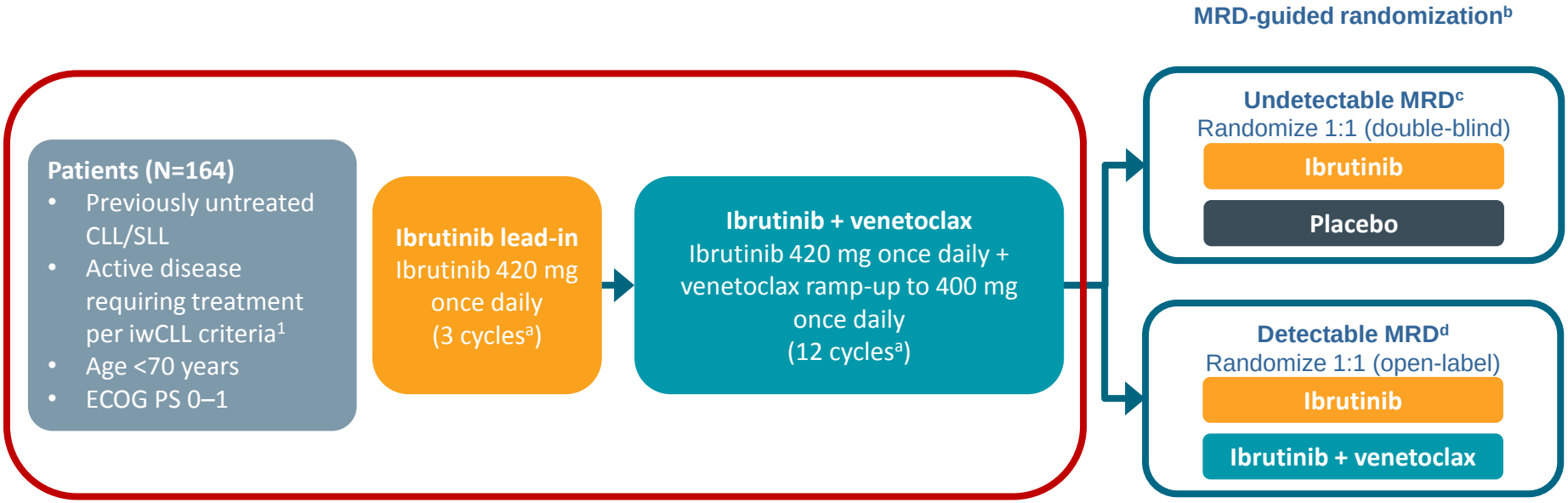


Ibrutinib Plus Venetoclax for First-Line Treatment of Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Results From the MRD Cohort of the Phase 2 CAPTIVATE Study

Constantine S. Tam, MD[1]; Tanya Siddiqi, MD[2]; John N. Allan, MD[3]; Thomas J. Kipps, MD, PhD[4]; Ian W. Flinn, MD, PhD[5]; Bryone J. Kuss, MBBS, PhD, FRACP, FRCPA[6]; Stephen Opat, FRACP, FRCPA, MBBS[7]; Paul M. Barr, MD[8]; Alessandra Tedeschi, MD[9]; Ryan Jacobs, MD[10]; Xavier C. Badoux, MBBS, FRACP, FRCPA[11]; Paolo Ghia, MD, PhD[12]; Juthamas Sukbuntherng, PhD[13]; Ahmed Hamed Salem, PhD, FCP[14]; Kristin Russell, BS[13]; Karl Eckert, BA[13]; Cathy Zhou, MS[13]; Joi Ninomoto, PharmD[13]; Danelle F. James, MD, MAS[13]; William G. Wierda, MD, PhD[15]

[1]Peter MacCallum Cancer Centre, St. Vincent's Hospital and University of Melbourne, Melbourne, VIC, Australia; [2]City of Hope National Medical Center, Duarte, CA, USA; [3]Weill Cornell Medicine, New York, NY, USA; [4]UCSD Moores Cancer Center, San Diego, CA, USA; [5]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [6]Flinders Medical Centre, Bedford Park, SA, Australia; [7]Monash University, Clayton, VIC, Australia; [8]Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, USA; [9]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [10]Levine Cancer Institute, Charlotte, NC, USA; [11]Ministry of Health, St. George Hospital, Kogarah, NSW, Australia; [12]Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy; [13]Pharmacyclics LLC, an AbbVie Company, Sunnyvale, CA, USA; [14]AbbVie, North Chicago, IL, USA; [15]Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX, USA.

CAPTIVATE-MRD Cohort: Study Design



- Results presented for prerandomization phase of the CAPTIVATE-MRD cohort (N=164) with 12 cycles of ibrutinib + venetoclax prior to MRD-guided randomization
- Time-limited therapy with 12 cycles of ibrutinib + venetoclax to be evaluated in separate fixed-duration cohort (N=159)

ECOG PS, Eastern Cooperative Oncology Group performance status; iwCLL, International Workshop on Chronic Lymphocytic Leukemia.
[a]1 cycle = 28 days; patients may have received 1 additional cycle while awaiting confirmation of undetectable MRD for randomization. [b]Stratified by *IGHV* mutation status. [c]Confirmed as having undetectable MRD ($<10^{-4}$ by 8-color flow cytometry) serially over at least 3 cycles in PB, and undetectable MRD in both PB and BM. [d]Defined as having detectable MRD or undetectable MRD not confirmed serially or not confirmed in both PB and BM.
1. Hallek M et al. *Blood*. 2008;111:5446-5456.

ASH 2019, CAPTIVATE-MRD; Tam et al.

High Rates of Undetectable MRD Achieved in PB and BM With Up to 12 Cycles of Combination

	Peripheral Blood n=163	Bone Marrow[a] n=155
Undetectable MRD in evaluable patients[b] (95% CI)	**75%** (67-81)	**72%** (64-79)

- In patients with undetectable MRD at cycle 16 in peripheral blood with matched bone marrow samples, 93% had undetectable MRD in both peripheral blood and bone marrow
- In the intention-to-treat population (N=164), undetectable MRD was achieved in 74% of patients in peripheral blood and in 68% of patients in bone marrow with up to 12 cycles of combination

[a]BM MRD assessment was scheduled after completion of 12 cycles of combination treatment.
[b]Patients with undetectable MRD at any postbaseline assessment; evaluable patients are those who had at least 1 MRD sample taken postbaseline.

ASH 2019, CAPTIVATE-MRD; Tam et al.

Selected First-line Phase III Trials

Trial	N	Randomization arms			
		Control	Investigational Arm		
UK FLAIR	1576	FCR	Ibr + R	Ibr	Ven + Ibr
CLL13	920	FCR / BR	Ven + G	Ven + R	Ven + Ibr + G
ACE-CL-311	780	FCR / BR	Acala + Ven	Acala + Ven + G	
CLL GLOW	200	Clb + G	Ven + Ibr		
EA9161	720	Ibr + G	Ibr + G + Ven		
A041702	454	Ibr + G	Ibr + G + Ven		
CLL17	?	Ibr	Ven + G	Ven + Ibr	

Unanswered Questions?

- What's the ideal firstline combination?
  - BCL2i + CD20 mAb
  - BCL2i + BTKi
  - BCL2i + BTKi + CD20 mAb
- Ideal treatment duration (can we stop Rx?)
- R/R CLL
  - Reversible BTKi (LOXO-305, SNS-062, ARQ-531)
  - CAR-T

CLL AND COVID-19

Management of CLL Patient

- No CLL specific data available at this time
- Given immunosuppression, we assume pts with CLL at high risk of severe complications
- Prevention: ‘Social Distancing’
  - Follow State/Country specific guidelines

CLL Patient: Not on active therapy

- Include
  - Early stage CLL on clinical observation
  - Patient with prior therapy (not on active Rx currently)
- Avoid ‘routine’ clinic / hospital visits
- Phone call / Telemedicine

CLL Patient: About to start therapy

- Include
  - Patients with CLL, about to initiate first or subsequent line of therapy
- Consider deferring therapy, if possible for at least 3 months
- If unavoidable, prefer non-myelosuppressive therapy

CLL Patient: Patients on active therapy

- Include
  - Patients with CLL receiving chemo-immunotherapy or targeted therapies
- Continue therapy for these patients
- Try to limit hospital / clinic visits

CLL Patient:
Patients on are COVID-19+

- For most pts, should be able to hold CLL treatment temporarily
- Follow the institutional guidelines for management of COVID+ pts
- May consider IVIG, if low (not to Rx COVID-19, but to prevent secondary infections)

Thank you!

njain@mdanderson.org

@NitinJainMD

(+1) 713-745-6080