Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 4 — Chronic Lymphocytic Leukemia

Wednesday, February 24, 2021
5:00 PM – 6:00 PM ET

Faculty

Paul M Barr, MD
Matthew S Davids, MD, MMSc
Kerry Rogers, MD

Moderator

Neil Love, MD

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Faculty

Paul M Barr, MD
Medical Director, Clinical Trials Office
Professor of Medicine
James P Wilmot Cancer Institute
University of Rochester Medical Center
Rochester, New York

Kerry Rogers, MD
Assistant Professor in the Division of Hematology
The Ohio State University
Columbus, Ohio

Matthew S Davids, MD, MMSc
Associate Professor of Medicine
Harvard Medical School
Director of Clinical Research, Division of Lymphoma
Dana-Farber Cancer Institute
Boston, Massachusetts

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Commercial Support

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Dr Love — Disclosures

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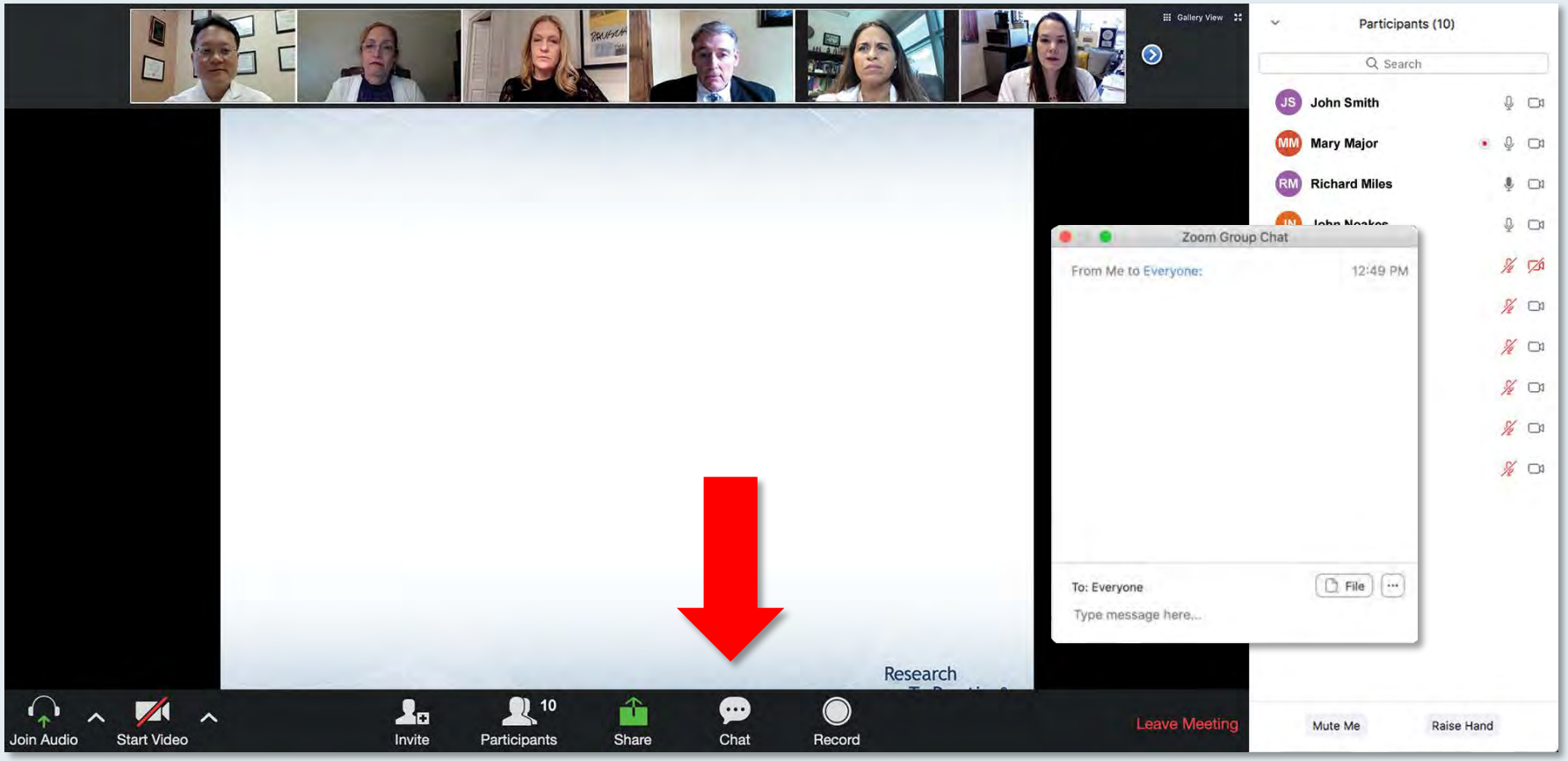

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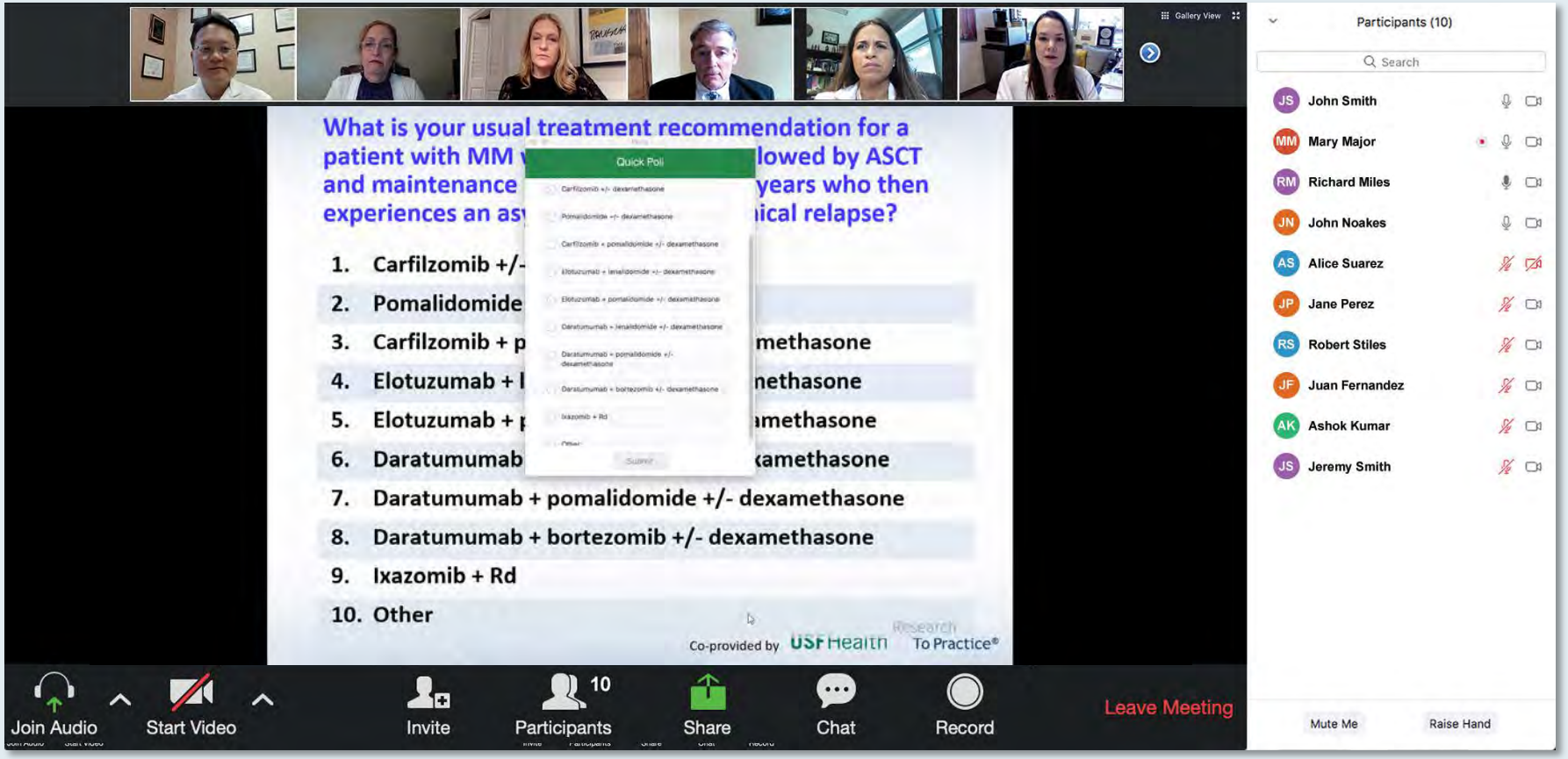

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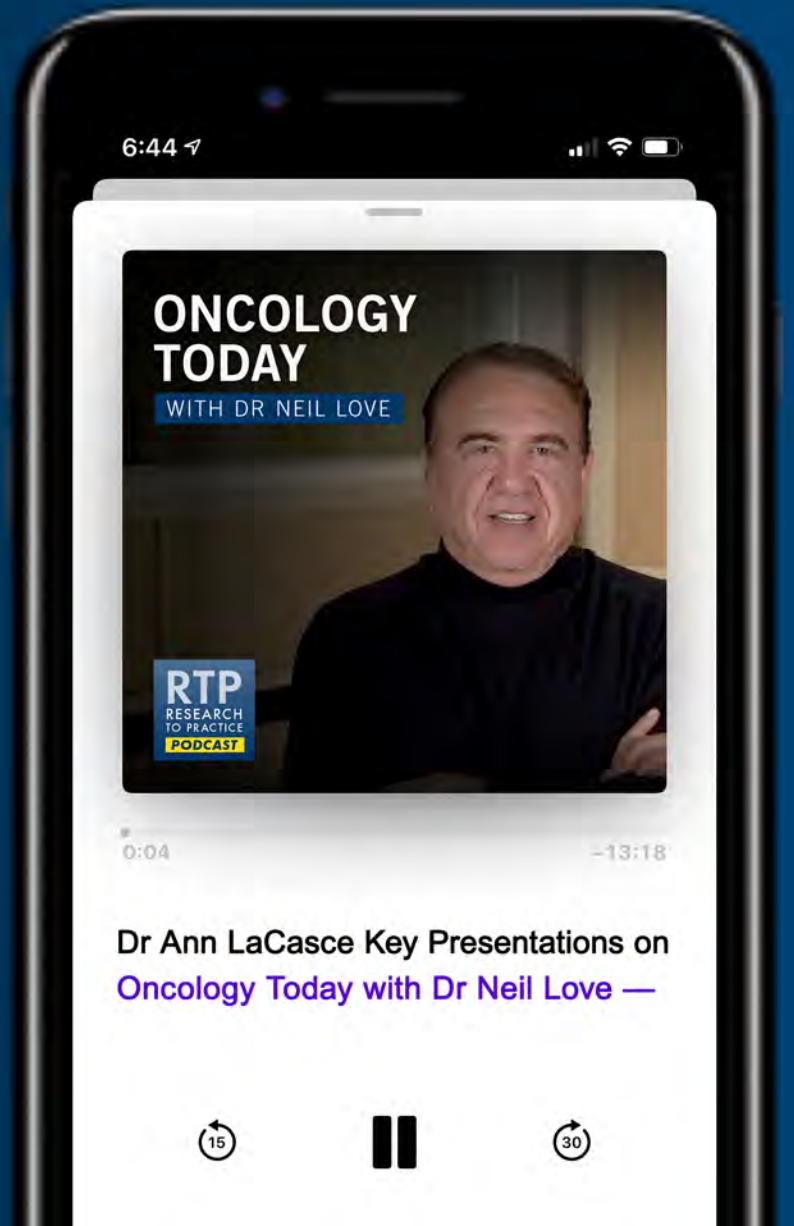

Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Prostate Cancer (Part 1 of a 3-Part Series)

Thursday, February 25, 2021
5:00 PM – 6:30 PM ET

Faculty

Tanya B Dorff, MD
Fred Saad, MD
A Oliver Sartor, MD
Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Renal Cell Carcinoma (Part 2 of a 3-Part Series)

Monday, March 1, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas E Hutson, DO, PharmD
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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Meet The Professor
Management of Ovarian Cancer

Tuesday, March 2, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas J Herzog, MD

Moderator

Neil Love, MD

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Meet The Professor
Management of Multiple Myeloma

Wednesday, March 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Morie A Gertz, MD, MACP

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Urothelial Bladder Carcinoma (Part 3 of a 3-Part Series)

Thursday, March 4, 2021
5:00 PM – 6:15 PM ET

Faculty

Arjun Balar, MD
Elisabeth I Heath, MD
Jonathan E Rosenberg, MD

Moderator

Neil Love, MD

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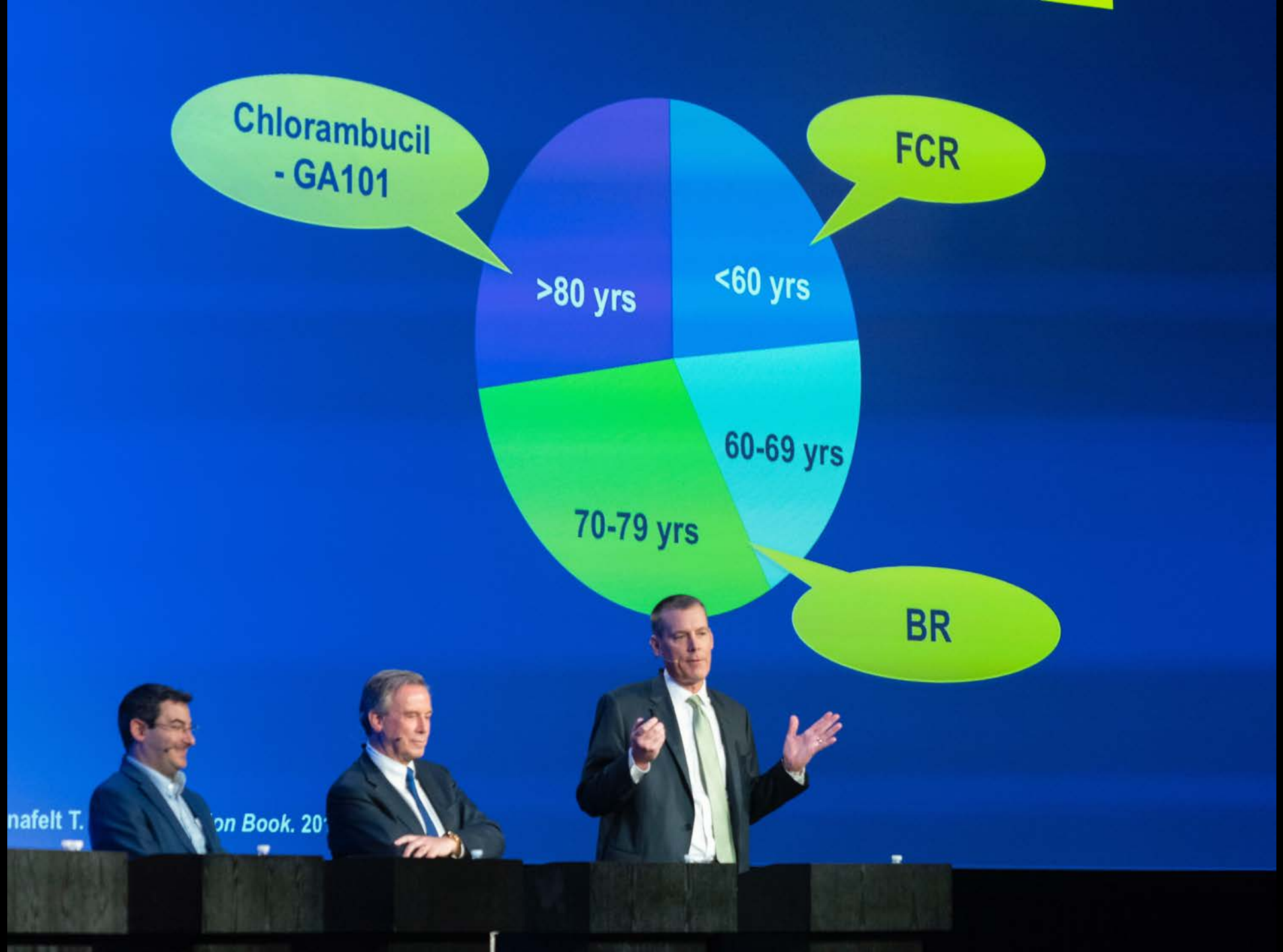
Neil Love, MD
Fac
ad S Kahl, M
Nastou
Sehn,
DELL


Jeremy Abram , MD
Bruce D Ches MD
Prof John G MD, DSc,

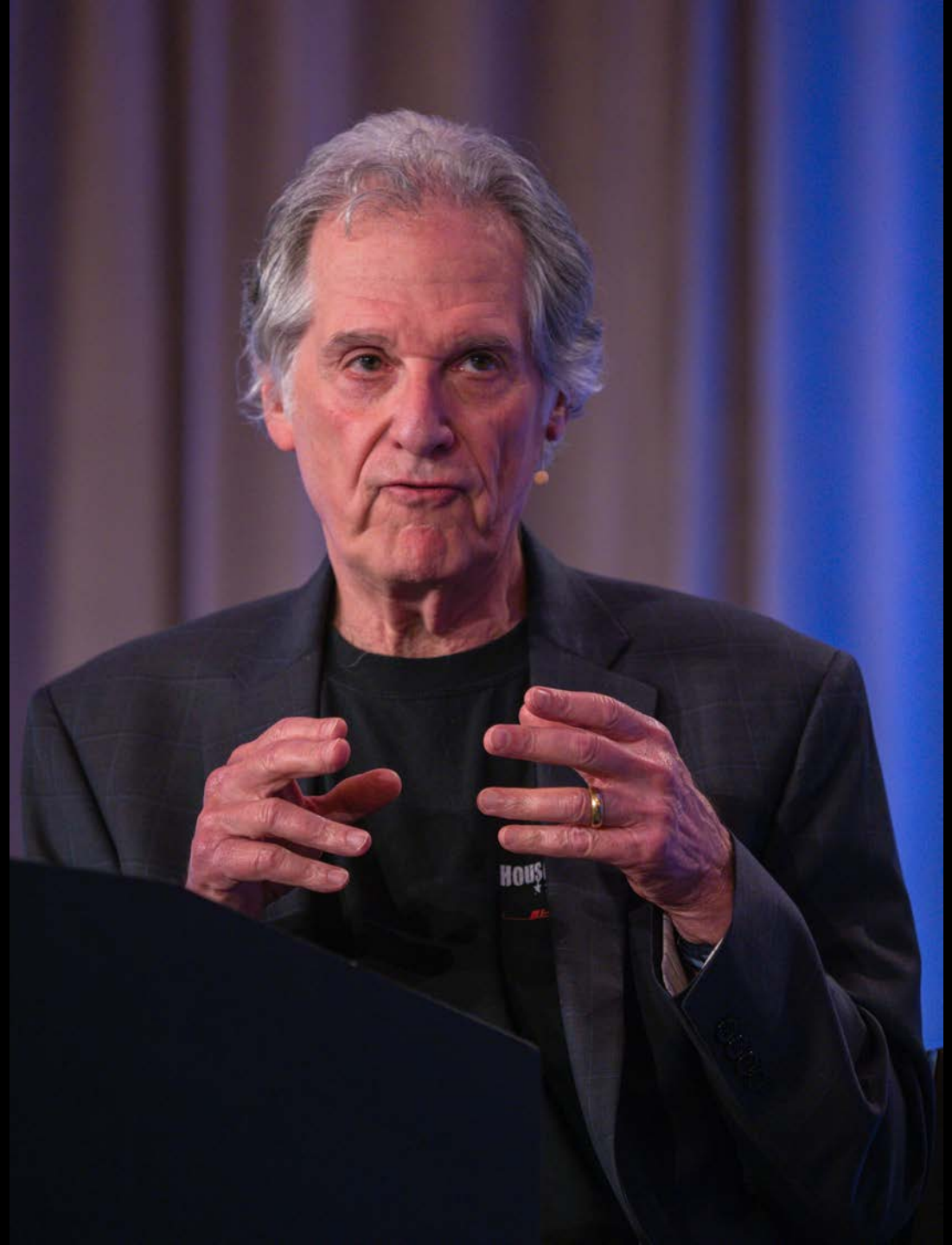

Acalabruti obinutuzumal
Obinutuzu + chlorambuc
Ven tuzumab


Biopsy of
lveme


Chlorambucil - GA101
FCR
>80 yrs
<60 yrs
60-69 yrs
70-79 yrs
BR

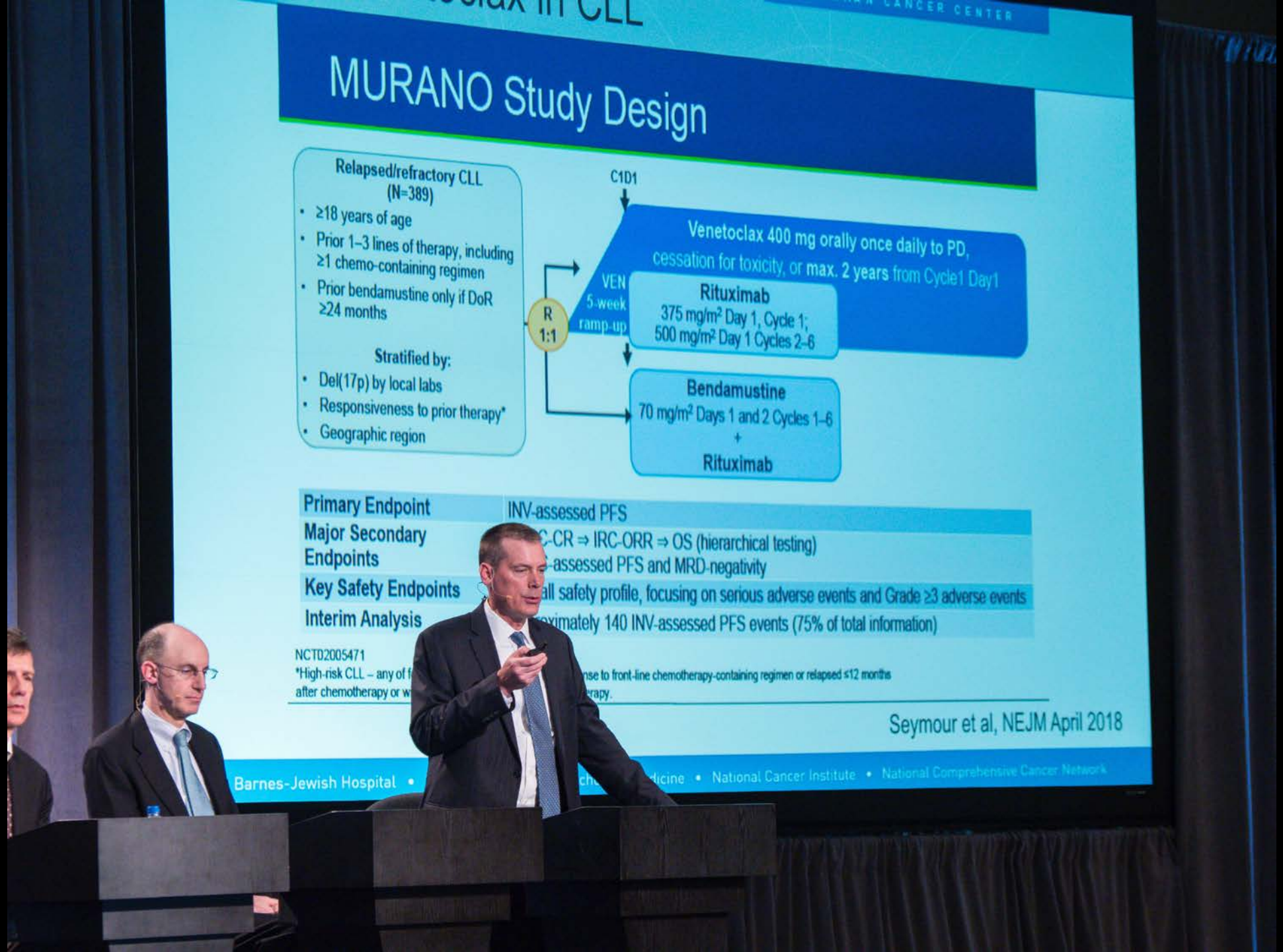

CLL patient requiring frontline Rx
1. 17p del/p53 mutation
– Ibrutinib or VO
• Would you stop V after 12 months?
2. IgVH unmutated (any age)
– VO or ibrutinib
3. IgVH mutated
– young and fit (<65)
• VO or ibrutinib
• Consider FCR
– age 65-80
• VO or ibrutinib
• Consider BR
– older > 80
• VO or ibrutinib
• Consider chlor uzumab


What is your usual preferred initial regi
mutated CLL without del(17p) or TP53
FCR
BR
Ibrutinib
Ibrutinib + rituximab
Ibrutinib + obinutuzumab
Acalabrutinib
Acalabrutinib + obinutuzumab
+ chlorambucil
+ obinutuzumab




Have you or would you order an NMO assay to inform the decision regarding
autoimmune after induction treatment?


Random National Survey of 100 General Medical Oncologists (October 2018)
Median Number of Patients in Your Practice
Breast Cancer
Number of Patients
Lung Cancer
100
Colorectal Cancer
58
Pancreatic Cancer
50
Gastric Cancer
12
8
14


MURANO Study Design
Relapsed/refractory CLL (N=389)
≥18 years of age
Prior 1–3 lines of therapy, including ≥1 chemo-containing regimen
Prior bendamustine only if DoR ≥24 months
Stratified by:
Del(17p) by local labs
Responsiveness to prior therapy*
Geographic region
R 1:1
C1D1
VEN 5-week ramp-up
Venetoclax 400 mg orally once daily to PD, cessation for toxicity, or max. 2 years from Cycle1 Day1
Rituximab
375 mg/m² Day 1, Cycle 1;
500 mg/m² Day 1 Cycles 2–6
Bendamustine
70 mg/m² Days 1 and 2 Cycles 1–6
+
Rituximab
Primary Endpoint
INV-assessed PFS
Major Secondary Endpoints
-CR ⇒ IRC-ORR ⇒ OS (hierarchical testing)
-assessed PFS and MRD-negativity
Key Safety Endpoints
ll safety profile, focusing on serious adverse events and Grade ≥3 adverse events
Interim Analysis
ximately 140 INV-assessed PFS events (75% of total information)
NCT02005471
*High-risk CL – any of f
nse to front-line chemotherapy-containing regimen or relapsed ≤12 months
after chemotherapy or w
rapy.
Seymour et al, NEJM April 2018
Barnes-Jewish Hospital •
dicine • National Cancer Institute • National Comprehensive Cancer Network


Rajni Sinha, MD
Rajni Sinha, MD


What initial treatment would you recommend for the 27-year-old patient in the previous scenario?
ABVD
14%
PET-adapted ABVD
33%
Brentuximab vedotin + AVD
25%
AVD
1%
BEACOPP
26%
Other chemotherapy
0%
1%
DELL


Case presentation: Dr Johl
63-year-old man with HL
• Presented with supraclavicular adenopathy, eczema and pruritus of the skin
• Core biopsy of neck lymph node: HL, nodular sclerosing, classical type
• PET/CT: Hypermetabolic lymphadenopathy above and below hemidiaphragms; splenomegaly with hypermetabolic splenic mass; hypermetabolic osseous lesions and hepatic mass
• Bone marrow biopsy: Normal
Case presentation: Dr Johl
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Optimal Selection of New
Molecules in the Treatment of
Chronic Lymphocytic Leukemia in
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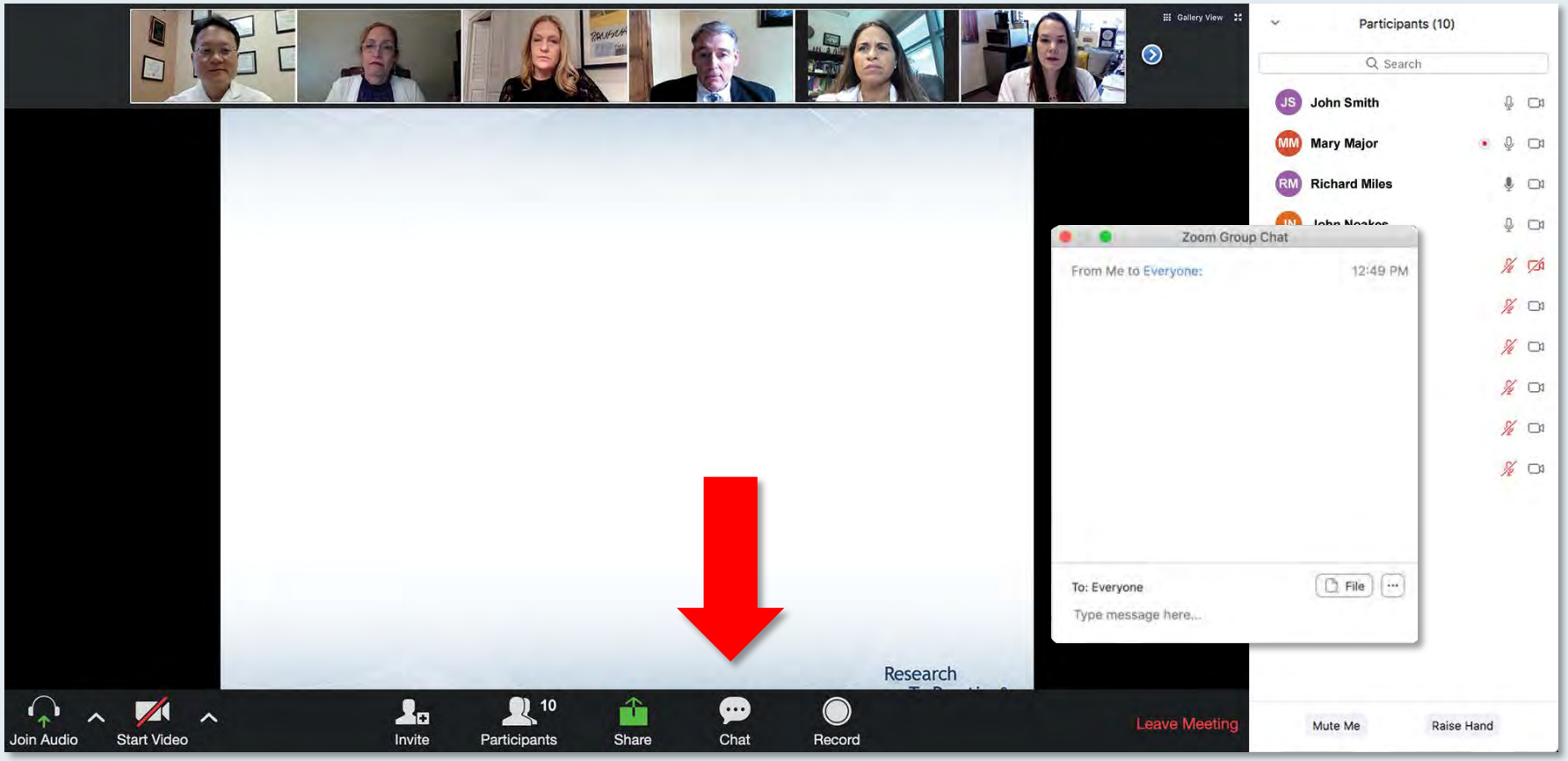

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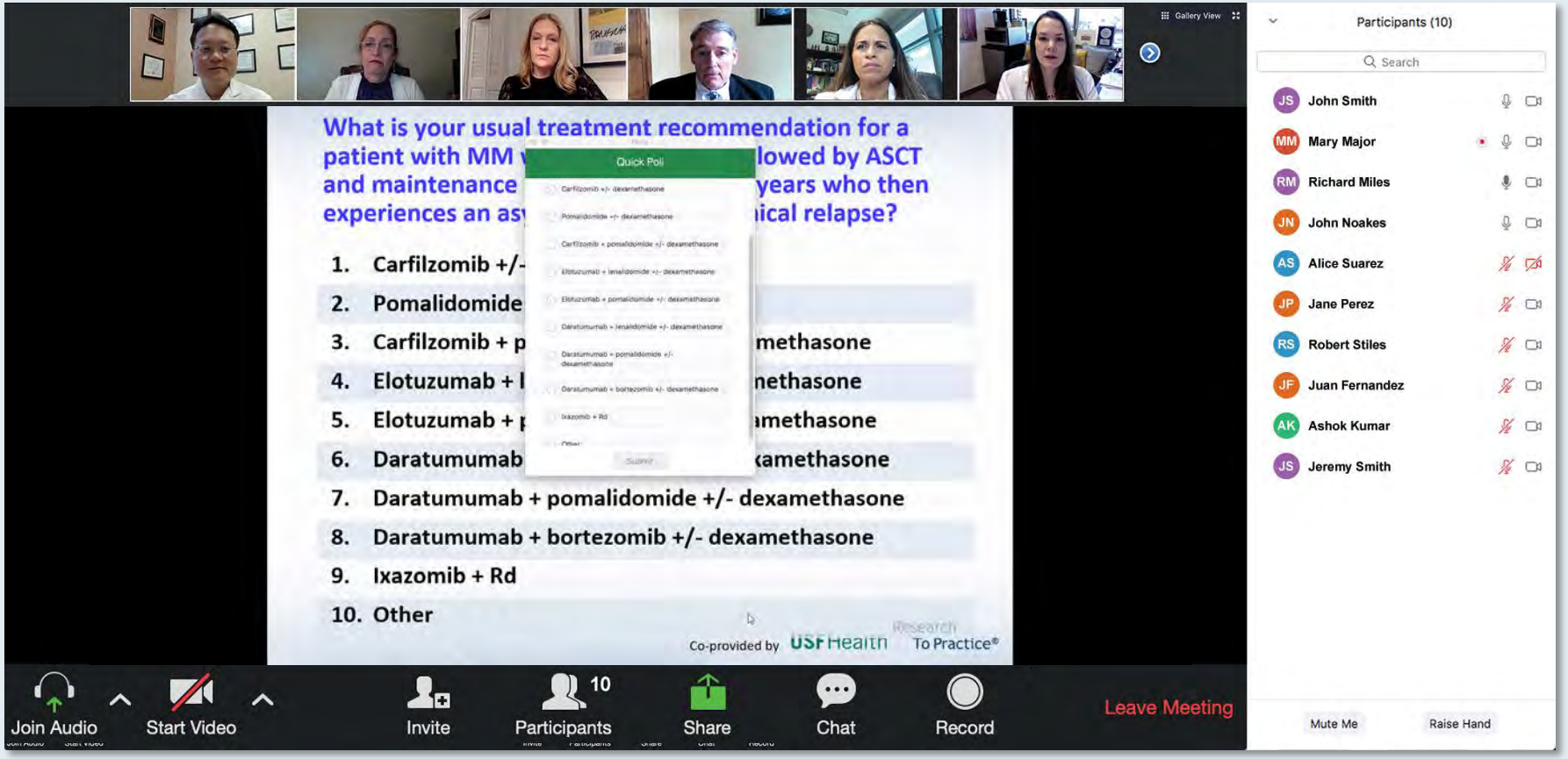

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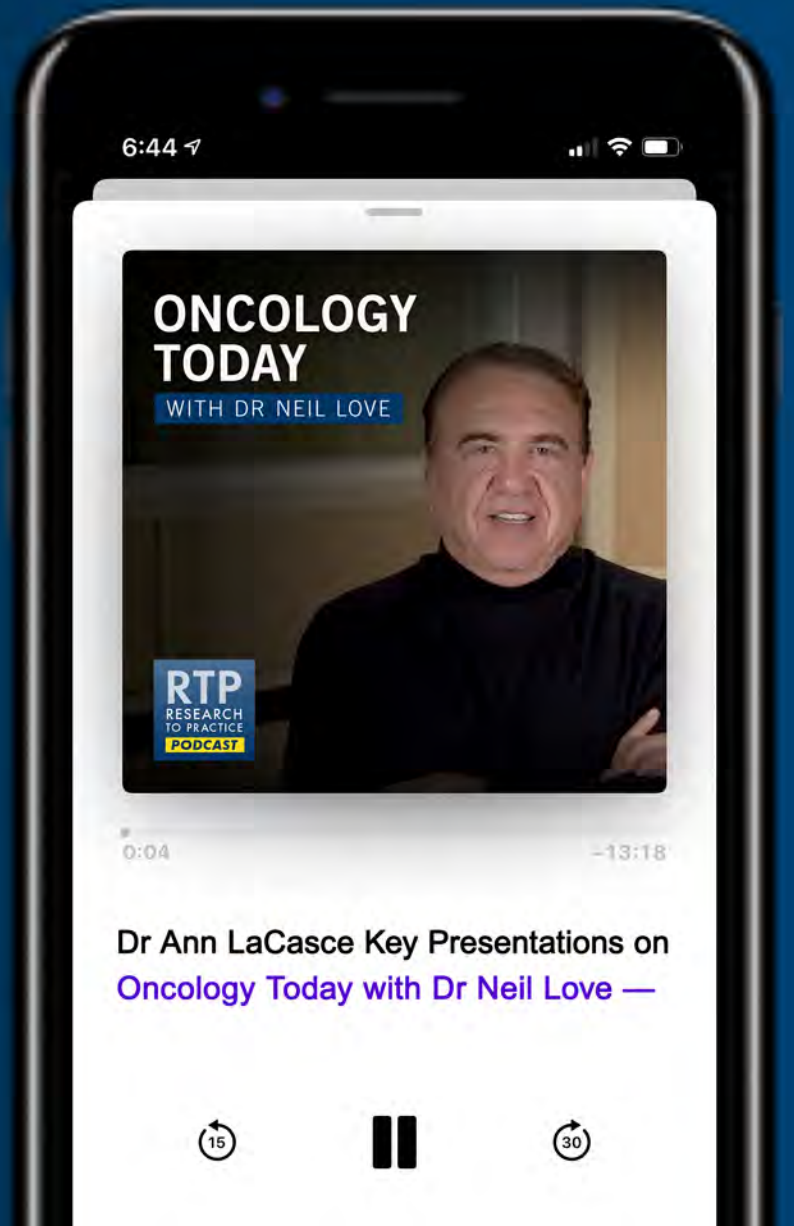

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Agenda

Module 1: BTK Inhibitors

- ASCEND, RESONATE-2, iLLUMINATE, BRUIN trials

Module 2: Bcl-2 Inhibitors

- MURANO, TAP CLARITY, CAPTIVATE, ACE-CL-003 trials

Module 3: Novel Strategies – U2 Regimen (Umbralisib/Ublituximab), CAR T-Cell Therapy

- UNITY-CLL, TRANSCEND CLL 004 trials

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Acalabrutinib Met Primary Efficacy Endpoint in Head-to-Head Trial Against Ibrutinib for Chronic Lymphocytic Leukemia

Press Release — January 25, 2021

"Positive high-level results from the ELEVATE-RR Phase III trial showed acalabrutinib met the primary endpoint demonstrating non-inferior progression-free survival (PFS) for adults with previously treated, high-risk chronic lymphocytic leukemia (CLL) compared to ibrutinib.

The trial also met a key secondary endpoint for safety, showing patients treated with acalabrutinib had statistically significantly lower incidence of atrial fibrillation compared to patients treated with ibrutinib. Atrial fibrillation is an irregular heart rate that can increase the risk of stroke, heart failure and other heart-related complications. Further hierarchical testing revealed no difference for Grade 3 or higher infections or Richter's transformation. There was a descriptive trend for numerically favorable overall survival. Overall, the safety and tolerability of acalabrutinib were consistent with the profile seen in the broader acalabrutinib clinical development program.

ELEVATE-RR is the first Phase III trial to compare two Bruton's tyrosine kinase (BTK) inhibitors in patients with CLL, the most common type of leukemia in adults."

https://www.astrazeneca.com/media-centre/press-releases/2021/calquence-met-primary-endpoint-against-ibrutinib.html

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Abstract 3140

Acalabrutinib vs Idelalisib plus Rituximab or Bendamustine plus Rituximab in Relapsed/Refractory Chronic Lymphocytic Leukemia: ASCEND Final Results

Paolo Ghia,[1] Andrzej Pluta,[2] Malgorzata Wach,[3] Daniel Lysak,[4] Tomas Kozak,[5] Martin Simkovic,[6] Iryna Kraychok,[7] Arpad Illes,[8] Javier de la Serna,[9] Sean Dolan,[10] Philip Campbell,[11] Gerardo Musuraca,[12] Abraham Jacob,[13] Eric J. Avery,[14] Jae Hoon Lee,[15] Denise Wang,[16] Priti Patel,[16] Wojciech Jurczak[17]

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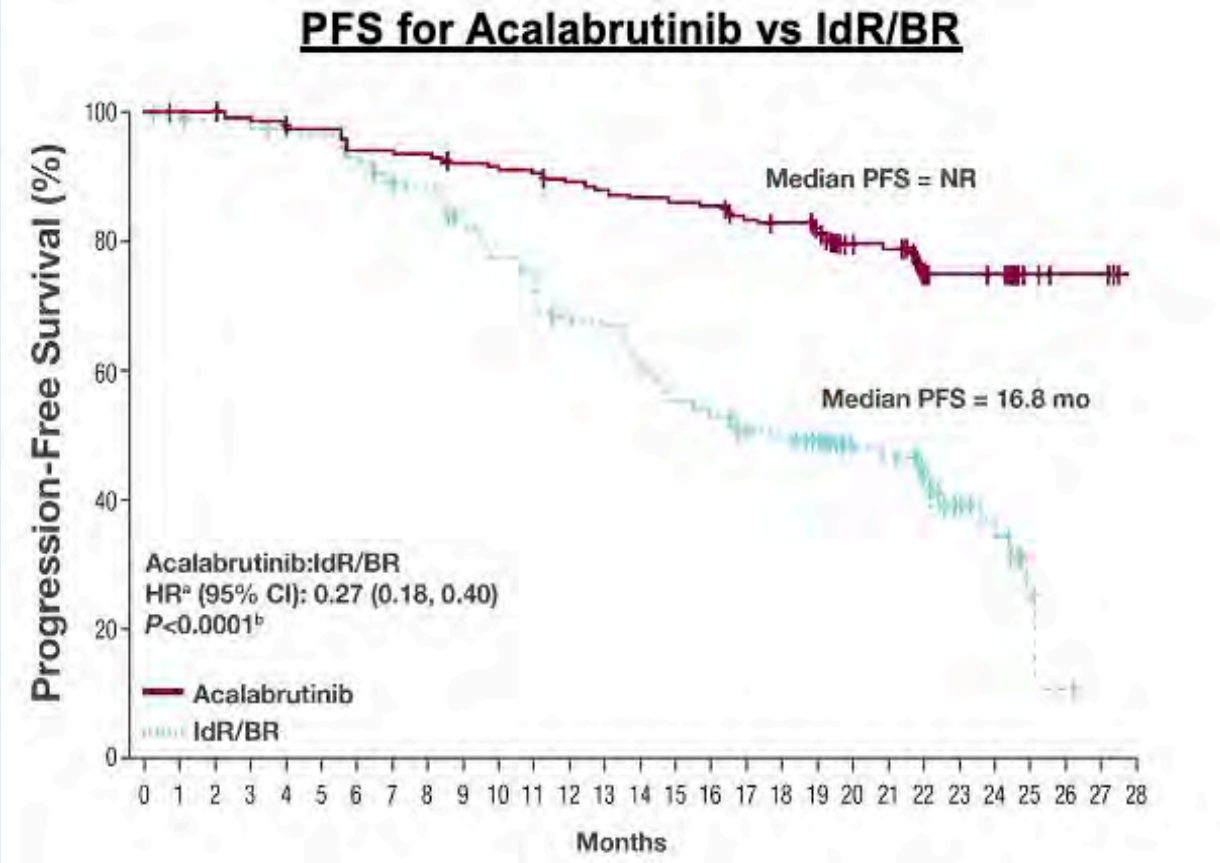
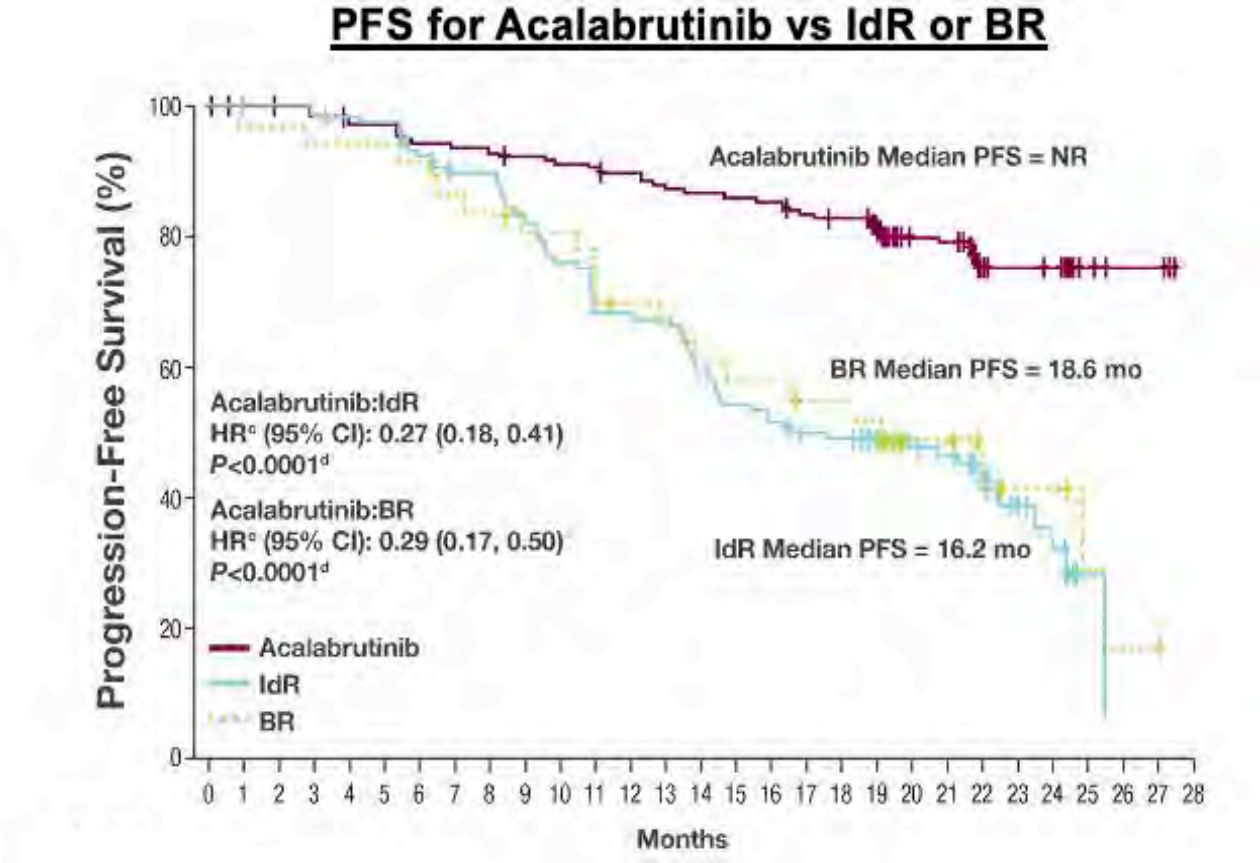
ASCEND Final Analysis: Progression-Free Survival





Ghia P et al. ASH 2020;Abstract 3140.

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Abstract 3146

Pooled Analysis of Cardiovascular Events From Clinical Trials Evaluating Acalabrutinib Monotherapy in Patients With Chronic Lymphocytic Leukemia (CLL)

Jennifer R. Brown,[1] John C. Byrd,[2] Paolo Ghia,[3] Jeff P. Sharman,[4] Peter Hillmen,[5] Deborah M. Stephens,[6] Clare Sun,[7] Wojciech Jurczak,[8] John M. Pagel,[9] Alessandra Ferrajoli,[10] Priti Patel,[11] Marshall Baek,[11] Tamara Lezhava,[11] Nataliya Kuptsova-Clarkson,[11] Javid Moslehi,[12] Richard R. Furman[13]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [3]Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy; [4]Willamette Valley Cancer Institute/US Oncology, Eugene, OR, USA; [5]St. James's University Hospital, Leeds, United Kingdom; [6]University of Utah Huntsman Cancer Institute, Salt Lake City, UT, USA; [7]National Heart, Lung, and Blood Institute, Bethesda, MD, USA; [8]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [9]Swedish Cancer Institute, Seattle, WA, USA; [10]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [11]Acerta Pharma, South San Francisco, CA, USA; [12]Vanderbilt University, Nashville, TN, USA; [13]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY, USA

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Pooled Analysis: Incidence of Cardiac Adverse Events with Acalabrutinib Monotherapy

Event	All Patients (N=782)	
	Any Grade	Grade ≥3[c]
Any cardiac AE,[a] n (%)[b], [number of events]	129 (17), [199]	37 (5), [51]
Most common cardiac AEs (preferred terms; occurring in ≥4 patients), n (%), [number of events]		
Atrial fibrillation	34 (4), [44]	10 (1), [11]
Palpitations	23 (3), [27]	0
Tachycardia	17 (2), [18]	0
Sinus tachycardia	11 (1), [13]	1 (0.1), [1]
Angina pectoris	10 (1), [11]	2 (0.3), [2]
Bradycardia	9 (1), [10]	2 (0.3), [2]
Cardiac failure	6 (0.8), [6]	3 (0.4), [3]
Acute myocardial infarction	5 (0.7), [6]	5 (0.7), [6]
Atrial flutter	4 (0.5), [4]	1 (0.1), [1]
Supraventricular tachycardia	4 (0.5), [4]	1 (0.1), [1]

- Among the 37 patients with grade ≥3 cardiac AEs, 18 (49%) were continuing acalabrutinib at data cutoff
  - 6 patients (16%) had discontinued acalabrutinib due to grade ≥3 cardiac AEs (acute myocardial infarction [n=2], cardiac failure congestive [n=2], cardiac failure [n=1], cardiac tamponade [n=1]), 4 patients (11%) to other AEs, 5 (14%) to PD, 3 (8%) to death, and 1 (3%) to other reasons
- Among 51 grade ≥3 cardiac events (G3, n=37; G4, n=12; G5, n=2[d]):
  - 16 (31%) led to dose delay and 6 (12%) led to acalabrutinib discontinuation
  - 36 (71%) were managed with concomitant meds; 43 (84%) resolved[e]

Brown JR et al. ASH 2020;Abstract 3146.

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Outcomes of First-Line Ibrutinib in Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma and High-Risk Genomic Features with up to 6.5 Years of Follow-Up: Integrated Analysis of Two Phase 3 Studies (RESONATE-2 and iLLUMINATE)

Burger JA et al.

ASH 2020;Abstract 2220.

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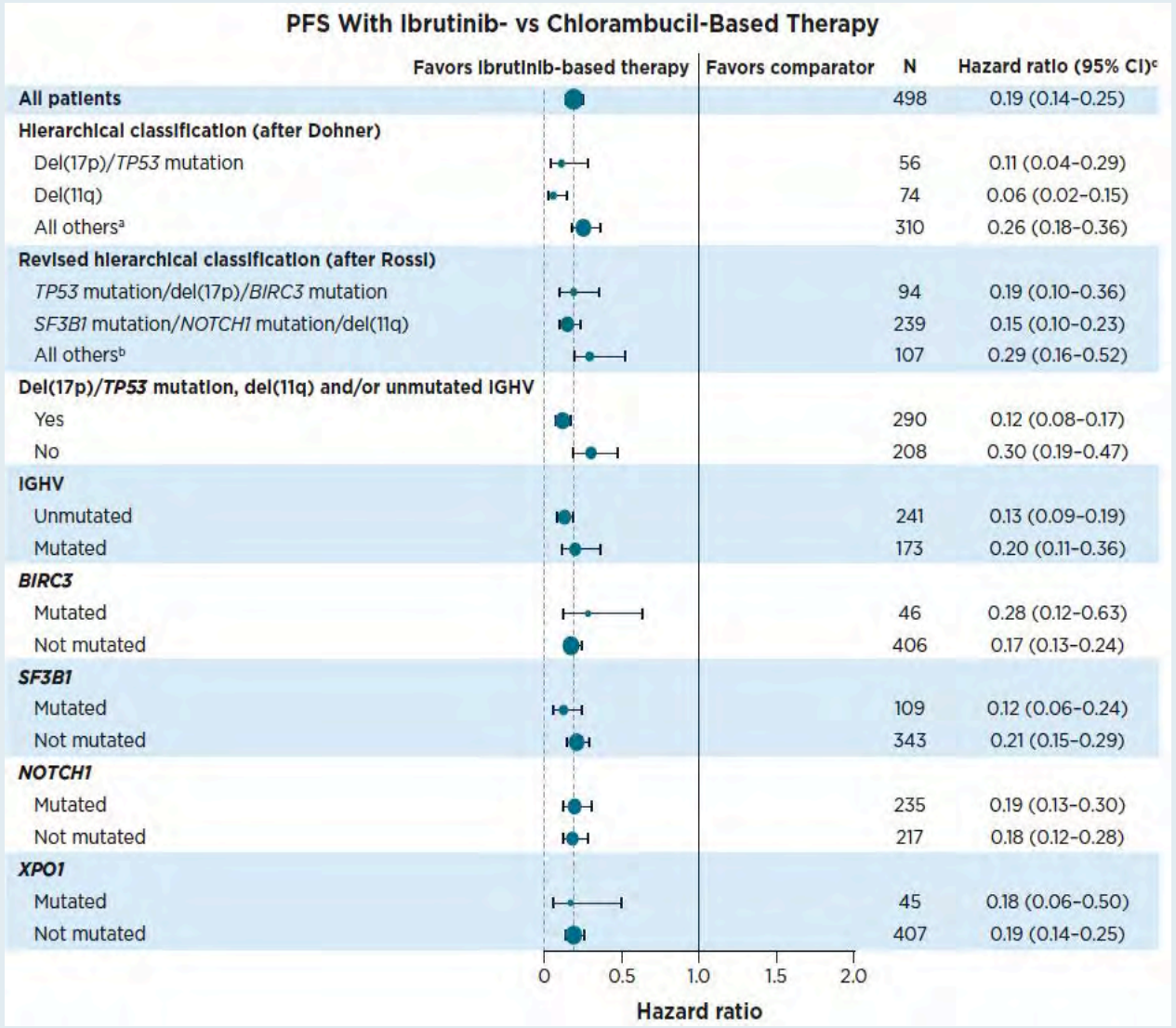
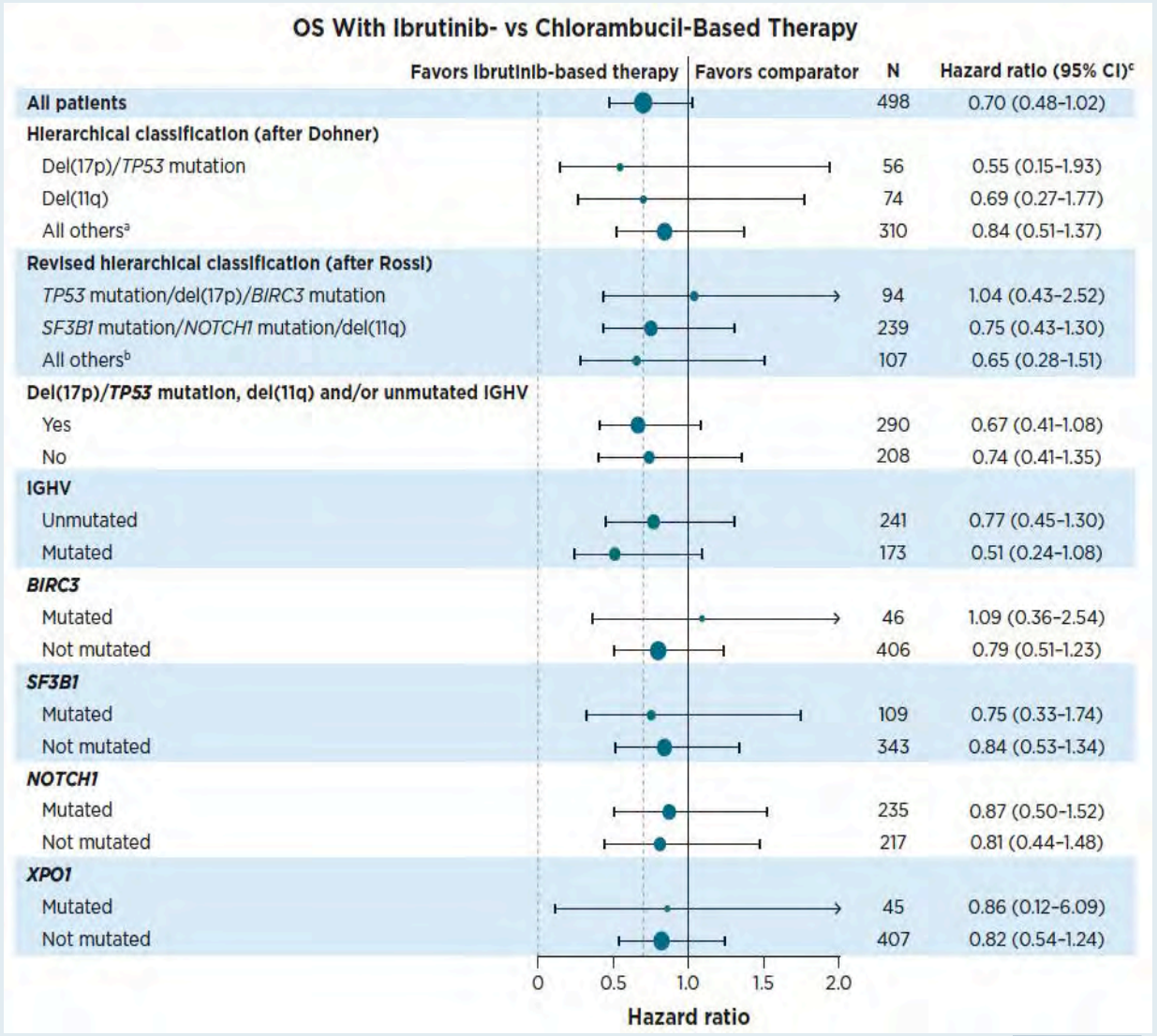
Integrated Analysis of RESONATE-2 and iLLUMINATE: Survival with Ibrutinib- versus Chlorambucil-Based Therapy by Specified Genomic Risk Features





Burger JA et al. ASH 2020;Abstract 2220.

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LOXO-305, A Next Generation, Highly Selective, Non-Covalent BTK Inhibitor In Previously Treated CLL/SLL: Results From The Phase 1/2 BRUIN Study

Anthony R. Mato[1], John M. Pagel[2], Catherine C. Coombs[3], Nirav N. Shah[4], Nicole Lamanna[5], Ewa Lech-Maranda[6], Toby A. Eyre[7], Jennifer A. Woyach[8], William G. Wierda[9], Chan Y. Cheah[10], Lindsey Roeker[1], Manish R. Patel[11], Bita Fakhri[12], Minal A. Barve[13], Constantine S. Tam[14], David Lewis[15], James N. Gerson[16], Alvaro Alencar[17], Justin Taylor[17], Omar Abdel-Wahab[1], Paolo Ghia[18], Stephen J. Schuster[16], Jessica Chen[19], Binoj Nair[20], Donald E. Tsai[20], Nora C. Ku[20], Matthew S. Davids[21], Jennifer R. Brown[21], Wojciech Jurczak[22]

Abstract 542

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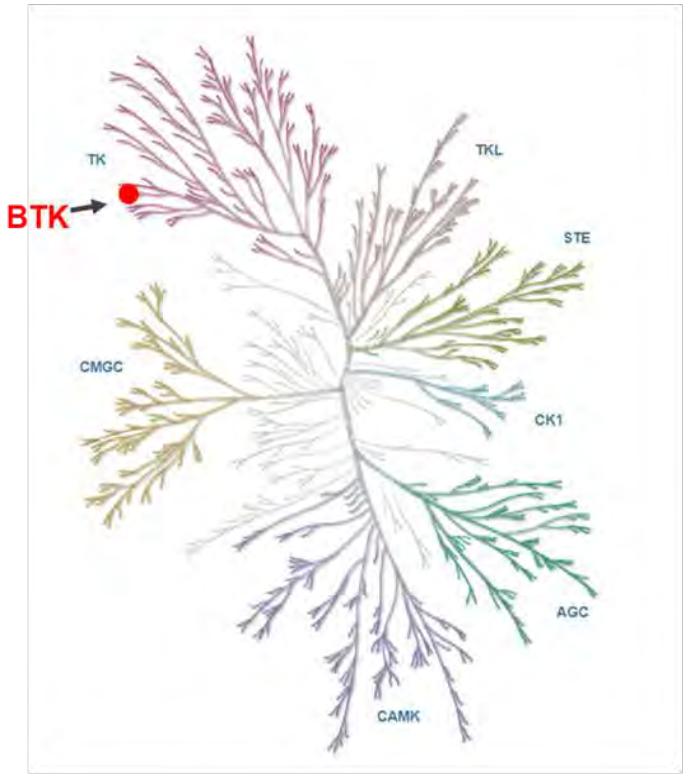
LOXO-305 is a Highly Potent and Selective Non-Covalent BTK Inhibitor

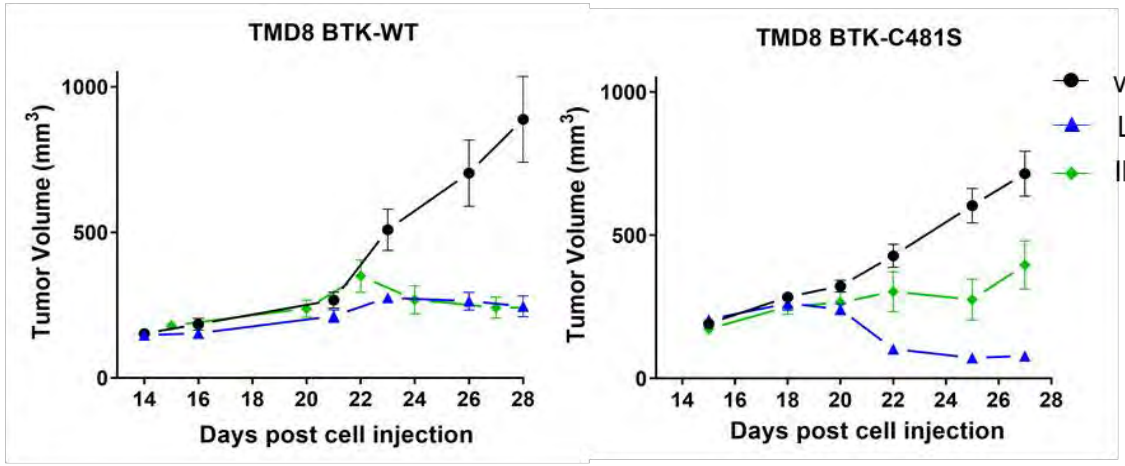
Kinome selectivity

Highly selective for BTK



Xenograft models

In vivo activity similarly efficacious as ibrutinib in WT; superior in C481S



- Nanomolar potency against WT & C481-mutant BTK in cell and enzyme assays[1,2]
- >300-fold selectivity for BTK vs 370 other kinases[1]
- Due to reversible binding mode, BTK inhibition not impacted by intrinsic rate of BTK turnover[1]
- Favorable pharmacologic properties allow sustained BTK inhibition throughout dosing interval[1]

BID, twice-daily; BTK, Bruton tyrosine kinase. Illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com). [1]Brandhuber et al. *Clin. Lymphoma Myeloma Leuk.* 2018;18:S216. [2]Mato et al. *Blood.* 2019:134 (Suppl 1):501.

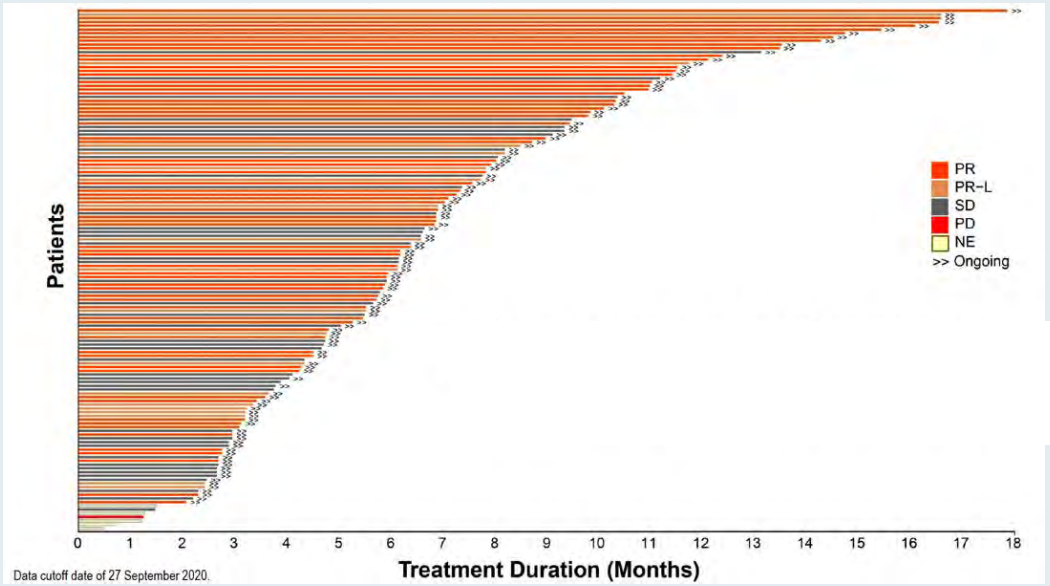
Mato AR et al. ASH 2020;Abstract 542.

BRUIN: Efficacy

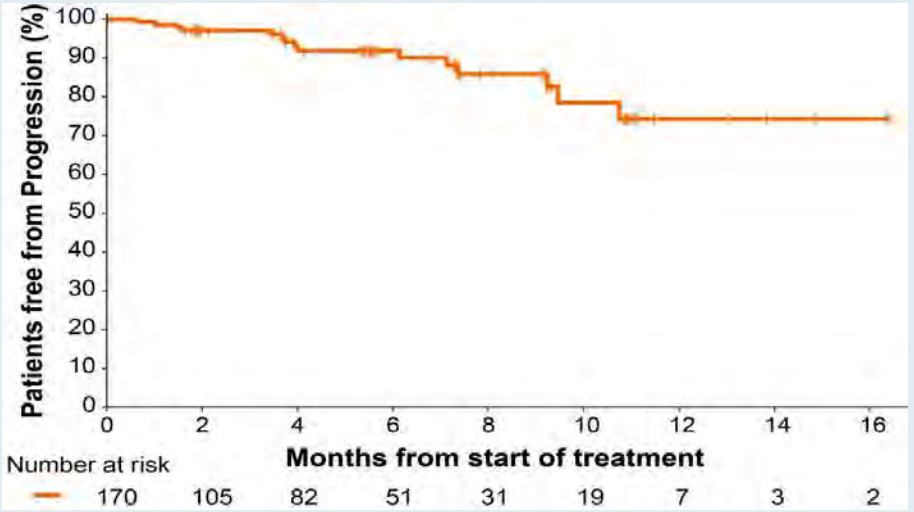
Response Rates		All Patients[a] (N=139)	BTK Pre-Treated Patients[a] (n=121)
ORR, % (95% CI)		63 (55-71)	62 (53-71)
Best response, n (%)	CR	0	0
	PR	69 (50)	57 (47)
	PR-L	19 (14)	18 (15)
	SD	45 (32)	41 (34)

- **ORR increased over time: PR/PR-L 63% to 86% from start of treatment to ≥10 months follow-up**
- **Median follow-up: 6 months (0.6-17.8+) for efficacy-evaluable[a] pts**
- **83 (94%) of responding patients with CLL/SLL are ongoing/in response**
  - **5 responders discontinued: 4 for PD, 1 in PR electively underwent transplantation**

Treatment Duration



PFS



Mato AR et al. ASH 2020;Abstract 542.

Courtesy of Matthew S Davids, MD, MMSc

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BRUIN: Safety

Adverse Events, at All Doses and Patients (N=323), n (%)		Treatment-Emergent AEs, (≥10%)[a]				Treatment-Related AEs	
		Any Grade	Grade 1	Grade 2	Grade 3	Any Grade	Grade 3/4
Fatigue		65 (20)	40 (12)	22 (7)	3 (1)	27 (8)	2 (<1)
Diarrhea		55 (17)	45 (14)	10 (3)	-	28 (9)	-
Contusion		42 (13)	37 (12)	5 (2)	-	29 (9)	-
AEs of special interest, [b,c]	Bruising	53 (16)	48 (15)	5 (2)	-	37 (12)	-
	Rash	35 (11)	30 (9)	5 (2)	-	18 (6)	-
	Arthralgia	16 (5)	13 (4)	3 (1)	-	5 (2)	-
	Hemorrhage	15 (5)	10 (3)	4 (1)	1 (<1)[d]	5 (2)	-
	Hypertension	15 (5)	2 (<1)	9 (3)	4 (1)	4 (1)	-
	AFib/Flutter	2 (<1)	-	2 (<1)[e]	-	-	-

- No DLTs reported and MTD not reached
- 5 (1.5%) discontinued due to treatment-related AEs
- 200 mg QD selected as recommended phase 2 dose

Mato AR et al. ASH 2020. Abstract 542.

Courtesy of Matthew S Davids, MD, MMSc

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What is your usual preferred initial regimen for a 60-year-old patient with CLL with IGHV mutation but without del(17p) or TP53 mutation who requires treatment?

1. FCR
2. BR
3. Ibrutinib
4. Ibrutinib + rituximab
5. Acalabrutinib
6. Acalabrutinib + obinutuzumab
7. Venetoclax + obinutuzumab
8. Other

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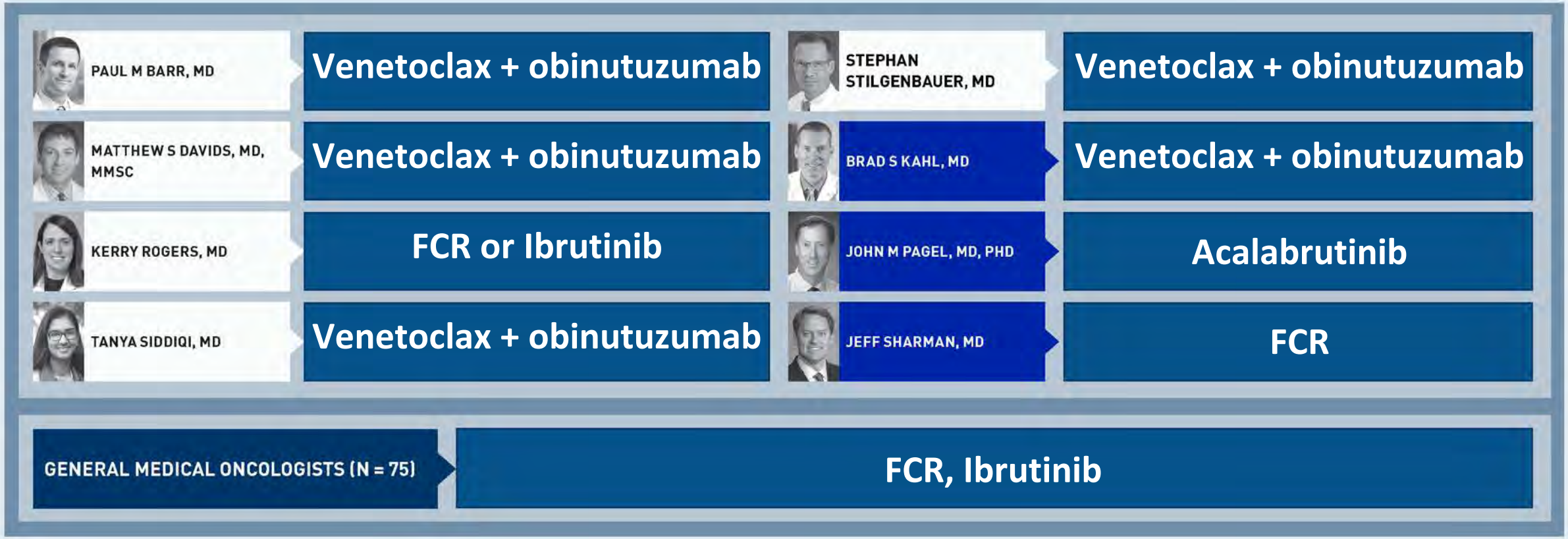
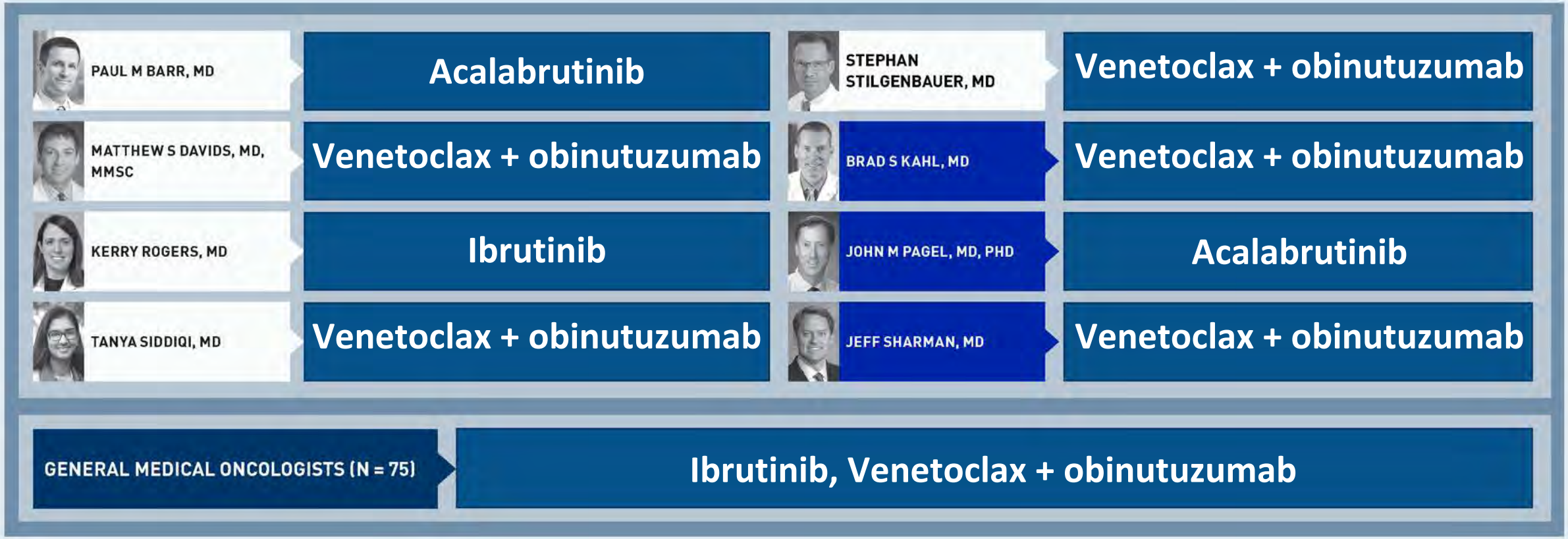
What is your usual preferred initial regimen for a 60-year-old patient with IGHV-mutated CLL without del(17p) or TP53 mutation who requires treatment?



FCR = fludarabine/cyclophosphamide/rituximab

What is your usual preferred initial regimen for a 60-year-old patient with IGHV-unmutated CLL without del(17p) or TP53 mutation who requires treatment?



What is your usual preferred initial regimen for a 75-year-old patient with CLL with IGHV mutation but without del(17p) or TP53 mutation who requires treatment?

1. FCR
2. BR
3. Ibrutinib
4. Ibrutinib + rituximab
5. Acalabrutinib
6. Acalabrutinib + obinutuzumab
7. Venetoclax + obinutuzumab
8. Other

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What is your usual preferred initial regimen for a 75-year-old patient with IGHV-mutated CLL without del(17p) or TP53 mutation who requires treatment?

 PAUL M BARR, MD	Venetoclax + obinutuzumab	 STEPHAN STILGENBAUER, MD	Venetoclax + obinutuzumab
 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab	 BRAD S KAHL, MD	Venetoclax + obinutuzumab
 KERRY ROGERS, MD	Acalabrutinib	 JOHN M PAGEL, MD, PHD	Acalabrutinib
 TANYA SIDDIQI, MD	Venetoclax + obinutuzumab	 JEFF SHARMAN, MD	Venetoclax + obinutuzumab
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Ibrutinib		

What is your usual preferred initial regimen for a 75-year-old patient with IGHV-unmutated CLL without del(17p) or TP53 mutation who requires treatment?

 PAUL M BARR, MD	Acalabrutinib	 STEPHAN STILGENBAUER, MD	Venetoclax + obinutuzumab
 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab	 BRAD S KAHL, MD	Venetoclax + obinutuzumab
 KERRY ROGERS, MD	Acalabrutinib	 JOHN M PAGEL, MD, PHD	Acalabrutinib
 TANYA SIDDIQI, MD	Acalabrutinib + obinutuzumab	 JEFF SHARMAN, MD	Venetoclax + obinutuzumab
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Ibrutinib, Acalabrutinib		

What is your usual preferred initial regimen for a 60-year-old patient with del(17p) CLL who requires treatment?

1. FCR
2. BR
3. Ibrutinib
4. Ibrutinib + rituximab
5. Acalabrutinib
6. Acalabrutinib + obinutuzumab
7. Venetoclax + obinutuzumab
8. Other

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What is your usual preferred initial regimen for a 60-year-old patient with del(17p) CLL who requires treatment?

 PAUL M BARR, MD	Acalabrutinib	 STEPHAN STILGENBAUER, MD	Venetoclax + obinutuzumab
 MATTHEW S DAVIDS, MD, MMSC	Ibrutinib	 BRAD S KAHL, MD	Acalabrutinib + obinutuzumab
 KERRY ROGERS, MD	Ibrutinib	 JOHN M PAGEL, MD, PHD	Acalabrutinib
 TANYA SIDDIQI, MD	Acalabrutinib + obinutuzumab	 JEFF SHARMAN, MD	Acalabrutinib
GENERAL MEDICAL ONCOLOGISTS (N = 75)	Ibrutinib, Venetoclax + obinutuzumab		

Agenda

Module 1: BTK Inhibitors

- ASCEND, RESONATE-2, iLLUMINATE, BRUIN trials

Module 2: Bcl-2 Inhibitors

- MURANO, TAP CLARITY, CAPTIVATE, ACE-CL-003 trials

Module 3: Novel Strategies – U2 Regimen (Umbralisib/Ublituximab), CAR T-Cell Therapy

- UNITY-CLL, TRANSCEND CLL 004 trials

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Five-year Analysis of MURANO Study Demonstrates Enduring Undetectable Minimal Residual Disease (uMRD) in a Subset of Relapsed/Refractory Chronic Lymphocytic Leukemia (R/R CLL) Patients Following Fixed-Duration Venetoclax-Rituximab (VenR) Therapy

Arnon P. Kater*[1], Thomas J. Kipps[2], Barbara F. Eichhorst[3], Peter Hillmen[4], James D'Rozario[5], Carolyn Owen[6], Sarit Assouline[7], Nicole Lamanna[8], Tadeusz Robak[9], Javier de la Serna[10], Ulrich Jaeger[11], Guillaume Cartron[12], Marco Montillo[13], Clemens Mellink[1], Brenda Chyla[14], Cameron Wilson[15], Jenny Wu[16], Yanwen Jiang[16], Marcus Lefebure[15], Michelle Boyer[15], John F. Seymour[17]

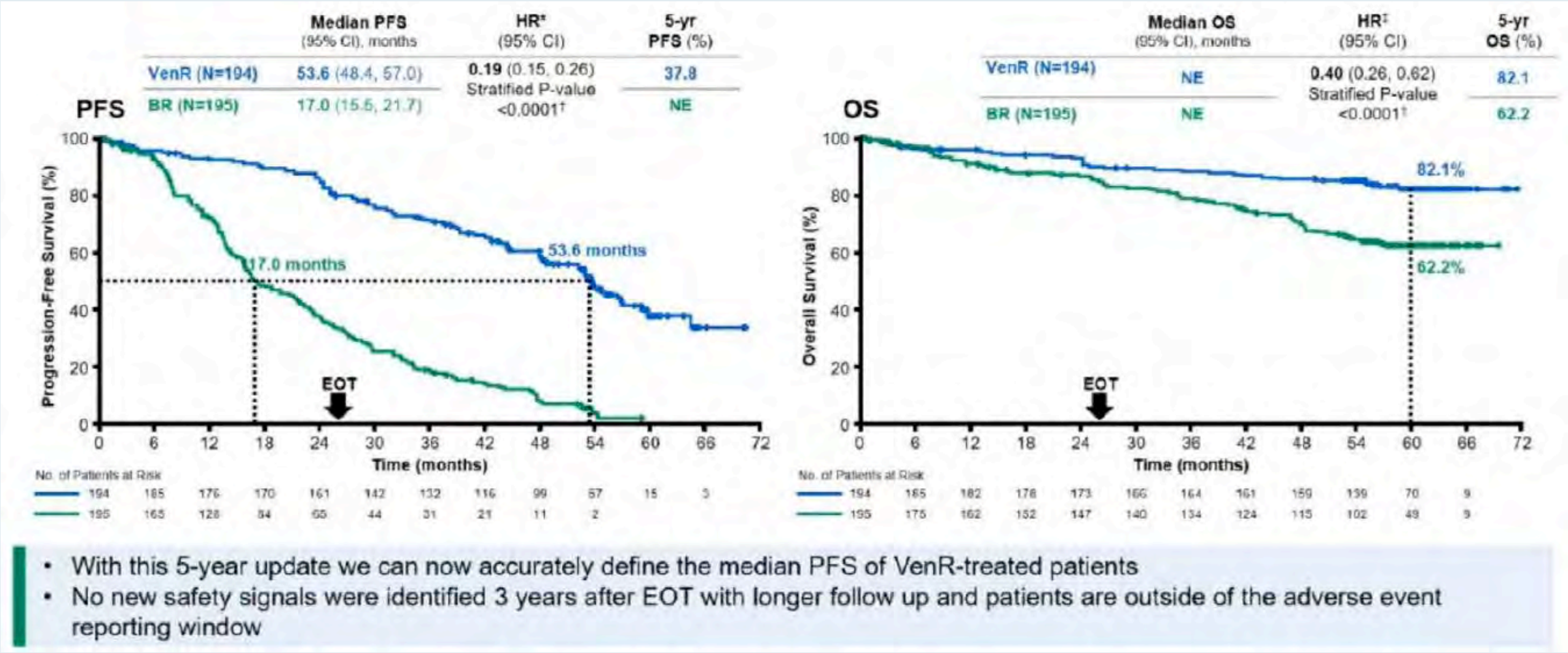
[1]Cancer Center Amsterdam, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands; [2]UCSD Moores Cancer Center, San Diego, CA, USA; [3]University of Cologne, Department I of Internal Medicine and Center of Integrated Oncology Aachen, Bonn, Cologne, Dusseldorf, German CLL Study Group, Cologne, Germany; [4]St. James's University Hospital, Leeds, United Kingdom; [5]The John Curtin School of Medical Research, Australian National University, Canberra, Australia; [6]University of Calgary, Calgary, Canada; [7]Segal Cancer Center, Lady Davis Institute, Jewish General Hospital, Montreal, Canada; [8]Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center, New York, NY, USA; [9]Medical University of Lodz, Copernicus Memorial Hospital, Lodz, Poland; [10]Hospital Universitario 12 de Octubre, Madrid, Spain; [11]Dept. of Medicine I, Division of Hematology and Hemostaseology, Medical University of Vienna, Vienna, Austria; [12]Centre Hospitalier Universitaire de Montpellier, Montpellier, France; [13]Department of Hematology, 12 Hematology, Niguarda Cancer Center, ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [14]AbbVie, North Chicago, IL, USA; [15]Roche Products Ltd, Welwyn, United Kingdom; [16]Genentech, Inc., South San Francisco, CA, USA; [17]Royal Melbourne Hospital, Peter MacCallum Cancer Centre and University of Melbourne, Melbourne, Australia.

Accepted as an Oral Presentation at the 62nd ASH Annual Meeting and Exposition

Abstract 125

RTP RESEARCH TO PRACTICE

MURANO: Survival



- With this 5-year update we can now accurately define the median PFS of VenR-treated patients
- No new safety signals were identified 3 years after EOT with longer follow up and patients are outside of the adverse event reporting window

Kater AP et al. ASH 2020;Abstract 125.

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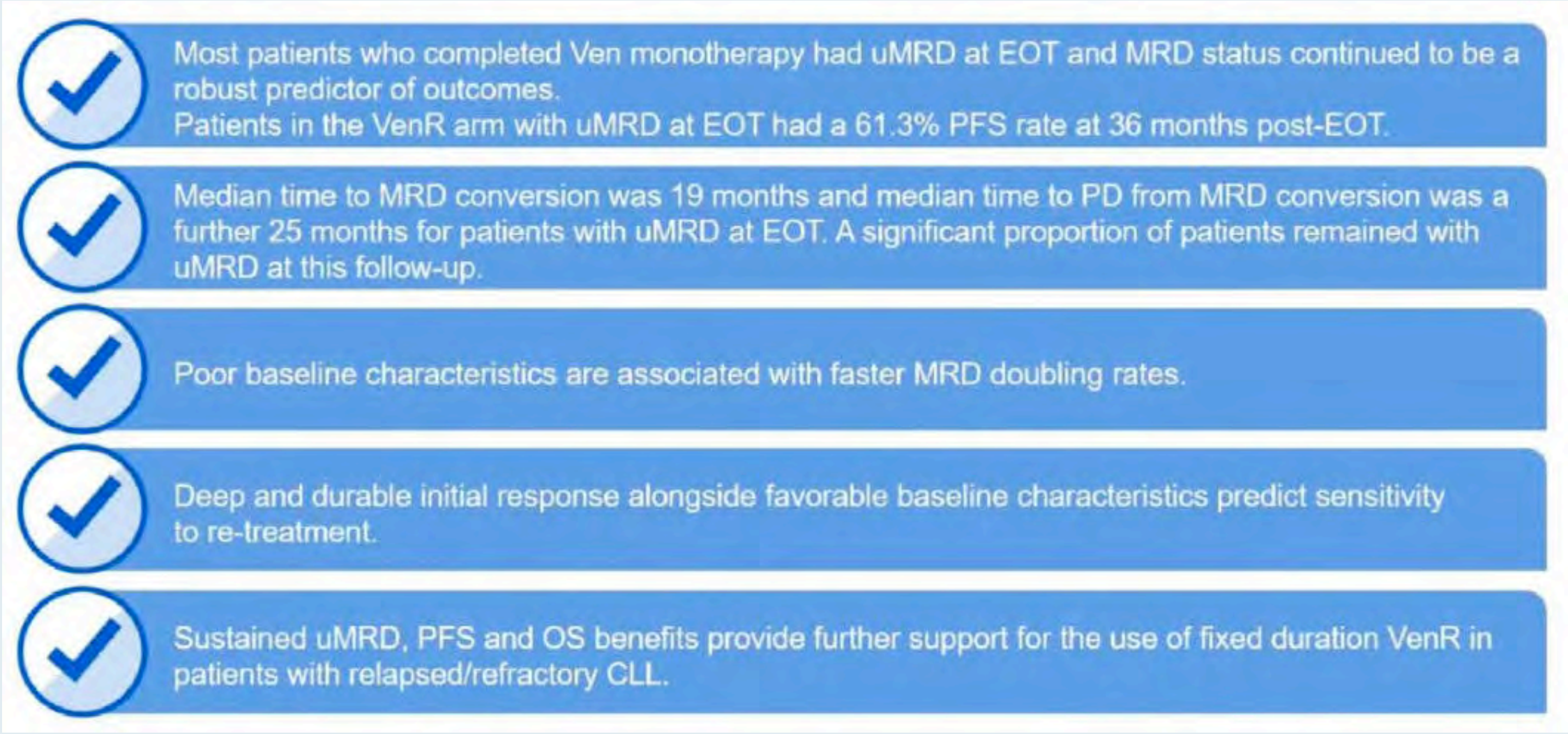
MURANO: Conclusions



Kater AP et al. ASH 2020;Abstract 125.

RTP RESEARCH TO PRACTICE

Efficacy of Subsequent Novel Targeted Therapies, Including Repeated Venetoclax-Rituximab (VenR), in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia (R/R CLL) Previously Treated with Fixed-Duration VenR in the MURANO Study

Harrup R et al.
ASH 2020;Abstract 3139.

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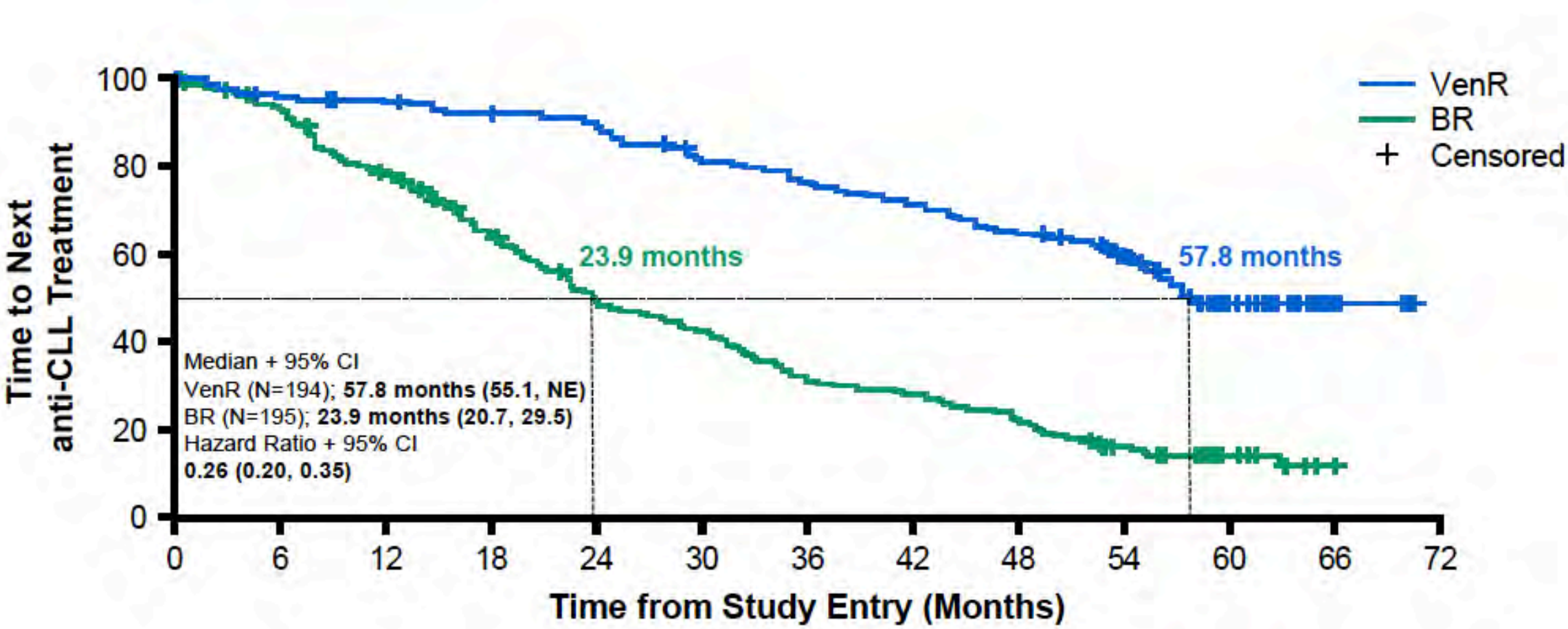
MURANO: TTNT with VenR versus BR



Harrup R et al. ASH 2020;Abstract 3139.

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Efficacy of Subsequent Novel Targeted Therapies in Patients Treated on the MURANO Trial: Conclusions

- 5-year follow-up data from the MURANO study demonstrated TTNT benefit with VenR versus BR.
- Initial VenR treatment was associated with improved time to second PFS event, indicating that early use of Ven over BR does not compromise efficacy of subsequent therapy.
- Response rates to subsequent BTKi therapy, re-treatment with Ven-based regimens or crossover to Ven-based regimens were high.
- Fixed-duration VenR is an effective approach in patients with R/R CLL and does not compromise response to subsequent therapy or OS.[1,2]

Harrup R et al. ASH 2020;Abstract 3139.

RTP RESEARCH TO PRACTICE

ASH Annual Meeting 2020 **Abstract Publication Number 3136**

Venetoclax Re-Treatment of Chronic Lymphocytic Leukemia Patients after a Previous Venetoclax-based Regimen

Meghan C. Thompson, MD[1], John N. Allan, MD[2], Kavita Sail, PhD[3], Beenish S. Manzoor, PhD, MPH[4], Jeffrey J. Pu, MD, PhD[5], Paul M. Barr, MD[6], Callie C. Coombs, MD[7], Stephen J. Schuster, MD[8], Alan Skarbnik, MD[9], Joanna M Rhodes, MD[10], Jacqueline C. Barrientos, MD[10], Lindsey E Roeker, MD[1], Lori A. Leslie, MD[11], Manali Kamdar, MD[12], Michael Y. Choi, MD[13], Martin Simkovic, MD, PhD[14], Frederick Lansigan, MD[15], Brittany Jane Hale, MD[15], Andrew D Zelenetz, MD, PhD[16], Alison J. Moskowitz, MD[1], Kurt S. Bantilan, MPH[1], Celina J. Komari, BS[1], Andre H. Goy, MD[1], Tatyana A. Feldman, MD[11], Richard R. Furman, MD[2] and Anthony R. Mato, MD[1]

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Study Design and Endpoints

- Multicenter, retrospective study
- 13 centers and the CLL Collaborative Study of Real-World Evidence (CORE) database
- Eligibility:
  - CLL patients treated with Ven-based regimen (any line of therapy, Ven1)
  - Then re-treated with second Ven-based regimen (Ven2) in a later line of therapy
- Data collected by investigators at individual sites
  - Demographics, prognostic disease characteristics, tumor lysis syndrome risk and incidence, clinical response and reasons for treatment discontinuation

- Primary endpoint:
  - Investigator-assessed ORR
  - CR: complete response, PR: partial response, SD: stable disease, PD: progression of disease, iwCLL 2018
- PFS estimated by Kaplan-Maier method
- All other analyses descriptive

Memorial Sloan Kettering Cancer Center
Weill Cornell Medicine
UPSTATE CANCER CENTER
UC San Diego Health
University of Colorado
UR MEDICINE
UNC
Penn
Hackensack Meridian John Theurer Cancer Center
NOVANT HEALTH
Northwell Health
Dartmouth-Hitchcock NORRIS COTTON CANCER CENTER
FAKULTNÍ NEMOCNICE HRADEC KRÁLOVÉ

Thompson MC et al. ASH 2020;Abstract 3136.

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Conclusions

- **ORR:** High ORR of 72.2% for Ven re-treatment
- **Heavily pretreated population:** Cohort studied had median 2 prior therapies, majority R/R (88%), BTKi exposed (60%)
- **Safety:** TLS rare event and majority were able to tolerate 400 mg daily
- **Improved outcomes with time:** Patients with CR to Ven re-treatment had a longer median follow-up than PR or SD patients
  - Potential for better responses with longer time on therapy?
- **Next steps:** Longer follow-up and prospective validation of Ven re-treatment → potential role of Ven re-treatment in sequencing algorithms

Thompson MC et al. ASH 2020;Abstract 3136.

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Continued Long Term Responses to Ibrutinib + Venetoclax treatment for Relapsed/Refractory CLL in The Blood Cancer UK TAP CLARITY Trial Ibrutinib Plus Venetoclax in Relapsed, Refractory CLL: Results of The Bloodwise TAP CLARITY Study

Talha Munir, Rebecca Boucher, Nichola Webster, Surita Dalal, Kristian Brock, Francesca Yates, Chhaya Sankhalpara, Donald Macdonald, Christopher Fegan, Alison McCaig, Anna Schuh, Andrew Pettitt, John Gribben, Piers Patten, Stephen Devereux, Adrian Bloor, Christopher Fox, Francesco Forconi, Andy Rawstron, Peter Hillmen

Abstract: 124
Saturday, December 5, 2020 09:30-11:00 AM
Presentation time: 09:45 AM

TAP CLARITY: MRD4 in Bone Marrow After 12 Months (Primary Endpoint)

All at Month 14	PB MRD negative	BM MRD negative	Trephine normal
All patients	**29/50 (58%)**	**20/50 (40%)**	**39/48 (81%)**
FCR/BR rel <36 months	14/20 (70%)	9/20 (45%)	18/19 (95%)
Prior idelalisib	6/9 (67%)	5/9 (56%)	7/9 (78%)

50/50 patients have reached at least Month 14 and have had a bone marrow MRD PB or BM <0.01% CLL cells (10^{-4}) by flow cytometry

Munir T et al. ASH 2020;Abstract 124.

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TAP CLARITY: Adverse Events

Toxicity	Grade 1&2, events (patients)	Grade 3, events (patients)	Grade 4, events (patients)	Any Grade, events (patients)
Atrial fibrillation / flutter	3 (3)	3 (2)	0 (0)	6 (5)
Blood Blister(s) / Bleeding	12 (8)	2 (2)	0 (0)	14 (10)
Bruising	38 (20)	0 (0)	0 (0)	38 (20)
Esophageal Hemorrhage	1 (1)	0 (0)	0 (0)	1 (1)
Eye Haemorrhage	5 (4)	1 (1)	0 (0)	6 (5)
Febrile Neutropenia	1 (1)	1 (1)	0 (0)	2 (2)
Haematoma (Retroperitoneal)	0 (0)	1 (1)	0 (0)	1 (1)
Neutrophil Count Decreased	3 (3)	24 (11)	10 (5)	37 (13)
Pleural Hemorrhage	1 (1)	0 (0)	0 (0)	1 (1)
Retroperitoneal Haematoma	0 (0)	1 (1)	0 (0)	1 (1)
Tumor Lysis Syndrome	0 (0)	1 (1)	0 (0)	1 (1)

Single case of tumour lysis syndrome (at 200mg dose) – increasing phosphate and creatinine. Managed by delaying venetoclax. Rapidly re-escalated with no further TLS

Recommendation in protocol to give G-CSF to keep the neutrophil count above 1 x 10^9/L.

Other side-effects were mild and/or manageable, most commonly neutropenia (3/37 grade 2, 34/37 grade 3/4). Two Suspected Unexpected Serious Adverse Reactions (SUSARs) were reported (abdominal pain and pemphigus), 47 Serious Adverse Events (SAEs), and 1156 Adverse Events (AEs) (of which 219 were grade 3 or 4) were reported.

2 Covid cases reported for CLARITY patients TN0 18, and TN0 30, both patients discharged with condition being stable.

Date of data lock: 06-Nov-2020

Munir T et al. ASH 2020;Abstract 124.

RTP RESEARCH TO PRACTICE

Ibrutinib Plus Venetoclax for First-Line Treatment of Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: 1-Year Disease-Free Survival Results From the MRD Cohort of the Phase 2 CAPTIVATE Study

William G. Wierda, MD, PhD[1]; Constantine S. Tam, MBBS, MD[2]; John N. Allan, MD[3]; Tanya Siddiqi, MD[4]; Thomas J. Kipps, MD, PhD[5]; Stephan Opat, FRACP, FRCPA, MBBS[6]; Alessandra Tedeschi, MD[7]; Xavier C. Badoux, MBBS, FRACP, FRCPA[8]; Bryone J. Kuss, MBBS, PhD, FRACP, FRCPA[9]; Sharon Jackson, MD[10]; Carol Moreno, MD, PhD[11]; Ryan Jacobs, MD[12]; John M. Pagel, MD, PhD[13]; Ian Flinn, MD, PhD[14]; Cathy Zhou, MS[15]; Edith Szafer-Glusman, PhD[15]; Joi Ninomoto, PharmD[15]; James P. Dean, MD, PhD[15]; Danelle F. James, MD, MAS[15]; Paolo Ghia, MD, PhD[16]

[1]Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Peter MacCallum Cancer Center & St. Vincent's Hospital and the University of Melbourne, Melbourne, VIC, Australia; [3]Weill Cornell Medicine, New York, NY, USA; [4]City of Hope National Medical Center, Duarte, CA, USA; [5]UCSD Moores Cancer Center, San Diego, CA, USA; [6]Monash University, Clayton, VIC, Australia; [7]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [8]Ministry of Health, Kogarah, NSW, Australia; [9]Flinders University and Medical Centre, Bedford Park, SA, Australia; [10]Middlemore Hospital, Auckland, New Zealand; [11]Hospital de la Santa Creu I Sant Pau, Autonomous University of Barcelona, Barcelona, Spain; [12]Levine Cancer Institute, Charlotte, NC, USA; [13]Swedish Cancer Institute Hematologic Malignancies Program, Seattle, WA, USA;
[14]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [15]Pharmacyclics LLC, an AbbVie Company, Sunnyvale, CA, USA; [16]Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy

Abstract 123

RTP RESEARCH TO PRACTICE

CAPTIVATE MRD Cohort: Rates of uMRD with 12 Cycles of Ibrutinib and Venetoclax

uMRD Rates With 12 Cycles of Combined Ibrutinib + Venetoclax

	Peripheral Blood n=163	Bone Marrow[a] n=155
Best response of undetectable MRD[1] in evaluable patients[b] (95% CI)	**75%** (69–82)	**72%** (65–79)

- In patients with uMRD in peripheral blood with matched bone marrow samples at Cycle 16, 93% had uMRD in both blood and bone marrow
- In all-treated patients (N=164), uMRD rate was 75% in peripheral blood and 68% in bone marrow

Wierda WG et al. ASH 2020;Abstract 123.

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CAPTIVATE MRD Cohort: Conclusions

- The 1-year DFS rate of 95% in patients with uMRD randomized to placebo after 12 cycles of combined ibrutinib + venetoclax supports a fixed-duration treatment approach
- 30-month PFS rates of >95% across all treatment arms compare favorably to other first-line fixed duration regimens including FCR (3-year PFS 73%)[1] and venetoclax + obinutuzumab (3-year PFS 82%)[2]
- Adverse events generally decreased after the first 6 months of ibrutinib + venetoclax treatment and no new safety signals emerged over time
- Ibrutinib + venetoclax is an all oral, once-daily, chemotherapy-free, fixed-duration regimen that provides highly concordant, deep MRD remissions in BM (72%) and PB (75%) in first-line CLL

Wierda WG et al. ASH 2020;Abstract 123.

RTP RESEARCH TO PRACTICE

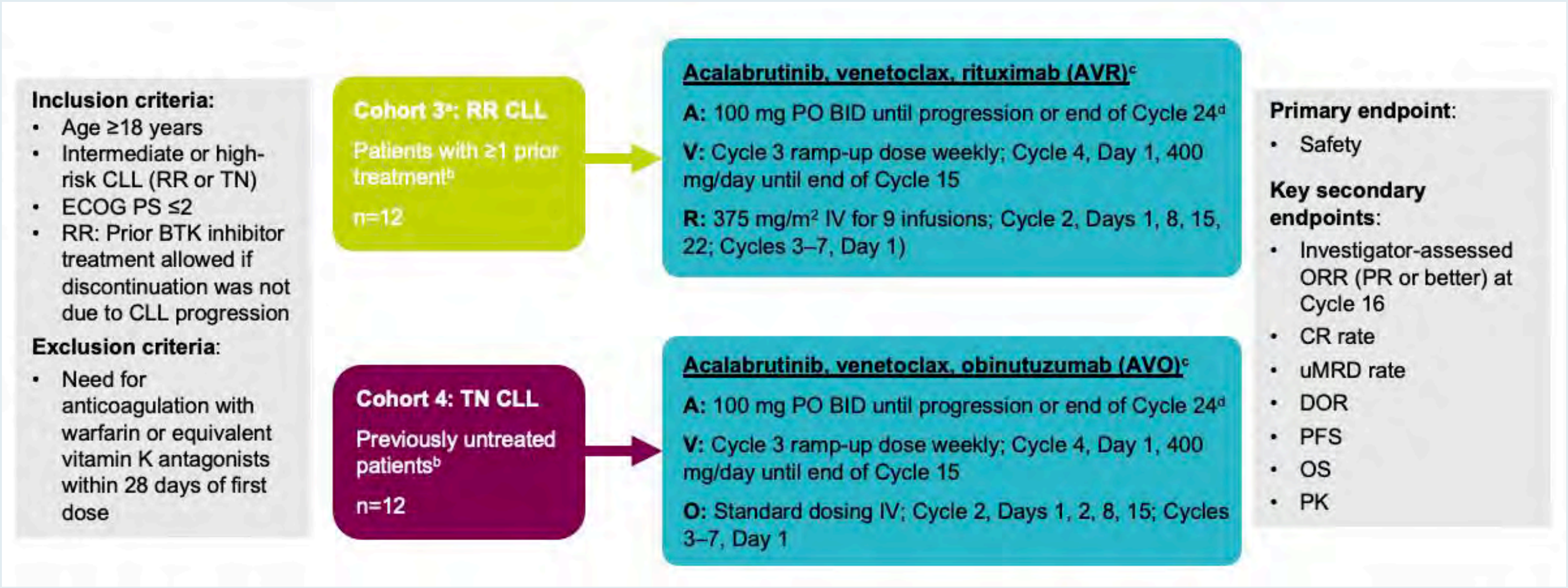
Abstract 1312

Acalabrutinib in Combination With Venetoclax and Obinutuzumab or Rituximab in Patients With Treatment-Naïve or Relapsed/Refractory Chronic Lymphocytic Leukemia

Jennifer A. Woyach,[1] James S. Blachly,[1] Kerry A. Rogers,[1] Seema A. Bhat,[1] Michael Grever,[1] Adam Kittai,[1] Mojgan Jianfar,[1] Gerard Lozanski,[1] David M Weiss,[1] Barbara L. Andersen,[1] Priti Patel,[2] Veerendra Munugalavadla,[2] Anna Butturini,[2] Yan Xu,[2] Min-Hui Wang,[2] John C. Byrd[1]

RTP RESEARCH TO PRACTICE

ACE-CL-003 Study Design



Woyach JA et al. ASH 2020;Abstract 1312.

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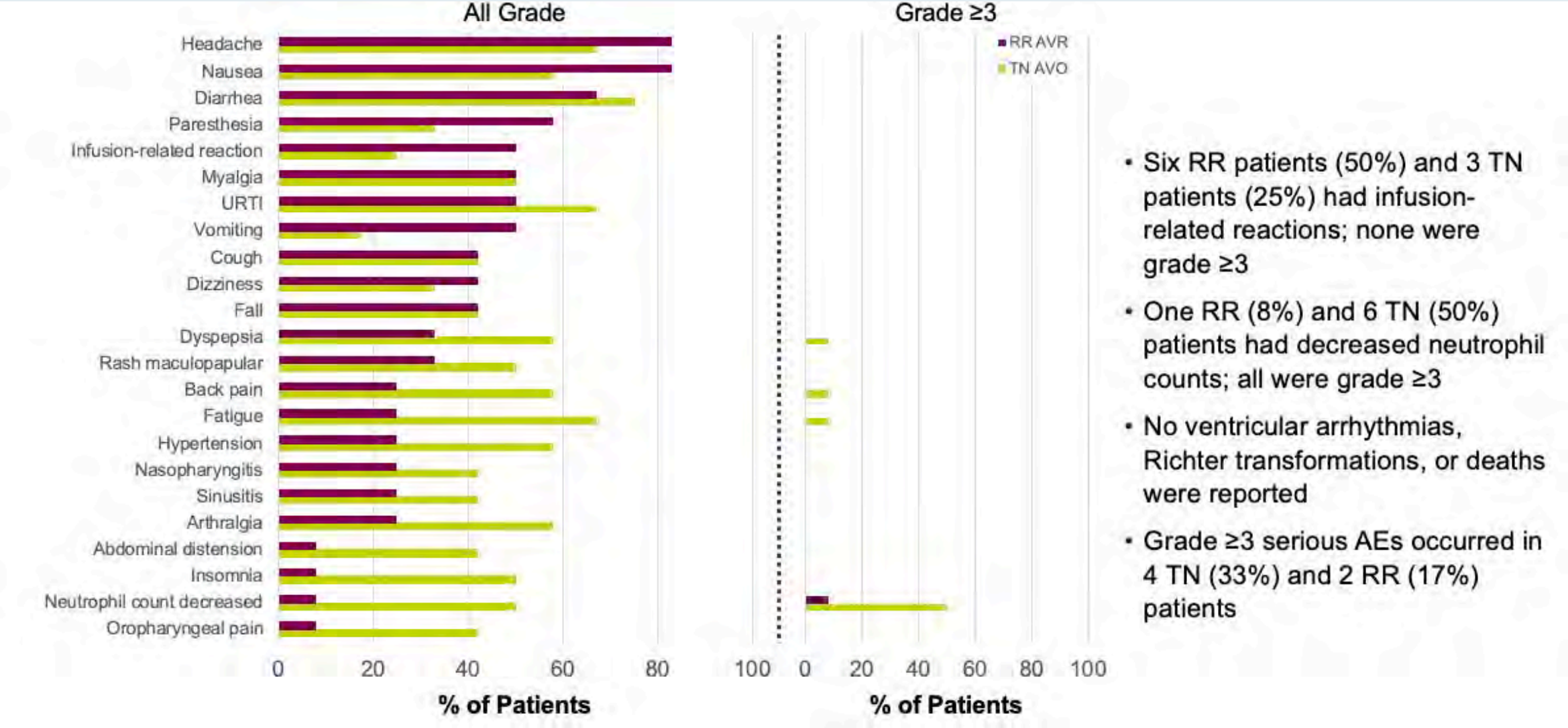
ACE-CL-003: Safety (Primary Endpoint)



- Six RR patients (50%) and 3 TN patients (25%) had infusion-related reactions; none were grade ≥3
- One RR (8%) and 6 TN (50%) patients had decreased neutrophil counts; all were grade ≥3
- No ventricular arrhythmias, Richter transformations, or deaths were reported
- Grade ≥3 serious AEs occurred in 4 TN (33%) and 2 RR (17%) patients

Woyach JA et al. ASH 2020;Abstract 1312.

RTP RESEARCH TO PRACTICE

ACE-CL-003: Conclusions

- This cohort analysis of CL-003 evaluated the safety and efficacy of acalabrutinib in triple combination with venetoclax and rituximab or obinutzumab in patients with RR and TN CLL
  - AEs were as expected based on each individual agents' safety profiles[1-4] and few patients discontinued treatment due to AEs
  - Most AEs of interest were low grade
    - One patient with prior history of atrial fibrillation experienced grade ≥3 atrial fibrillation in the RR CLL cohort
  - ORR was 92% in RR and 100% in TN patients after 16 cycles, and 50% of patients in each cohort had achieved CR or CRi with median follow-up of 27.7 and 26.0 months, respectively
  - Overall uMRD rate was 71% (67% in RR patients and 75% in TN patients)
    - All patients with CR or CRi achieved uMRD
  - Median DOR, PFS, and OS were not reached
- Triple combination therapy with acalabrutinib plus an anti-CD20 antibody and a BCL-2 inhibitor is feasible based on tolerability and yielded high CR and uMRD rates in both RR and TN CLL

Woyach JA et al. ASH 2020;Abstract 1312.

RTP RESEARCH TO PRACTICE

Updated Safety and Efficacy Results from a Phase 2 Study of Acalabrutinib, Venetoclax and Obinutuzumab (AVO) for Frontline Treatment of Chronic Lymphocytic Leukemia (CLL)

Matthew S. Davids, MD, MMSc[1], Benjamin L. Lampson, MD, PhD[1], Svitlana Tyekucheva, PhD[2], Jennifer L. Crombie, MD[1], Samuel Ng, MD, PhD[1], Austin I. Kim, MD[1], Matthew Weinstock, MD[3], Jessica C. Lowney,[1] Samantha Pazienza[1], Josie Montegaard, NP[1], Victoria Patterson, RN[1], Caron A. Jacobson, MD[1], Ann S. LaCasce, MD, MMSc[1], Philippe Armand, MD, PhD[1], Jon E. Arnason, MD[3], David C. Fisher, MD[1], Jennifer R. Brown, MD, PhD[1]

[1]Dept. of Medical Oncology, Dana-Farber Cancer Institute, Boston, USA;
[2]Dept. of Biostatistics, Dana-Farber Cancer Institute, Boston, MA; [3]Beth Israel Deaconess Medical Center, Boston, MA

Abstract 2216
2020 Virtual ASH Annual Meeting

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Phase II Study of Acalabrutinib, Venetoclax and Obinutuzumab: Conclusions

- AVO is highly active as front-line CLL therapy (uMRD BM 77% after 15 cycles of therapy) in a population enriched for high-risk disease and similar results in high-risk patients
- The safety profile of AVO is favorable, with low risk of Gr ≥3 infection, afib, and infusion-related reactions (2% each) and no major bleeding or febrile neutropenia
- No TLS due to ven was observed with a more convenient 4-week ven ramp-up
- Accrual to a *TP53*-aberrant cohort is ongoing (NCT03580928)
- A phase 3 trial of AVO vs AV vs chemoimmunotherapy in ~780 patients with previously untreated CLL is now accruing (ACE-CL-311, NCT03836261)

Davids MS et al. ASH 2020;Abstract 2216.

RTP RESEARCH TO PRACTICE

Updated Results from a Phase I/II Study of Duvelisib and Venetoclax in Patients with Relapsed or Refractory CLL/SLL or Richter's Syndrome

Jennifer L. Crombie, MD[1], Svitlana Tyekucheva, PhD[2], Zixu Wang, MS[2], Alexandra Savell, BA[1], Lisa Brennan, RN[1], Jessica Lowney, BA[1], Karen Francoeur, RN[3], Josie Montegaard, NP[1], Austin Kim, MD[1], Jacob Soumerai, MD[4], Jon Arnason, MD[5], Alan Louie Cruz, MD[6], Sigrid Berg, MD[6], David C. Fisher, MD[1], Jennifer R. Brown, MD, PhD[1], Matthew S. Davids, MD, MMSc[1]

[1]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; [2]Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, MA; [3]Verastem Oncology, Needham, MA; [4]Center for Lymphoma, Massachusetts General Hospital, Boston, MA; [5]Beth Israel Deaconess Medical Center, Boston, MA; [6]Northern Light Cancer Care, Brewer, ME

2020 ASH Virtual Meeting
Abstract #3141

RTP RESEARCH TO PRACTICE

Phase I/II Study of Duvelisib and Venetoclax: Conclusions

- DUV + VEN and is active for pts with R/R CLL/SLL, including those who have relapsed after BTKi
- DUV + VEN has a manageable safety profile and the most common AEs were cytopenias and fatigue
- High rates of CR and uMRD have been seen for this 1-year, MRD-guided, time limited, all oral regimen
- This phase II study is actively accruing at multiple centers (NCT03534323)

Crombie JL et al. ASH 2020;Abstract 3141.

RTP RESEARCH TO PRACTICE

What would be your most likely approach for a patient with newly diagnosed CLL to whom you decide to administer up-front venetoclax/obinutuzumab and who has detectable MRD after completing 1 year of treatment?

1. Continue treatment
2. Discontinue treatment

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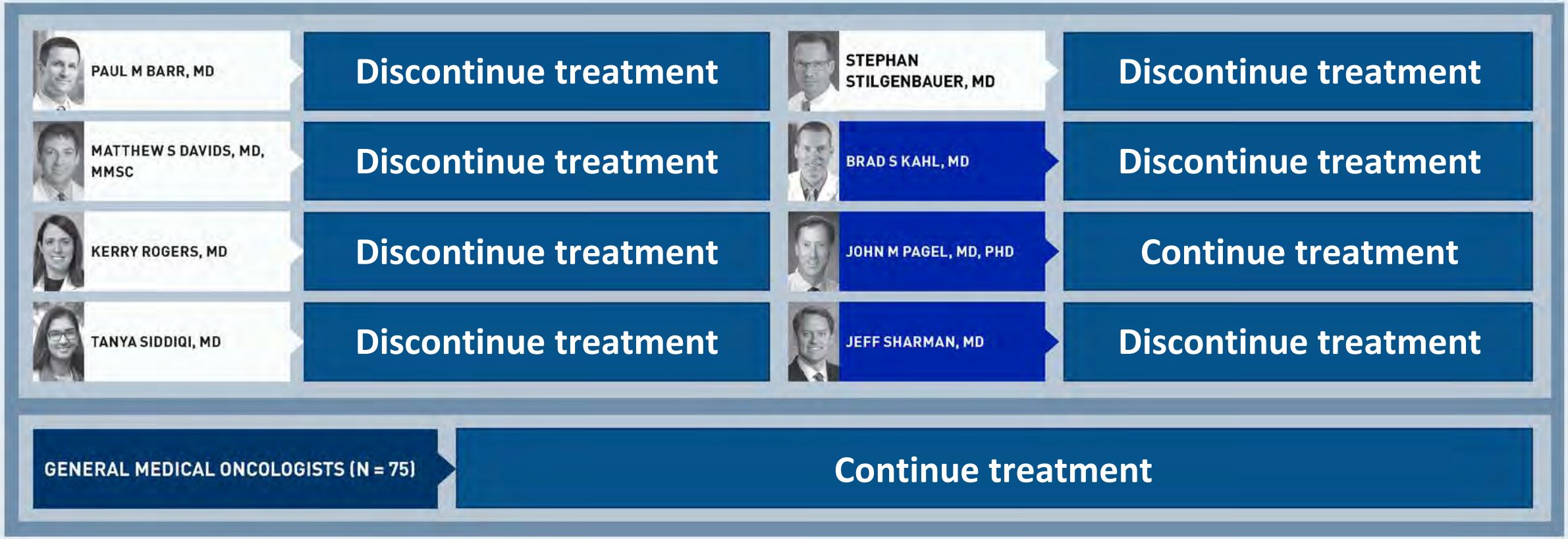
What would be your most likely approach for a patient with newly diagnosed CLL to whom you decide to administer up-front venetoclax/obinutuzumab who has detectable MRD after completing 1 year of treatment?



Agenda

Module 1: BTK Inhibitors

- ASCEND, RESONATE-2, iLLUMINATE, BRUIN trials

Module 2: Bcl-2 Inhibitors

- MURANO, TAP CLARITY, CAPTIVATE, ACE-CL-003 trials

Module 3: Novel Strategies – U2 Regimen (Umbralisib/Ublituximab), CAR T-Cell Therapy

- UNITY-CLL, TRANSCEND CLL 004 trials

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Phase 3 Study of Umbralisib Combined With Ublituximab vs Obinutuzumab Plus Chlorambucil in Patients With Chronic Lymphocytic Leukemia: Results From UNITY-CLL

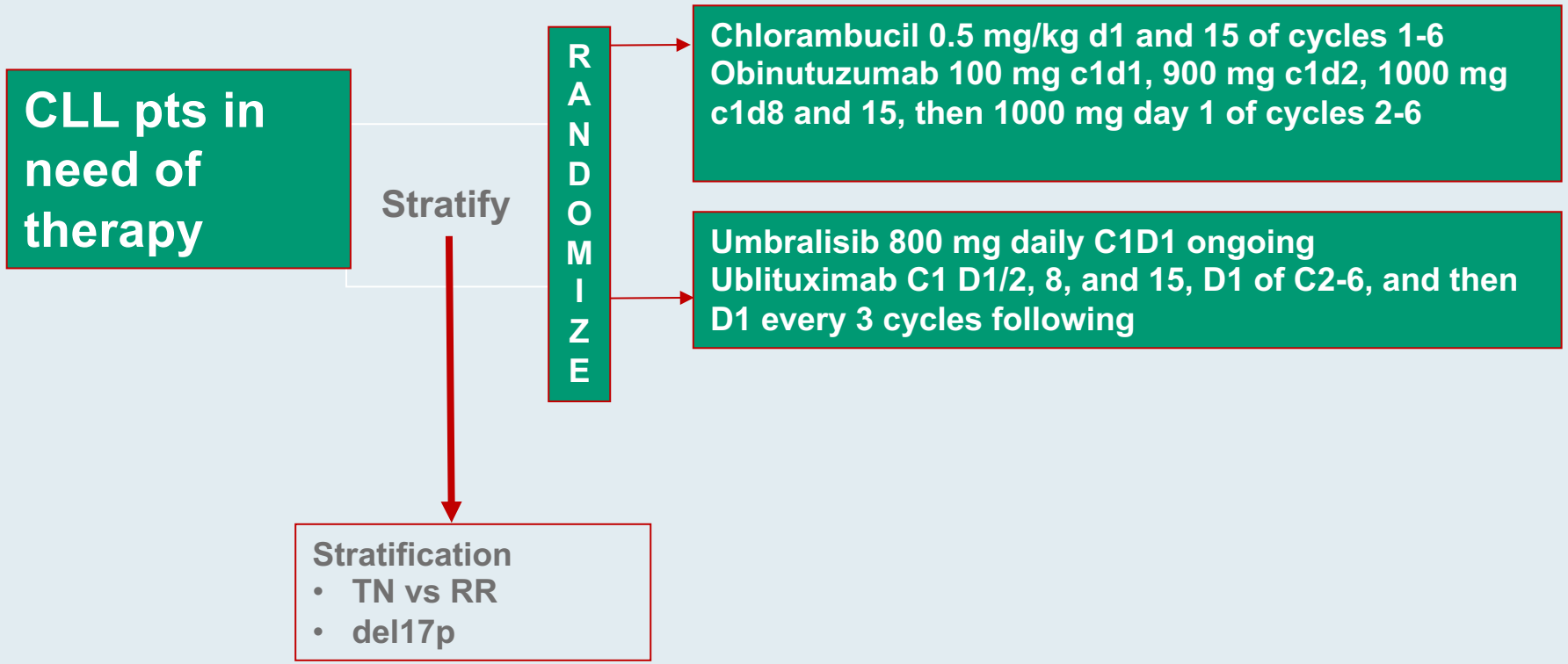
John G. Gribben, MD DSc[1], Wojciech Jurczak, MD, PhD[2], Ryan W. Jacobs, MD[3], Sebastian Grosicki, MD, PhD[4], Krzysztof Giannopoulos, MD, PhD[5], Tomasz Wrobel, MD PhD[6], Syed F. Zafar, MD[7], Jennifer L. Cultrera, MD[8], Suman Kambhampati, MD[9], Alexey Danilov, MD[10], John M. Burke, MD[11], Jerome Goldschmidt, MD[12], Douglas F. Beach, MD[13], Scott F. Huntington, MD, MPH[14], Javier Pinilla Ibarz, MD, PhD[15], Jeff P Sharman, MD[16], Tanya Siddiqi, MD[17], Danielle M. Brander, MD[18], John M. Pagel, MD PhD[19], Kathryn S. Kolibaba, MD[20], Monika Dlugosz-Danecka, MD, PhD[2], Nilanjan Ghosh, MD, PhD[3], Peter Sportelli, BS[21], Hari P. Miskin, MSc[21], Owen A. O'Connor, MD, PhD[21], Michael S. Weiss[21] and Ian W. Flinn, MD, PhD[22]

Abstract 543

RTP RESEARCH TO PRACTICE

UNITY-CLL Phase III Study Design

- 421 total patients
- 57% TN
- 56% IGHV unmutated
- 10% del17p

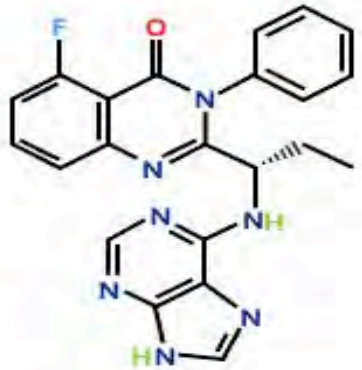
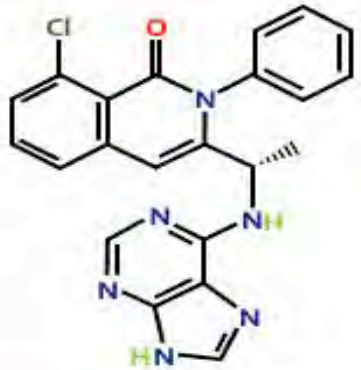
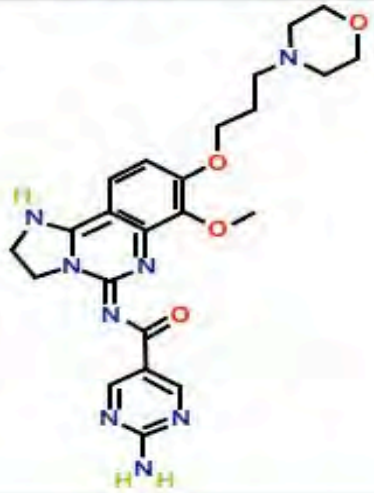


Gribben JG et al. ASH 2020;Abstract 543.

Courtesy of Jennifer Woyach, MD

RTP RESEARCH TO PRACTICE

Umbralisib – Dual Inhibitor of PI3Kδ and CK1ε

	Umbralisib[1]	Idelalisib[1]	Duvelisib[1]	Copanlisib[2]
				
Isoform	**K_d (nM)**			
PI3kα	>10000	600	40	0.04
PI3Kβ	>10000	19	0.89	1.5
PI3Kγ	1400	9.1	0.21	0.31
PI3Kδ	6.2	1.2	0.047	0.068
CK1ε	180	>30,000	>30,000	>6,000

- Umbralisib is an oral, once daily, dual inhibitor of PI3Kδ and CK1ε
- Umbralisib has >1000-fold greater selectivity for PI3Kδ compared to α and β isoforms[3]
- Umbralisib is also **>200-fold** more selective for PI3Kδ relative to **PI3Kγ**

Gribben JG et al. ASH 2020;Abstract 543.

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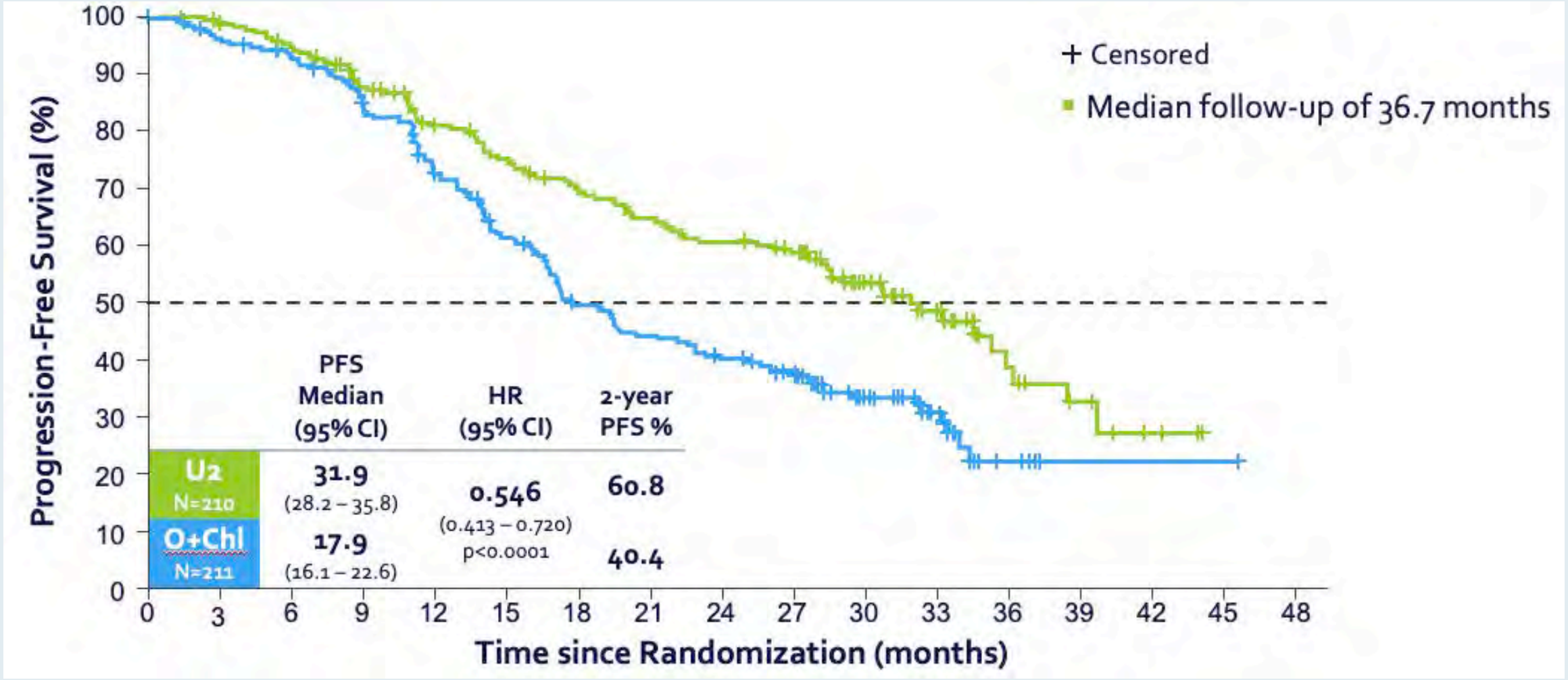
UNITY-CLL: Progression-Free Survival (Primary Endpoint)



Gribben JG et al. ASH 2020;Abstract 543.

RTP RESEARCH TO PRACTICE

UNITY-CLL: Adverse Events

AEs, n (%)	U2 N=206 Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	O+Chl N=200 Any Grade	Grade 1	Grade 2	Grade 3	Grade 4
Diarrhea	115 (56)	53 (26)	37 (18)	25 (12)	-	43 (22)	25 (13)	13 (7)	5 (3)	0
Nausea	105 (51)	68 (33)	34 (17)	3 (2)	-	75 (38)	49 (25)	24 (12)	2 (1)	0
IRR	95 (46)	13 (6)	78 (38)	3 (2)	1 (0.5)	50 (25)	6 (3)	37 (19)	7 (4)	0
Fatigue	72 (35)	35 (17)	33 (16)	4 (2)	-	60 (30)	37 (19)	17 (9)	6 (3)	0
Neutropenia	69 (34)	1 (0.5)	4 (2)	27 (13)	37 (18)	79 (40)	6 (3)	3 (2)	41 (21)	29 (15)
Cough	59 (29)	36 (18)	23 (11)	-	-	36 (18)	25 (13)	11 (6)	0	0
Headache	53 (26)	41 (20)	11 (5)	1 (0.5)	-	36 (18)	26 (13)	9 (5)	1 (0.5)	0
Pyrexia	51 (25)	34 (17)	16 (8)	1 (0.5)	-	39 (20)	24 (12)	13 (7)	2 (1)	0
Chills	50 (24)	26 (13)	23 (11)	1 (0.5)	-	33 (17)	24 (12)	9 (5)	0	0
URTI	45 (22)	10 (5)	35 (17)	-	-	24 (12)	6 (3)	16 (8)	2 (1)	0
Dizziness	44 (21)	33 (16)	9 (4)	2 (1)	-	18 (9)	16 (8)	2 (1)	0	0
Thrombocytopenia	19 (9)	6 (3)	6 (3)	3 (2)	4 (2)	45 (23)	6 (3)	13 (7)	21 (11)	5 (3)

Gribben JG et al. ASH 2020;Abstract 543.

RTP RESEARCH TO PRACTICE

TRANSCEND CLL 004: Phase 1 Cohort of Lisocabtagene Maraleucel (liso-cel) in Combination with Ibrutinib for Patients with Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

William G. Wierda,[1] Kathleen A. Dorritie,[2] Javier Munoz,[3] Deborah M. Stephens,[4] Scott Solomon,[5] Heidi H. Gillenwater,[6] Lucy Gong,[6] Lin Yang,[6] Ken Ogasawara,[7] Jerill Thorpe,[6] Tanya Siddiqi[8]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA, USA; [3]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [4]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [5]Immunotherapy Program, Northside Hospital Cancer Institute, Atlanta, GA, USA; [6]Bristol Myers Squibb, Seattle, WA, USA; [7]Bristol Myers Squibb, Princeton, NJ, USA; [8]City of Hope National Medical Center, Duarte, CA, USA

Presentation 544

Updated Follow-Up of Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Treated with Lisocabtagene Maraleucel in the Phase 1 Monotherapy Cohort of TRANSCEND CLL 004, Including High-Risk and Ibrutinib-Treated Patients

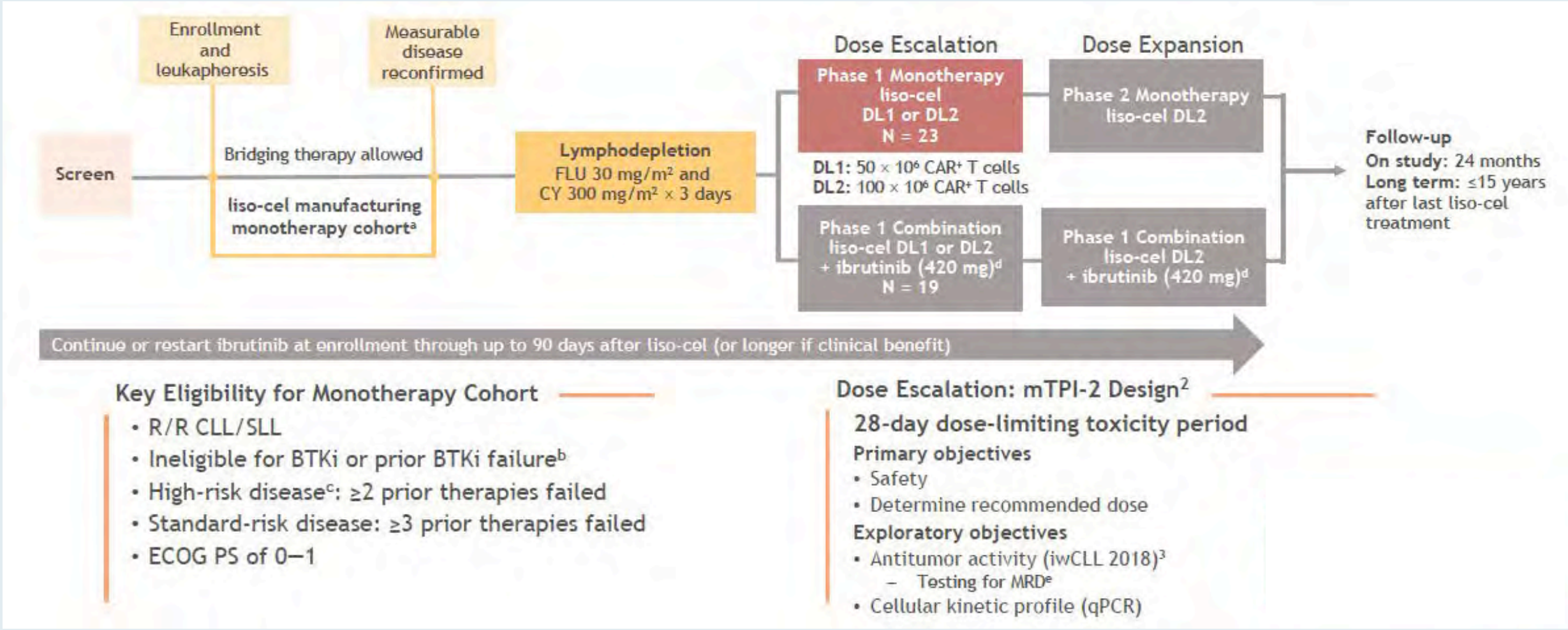
Tanya Siddiqi,[1] Jacob D. Soumerai,[2] Kathleen A. Dorritie,[3] Deborah M. Stephens,[4] Peter A. Riedell,[5] Jon Arnason,[6] Thomas J. Kipps,[7] Heidi H. Gillenwater,[8] Lucy Gong,[8] Lin Yang,[8] Ken Ogasawara,[9] William G. Wierda[10]

[1]City of Hope National Medical Center, Duarte, CA, USA; [2]Center for Lymphoma, Massachusetts General Hospital Cancer Center, Boston, MA, USA; [3]UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA, USA; [4]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [5]University of Chicago Medical Center, Chicago, IL, USA; [6]Beth Israel Deaconess Medical Center, Boston, MA, USA; [7]Moores Cancer Center, University of California San Diego Health, San Diego, CA, USA; [8]Bristol Myers Squibb, Seattle, WA, USA; [9]Bristol Myers Squibb, Princeton, NJ, USA; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Presentation 546

RTP RESEARCH TO PRACTICE

TRANSCEND CLL 004: Study Design



Key Eligibility for Monotherapy Cohort

- R/R CLL/SLL
- Ineligible for BTKi or prior BTKi failure[b]
- High-risk disease[c]: ≥2 prior therapies failed
- Standard-risk disease: ≥3 prior therapies failed
- ECOG PS of 0–1

Dose Escalation: mTPI-2 Design[2]

28-day dose-limiting toxicity period

Primary objectives

- Safety
- Determine recommended dose

Exploratory objectives

- Antitumor activity (iwCLL 2018)[3]
  - Testing for MRD[e]
- Cellular kinetic profile (qPCR)

Wierda WG et al. ASH 2020;Abstract 544; Siddiqi T et al. ASH 2020;Abstract 546.

RTP RESEARCH TO PRACTICE

TRANSCEND CLL 004 Study: Liso-cel with Ibrutinib

- 19 patients included
- Median 4 prior therapies
- 74% had BTKi as last therapy and 53% had also received venetoclax
- 74% CRS, 1 grade 3; 16% G3+ neurologic events
- ORR 95%, 47% CR/CRi
- 83% maintained response at 3 months
- 79% had uMRD in marrow

Wierda WG et al. ASH 2020;Abstract 544.

Courtesy of Jennifer Woyach, MD

RTP RESEARCH TO PRACTICE

TRANSCEND CLL 004 Study: Liso-cel Monotherapy

- Study schema same as previous, but without ibrutinib
- 23 pts evaluable for safety, 22 for efficacy
- Median 6 prior therapies, all with prior ibr and 48% with ven too
- ORR 82%, CR/CRi 45%
- Median PFS 18 months, 5/8 progressions were RT
- G3+ CRS 9%, G3+ neuro events 22%

Siddiqi T et al. ASH 2020;Abstract 546.

Courtesy of Jennifer Woyach, MD

RTP RESEARCH TO PRACTICE

SHEBA Tel HaShomer | Cancer Center

Safety and Efficacy of CD19-CAR T Cells in Richter's Transformation after Targeted Therapy for Chronic Lymphocytic Leukemia

Ohad Benjamini, Avichai Shimoni, Michal Besser, Noga Shem-Tov, Ivetta Danylesko, Ronit Yerushalmi, Drorit Grizim Merkel, Tamar Tadmor, David Lavie, Riva Fineman, Elad Jacobi, Arnon Nagler, Abraham Avigdor

ASH 2020;Abstract 545

RTP RESEARCH TO PRACTICE

CD19 CAR T-cell Tx toxicity

pts N	Age at CART	CRS grade	CRS therapy	ICANS grade	ICANS therapy
1	67	3	tocilizumab, NA	3	levetiracetam steroids
2	63	4	tocilizumab, NA	3	levetiracetam steroids
3	73	1	none	1	levetiracetam
4	65	1	none	0	none
5	64	1	none	0	none
6	62	0	none	0	none
7	62	1	none	0	none
8	54	3	tocilizumab	0	none
9	60	1	none	3	levetiracetam steroids

CRS cytokine release syndrome, immune effector cell–associated neurotoxicity syndrome ICANS, NA noradrenaline,

- 7 patients developed CRS
  4 patients had grade 1 and 3 grade 3-4
- 4 patients had CNS toxicity, 3 grade 3
- 75% percent (6/8) developed neutropenia
- 2 had infections after CAR T-cell therapy

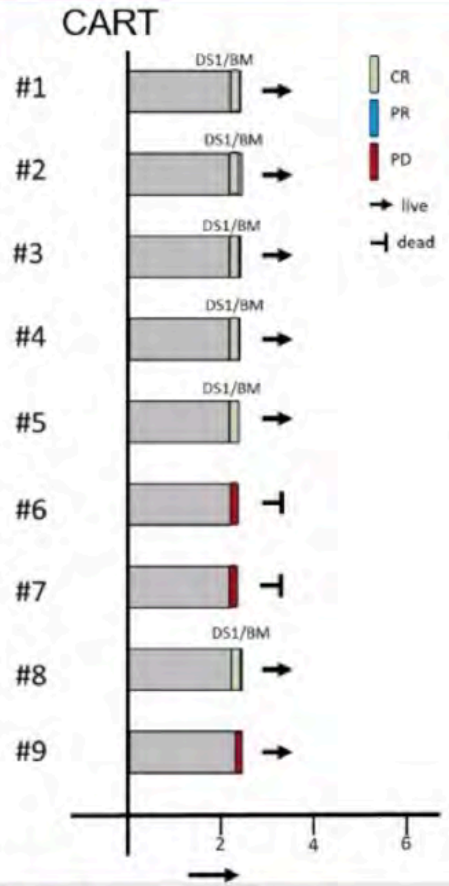
There were no fatalities due to CAR T-cell toxicity

SHEBA Tel HaShomer | Cancer Center

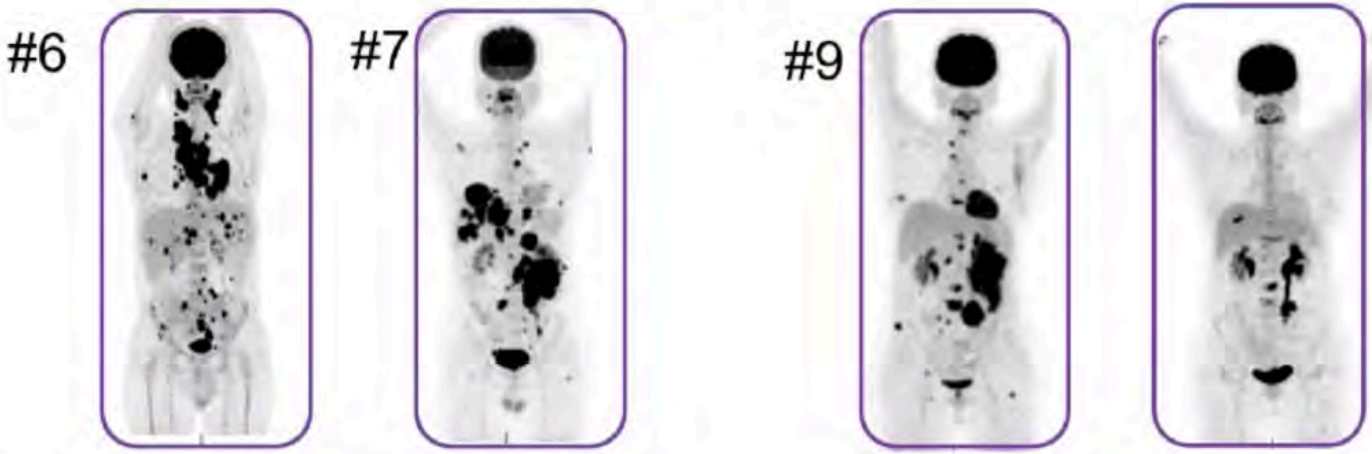
Benjamini O et al. ASH 2020;Abstract 545.

RTP RESEARCH TO PRACTICE

Initial response to CAR T-cell Tx



- 67% (6/9) of patients responded - all achieved CR
- 3 were refractory to CAR T cell Tx
  - 2 died within 8 weeks
  - 1 responded to chemotherapy



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Benjamini O et al. ASH 2020;Abstract 545.

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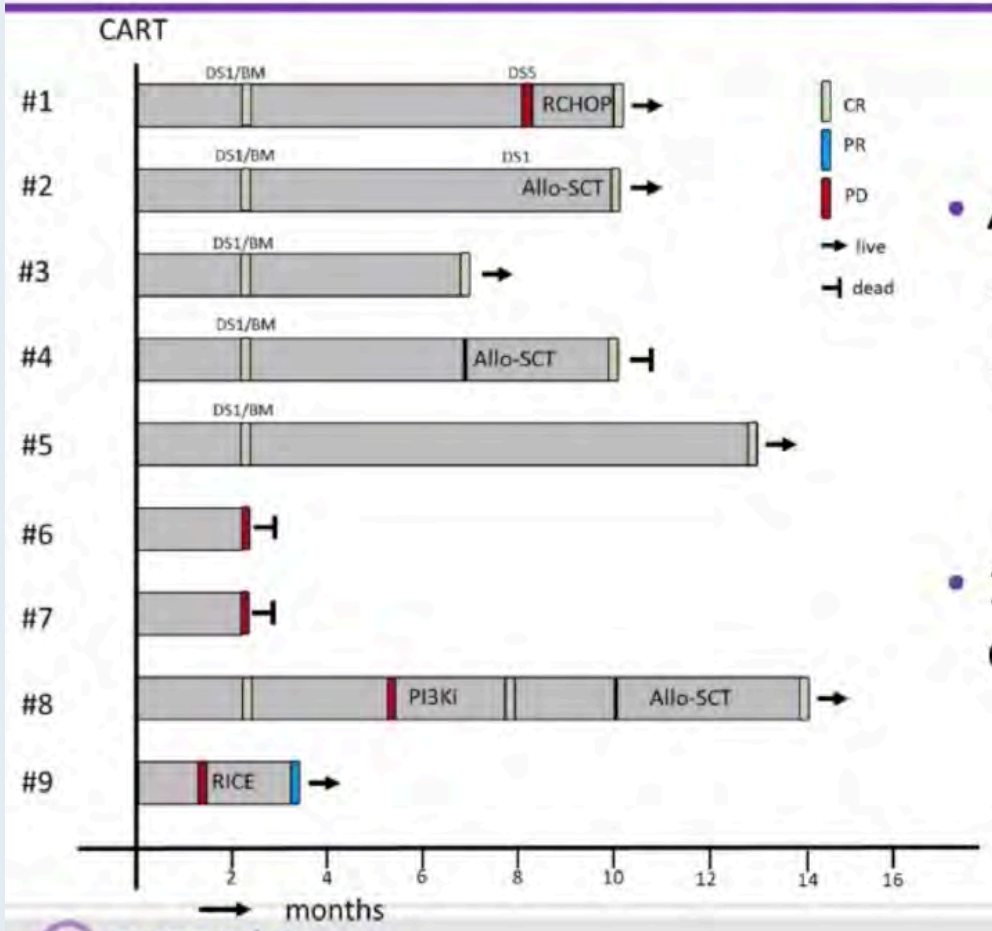
Outcome post CAR T-cell Tx



- After initial CR in 6 patients, 2 progressed
  - 1 responded to R-CHOP
  - 1 progressed with PLL, responded to duvelisib and underwent second allo-SCT in CR
- 1 patient in CR proceeded to allo-SCT and died due to severe GVHD

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Benjamini O et al. ASH 2020;Abstract 545.

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Prostate Cancer (Part 1 of a 3-Part Series)

Thursday, February 25, 2021
5:00 PM – 6:30 PM ET

Faculty

Tanya B Dorff, MD
Fred Saad, MD
A Oliver Sartor, MD
Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.