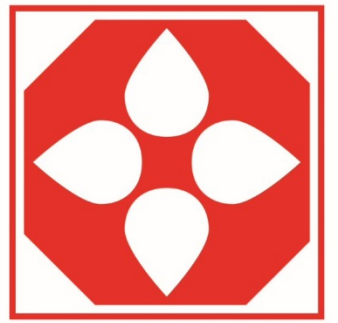
Ed Forum: ASH 2020 Comes to You!

February 4, 2021

10:00 AM PT, 11:00 AM MT,
12:00 PM CT, 1:00 PM ET



This program was made possible by grant support from

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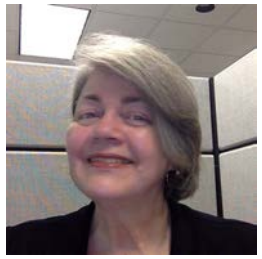
Agenda and Speakers

1:00 PM EST	Welcome	Patricia Koffman
1:05 PM	Encouraging Updates on Drugs in Development + the Sad State of **Test Before Treat™**	Dr. Anthony Mato
1:30 PM	CAPTIVTE Trial (I + V) and CAR-T Research: Lisocel + Ibrutinib	Dr. William Wierda
1:55 PM	New Combinations, New Sequences, New Ways to Measure Disease + CAR-T for Richters	Dr. Brian Koffman
2:15 PM	The Importance of ASH from a Caregiver's Perspective	Linda Lannom
2:25 PM	CLL Society's Programs & Services	Robyn Brumble
2:30 PM	Audience Q&A	Drs. Koffman, Mato, and Wierda
2:57 PM	Closing Remarks	Dr. Brian Koffman

Patricia Koffman
Co-Founder &
Communications Director
CLL Society

William G. Wierda, MD, PhD
The University of Texas MD
Anderson Cancer Center

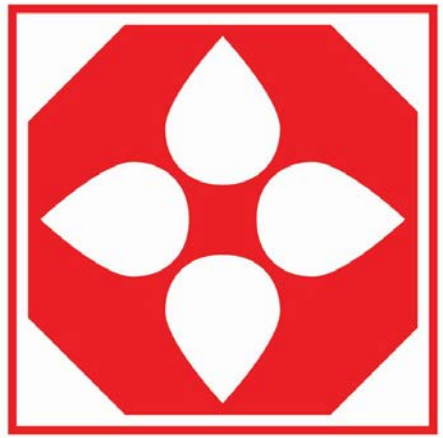


Linda Lannom
Patient Advocate,
Co-Facilitator, CLL Society
Oberlin, OH CLL Support Group

Anthony Mato, MD, MSCE
Memorial Sloan Kettering
Cancer Center

Brian Koffman, MDCM (retired), MS Ed
Co-Founder, EVP and Chief
Medical Officer,
CLL Society

Robyn Brumble, RN
Director of Scientific Affairs
CLL Society



CLL SOCIETY

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ASH 2020 CLL CAPTIVATE TRANSCEND CLL 004

William G. Wierda MD,PhD

Professor of Medicine

Section Head, CLL

Department of Leukemia

U.T. M.D. Anderson Cancer Center

Houston, TX USA

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

Phase 2 CAPTIVATE Study MRD Cohort

Patients (N=164)
- Previously untreated CLL/SLL
- Active disease requiring treatment per iwCLL criteria[1]
- Age <70 years
- ECOG PS 0–1

Ibrutinib lead-in
Ibrutinib 420 mg once daily
(3 cycles[a])

Ibrutinib + Venetoclax
Ibrutinib 420 mg once daily + venetoclax ramp-up to 400 mg once daily
(12 cycles[a])

MRD-guided randomization
Stratified by IGHV mutation status

Confirmed uMRD
Randomize 1:1 (double-blind)
- Placebo
- Ibrutinib

uMRD not confirmed
Randomize 1:1 (open-label)
- Ibrutinib
- Ibrutinib + Venetoclax

- **Confirmed undetectable MRD (uMRD):** defined as having uMRD ($<10^{-4}$ by 8-color flow cytometry) serially over at least 3 cycles, and undetectable MRD in both PB and BM
- **uMRD Not Confirmed:** Defined as having detectable MRD or uMRD not confirmed serially or not confirmed in both PB and BM
- **Primary endpoint:** 1-year DFS rate in patients with Confirmed undetectable MRD (uMRD) randomized to placebo vs ibrutinib
  - DFS rate: proportion of patients who remain free of MRD relapse ($\geq 10^{-2}$ confirmed on 2 separate occasions), and without disease progression or death
- **Key secondary endpoints:** rates of uMRD, response, PFS, TLS risk reduction, and safety

DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; TLS, tumor lysis syndrome.

[a]1 cycle = 28 days. 1. Hallek M et al. *Blood*. 2008;111:5446-5456.

Wierda et al. ASH 2020 Abstract #123

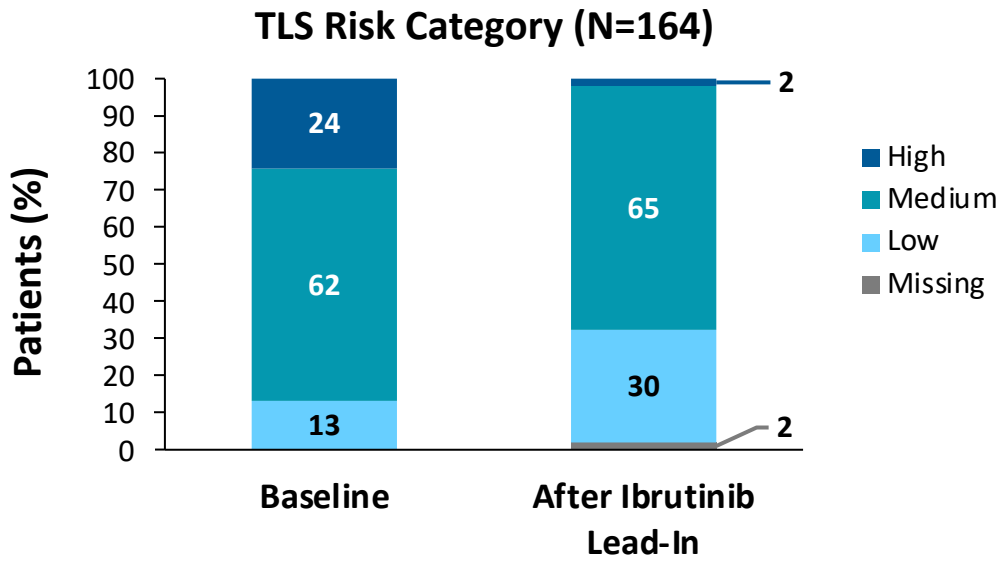
Baseline Characteristics in All-Treated Patients (N=164)

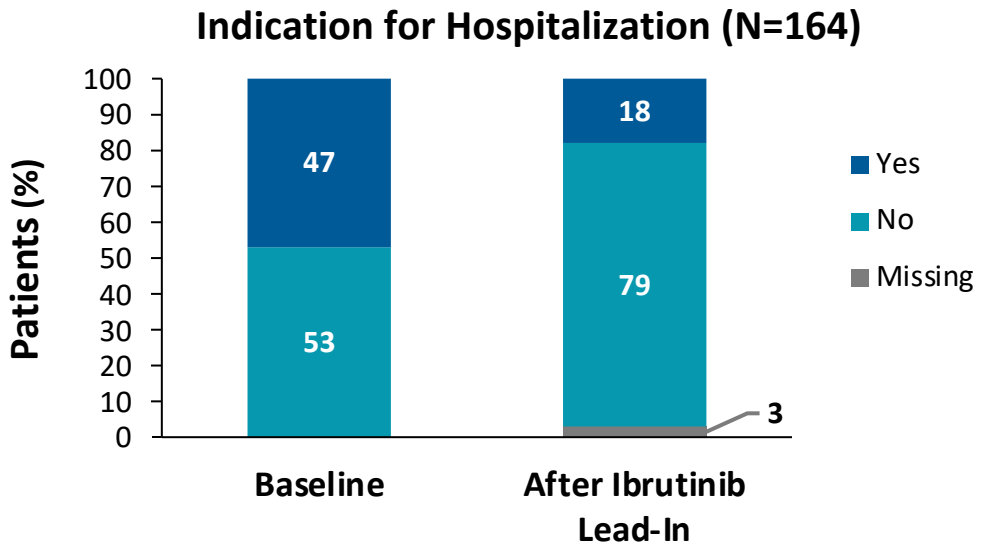
Characteristic	All Treated Population N=164
Median age (range), years	58 (28–69)
Rai stage III/IV disease, n (%)	53 (32)
High-risk features, n (%)	
del(17p)/*TP53* mutation	32 (20)
del(11q)[a]	28 (17)
Complex karyotype[b]	31 (19)
Unmutated IGHV	99 (60)
Any cytopenia, n (%)	59 (36)
ANC ≤1.5 × 10^9/L	14 (9)
Hemoglobin ≤11 g/dL	35 (21)
Platelets ≤100 × 10^9/L	30 (18)
Lymph node diameter, n (%)	
≥5 cm	53 (32)
Median ALC × 10^9/L (range)	56 (1–419)
ALC ≥25 × 10^9/L, n (%)	125 (76)

ALC, absolute lymphocyte count; ANC, absolute neutrophil count; CrCl, creatinine clearance.
[a]Without del(17p) per Dohner hierarchy. [b]Defined as ≥3 abnormalities by conventional CpG-stimulated cytogenetics by central lab.

Wierda et al. ASH 2020 Abstract #123

3 Cycles of Ibrutinib Lead-In Reduces TLS Risk and Hospitalization





- After ibrutinib lead-in, 90% of patients with baseline high TLS risk shifted to medium or low TLS risk categories[1]
- Among 77 patients for whom hospitalization would have been indicated[a] with venetoclax initiation, hospitalization was no longer indicated in 51 patients (66%) after ibrutinib lead-in
- Overall, 131/159 patients (82%) initiated venetoclax post-ibrutinib lead-in without hospitalization

TLS, tumor lysis syndrome.

[a]Defined as patients with high TLS risk or patients with medium TLS risk and CrCl <80 mL/min at baseline.

1. Siddiqi T et al. EHA 2020, Abstract #S158.

Wierda et al. ASH 2020 Abstract #123

High Rate of uMRD With 12 Cycles of Combined Ibrutinib + 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

CI, confidence interval.
[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.

1. Siddiqi T et al. EHA 2020, Abstract #S158.

Wierda et al. ASH 2020 Abstract #123

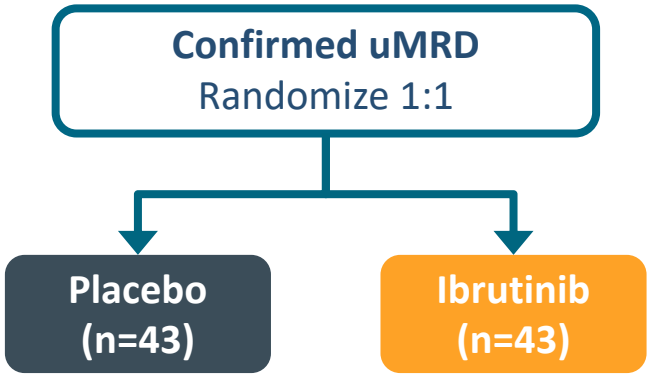
Baseline Characteristics By Randomized Treatment Arm

Characteristic	Confirmed uMRD (n=86)		uMRD Not Confirmed (n=63)	
	Placebo (n=43)	Ibrutinib (n=43)	Ibrutinib (n=31)	Ibrutinib + Venetoclax (n=32)
Median age (range), year	61 (43–69)	56 (34–69)	58 (28–69)	56 (37–69)
Rai stage III/IV disease, n (%)	**15 (35)**	**8 (19)**	**14 (45)**	**11 (34)**
High-risk features, n (%)				
del(17p)/*TP53* mutation	**2 (5)**	**13 (30)**	**5 (16)**	**8 (25)**
del(11q)[a]	8 (19)	10 (23)	3 (10)	2 (6)
Complex karyotype[b]	**4 (9)**	**13 (30)**	5 (16)	4 (13)
Unmutated IGHV	30 (70)	30 (70)	14 (45)	15 (47)
Any cytopenia, n (%)	19 (44)	6 (14)	13 (42)	14 (44)
ANC ≤1.5 × 10^9/L	**5 (12)**	**0**	**2 (6)**	**4 (13)**
Hemoglobin ≤11 g/dL	**14 (33)**	**2 (5)**	9 (29)	7 (22)
Platelets ≤100 × 10^9/L	4 (9)	4 (9)	9 (29)	9 (28)
Lymph node diameter, n (%)				
≥5 cm	**18 (42)**	**10 (23)**	**7 (23)**	**11 (34)**
Median ALC × 10^9/L (range)	53 (1–235)	56 (2–256)	85 (1–342)	87 (3–419)
ALC ≥25 × 10^9/L, n (%)	32 (74)	34 (79)	25 (81)	24 (75)

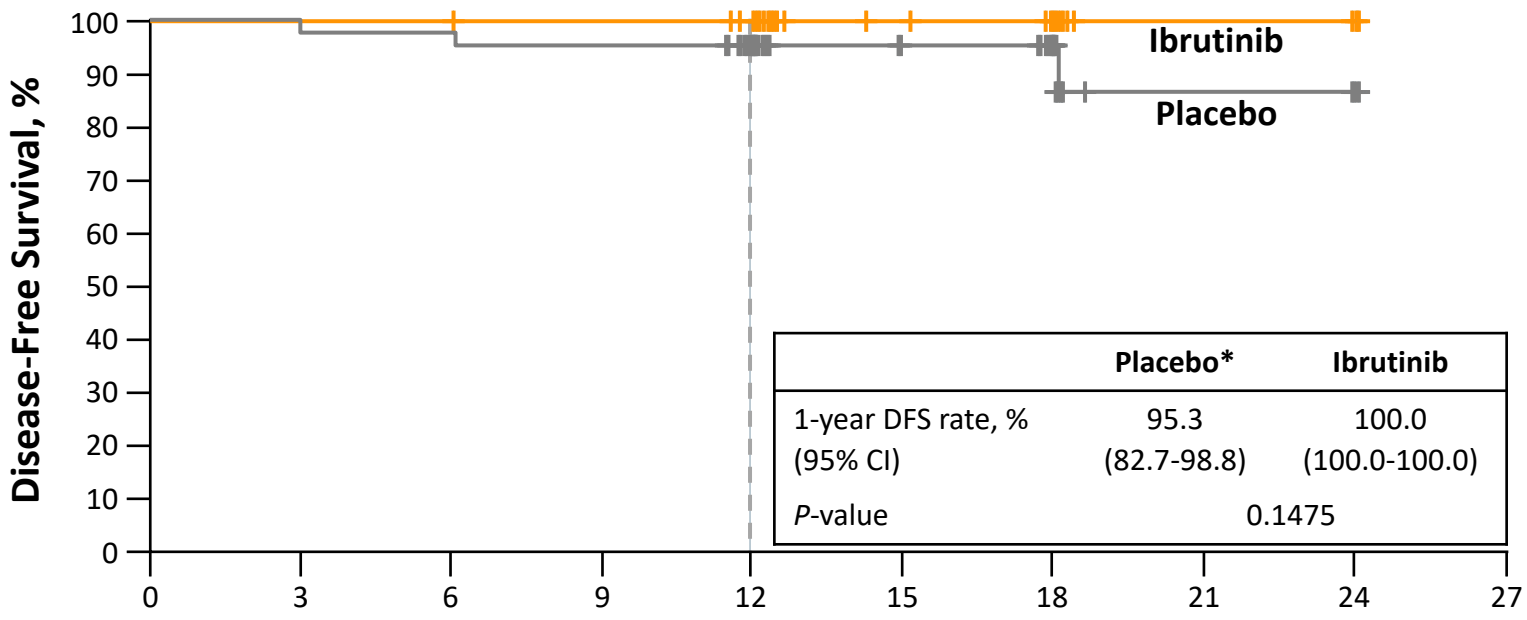
[a]Without del(17p) per Dohner hierarchy. [b]Defined as ≥3 abnormalities by conventional CpG-stimulated cytogenetics.

Wierda et al. ASH 2020 Abstract #123

1-year DFS After Randomization in Patients with Confirmed uMRD



- DFS: freedom from MRD relapse ($\geq 10^{-2}$ confirmed on 2 separate occasions), and without disease progression or death
- Median follow-up time 16.6 months post-randomization



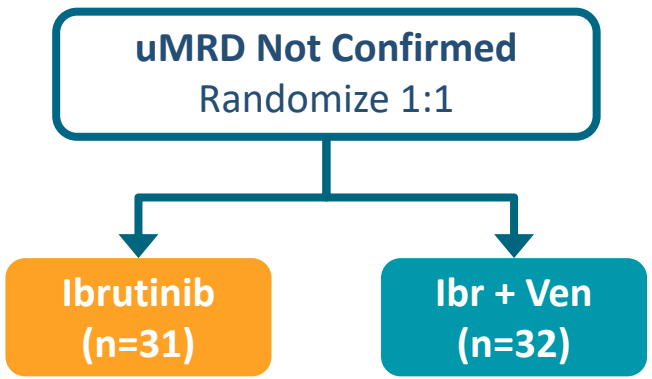
	Placebo*	Ibrutinib
1-year DFS rate, % (95% CI)	95.3 (82.7-98.8)	100.0 (100.0-100.0)
P-value	0.1475	

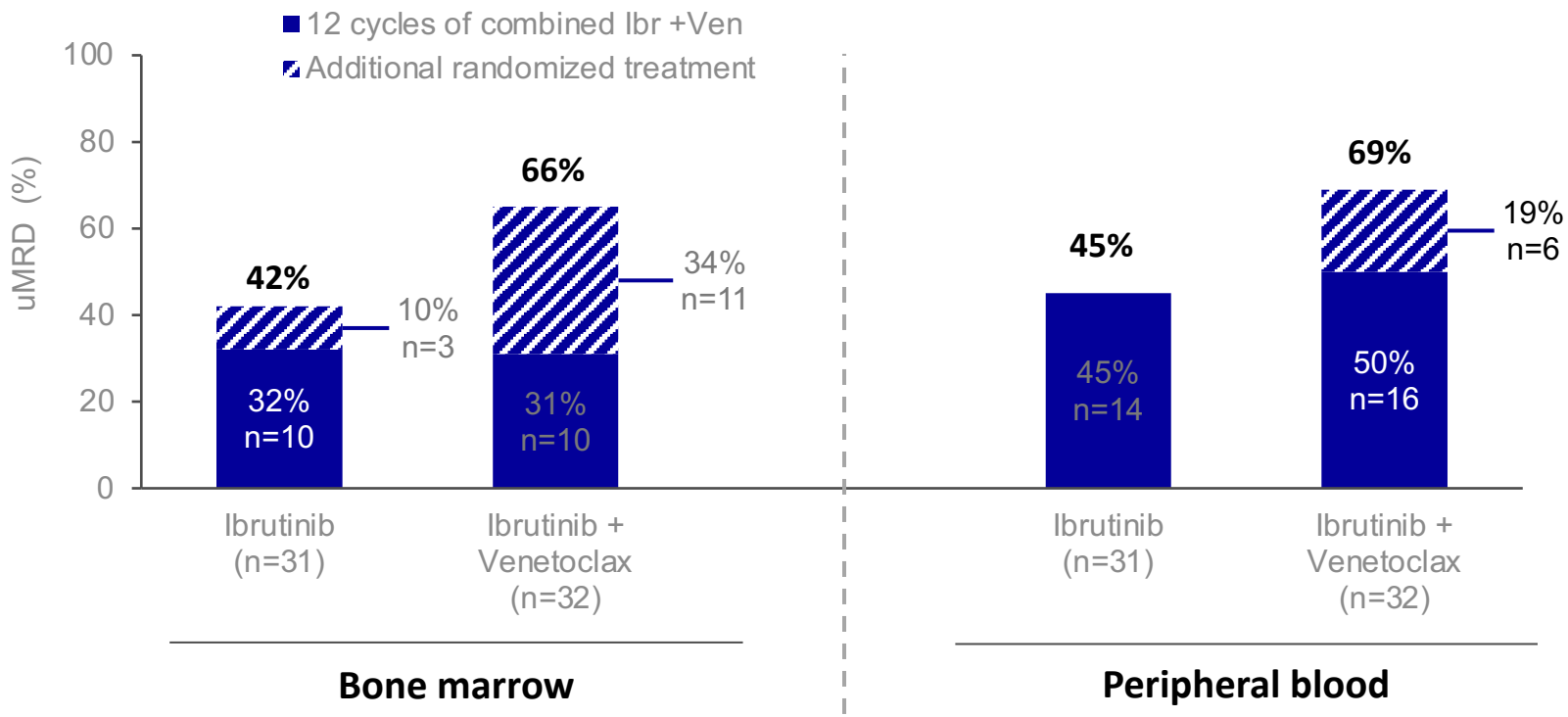
Patients at Risk										
Ibrutinib	43	43	43	42	40	24	21	5	3	0
Placebo	43	43	42	41	35	21	17	3	3	0

*The 3 DFS events in placebo arm were disease progression in 2 patients and MRD relapse in 1 patient.
Tick marks indicate patients with censored data.
DFS, disease-free survival.

Wierda et al. ASH 2020 Abstract #123

Best Overall uMRD Rates in uMRD Not Confirmed Population





- In patients without confirmed uMRD[a] after 12 cycles of combined ibrutinib + venetoclax, increases in uMRD were greater with continued ibrutinib + venetoclax versus ibrutinib alone

[a]Confirmed uMRD defined as having uMRD ($<10^{-4}$ by 8-color flow cytometry) serially over at least 3 cycles, and undetectable MRD in both PB and BM.

Wierda et al. ASH 2020 Abstract #123

Summary of AEs Leading to Dose Modification or Discontinuation By Randomized Treatment Arm

	Confirmed uMRD (n=86)		uMRD Not Confirmed (n=63)	
	Placebo (n=43)	Ibrutinib (n=43)	Ibrutinib (n=31)	Ibrutinib + Venetoclax (n=32)
AEs leading to dose reduction before randomization[a], n (%)				
Placebo/ibrutinib	4 (9)	4 (9)	5 (16)	7 (22)
Venetoclax	6 (14)	3 (7)	2 (6)	3 (9)
AEs leading to discontinuation before randomization, n (%)				
Placebo/ibrutinib	0	0	0	0
Venetoclax	0	1 (2)	0	0
AEs leading to dose reduction after randomization[a], n (%)				
Placebo/ibrutinib	1 (2)	3 (7)	2 (6)	2 (6)
Venetoclax	NA	NA	NA	0
AEs leading to discontinuation after randomization, n (%)				
Placebo/ibrutinib	0	0	1 (3)	2 (6)[b]
Venetoclax	NA	NA	NA	2 (6)[b]

[a]Dose reductions during pre-randomization in all-treated patients (N=164) occurred in 15% for ibrutinib (n=24) and 10% for venetoclax (n=16).

[b]The same 2 patients had AEs leading to discontinuation of both ibrutinib and venetoclax.

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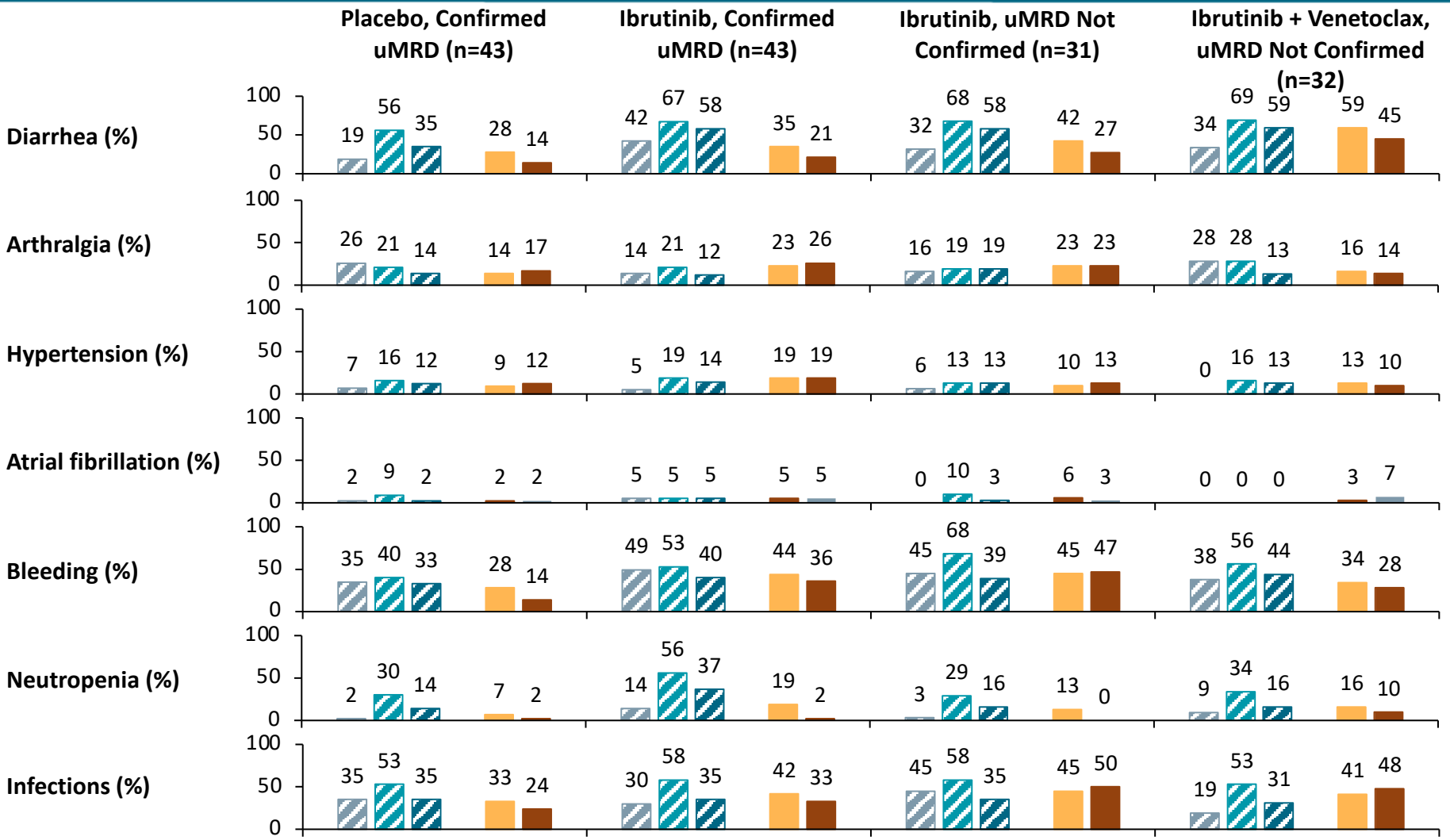
Prevalence of AEs of Interest (Any Grade) Over Time By Randomized Treatment Arm



Prevalence of AEs was generally highest during the first 6 months of pre-randomization ibrutinib + venetoclax and decreased over time irrespective of subsequent randomized treatment

- Ibrutinib lead-in, 1-3 mo
- Ibrutinib + Venetoclax, pre-randomization 4-9 mo
- Ibrutinib + Venetoclax, pre-randomization 10-15 mo
- Post-randomization 1-6 mo
- Post-randomization 7-12 mo*

*At post-randomization 7-12 months, Confirmed uMRD group: Placebo (n=42), Ibrutinib (n=42); uMRD Not Confirmed group: Ibrutinib (n=30); Ibrutinib + Venetoclax (n=29).

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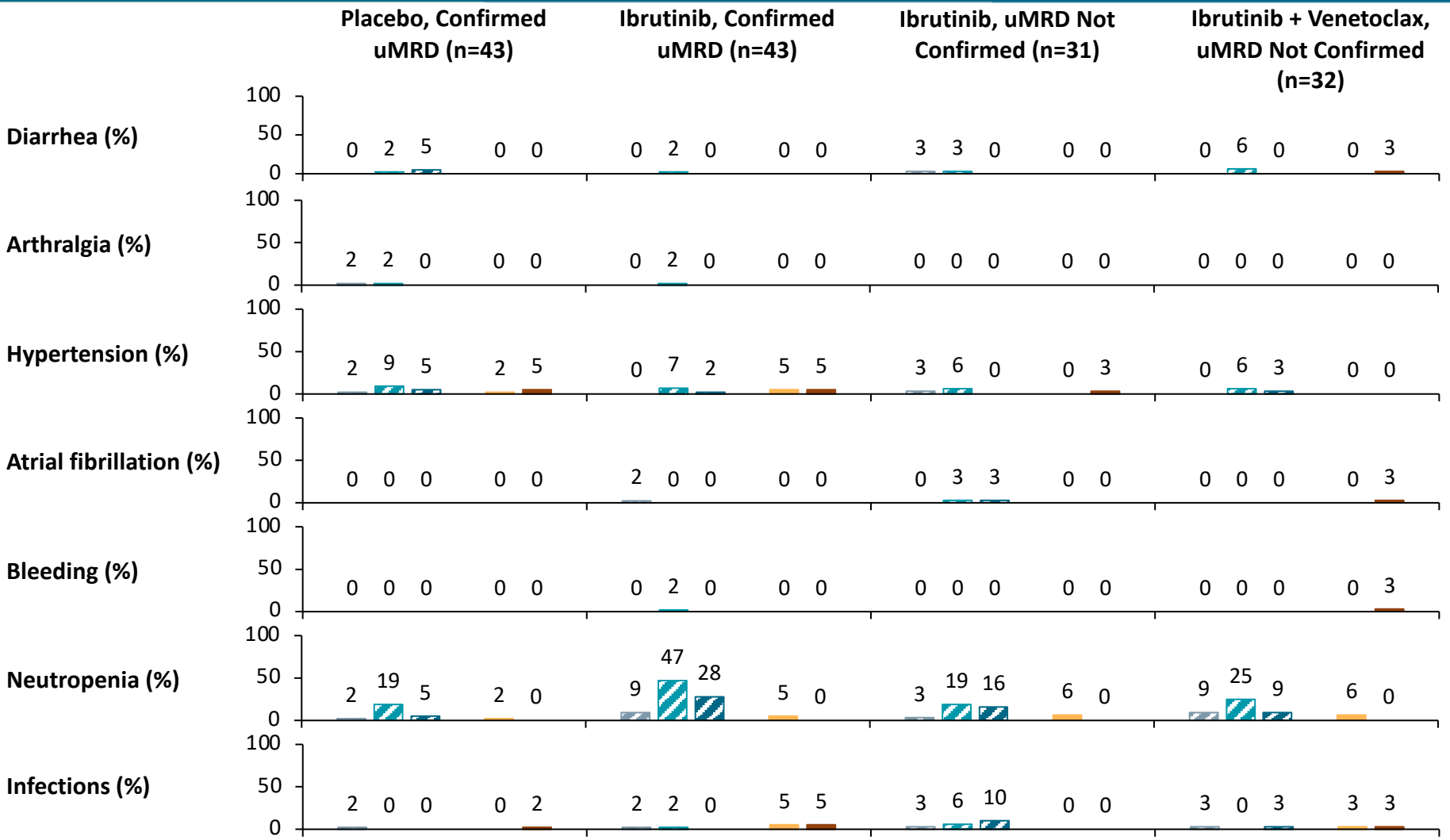
Prevalence of AEs of Interest (Grade ≥3) Over Time By Randomized Treatment Arm



Grade ≥3 AEs were infrequent across all randomized treatment arms

- Ibrutinib lead-in, 1-3 mo
- Ibrutinib + Venetoclax, pre-randomization 4-9 mo
- Ibrutinib + Venetoclax, pre-randomization 10-15 mo
- Post-randomization 1-6 mo
- Post-randomization 7-12 mo*

*At post-randomization 7-12 months, Confirmed uMRD group: Placebo (n=42), Ibrutinib (n=42); uMRD Not Confirmed group: Ibrutinib (n=30); Ibrutinib + Venetoclax (n=29).

Wierda et al. ASH 2020 Abstract #123

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]

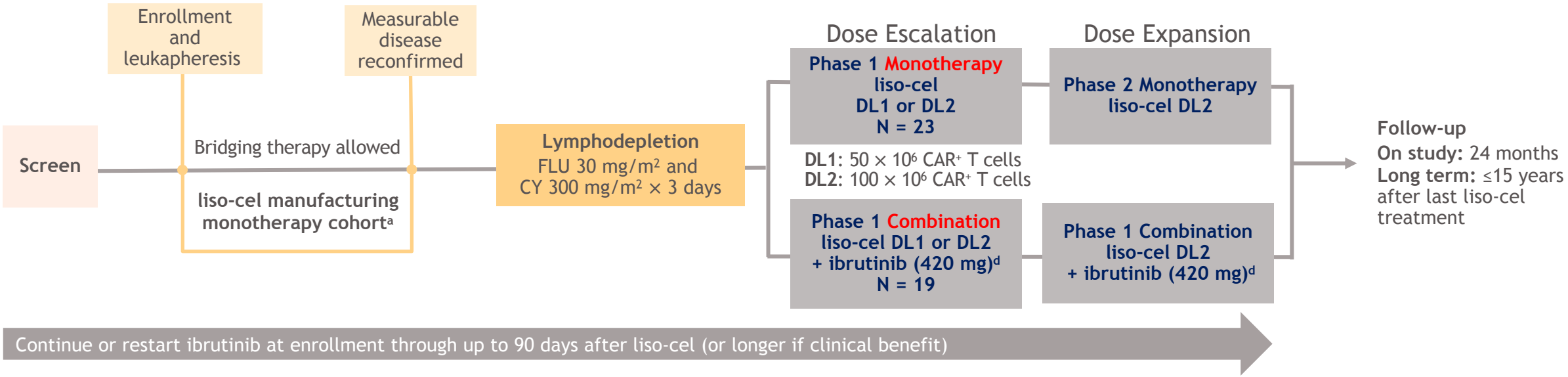
[1]City of Hope National Medical Center, Duarte, CA, USA; [2]Center for Lymphoma, Massachusetts General Hospital Cancer Center, Boston, MA, USA; [3]UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA, USA; [4]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [5]University 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

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

TRANSCEND CLL 004 Phase 1/2 Study Design[1] of liso-cel, a CD19-Directed, Defined Composition, CAR T Cell Product



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)

[a]Liso-cel conforming product was successfully manufactured for 23 of 24 patients in the monotherapy phase 1 cohort; one patient who received nonconforming product was excluded from the safety-evaluable population (N = 23). [b]Defined as patients whose disease progressed on BTKi. [c]Complex cytogenetic abnormalities, del(17p), *TP53* mutated, or unmutated *IGHV*. [d]Lower dose was used if prior dose reduction was necessary to manage toxicity. [e]MRD was assessed in blood by flow cytometry and/or in bone marrow by next-generation sequencing (both with a sensitivity of $\leq 10^{-4}$).
CY, cyclophosphamide; DL, dose level; FLU, fludarabine; iwCLL, International Workshop on CLL; mTPI, modified toxicity probability interval.

1. ClinicalTrials.gov. NCT03331198; 2. Guo W, et al. *Contemp Clin Trials*. 2017;58:23-33; 3. Hallek M, et al. *Blood*. 2018;131:2745-2760

Siddiqi et al. ASH 2020 Abstract #546

TRANSCEND CLL 004 (Mono): Treatment-Emergent AEs, Cytokine Release Syndrome, and Neurological Events

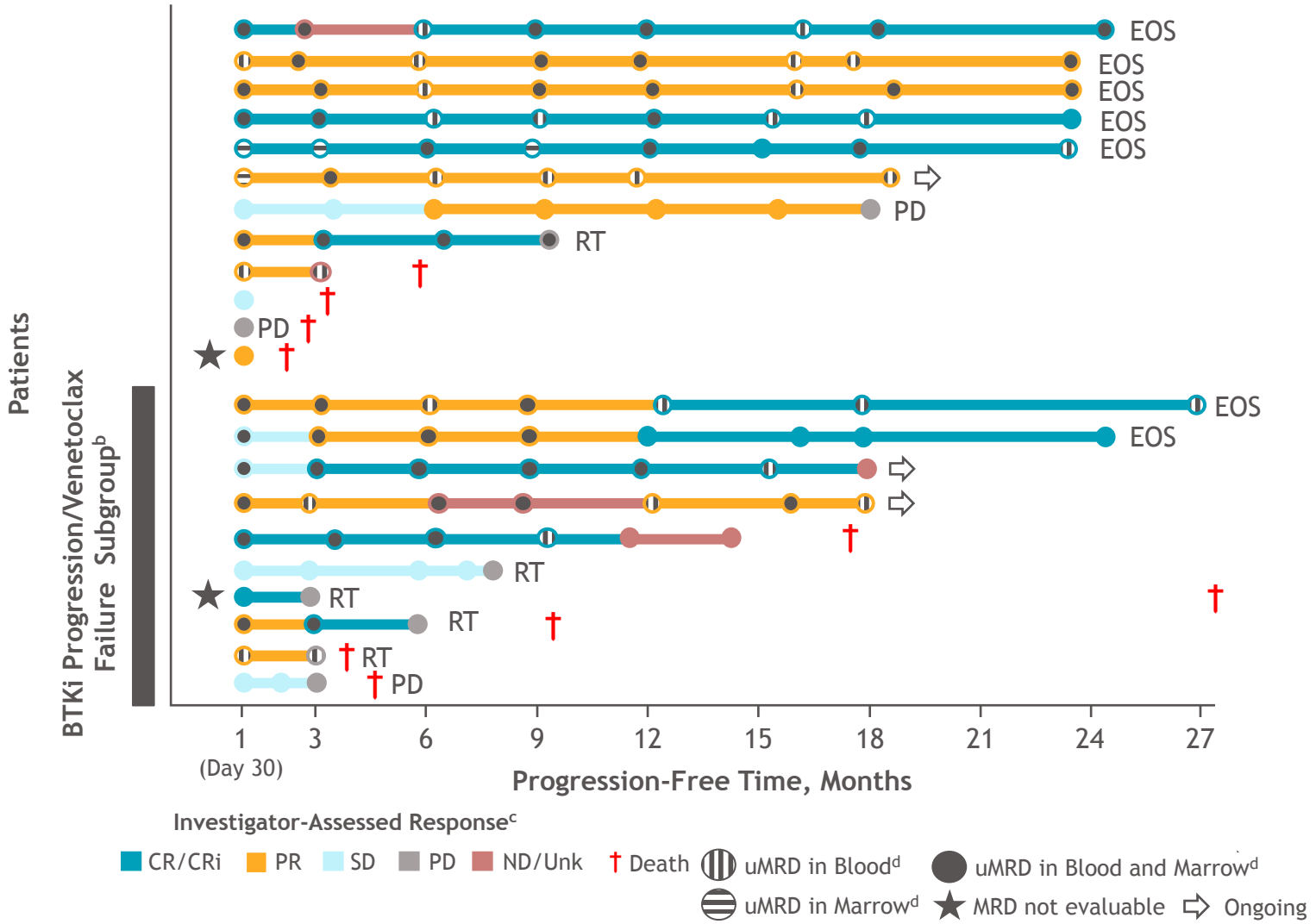
- Dose-limiting toxicities were reported for 2 patients at DL2, which resolved
- No late or delayed AEs of concern have emerged with longer follow-up

Parameter	Monotherapy Cohort (N = 23)	BTKi Progression/Venetoclax Failure Subgroup[c] (n = 11)
Common grade 3/4 treatment-emergent AEs (TEAEs), n (%)		
Anemia	17 (74)	7 (64)
Thrombocytopenia	16 (70)	6 (55)
Neutropenia/neutrophil count decrease	16 (70)	8 (73)
Leukopenia	10 (43)	2 (18)
Cytokine release syndrome (CRS)[d]		
All-grade CRS, n (%)	17 (74)	7 (64)
Median time to CRS onset, days (range)	3 (1–10)	1 (1–10)
Median duration of CRS, days (range)	12 (2–50)	15 (5–50)
Grade 3 CRS,[a] n (%)	**2 (9)**	2 (18)
Neurological events (NEs)		
All-grade NEs, n (%)	9 (39)	5 (46)
Median time to NE onset, days (range)	4 (2–21)	4 (2–21)
Median duration of NE, days (range)	20.5 (6–50)	38 (6–50)
Grade ≥3 NEs,[b] n (%)	**5 (22)**	3 (27)
Management of CRS and/or NEs, n (%)		
Tocilizumab only	6 (26)	1 (9)
Corticosteroids only	1 (4)	1 (9)
Tocilizumab and corticosteroids	8 (35)	4 (36)

[a]No grade 4 or 5 CRS events were reported. [b]NEs were not mutually exclusive: encephalopathy (n = 3), aphasia (n = 1), confusional state (n = 1), muscular weakness (n = 1), and somnolence (n = 1). [c]Defined as patients whose disease progressed on BTKi and failed venetoclax due to progression, intolerance, or failure to respond after at least 3 months of therapy. [d]Based on Lee criteria (Lee et al, *Blood*. 2014;124:188–195).

Siddiqi et al. ASH 2020 Abstract #546

TRANSCEND CLL 004 (**Mono**): Patient Response at 24-Month Median Follow-Up



- ORR was 82% (CR/CRi, 46%; PR, 36%), with 68% (n = 15/22)[a] of patients achieving a rapid response within 30 days
- 27% (n = 6/22) of patients had a deepening of response
- Response was durable. At 12 months, 50% (n = 11/22) were in response and only 2 of these responders progressed beyond 12 months
- Four of the 15 patients with uMRD (blood) response (CR or PR) have progressed, with 3 due to Richter transformation (RT)
- The subgroup also demonstrated rapid and durable responses
- Four of 6 progression events in the subgroup were due to RT

[a]One patient had RT before lymphodepleting chemotherapy and was excluded from the efficacy analysis. [b]Defined as patients whose disease progressed on BTKi and failed venetoclax due to progression, intolerance, or failure to respond after at least 3 months of therapy. [c]Evaluated according to iwCLL 2018 criteria. [d]Assessed in blood by flow cytometry and/or in bone marrow by next-generation sequencing (both with a sensitivity of $\leq 10^{-4}$). CRi, CR with incomplete blood count recovery; EOS, end of study; ND, not done; Unk, unknown.

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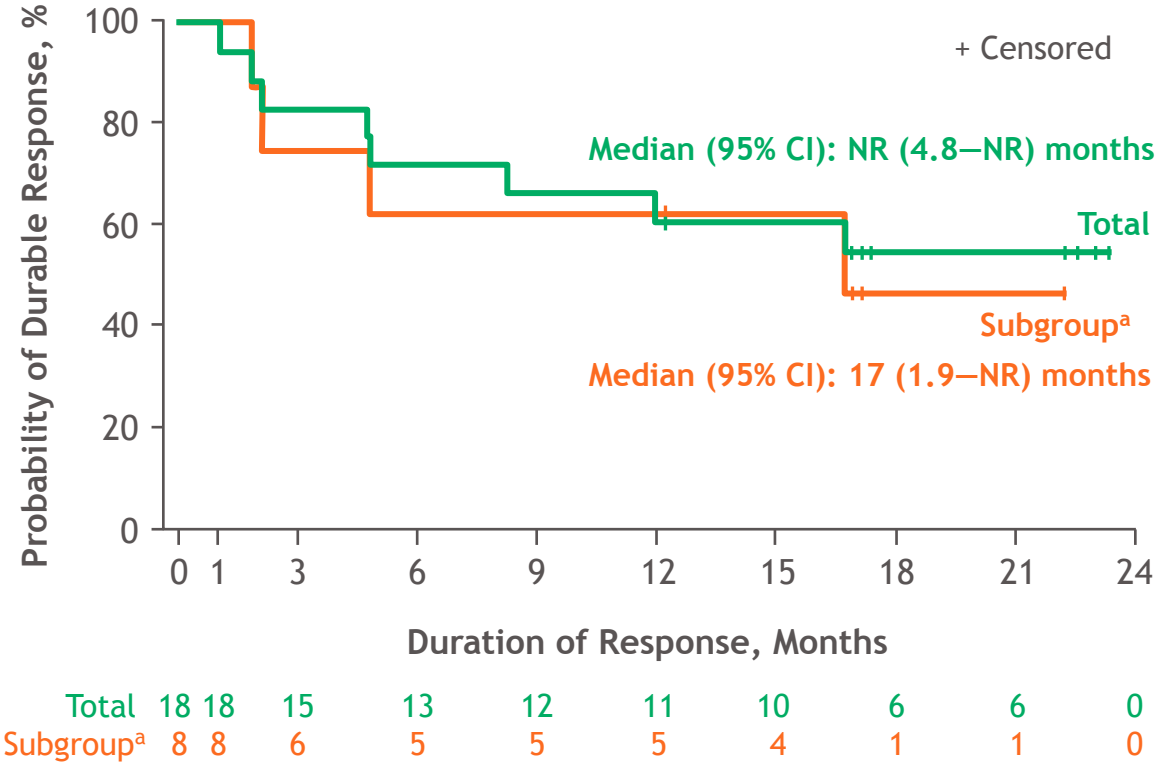
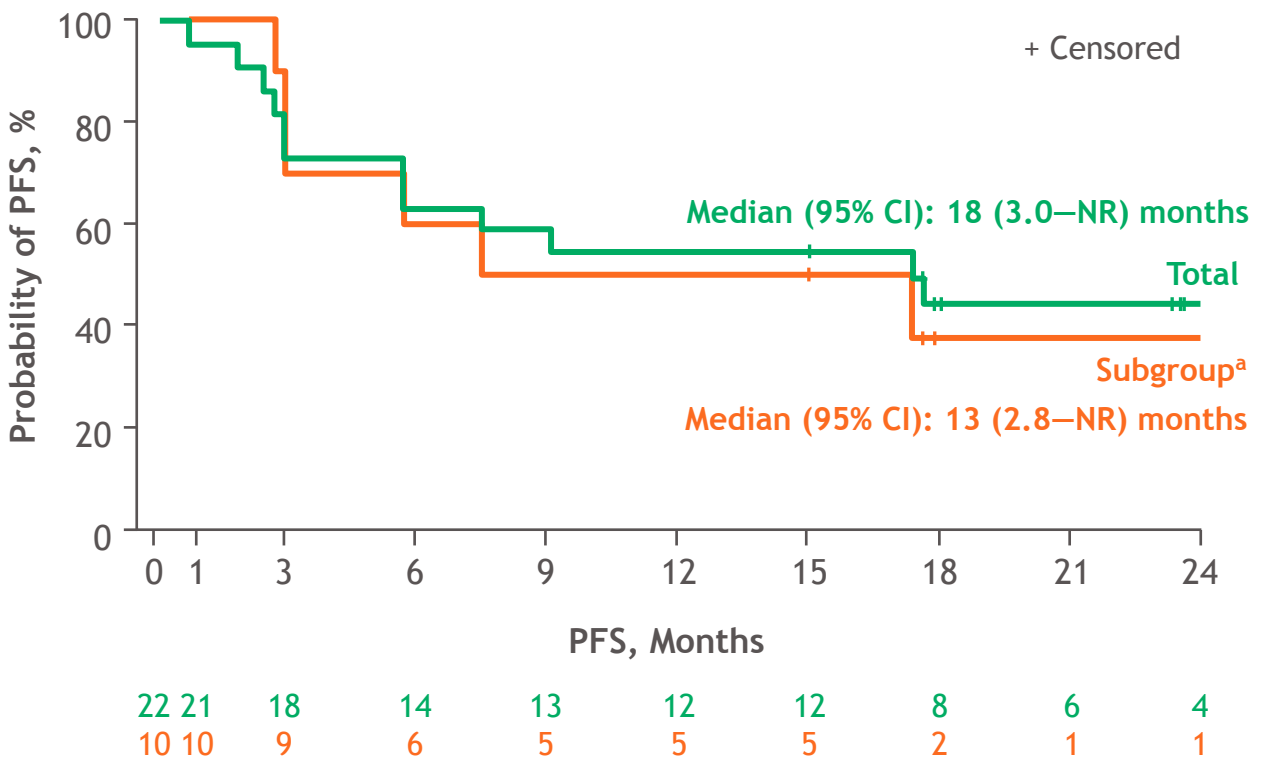
TRANSCEND CLL 004 (Mono): Duration of Response and PFS at 24-Month Median Follow-Up





[a]Defined as patients whose disease progressed on BTKi and failed venetoclax due to progression, intolerance, or failure to respond after at least 3 months of therapy.
NR, not reached.

Siddiqi et al. ASH 2020 Abstract #546

TRANSCEND CLL 004 (Combo): Demographic and Baseline Disease Characteristics

Characteristic	Combination Cohort (N = 19)	DL1 + Ibrutinib (n = 4)	DL2 + Ibrutinib (n = 15)
Median age, y (range)	61 (50–77)	58 (50–70)	61 (51–77)
Male, n (%)	12 (63)	2 (50)	10 (67)
Median time since diagnosis, mo (range)	121 (21–252)	84 (31–176)	127 (21–252)
Bulky disease ≥5 cm, n (%)[a]	6 (32)	0	6 (40)
Median SPD, cm^2 (range)	30 (2–193)	27 (2–55)	32 (3–193)
Median BALL risk score[1] (range)	2 (0–3)	2.5 (1–3)	1 (0–3)
Median LDH, U/L (range)	202 (104–604)	182.5 (104–428)	202 (106–604)
Stage, n (%)			
Rai stage III/IV	9 (47)	2 (50)	7 (47)
Binet stage C	9 (47)	2 (50)	7 (47)
High-risk feature (any), n (%)	18 (95)	4 (100)	14 (93)
Del(17p)	8 (42)	2 (50)	6 (40)
TP53 mutated	6 (32)	1 (25)	5 (33)
Complex karyotype[b]	8 (42)	3 (75)	5 (33)
Median no. of lines of prior therapy (range)	4 (1–10)	4.5 (1–5)	3 (2–10)
Prior ibrutinib, n (%)	19 (100)	4 (100)	15 (100)
Ibrutinib relapsed/refractory, n (%)	19 (100)	4 (100)	15 (100)
Prior BTKi and venetoclax, n (%)	11 (58)	2 (50)	9 (60)
Received bridging therapy, n (%)	8 (42)	2 (50)	6 (40)

[a]Bulky disease defined as ≥1 lesion with longest diameter of ≥5 cm. [b]At least 3 chromosomal aberrations.
BALL, β_2 microglobulin, anemia, LDH, last therapy; BTKi, Bruton tyrosine kinase inhibitor; SPD, sum of the product of perpendicular diameters.
1. Soumerai JD, et al. *Lancet Haematol*. 2019;6:e366-e374.

Wierda et al. ASH 2020 Abstract #544

TRANSCEND CLL 004 (Combo): Treatment-Emergent AEs, Cytokine Release Syndrome, and Neurological Events

- The combination of liso-cel and ibrutinib was well tolerated, with no reported dose-limiting toxicities
- No grade 5 AEs or grade 4 CRS or NEs were reported

Parameter	Combination Cohort (N = 19)	DL1 + Ibrutinib (n = 4)	DL2 + Ibrutinib (n = 15)
Common grade 3/4 treatment-emergent AEs (TEAEs), n (%)	18 (95)	4 (100)	14 (93)
Neutropenia/neutrophil count decrease	17 (89)	3 (75)	14 (93)
Anemia	9 (47)	3 (75)	6 (40)
Febrile neutropenia	5 (26)	1 (25)	4 (27)
Cytokine release syndrome (CRS)[a]			
All-grade CRS, n (%)	14 (74)	4 (100)	10 (67)
Median time to CRS onset, days (range)	6.5 (1–13)	8 (6–13)	5.5 (1–8)
Median duration of CRS, days (range)	6 (3–13)	6.5 (4–7)	5.5 (3–13)
Grade 3 CRS, n (%)	**1 (5)**	**1 (25)**	**0**
Neurological events (NEs)			
All-grade NEs, n (%)	6 (32)	2 (50)	4 (27)
Median time to NE onset, days (range)	8 (5–12)	9 (6–12)	8 (5–10)
Median duration of NE, days (range)	6.5 (1–8)	8 (8–8)	5 (1–7)
Grade 3 NEs,[b] n (%)	**3 (16)**	**0**	**3 (20)**
Management of CRS and/or NEs, n (%)			
Tocilizumab only	2 (11)	0	2 (13)
Corticosteroids only	3 (16)	2 (50)	1 (7)
Tocilizumab and corticosteroids	3 (16)	1 (25)	2 (13)

[a]Based on Lee criteria (Lee et al, *Blood*. 2014;124:188-195). [b]NEs were not mutually exclusive: aphasia (n = 1), ataxia (n = 1), and encephalopathy (n = 1).

Wierda et al. ASH 2020 Abstract #544

TRANSCEND CLL 004 (Combo): Ibrutinib-Related TEAEs Rarely Resulted in Dose Reduction or Discontinuation

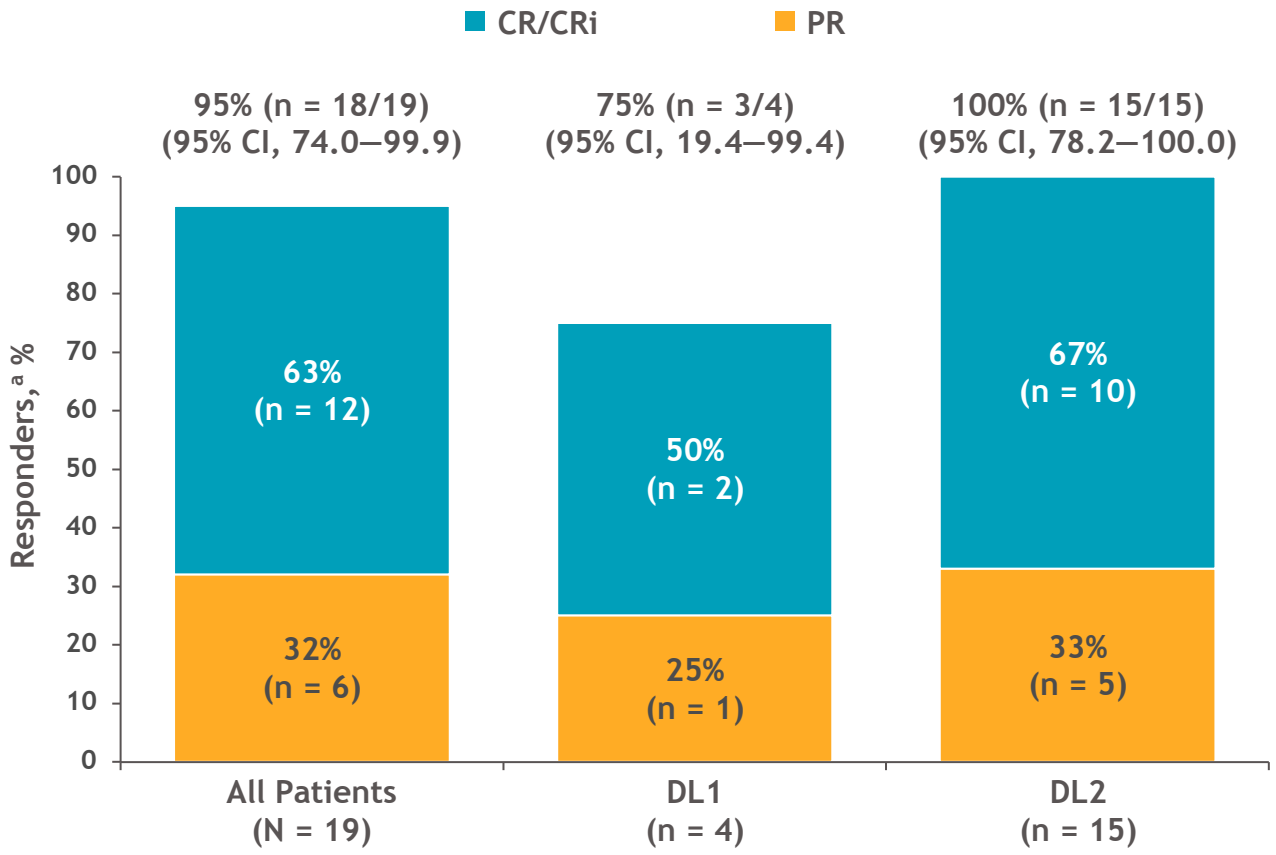
Parameter	Combination Cohort (N = 19)	DL1 + Ibrutinib (n = 4)	DL2 + Ibrutinib (n = 15)
Ibrutinib-related TEAEs, n (%) Grade 3/4 ibrutinib-related TEAEs	15 (79) 7 (37)	3 (75) 2 (50)	12 (80) 5 (33)
Ibrutinib dose reduced due to TEAE, n (%)	2 (11)	0	2 (13)
Ibrutinib discontinued due to TEAE, n (%)	4 (21)	1 (25)	3 (20)
Received ≥90 days of ibrutinib after liso-cel,[a] n (%)	14 (74)	3 (75)	11 (73)
Median total duration of ibrutinib therapy, days (range)	141 (65—421)	161.5 (94—285)	141 (65—421)
Median duration of ibrutinib therapy after liso-cel infusion, days (range)	97 (14—388)	132 (59—197)	97 (14—388)

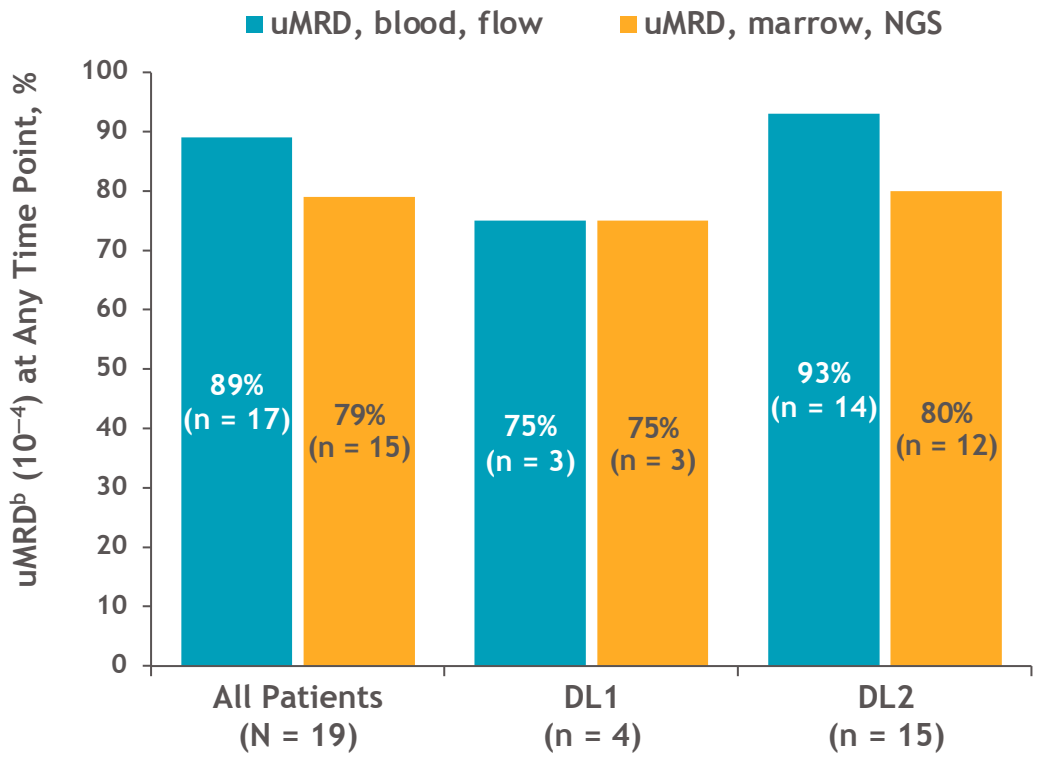
[a]Four patients were still receiving ibrutinib.

- Grade 3/4 ibrutinib-related TEAEs included: anemia (n = 4), neutropenia/neutrophil count decrease (n = 4), atrial fibrillation (n = 1), hypertension (n = 1), lung infection (n = 1), staphylococcal infection (n = 1), and thrombocytopenia (n = 1)
- TEAEs/toxicities leading to ibrutinib dose reduction (all resolved):
  - Grade 2 atrial fibrillation and grade 2 fatigue
- TEAEs leading to ibrutinib discontinuation (all resolved):
  - Grade 3 atrial fibrillation, grade 2 red blood cell aplasia (related to liso-cel), grade 2 fatigue, and grade 1 palpitations

Wierda et al. ASH 2020 Abstract #544

TRANSCEND CLL 004 (Combo): Best Overall Response and uMRD (≤10^{-4}) at 10-Month Follow-Up



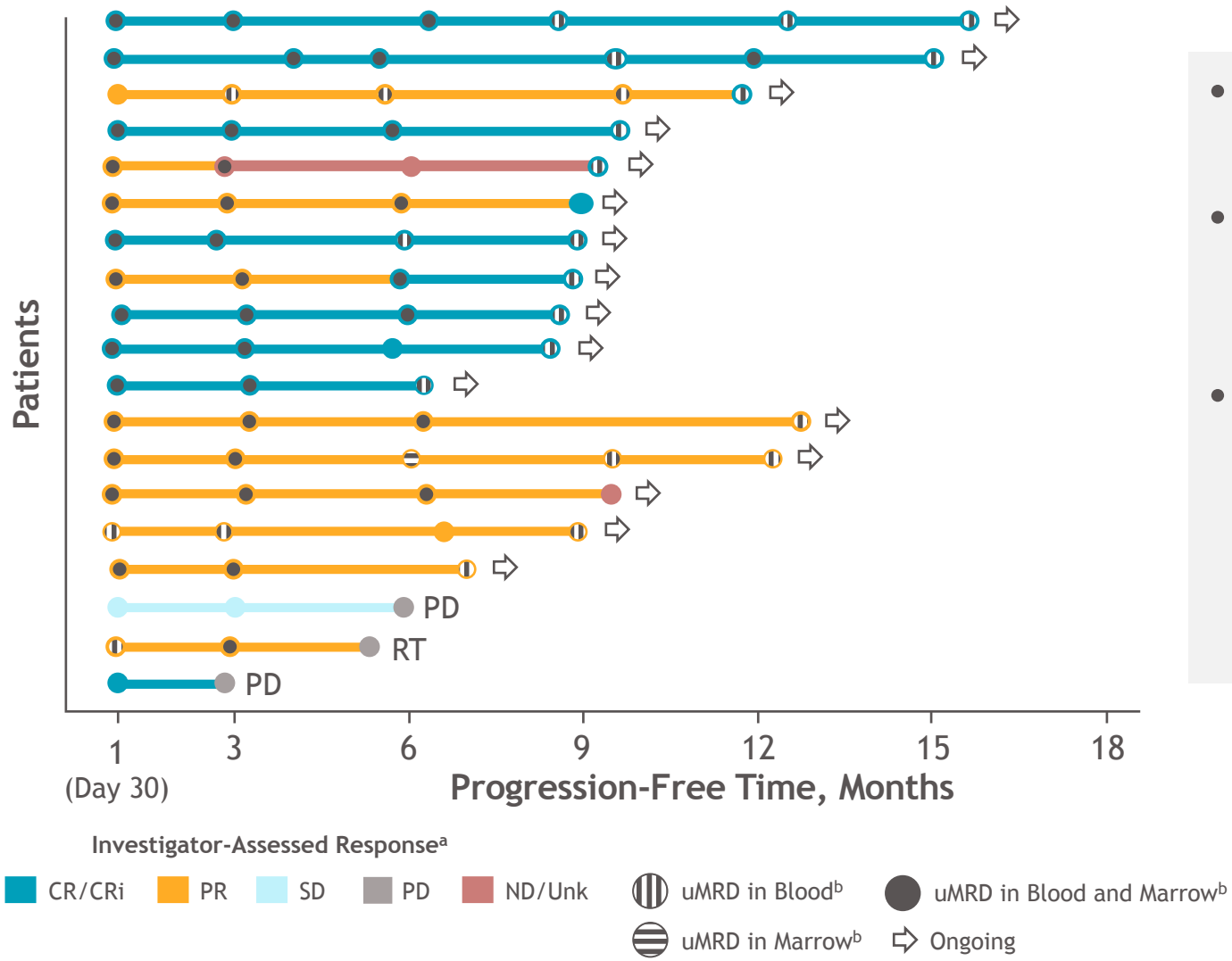


- No patients had PD during the first month after liso-cel
- One patient at DL1 had SD for 6 months but later progressed

[a]Evaluated according to iwCLL 2018 criteria. [b]Assessed in blood by flow cytometry and/or in bone marrow by NGS.
CRi, CR with incomplete blood count recovery; NGS, next-generation sequencing.

Wierda et al. ASH 2020 Abstract #544

TRANSCEND CLL 004 (Combo): Patient Responses over Time at 10-Month Follow-Up

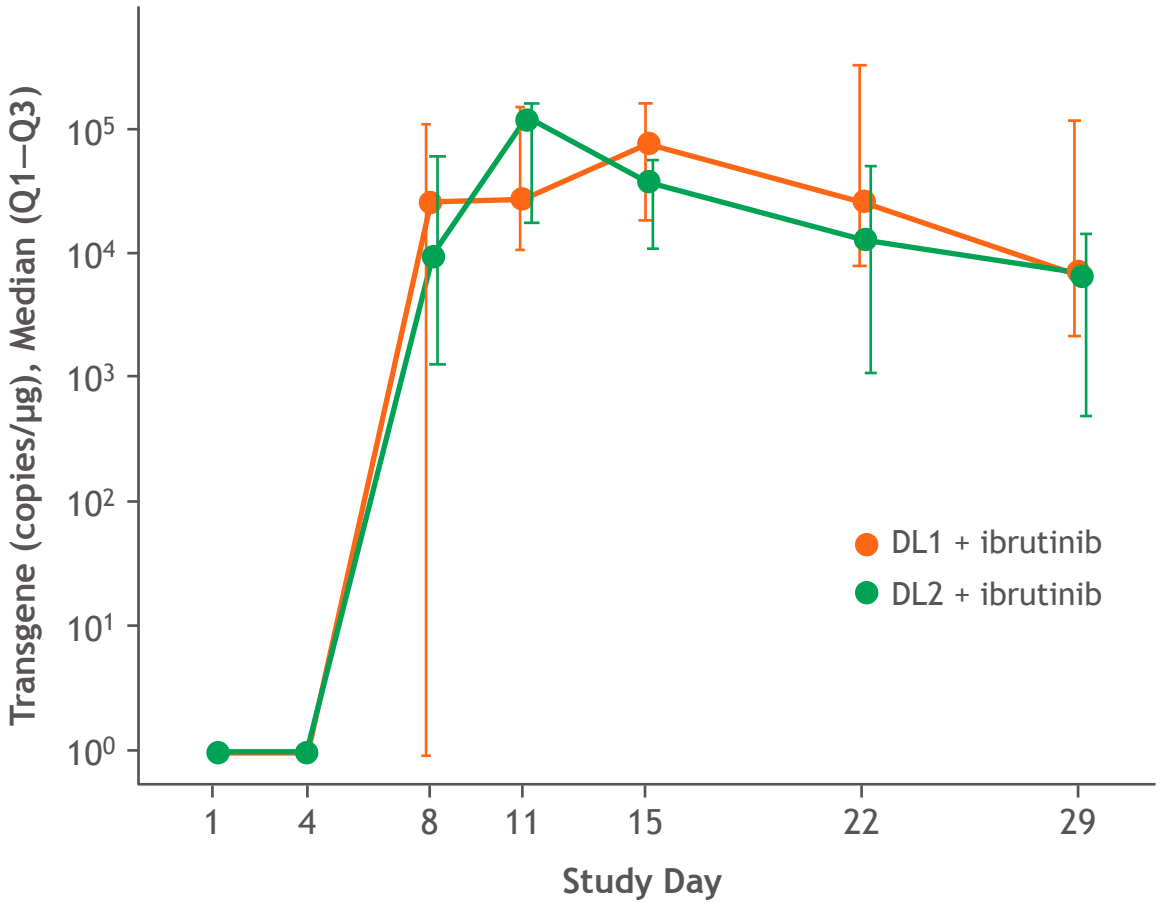


- All responders (n = 18/19) achieved a response by Day 30 after liso-cel
- Among 18 patients with ≥6 months of follow-up, 89% (n = 16/18) maintained or improved response from Day 30
- Of 17 patients who achieved uMRD in blood:
  - All achieved this response by Day 30
  - Only 1 later progressed due to Richter transformation (RT)

[a]Evaluated according to iwCLL 2018 criteria. [b]Assessed in blood by flow cytometry and/or in bone marrow by NGS.
ND, not done; Unk, unknown.

Wierda et al. ASH 2020 Abstract #544

TRANSCEND CLL 004 (Combo): Cellular Kinetics — Expansion and Persistence



Parameter[a,b]	Combination Cohort (N = 19)	DL1 + Ibrutinib (n = 4)	DL2 + Ibrutinib (n = 15)
C_{max} (copies/µg)	128,000 (47,100–344,000)	201,000 (91,400–309,000)	128,000 (45,100–377,000)
t_{max} (day)	11 (10–15)	12 (8.5–18)	11 (10–15)
$AUC_{0–28d}$ (day × copies/µg)	682,000 (390,000–2,720,000)	1,700,000 (536,000–3,000,000)	615,000 (348,000–1,800,000)

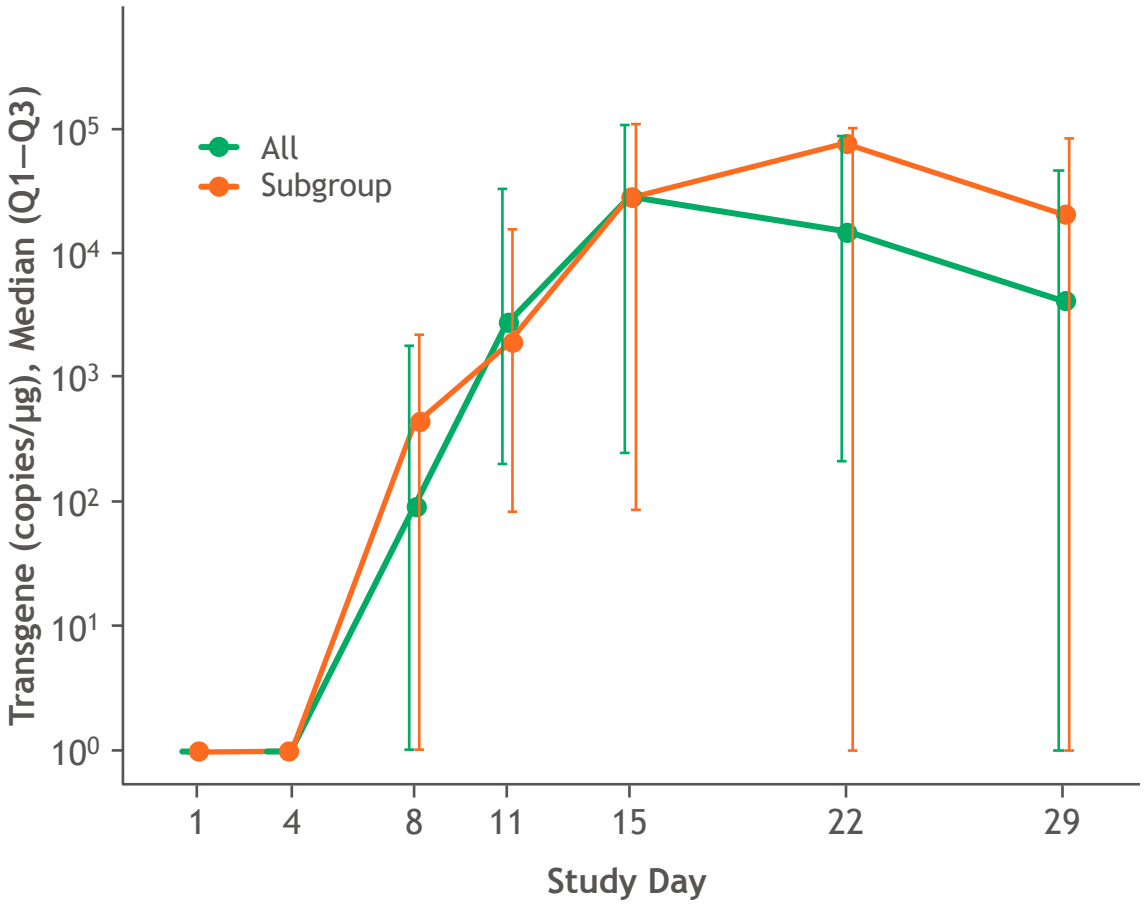
[a]Median (interquartile range, Q1–Q3). [b]Evaluated using qPCR.

- Long-term persistence
  - 38% of patients (n = 6/16) at 6 months
  - 20% of patients (n = 1/5) at 12 months

$AUC_{0–28d}$, area under the curve for transgene levels from 0 to 28 days postinfusion; C_{max}, maximum transgene levels; Q, quartile; t_{max}, time to C_{max}.

Wierda et al. ASH 2020 Abstract #544

TRANSCEND CLL 004 (**Mono**): Cellular Kinetics—Expansion and Persistence



Parameter[a,b]	Monotherapy Cohort (N = 23)	BTKi Progression/Venetoclax Failure Subgroup[c] (n = 11)
C_{max} (copies/µg)	67,300 (2510–139,000)	67,300 (982–163,000)
t_{max} (day)	15 (14–21)	20 (15–21)
$AUC_{0–28d}$ (day × copies/µg)	470,000 (17,400–1,740,000)	664,000 (7810–1,960,000)

[a]Median (interquartile range, Q1–Q3). [b]Evaluated using qPCR. [c]Defined as patients whose disease progressed on BTKi and failed venetoclax due to progression, intolerance, or failure to respond after at least 3 months of therapy.

- Long-term persistence
  - 50% of patients (n = 6/12) at 12 months
  - 18% of patients (n = 2/11) at 18 months

$AUC_{0–28d}$, area under the curve for transgene levels from 0 to 28 days postinfusion; C_{max}, maximum transgene levels; Q, quartile; t_{max}, time to C_{max}.

Siddiqi et al. ASH 2020 Abstract #546

CAPTIVATE AND TRANSCEND Conclusions for ASH2020 in CLL

- Combined targeted therapy (ibrutinib + venetoclax) results in deep remissions (uMRD) with fixed-duration treatment correlated also with long progression-free and overall survival
- CD19-CAR-T ± ibrutinib well-tolerated with durable remissions in refractory CLL

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ASH 2020: A Review of The Most Notable CLL Abstracts

Presented By: Dr. Brian Koffman

February 4, 2021

Introduction & Overview of ASH 2020

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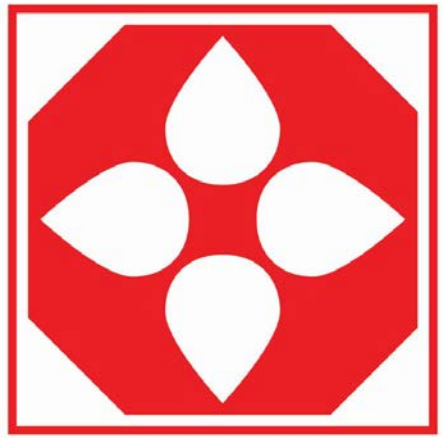
- New information pertaining to CLL:
  - COVID-19
  - Monitoring Response & Guiding Therapy
  - First Line Ibrutinib
  - Re-treating with Venetoclax
  - Acalabrutinib
  - New Drugs & Combination Therapies
  - CAR T



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COVID-19

Worldwide Examination of Patients with CLL Hospitalized for COVID-19

Worldwide Examination of Patients with CLL Hospitalized for COVID-19

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- There were 411 hospitalized CLL patients studied
- Symptoms were as expected:
  - Fever (>100.3° F) was present in 88% of patients
  - Lymphocyte counts were either abnormally up or down
  - About half were coughing and/or experienced shortness of breath
  - Of those admitted to the hospital, 90% needed supplemental oxygen
- For patients who had serious disease and were sick enough to be hospitalized, the mortality rate was 30-35%

Worldwide Examination of Patients with CLL Hospitalized for COVID-19

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- Difficult to predict who has worse odds of dying from COVID-19, but advanced age and co-morbidities increase the risk
- There might be a suggestion that chemo-immunotherapy treatment increases the risk of mortality
- There was no signal that ibrutinib or acalabrutinib help or hurt outcomes
- Could be due to most of those hospitalized that were on these novel agents had their medications held upon admission
- CAVEAT: Data was collected early on in the pandemic, and only studied patients who were symptomatic enough to report to their oncologist

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Monitoring Response & Guiding Therapy

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The Clinical Relevance of Residual, Persistent and Elongated Abnormal Sized Nodes By Longest Diameter in Patients with Chronic Lymphocytic Leukemia, Otherwise in a Complete Remission

The Clinical Relevance of Residual, Persistent and Elongated Abnormal Sized Lymph Nodes

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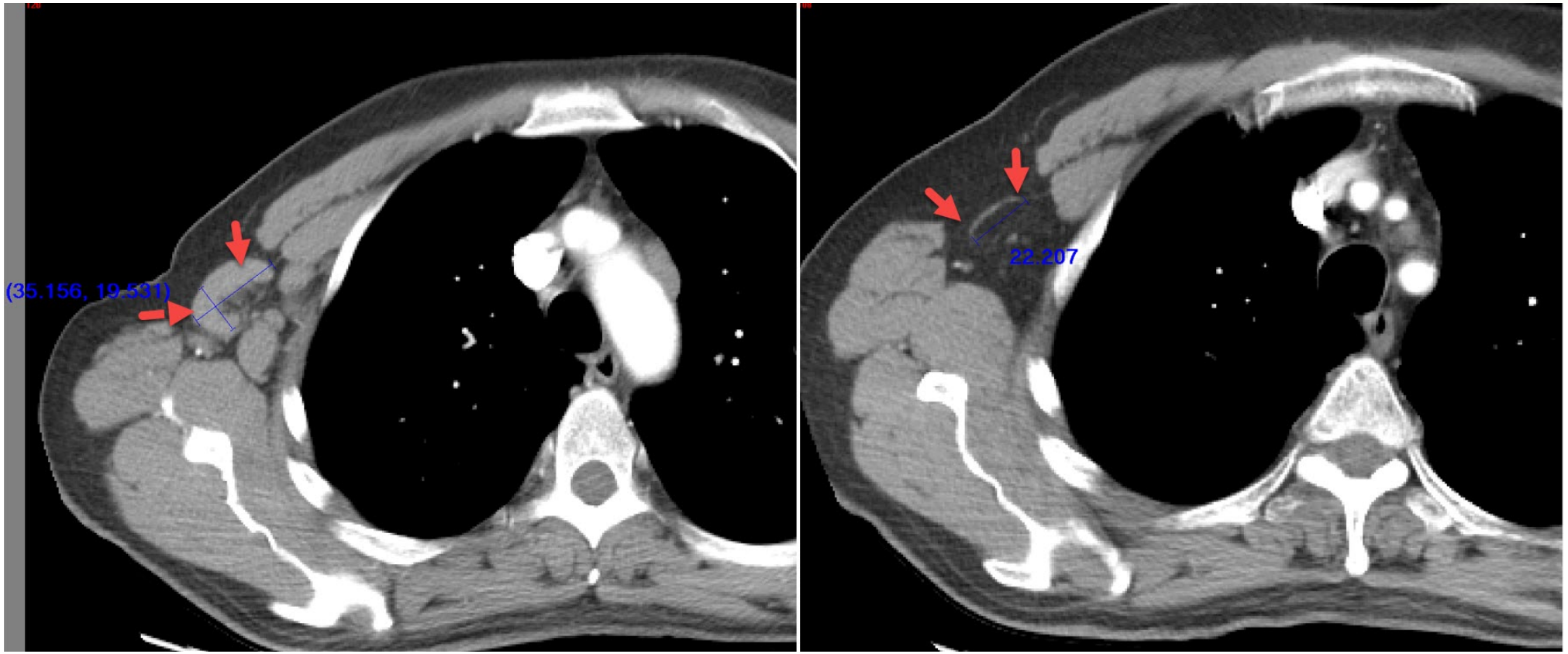
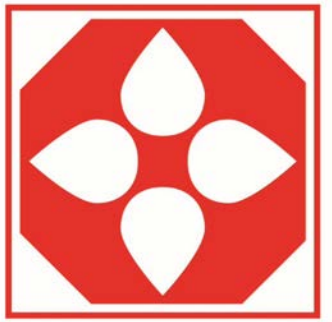
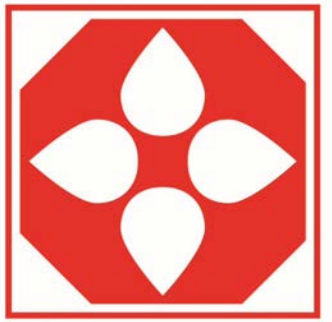


The Clinical Relevance of Residual, Persistent and Elongated Abnormal Sized Nodes By Longest Diameter in CLL Patients otherwise in a Complete Remission



- There were 1,168 patients across multiple phase III CLL clinical trials where targeted agents were studied
- Of those, 161 (13.8%) had an overall response of partial remission (PR) due to findings of abnormal Longest Diameter (LDi+) nodes on imaging (per iwCLL criteria >1.5 cm), even though the rest of the disease burden had normalized
- CBC and ALC were normal in all 161 patients
- Bone marrow was available for 31 patients and was negative complete remission (CR) in all

The Clinical Relevance of Residual, Persistent and Elongated Abnormal Sized Nodes By Longest Diameter in CLL Patients otherwise in a Complete Remission



- These patients continued to have a sustained response of CR in all other parameters for multiple follow up visits, with a median follow up of about 6 months
- An adaptation of the iwCLL criteria is proposed to allow hematologists/oncologists to update/override the radiology assessment from PR to CR based on clinical judgment if all other components of the oncology review (e.g., blood counts, bone marrow, target lesions, organ assessments) meet CR criteria

MRD-Driven Time Limited Therapy with Zanubrutinib, Obinutuzumab, and Venetoclax (BOVen) in Previously Untreated Chronic Lymphocytic Leukemia

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MRD-Driven Time Limited Therapy with Zanubrutinib, Obinutuzumab, and Venetoclax (BOVen) in Previously Untreated CLL

- Treatment duration was determined by a pre-specified uMRD endpoint (min 8 to max 24 cycles)
- Beginning C7D1 then every 2 cycles, patients with uMRD by flow cytometry at a sensitivity ≥10-4 (uMRD-FC4) in peripheral blood (PB) underwent bone marrow (BM) assessment in ≤14 days for MRD, with PB MRD-FC4 reassessed after 2 additional cycles
- Patients with uMRD-FC4 in PB on 2 consecutive measurements and in BM discontinued therapy and entered post-treatment surveillance

MRD-Driven Time Limited Therapy with Zanubrutinib, Obinutuzumab, and Venetoclax (BOVen) in Previously Untreated CLL

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- Of the 39 patients studied, with a median age of 59, 66% had high or very high risk CLL and 15.4% had 17p del and/or TP53 mutation
- The most common AEs (adverse events) were low neutrophils (56%), low platelets (49%), diarrhea (46%), bruising (41%), infusion related reaction (41%), nausea (26%), and myalgia (23%)
- At a median follow up of 14+ months, 92% of patients (34/37) achieved uMRD-FC4 in PB (peripheral blood) and 84% (31/37) in BM (bone marrow)
- Twenty-nine patients (77%) achieved the pre-specified MRD endpoint and discontinued treatment per protocol
- The value of MRD directed treatment duration will continue to be evaluated with ongoing follow-up

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First Line Ibrutinib

Outcomes of First-Line Ibrutinib in Patients with CLL and High-Risk Genomic Features with up to 6.5 Years Follow-up: Integrated Analysis of Two Phase 3 Studies (RESONATE-2 and iLLUMINATE)

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Outcomes of First-Line Ibrutinib in Patients with CLL and High-Risk Genomic Features with up to 6.5 Years Follow-up

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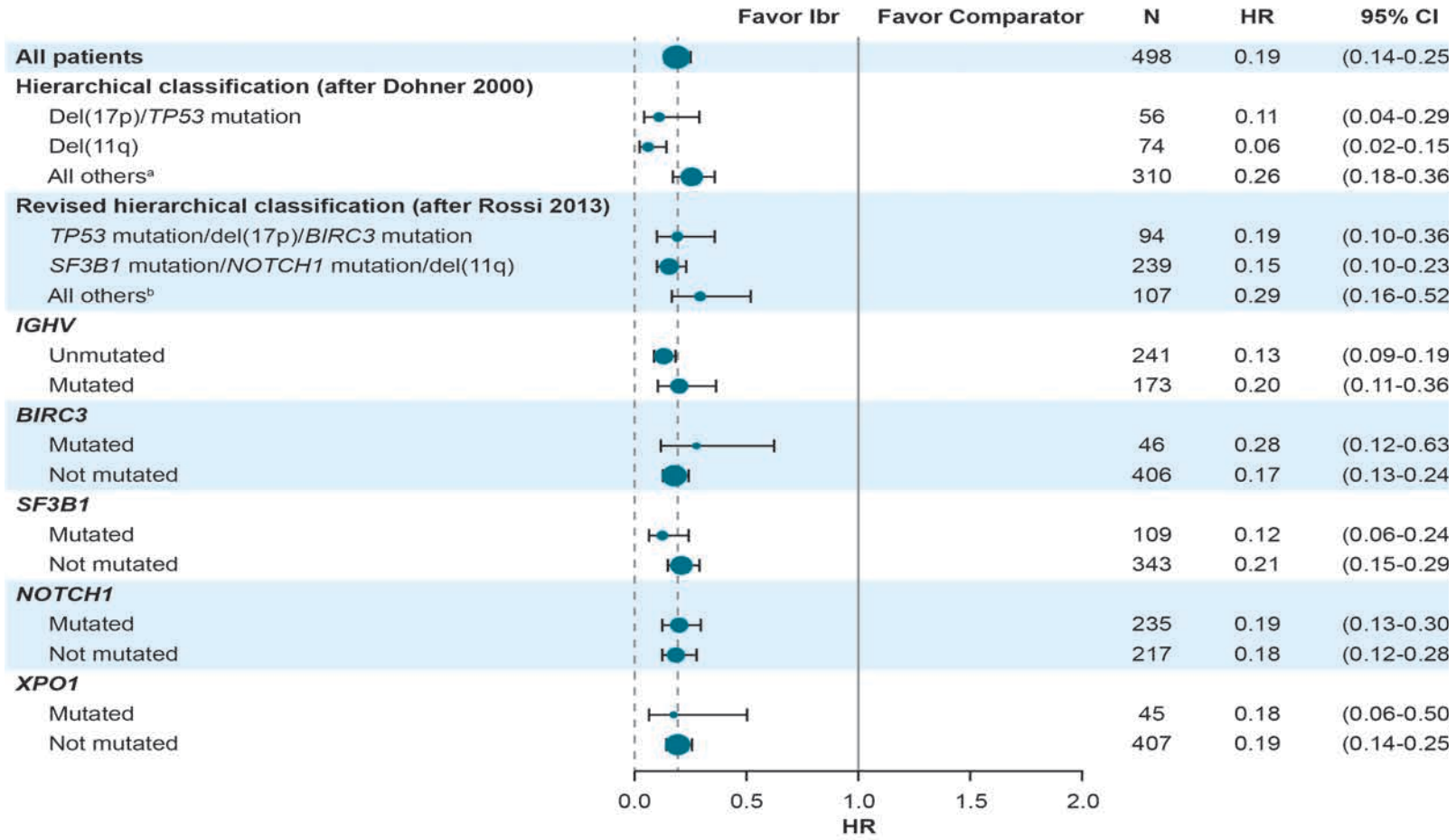
Figure. PFS outcomes in ibr- vs clb-treated pts with specified genomic risk features



[a]Neither del17p/*TP53* mutation nor del(11q).
[b]Neither *TP53* mutation/del(17p)/*BIRC3* mutation, nor *SF3B1*/*NOTCH1* mutations/del(11q).

Outcomes of First-Line Ibrutinib in Patients with CLL and High-Risk Genomic Features with up to 6.5 Years Follow-up

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Table. Efficacy outcomes in ibr-treated pts with vs without genomic risk features

Risk Factor Present	Risk Factor Present, Yes vs No	
	PFS, 42-mo Rates[a] and HR (95% CI)	ORR and RR (95% CI)
Hierarchical classification (after Dohner 2000)[b]		
Del(17p)/*TP53* mutation (Yes n=29; No n=172)	79% vs 75% 0.83 (0.37-1.82)	90% vs 91% 0.99 (0.87-1.13)
Del(11q) (Yes n=38; No n=172)	82% vs 75% 0.85 (0.44-1.63)	97% vs 91% 1.07 (1.00-1.15)
Revised hierarchical classification (after Rossi 2013)[c]		
TP53 mutation/del(17p)/*BIRC3* mutation (Yes n=49; No n=62)	72% vs 73% 1.05 (0.54-2.04)	86% vs 87% 0.98 (0.85-1.14)
SF3B1 mutation/*NOTCH1* mutation/del(11q) (Yes n=128; No n=62)	80% vs 73% 0.82 (0.48-1.43)	96% vs 87% 1.10 (1.00-1.22)
Unmutated *IGHV* (Yes n=124; No n=81)	72% vs 87% 1.79 (0.99-3.24)	92% vs 93% 0.99 (0.92-1.08)
BIRC3 mutated (Yes n=24; No n=219)	63% vs 78% 1.60 (0.79-3.22)	83% vs 92% 0.90 (0.75-1.09)
SF3B1 mutated (Yes n=58; No n=185)	82% vs 75% 0.75 (0.42-1.35)	93% vs 91% 1.03 (0.94-1.12)
NOTCH1 mutated (Yes n=116; No n=127)	76% vs 77% 1.05 (0.65-1.69)	91% vs 92% 0.98 (0.91-1.06)
XPO1 mutated (Yes n=24; No n=219)	78% vs 77% 0.95 (0.41-2.19)	96% vs 91% 1.06 (0.96-1.16)

[a]By Kaplan-Meier estimates.
[b]Compared with neither del(17p)/*TP53* mutation nor del(11q).
[c]Compared with neither *TP53* mutation/del(17p)/*BIRC3* mutation nor *SF3B1* mutation/*NOTCH1* mutation/del(11q).

Outcomes of First-Line Ibrutinib in Patients with CLL and High-Risk Genomic Features with up to 6.5 Years Follow-up

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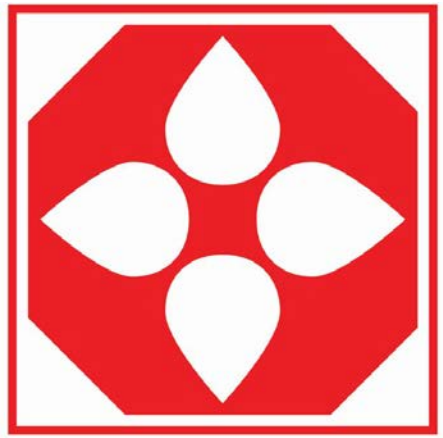
- With up to 79 months follow-up, this analysis across two phase-3 studies of 498 patients undergoing 1st line ibrutinib (ibr)-based treatment showed similar PFS (progression free survival) and ORR (overall response rate) for ibr-treated patients **with or without high-risk genomic features**
- This analysis demonstrated the efficacy of first-line ibr-based treatment irrespective of cytogenetic and mutational risk features, including those with unmutated IGHV, NOTCH1 mutation, and those with the highest risk classification of del(17p)/TP53 mutation/BIRC3 mutation
- This has proven to be less true when ibr is used in later lines of therapy



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Venetoclax

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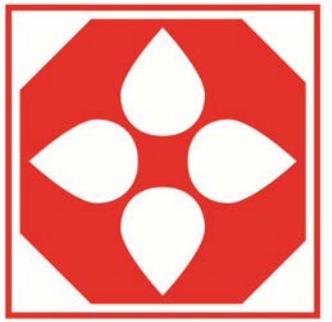
Venetoclax Re-Treatment of Chronic Lymphocytic Leukemia (CLL) Patients after a Previous Venetoclax-Based Regimen

Venetoclax Re-Treatment of Chronic Lymphocytic Leukemia (CLL) Patients after a Previous Venetoclax-Based Regimen



- Studied 25 patients from 13 centers who were treated with venetoclax based therapy (Ven1), then relapsed and retreated with a second Ven-based regimen (Ven2) in a later line of therapy (LOT)
- With a median duration of exposure of 15 months (64% pts >12 months) for Ven1, the ORR was 88% (CR: 48%)
- Median time was 8.7 months (36% >12 months) between Ven1 and the initiation of Ven2
- Reasons for Ven2 initiation were either CLL progression (87.5%) or MRD-positive relapse (12.5%)
- Overall response rate (ORR) was 72.2%
- Out of 25 pts re-treated with Ven, 68% remain on Ven2, and 4 patients progressed

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 (Tx)

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MURANO 5-Yr Analysis: Progression Free Survival (PFS) and Overall Survival (OS)

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Outcome	VenR (n = 194)	BR (n = 195)
Median PFS, mos	53.6	17.0
5-yr PFS, %	37.8	Not evaluable
▪ HR (95% CI)	0.19 (0.15-0.26)	
▪ *P* value	< .0001	
5-yr OS, %	82.1	62.2
▪ HR (95% CI)	0.40 (0.26-0.62)	
▪ *P* value	< .0001	

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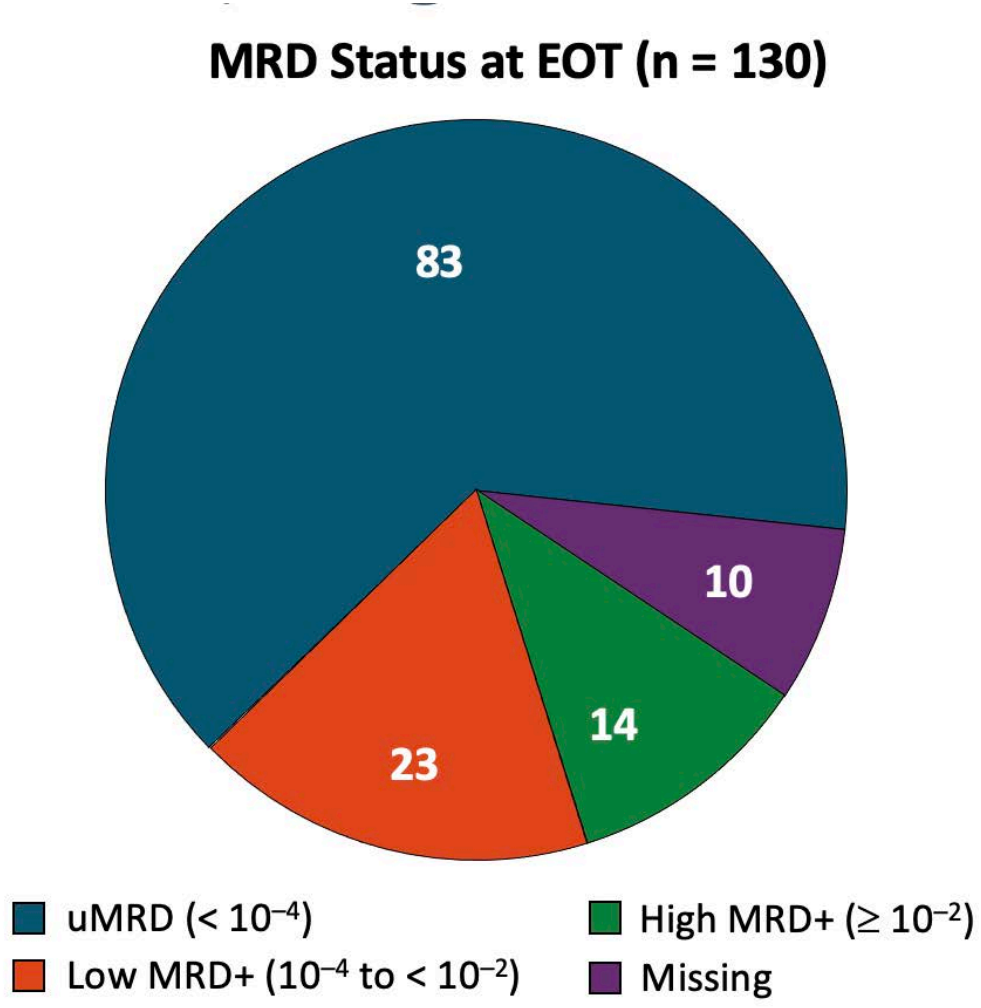
MURANO 5-Yr Analysis: Conclusions



- In patients with relapsed/refractory CLL, 5-yr PFS for patients who received venetoclax + rituximab was 37.8%
  - uMRD at EOT with venetoclax + rituximab associated with 61.3% PFS at 36 months post-EOT
  - Median time to MRD conversion with venetoclax + rituximab: 19 months
  - Median time to PD from MRD conversion with venetoclax + rituximab: 25 months
  - uMRD sustained at follow-up with venetoclax + rituximab: ~ 40%

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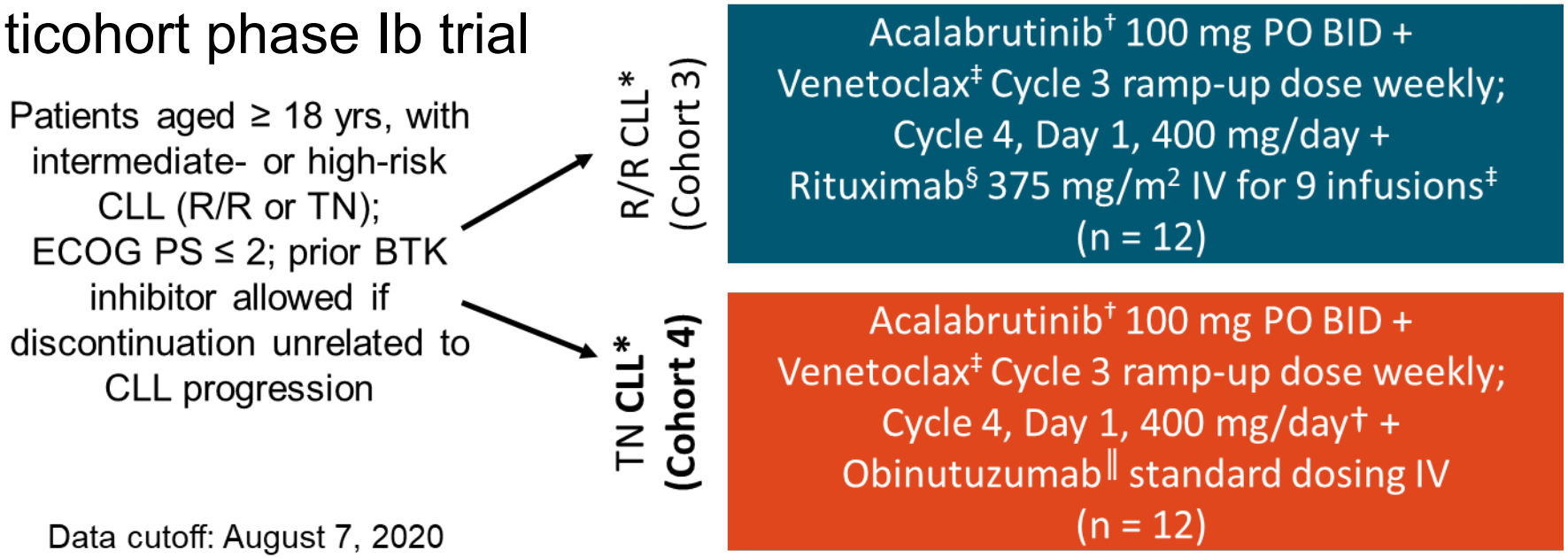
ASH 2020: More Notable CLL Abstracts

Acalabrutinib+

Phase Ib ACE-CL-003: Acalabrutinib Combined With Venetoclax and Obinutuzumab or Rituximab in Treatment-Naive or Relapsed/Refractory CLL

Acalabrutinib + Venetoclax + Anti-CD20 Ab in CLL (ACE-CL-003): Study Design

- Multicohort phase Ib trial



*Samples for PK analyses will be obtained from first 8 patients enrolled in each arm. †Acalabrutinib until PD, end of cycle 24, or investigator decision based on MRD and clinical response. ‡Venetoclax until end of cycle 15. §Rituximab on cycle 2, Days 1, 8, 15, 22; cycles 3-7, Day 1. Obinutuzumab on cycle 2, Days 1, 2, 8, 15; cycles 3-7, Day 1.

- Primary endpoint: safety
- Key secondary endpoints: ORR (per investigator) at Cycle 16, CR rate, uMRD rate, DoR, PFS, OS, PK

Woyach. ASH 2020. Abstr 1312. NCT02296918

ACE-CL-003: Safety

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- There were six (50%) relapsed/refractory (R/R) patients, and three (25%) Treatment Naïve (TN) patients that experienced infusion-related mild or moderate reactions
- Seriously decreased neutrophil counts in one R/R patient (8%), and in half of TN patients
- **No ventricular heart irregularities, Richter Transformations, tumor lysis syndrome (TLS) or deaths**
- Only 1 out of 24 patients had atrial fibrillation, and 42% had hypertension
- Serious (grade ≥ 3) AEs (adverse events) occurred in four (33%) TN patients, and two (17%) R/R patients
- Serious (grade ≥ 3) infections occurred in three TN patients, and none in R/R patients

Woyach. ASH 2020. Abstr 1312.

ACE-CL-003: Summary & Results

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- Triple combination of acalabrutinib + venetoclax + rituximab or obinutuzumab was associated with a safety profile expected for each individual agent:
  - Few patients discontinued treatment due to an AE (one in R/R; two in TN)
- Deep and durable responses were observed:
  - ORR: 92% in R/R and 100 in TN; CR/CRi rate: 50% in each cohort
  - Overall uMRD rate: 71% (67% in R/R; 75% in TN)
  - uMRD in all patients with CR or CRi
  - Median DoR (duration of response), PFS and OS not reached

Woyach. ASH 2020. Abstr 1312.

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

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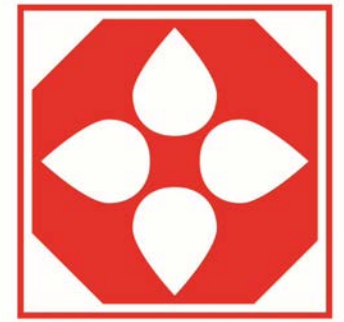
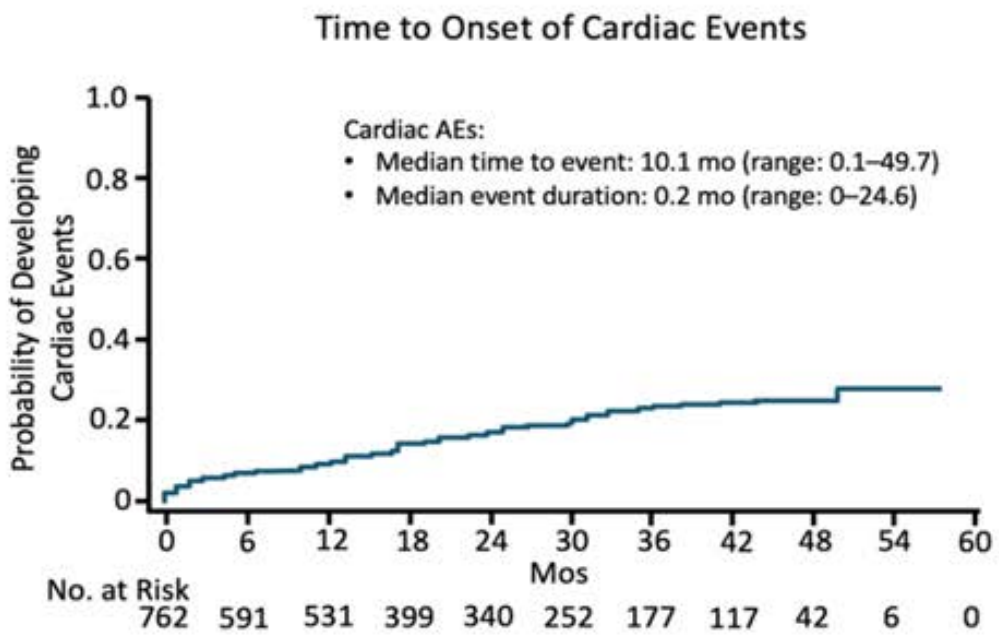
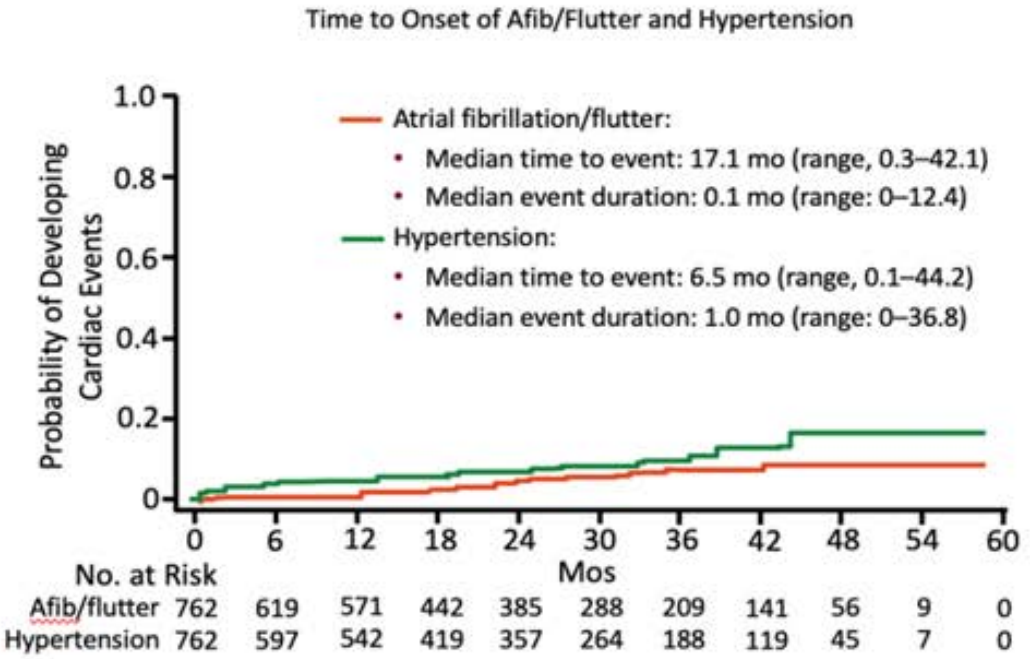
Pooled Cardiovascular Safety Analysis for Acalabrutinib

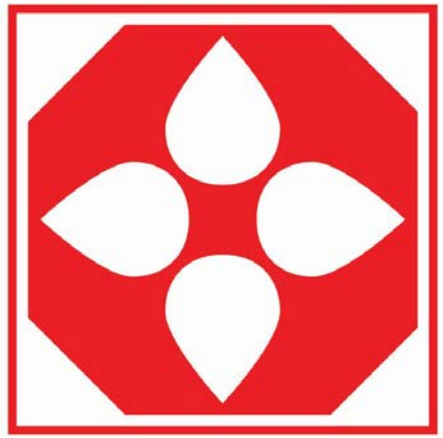


- A prior history of an arrhythmia was found in the 7 of 38 patients (18%) that developed atrial fibrillation or atrial flutter
- Preexisting hypertension was found in 46 of 67 patients (69%), and 18 (27%) had risk factors





Brown. ASH 2020. Abstr 3146



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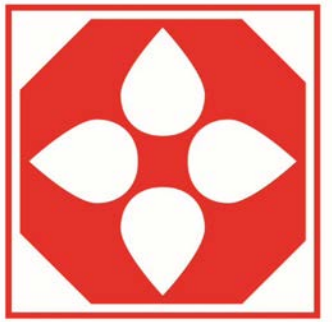
New Drugs and Combination Therapies

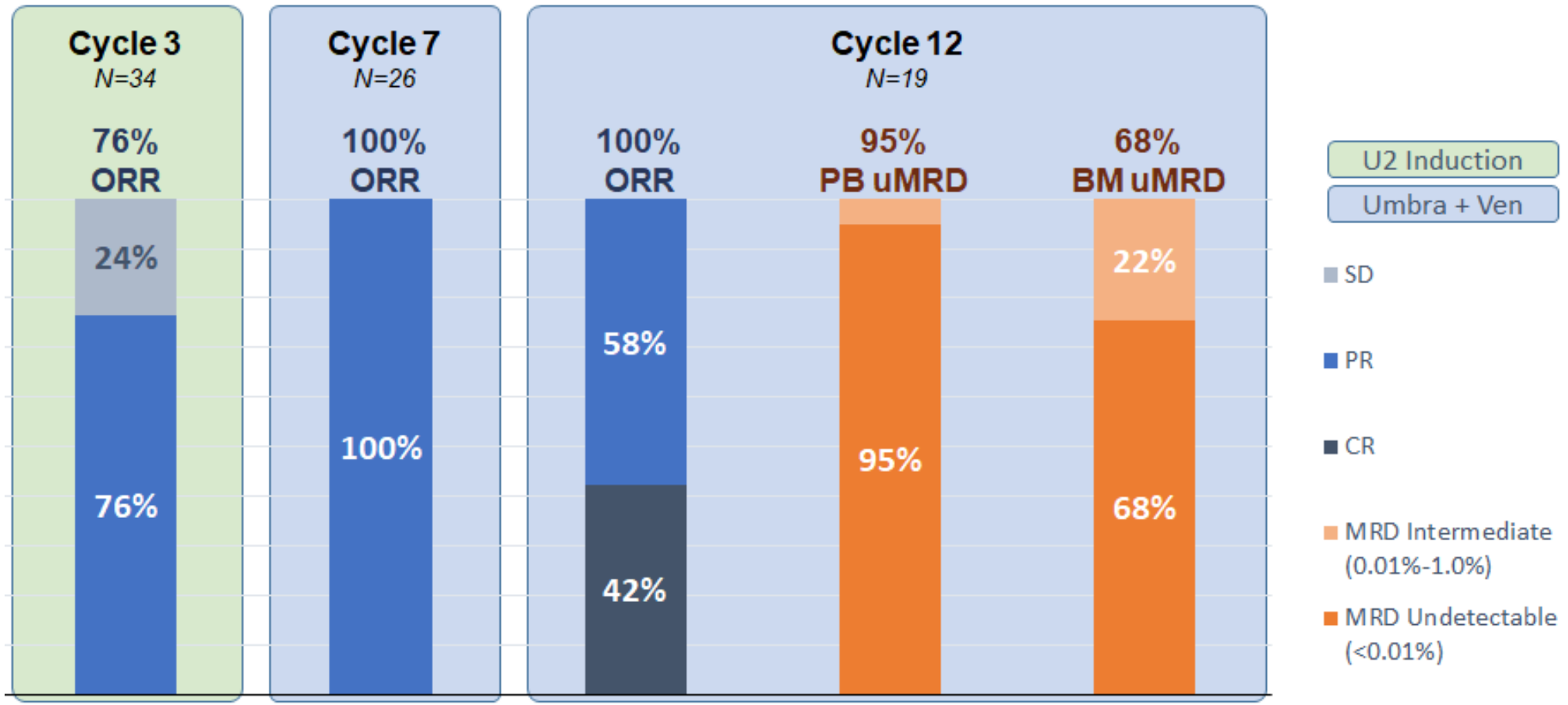
A Phase 1/2 Study of Umbralisib, Ublituximab, and Venetoclax (U2-Ven) in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL)

Umbralisib, Ublituximab, and Venetoclax (U2-Ven) in Patients with R/R CLL

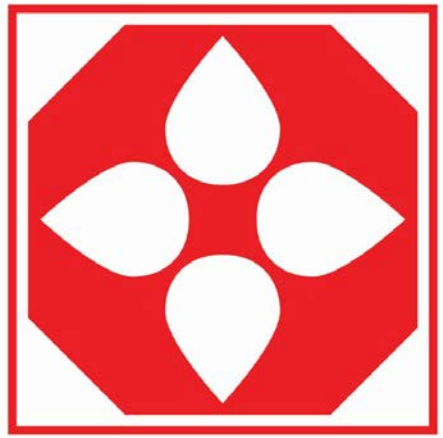


- Out of 40 patients, 20 (50%) had prior ibrutinib therapy
  - In those with prior ibrutinib, 11 (55%) were BTK refractory
  - BTK resistance mutations were found in eight cases
- High-risk genetic features included unmutated IGHV genes (20), del17p (8), del11q (11), TP53 mutated (4), NOTCH1 mutated (5) and SF3B1 mutated (2)
- The most common AEs were infusion related reactions (63%), anemia (55%), low platelets (53%), low neutrophils (53%), low white blood cells (50%), decreased renal function (50%), fatigue (45%), diarrhea (43%), nausea (38%), ↑ AST marker for liver inflammation (30%)
- No tumor lysis syndrome (TLS)

Umbralisib, Ublituximab, and Venetoclax (U2-Ven) in Patients with R/R CLL



Note: Cycle 3 & 7 Assessments were by CT only without BM, therefore CR could not be assessed



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CAR-T

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

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

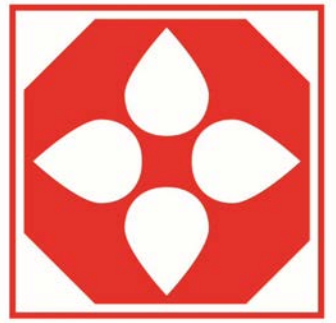


Table: Charachteristics, pre and post transformation Tx and response to CAR T-cell in CLL and Richter's transformation

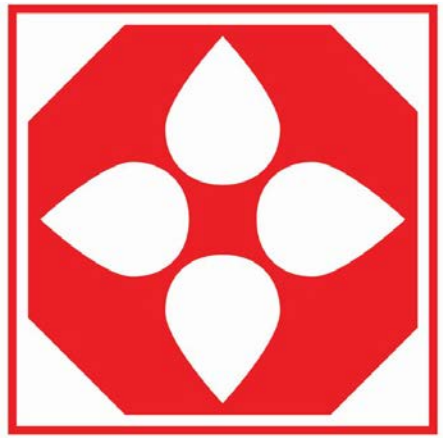
pts N	Age at CART	FISH / $TP53^{mut}$	non targeted therapies	targeterd therapy	type of transformation	transformation therapies	disease status at CART	CRS grade	CNS grade	response to CART	follow up months	status last follow up
1	67	del17p/$TP53^{mut}$	FCR	Ibrutinib/ venetoclax	accelerated	Venetoclax	PD	3	3	CR	6	Live
2	63	del17p	BR	Ibrutinib/ venetoclax	DLBCL	R-CHOP	PD	4	3	CR	6	Live post allo-SCT
3	73	n/a	FCR	Ibrutinib	DLBCL	R-CHOP, HD-MTX R-GDP	PD	1	1	CR	5	Live
4	65	n/a	FCR	Ibrutinib/ venetoclax	DLBCL	R-CHOP	PD	1	0	CR	4	Live post allo-SCT
5	64	$TP53^{mut}$	BR	Ibrutinib/ venetoclax	DLBCL	R-CHOP	PD	1	0	CR	10	Live
6	62	del11q	FCO	Ibrutinib	DLBCL	R-CHOP, R-Venetoclax+Benda	PD	0	0	PD	1	Dead
7	62	del17p/del11q	none	venetoclax	DLBCL	R-CHOP	PD	1	0	PD	2	Dead
8	54	del17p	FCR alemtuzumab	Ibrutinib/ venetoclax	Prolymphocytic	Ibrutinib,R-venetoclax Allo-SCT	PD	3	0	PD	2	Live

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

- After infusion of CAR T-cells, seven patients had cytokine release syndrome (CRS) that required tocilizumab
  - Four had grade 1
  - Three had grade 3-4
- Three patients had CNS toxicity, two with grade 3
- No fatalities attributed to CAR T-cell toxicity
- There were two fatalities due to disease progression
- All 71% (5/8) responders achieved complete response with DS1 in PET CT scan on day 28
- After median follow-up duration of 6 (4-10) months, two patients went on to having an allogeneic stem cell transplant (allo-SCT)

Summary: A glimpse at the Present and the Promise of the Future

- Symptomatic COVID-19 is dangerous for CLL patients.
- Don’t worry about persistent slightly enlarged lymph nodes.
- MRD status is probably much more important that a complete remission.
- Acalabrutinib is associated with few cardiac problems.
- Ibrutinib as monotherapy works very well frontline regardless of risk factors.
- Deep and durable responses are possible with many targeted combinations:
  - Zanubrutinib, Venetoclax and Obinutuzumab (BOVen)
  - Venetoclax and Rituximab (Murano)
  - Umbralisib, Ublituxumab and Venetoclax (U2- Ven)
  - Acalabrutinib and Venetoclax with Obinutuzumab or Rituximab (ACE-CL-003)
- CAR-T therapy is promising in Richter’s Transformation



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Thank You

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The Importance of ASH from a Caregiver's Perspective

Linda Lannom

February 4, 2021

Background

- Diagnosed by PCP in 2012
- Referred to a community hematologist/oncologist
- Switched to a hematologist/oncologist at an NCI-designated Comprehensive Cancer Center

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Discovery of Resources

- National Institutes of Health Natural History Study of CLL
- Brian Koffman's blog, *Learning from and about cancer (chronic lymphocytic leukemia or CLL)*
- Listservs for CLL patients and caregivers
- *CLL Topics*
- PubMed
- Professional meetings

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Professional Meetings

- ASCO American Society for Clinical Oncology
- ASH American Society for Hematology

What does ASH offer?

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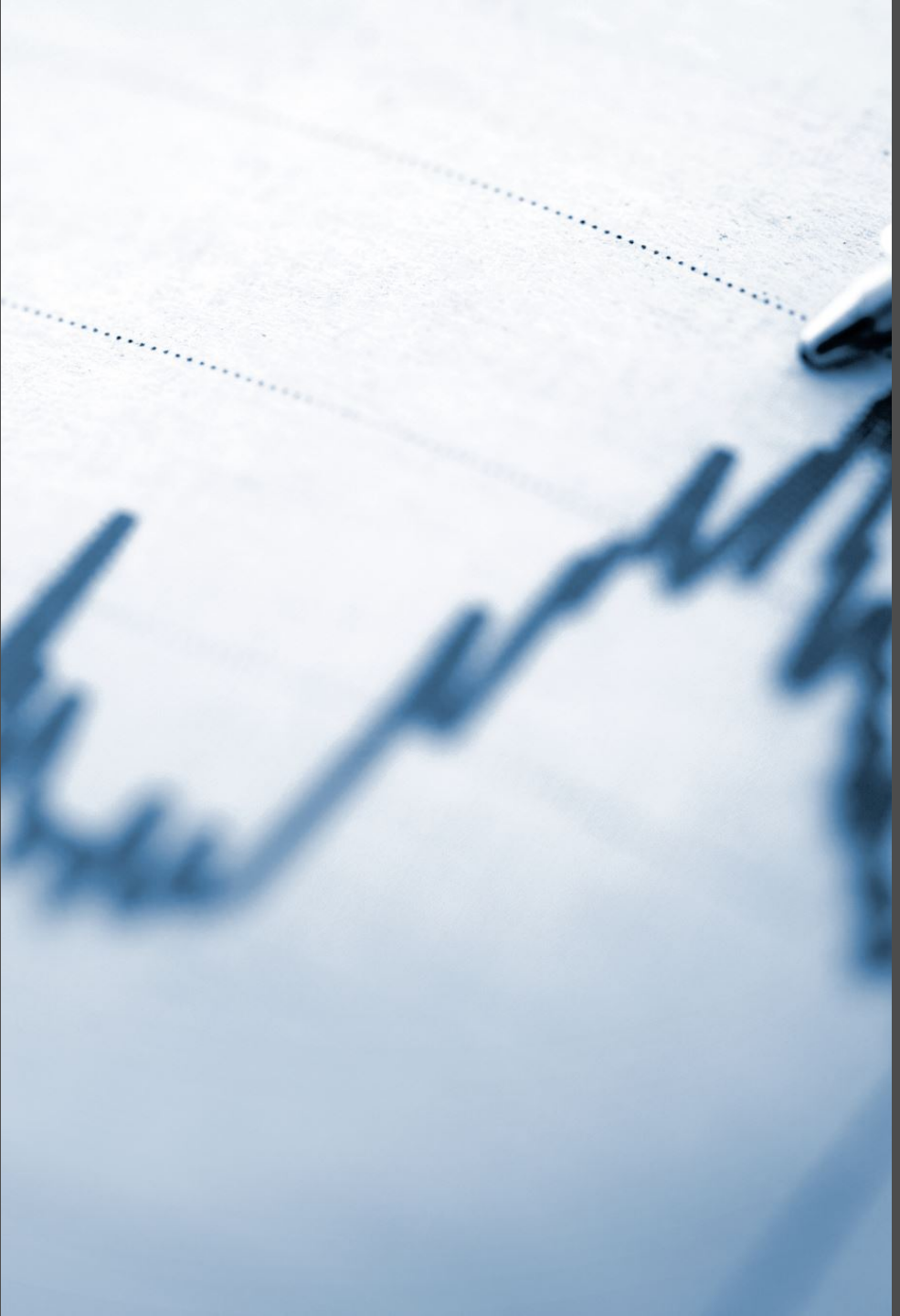
- General Sessions, e.g., **Fireside Chat with Anthony Fauci**
- Scientific Program, e.g., **Challenges in Cell Therapy: Relapse and Toxicities**
- Special Interest Sessions, e.g., **The 2020 Pandemic: Latest Insights on COVID-19**
- Oral and Poster Sessions, including the ability to search through the paper abstracts and posters on CLL
- Education Program, e.g., **A Map for the Changing Landscape of CLL**



What CLL topics does ASH cover?

In 2020…

- Phase III UNITY CLL trial
- Phase II CAPTIVATE study
- Phase I cohort of liso-cel in combination with ibrutinib
- Phase I/II BRUIN study of LOXO-305

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Why is it important for CLL patients and caregivers to know about this stuff?

- CLL is still (mostly) an incurable disease that shortens the lives of too many
- We need to be on the lookout for the next best treatment
- The newest clinical trial results are presented at professional meetings

An Example…

- **Dx in 2012**
- **W&W until 2014**
- **BR in the ALLIANCE trial in 2014**
- **A Phase II Study Using ACP-196 in Patients with Relapsed/Refractory and Treatment Naive Deletion 17p CLL/SLL**
- Uh, oh…

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An Example (con't.)

- Support groups matter, too!
- It's not just what you know, it's also who you know.

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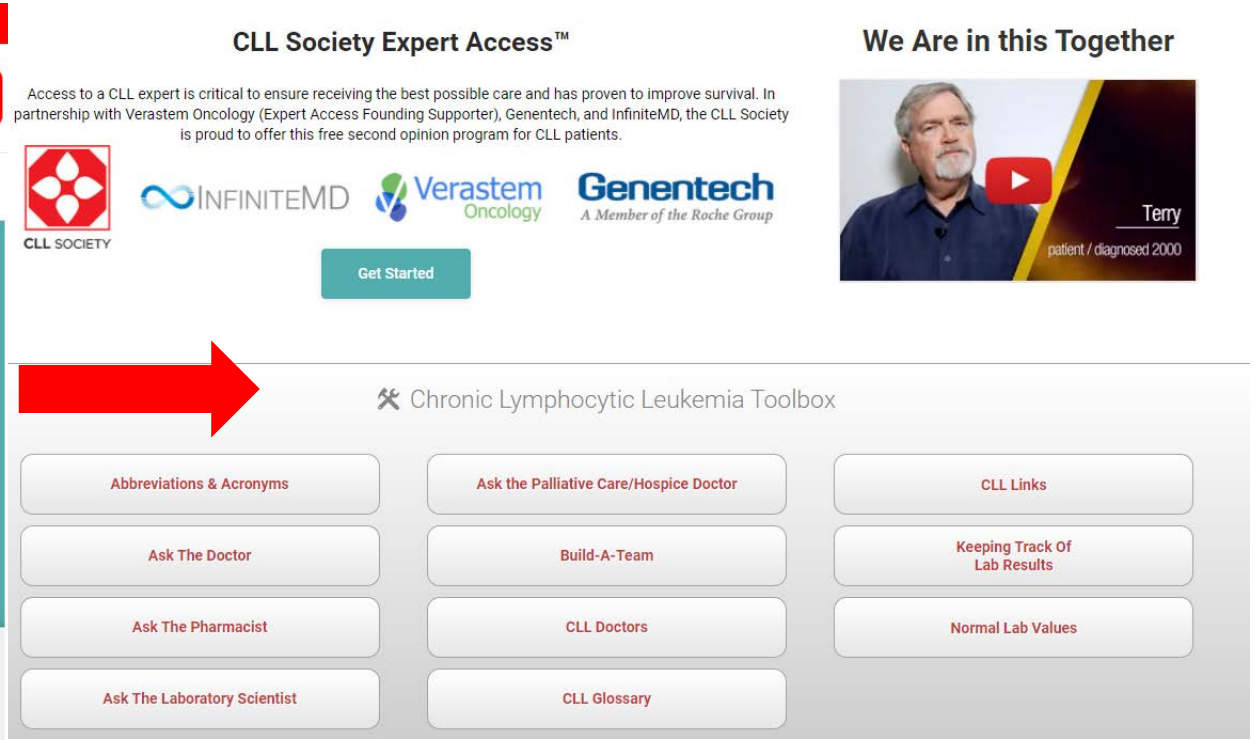
CLL Society's Programs & Services

Robyn Brumble, RN
Director of Scientific Affairs
CLL Society

CLL Society Website



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Conference Coverage

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Category Archives: 2020 Conference

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ASCO 2020 "Top 12" #1: Fixed-duration venetoclax-obinutuzumab for previously untreated patients with chronic lymphocytic leukemia: Follow-up of efficacy and safety results from the multicenter, open-label, randomized, phase III CLL14 trial

ASCO 2020 "Top 12" #1: Fixed-duration venetoclax-obinutuzumab for previously untreated patients with chronic lymphocytic leukemia: Follow-up of efficacy and safety...

August 26, 2020 / 2020 Conferences

ASCO 2020 "To... Acalabrutinib ir... chronic lymphocytic leukemia: Mature results from phase II study demonstrating durable remissions and long-term tolerability

#2 At virtual ASCO 2020, Dr. John Byrd led a group of researchers to report the latest from the first...

August 20, 2020 / 2020 Conferences

ASCO 2020 Top 12" #3: A ...ulticenter phase II study of venetoclax plus dose-adjusted R-EPOCH (VR-EPOCH) for Richter's syndrome

In short videos with accompanying text, Dr. Brian Koffman, the Executive Vice President (EVP) and Chief Medical Officer (CMO) of...

July 24, 2020 / 2020 Conferences

ASCO 2020 Top 12" #4: Long-term follow-up of anti-CD19 CAR T-cell therapy for B-cell lymphoma and chronic lymphocytic leukemia.

ASCO 2020 Top 12" #5: Survival trend of chronic lymphocytic leukemia and prognostic factors in the United States: An analysis

ASCO 2020 Top 12" #6: Cause of death in patients with newly

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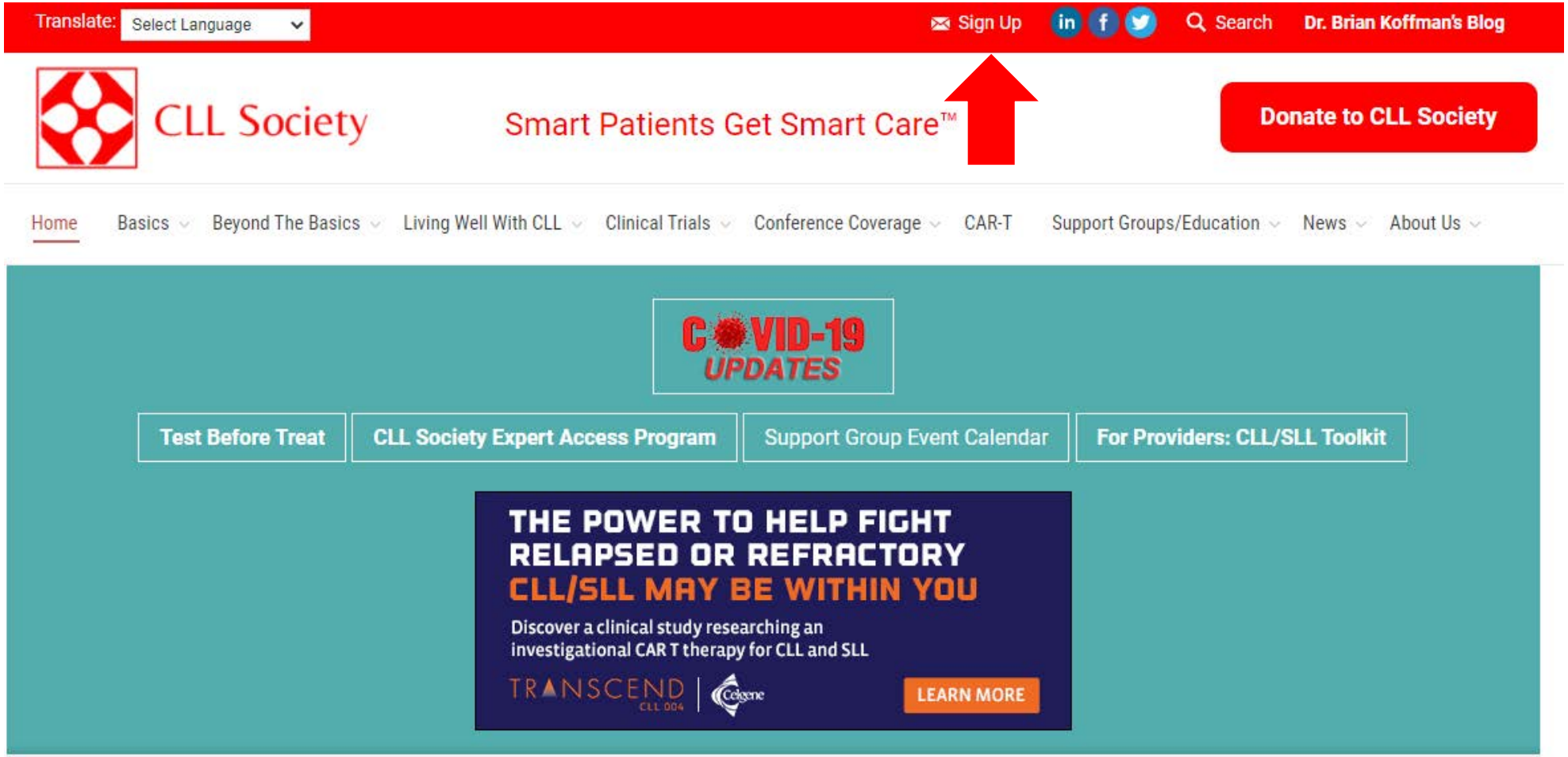

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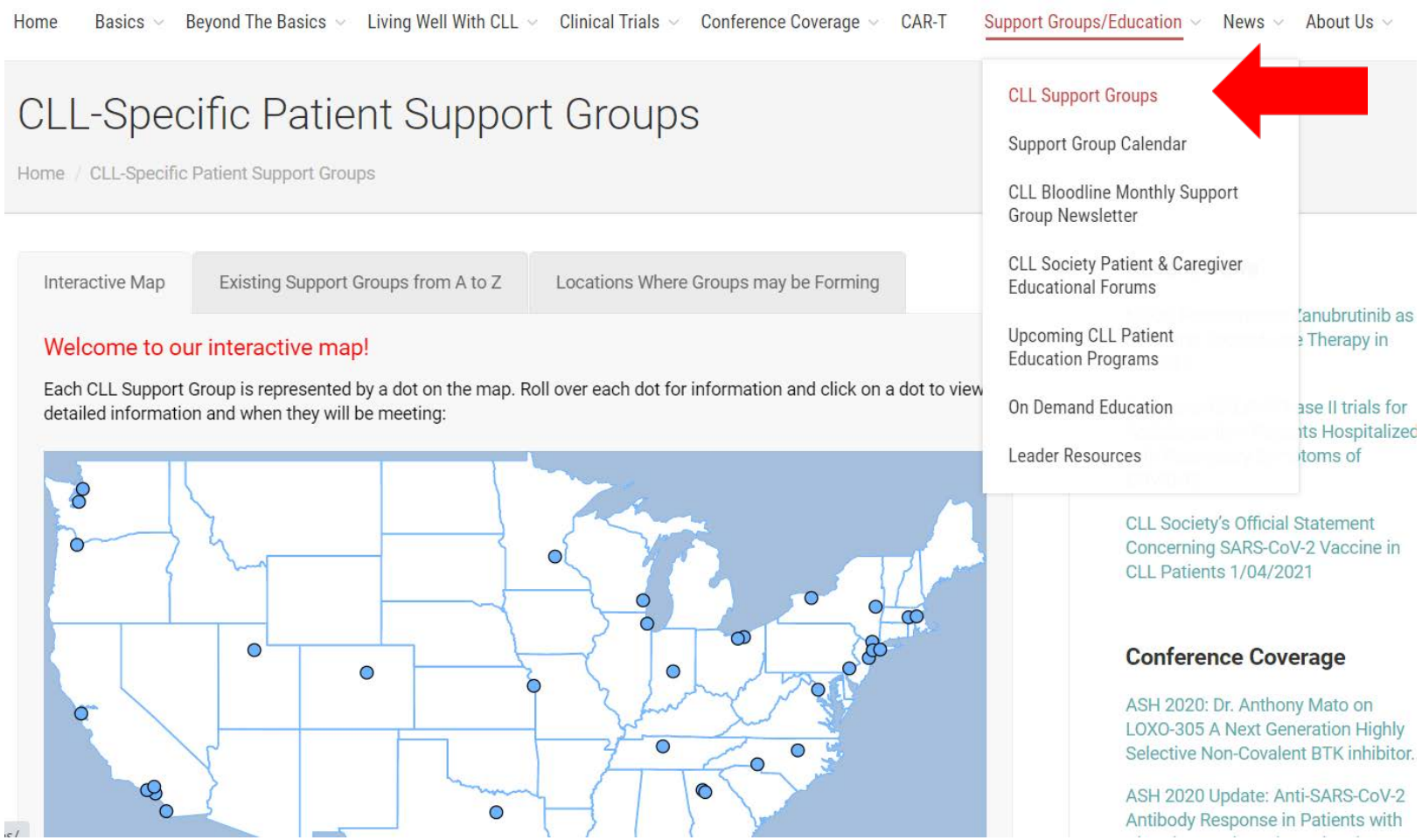
Support Groups



95% would recommend their CLL Society Support Group to other CLL patients and families.

89% are more knowledgeable about CLL since attending their local CLL Society Support Group.

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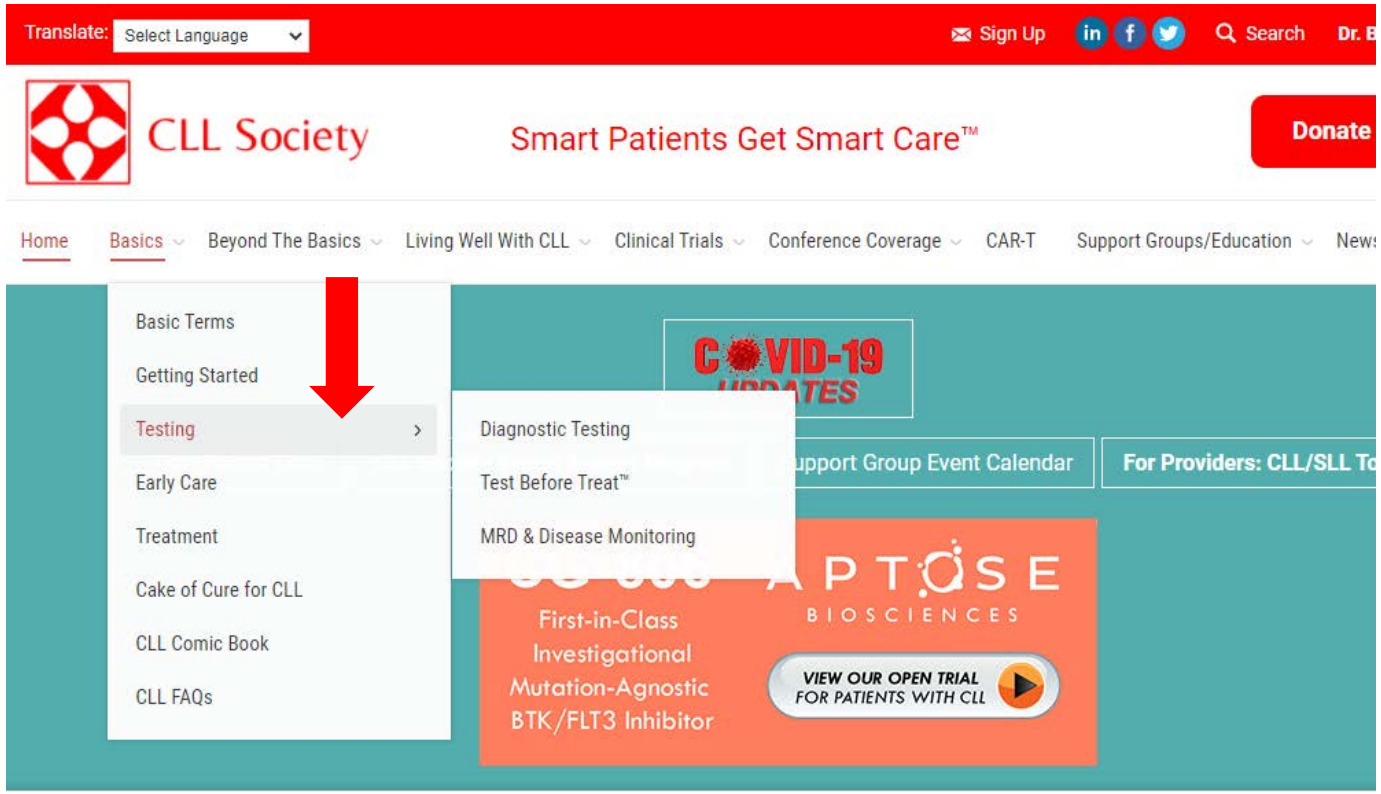
Testing



What Doctors Say About Test Before Treat™

What critical concern could compel these CLL Experts from some of the top research centers around the world, to come before our cameras and speak so urgently to you, our readers? The answer: **Test Before Treat™!** The truth is that critical tests which can predict which patients will do well on or fail certain medications and should be done before each and *every* treatment decision, are often *not* being done... or *are* being done and the results are ignored. Take our patients' stories to heart. Print out our one-pager. Share it with your doctor. **Smart Patients Get Smart Care™.**

Read More

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- The Orange County CLL Support Group
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Medical Advisory Board

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The CLL Society Medical & Scientific Advisory Board is comprised of distinguished physician-scientist researchers who specialize in CLL as well as respected doctors who treat a significant number of CLL patients in their practice. The board advises the CLL Society on the latest research in CLL and advances in medical treatment, as well as issues related to patient care.

Farrukh T. Awan, M.D.

Associate Professor of Internal Medicine
Director of Lymphoid Malignancies Program
Harold C. Simmons Comprehensive Cancer Center
University of Texas Southwestern Medical Center
Dallas, TX

Recent News

NCCN Recommends Za
First-Line, Second-Line
CLL/SLL

Update on CALAVI Pha
Acalabrutinib in Patient
with Respiratory Sympt
COVID-19

CLL Society's Official Statement Concerning SARS-CoV-2 Vaccine in CLL Patients 1/04/2021

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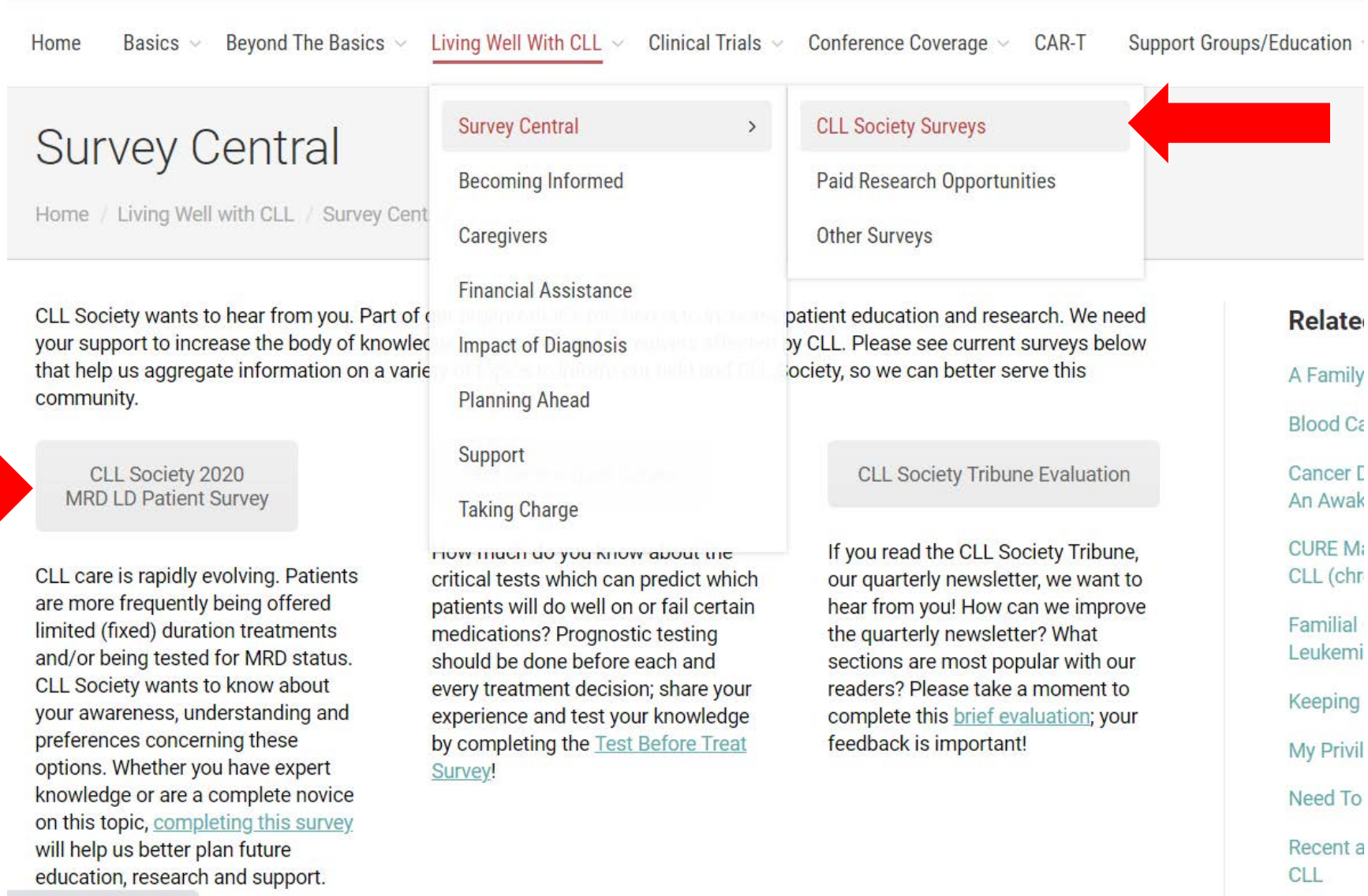
Patient & Caregiver Surveys



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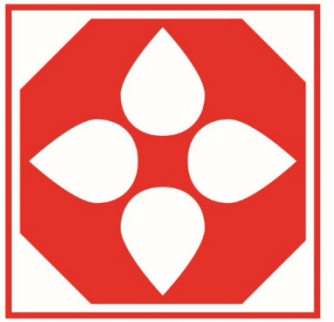
Audience Questions & Answers



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