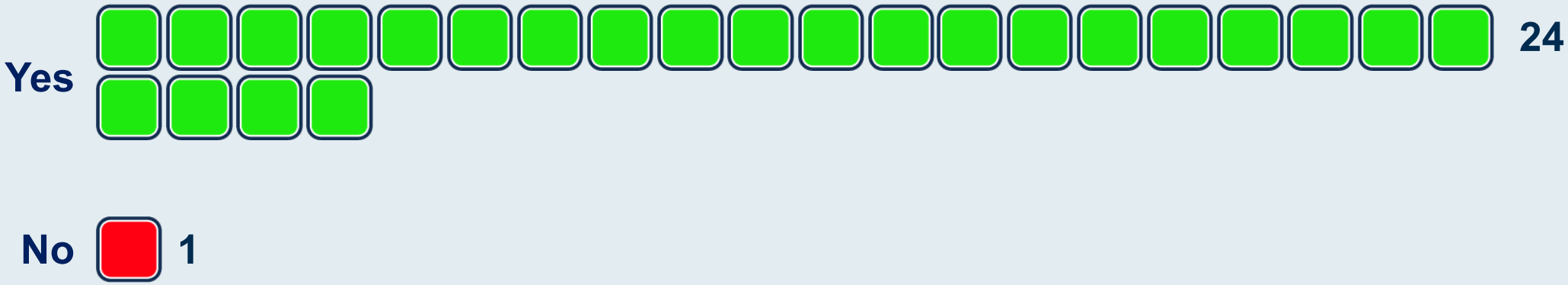
Promising Investigational Agents and Strategies in CLL

Alexey V. Danilov, MD, PhD
Professor, Department of Hematology and Transplantation
Co-Director, Toni Stephenson Lymphoma Center
City of Hope National Medical Center

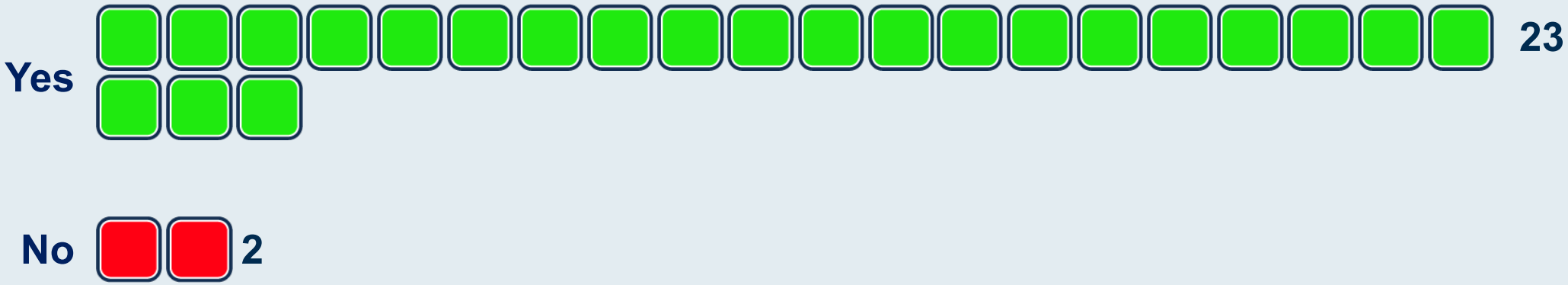
City of Hope.

If you could access one of the novel noncovalent BTK inhibitors (eg, pirtobrutinib) for your patients with relapsed CLL today, would you want to use it in clinical practice?



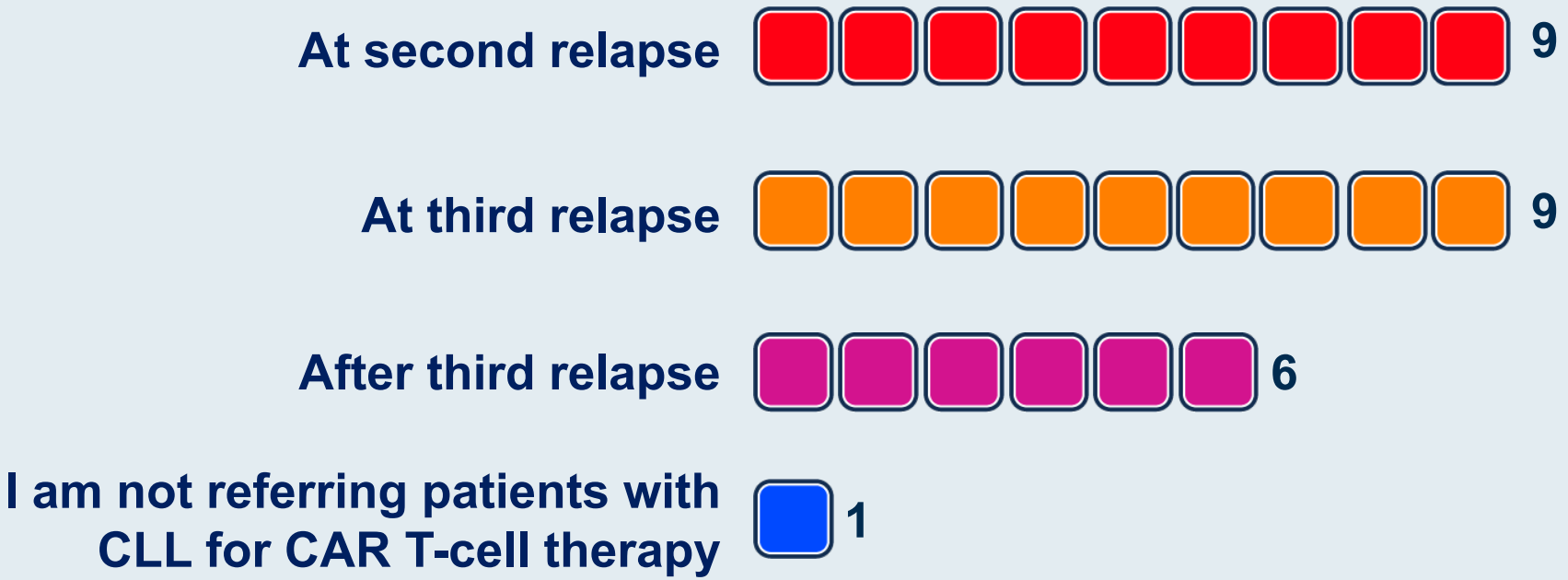
Survey of 25 US-based clinical investigators

In your opinion, will CAR T-cell therapy eventually become a part of the standard treatment algorithm for patients with CLL?



Survey of 25 US-based clinical investigators

At what point in the treatment course are you referring patients with multiregimen-relapsed CLL for consultation regarding CAR T-cell therapy?



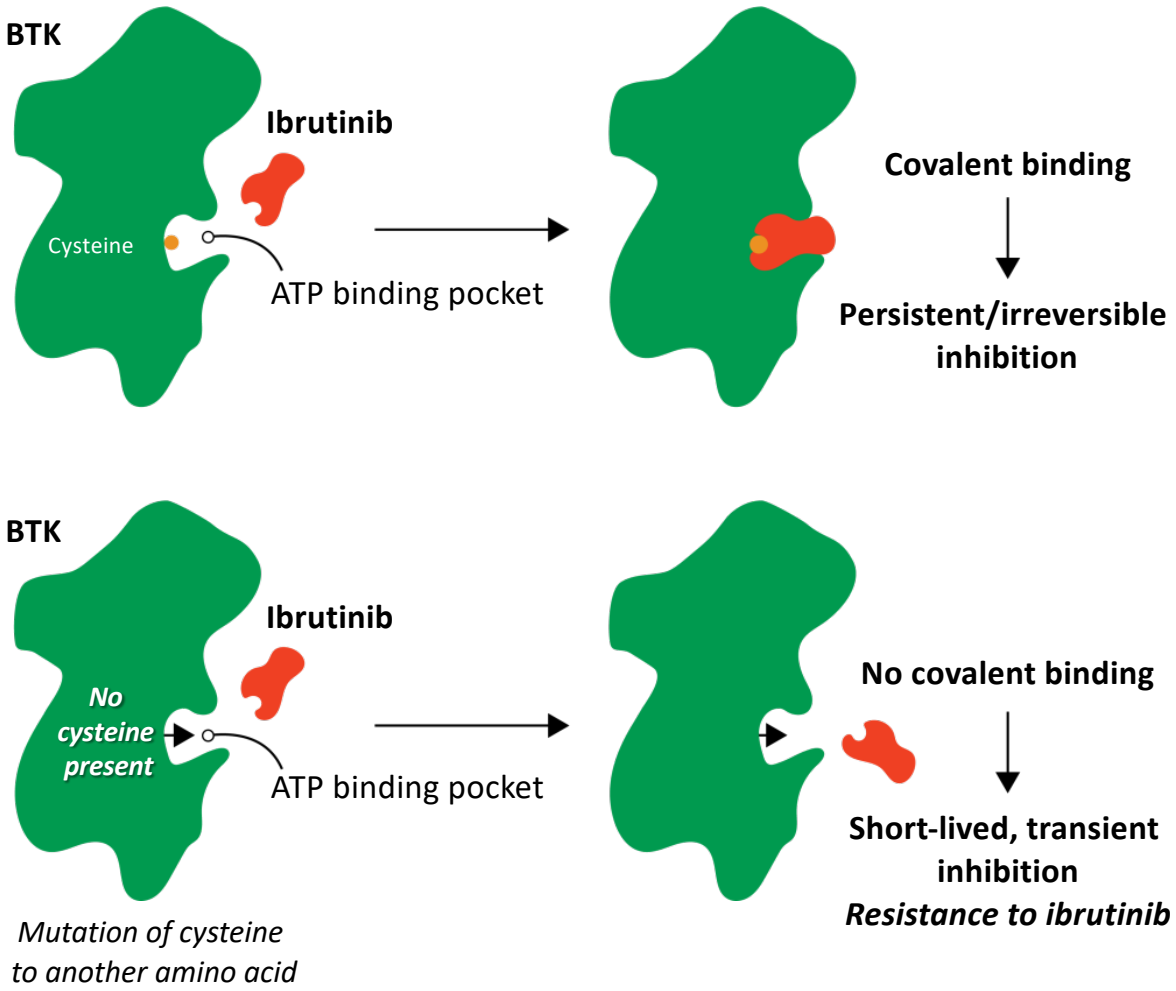
Survey of 25 US-based clinical investigators

Promising Investigational Agents and Strategies in CLL

Alexey V. Danilov, MD, PhD
Professor, Department of Hematology and Transplantation
Co-Director, Toni Stephenson Lymphoma Center
City of Hope National Medical Center

City of Hope.

Reversible Non-C481–Binding BTK Inhibitors



Several **reversible** BTK inhibitors designed to overcome resistance mutations are in development

BTK Inhibitors in clinic and development

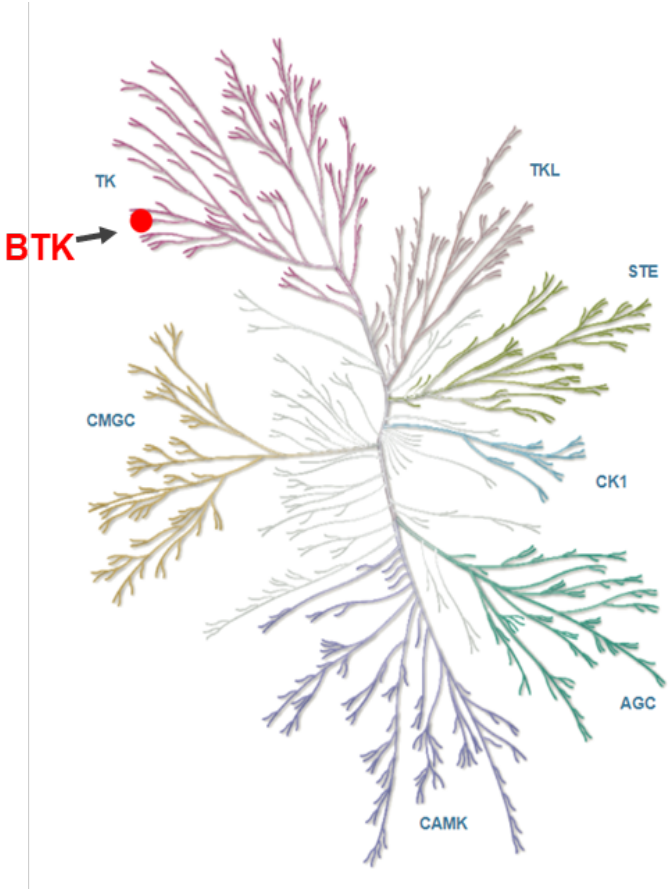
		TEC Family Kinases IC_{50} (nM)				Other Kinases IC_{50} (nM)
	BTK	ITK	Tec#	TXK*	BMX*	Notable Target Kinases
Covalent	Ibrutinib[2]	0.5	10.7	78	2.0[3]	0.8	> 10 more: EGFR family
Covalent	Acalabrutinib[3]	5.1	>1000	93	368	46	Selective
Covalent	Zanubrutinib[4]	0.22	30	1.9	n/a	n/a	
Covalent	**Vecabrutinib[1]**	**3**	**14**	**14**	**474**	**224**	**Selective: only 4, including SRC family, NEK11**
Noncovalent	**ARQ 531[5]**	**4.23**	**>10000**	**5.8**	**36.4**	**5.23**	**> 20 more: SRC & TRK families, RAF1, MEK1**
Noncovalent	**LOXO-305[6] (Pirtobrutinib)**	**8.7**	**>15597**	**181**	**220**	**1410**	**Very Selective**
Noncovalent	**CG-806[7] (luxeptinib)**	**8.4**	**4.3**	**>1000**	**n/a**	**14.5**	**18 w/ IC50 < 10 nM: FLT3 (wt, ITD) c-MET, TRK family & Aurora kinases**

1. Honigberg. Proc Natl Acad Sci U S A. 2010;107:13075. 2. Byrd. NEJM. 2016;374:323. 3. Tam. ASH 2016. Abstract 623. 4. Neuman. ASH 2016. Abstract 642. 5. Eathiraj. Pan Pacific Lymphoma Conference. 2016. 6. Guisot. ASH 2016. Abstract 642. 7. REF

Pirtobrutinib (LOXO-305) is a Highly Potent & selective Non-Covalent BTK Inhibitor
Phase 1/2 BRUIN study

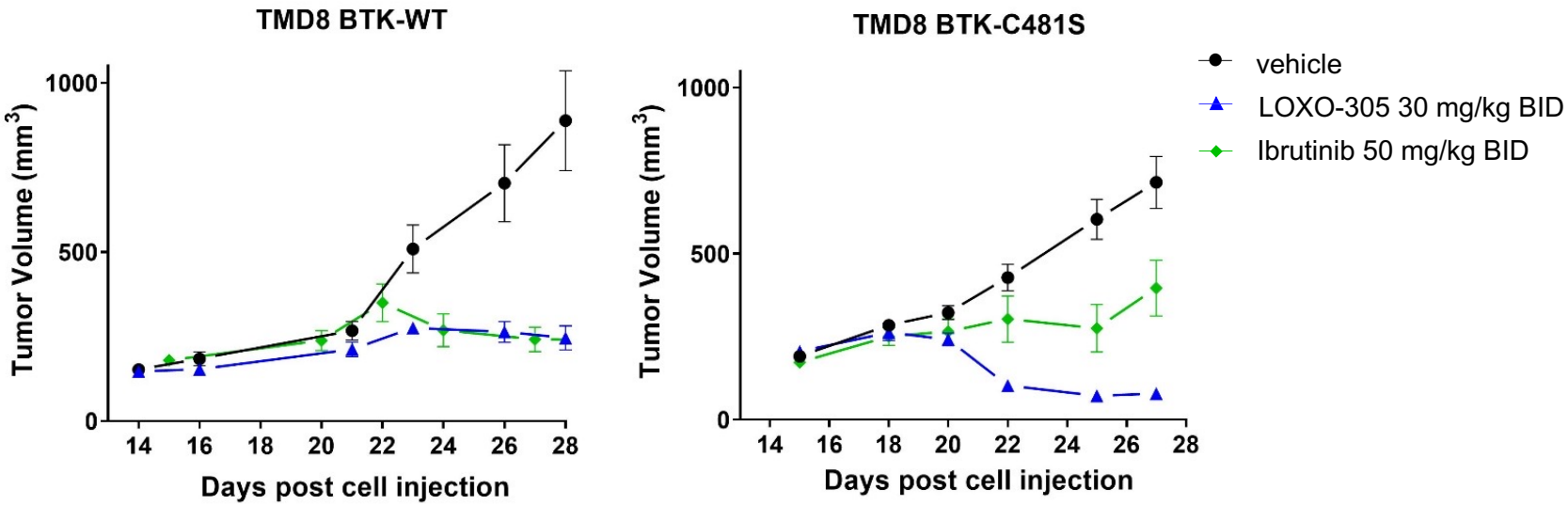
Kinome selectivity

Highly selective for BTK



Xenograft models

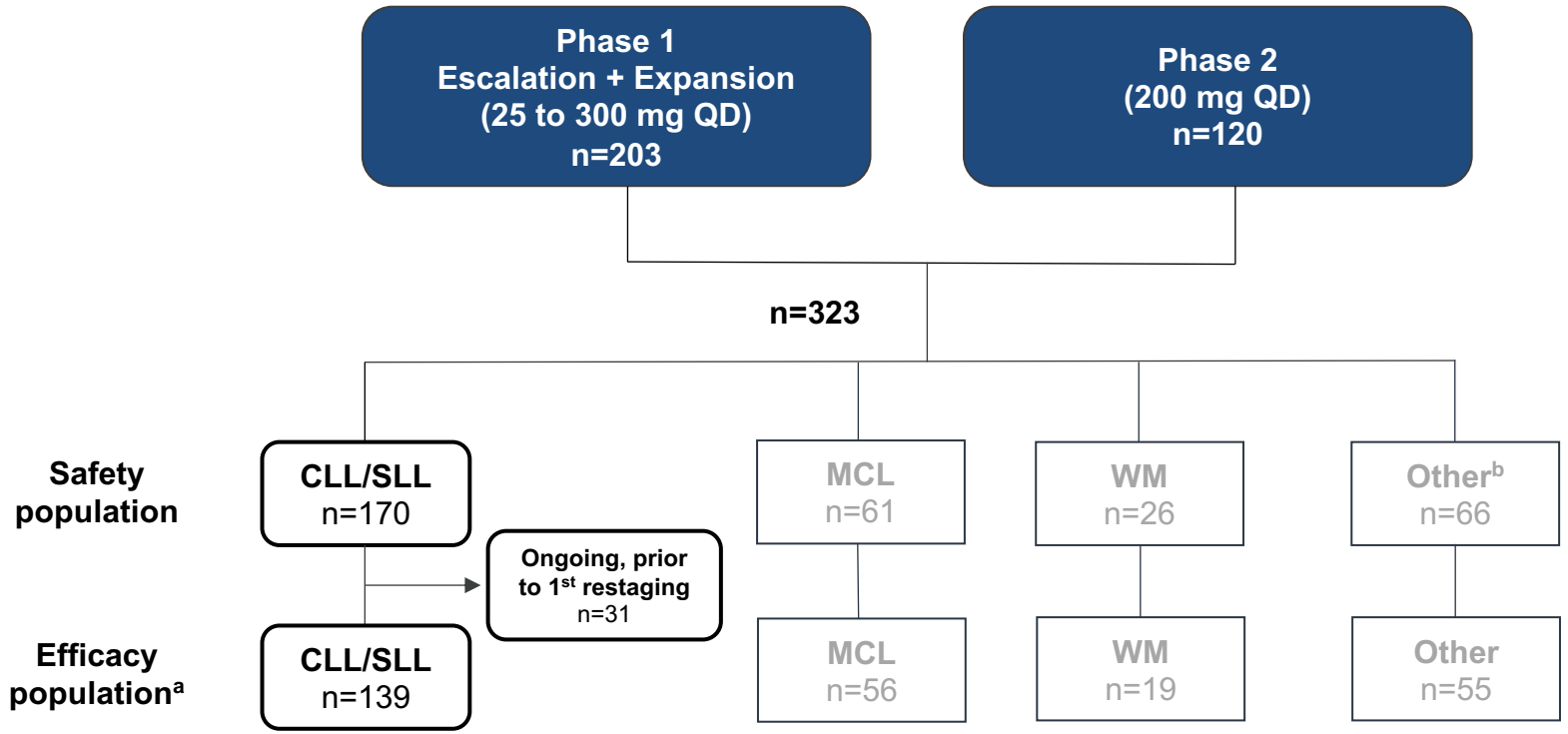
In vivo activity similarly efficacious as ibrutinib in WT; superior in C481S



- 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.

Phase 1/2 BRUIN Study: Design, Eligibility and Enrollment



Phase 1 3+3 design

- 28-day cycles
- Intra-patient dose escalation allowed
- Cohort expansion permitted at doses deemed safe

Eligibility

- Age ≥18
- ECOG PS 0-2
- CLL or other B-cell NHL
- Active disease and in need of treatment
- Previously treated

Key endpoints

- Safety/tolerability
- Determine MTD & recommended phase 2 dose
- Pharmacokinetics
- Efficacy according to ORR & DOR based on disease criteria (iwCLL, IWWM, Lugano)

Data cutoff date of 27 September 2020. [a]Efficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. [b]Other includes DLBCL, FL, MZL, Richter's transformation, B-PLL, Hairy Cell Leukemia, and other transformation. All response data presented based on investigator assessment.

BRUIN: CLL/SLL Patient Characteristics

Characteristics	n=170
Median age, years (range)	69 (36-88)
Female, n (%)	61 (36)
Male, n (%)	109 (64)
ECOG PS[a], n (%)	
0	87 (51)
1	69 (41)
2	13 (8)
Median number prior lines of systemic therapy (range)	3 (1-11)
BTK pre-treated	4 (1-11)
Prior therapy, n (%)	
BTK inhibitor	**146 (86)**
Chemotherapy	140 (82)
Anti-CD20 antibody	153 (90)
BCL2 inhibitor	57 (34)
PI3K inhibitor	36 (21)
Lenalidomide	14 (8)
Autologous stem cell transplant	0
Allogeneic stem cell transplant	3 (2)
CAR-T	10 (6)
Reason discontinued any prior BTKi, n (%)[b]	
Progressive disease	**98 (67)**
Toxicity/other[c]	**48 (33)**

Baseline Molecular Characteristics[d]	
Mutation status, n (%)	
BTK C481-mutant	25 (27)
BTK Wildtype	66 (73)
PLCG2-mutant	4 (4)
High Risk Molecular Findings, n (%)	
17p deletion	20 (25)
TP53 mutation	27 (30)
17p13 deletion + TP53 mutant	18 (22)
IGHV unmutated	71 (88)
11q deletion	15 (19)

Data cutoff date of 27 September 2020. Total % may be different than the sum of the individual components due to rounding. [a]Patients with missing ECOG PS status: n=1. [b]Calculated as percent of patients who received prior BTK inhibitor. [c]Other includes patients who completed treatment and those who discontinued voluntarily or due to physician's decision. [d]Molecular characteristics were determined centrally, in those patients with sufficient sample to pass assay quality control. 91 patients were tested for BTK and PLCG2, 81 patients for 17p13 deletion, 91 patients for TP53, 81 patients for 17p13 deletion + TP53, 81 patients for IGHV and 81 patients for 11q deletion.

BRUIN: Pirtobrutinib (LOXO-305) Safety Profile

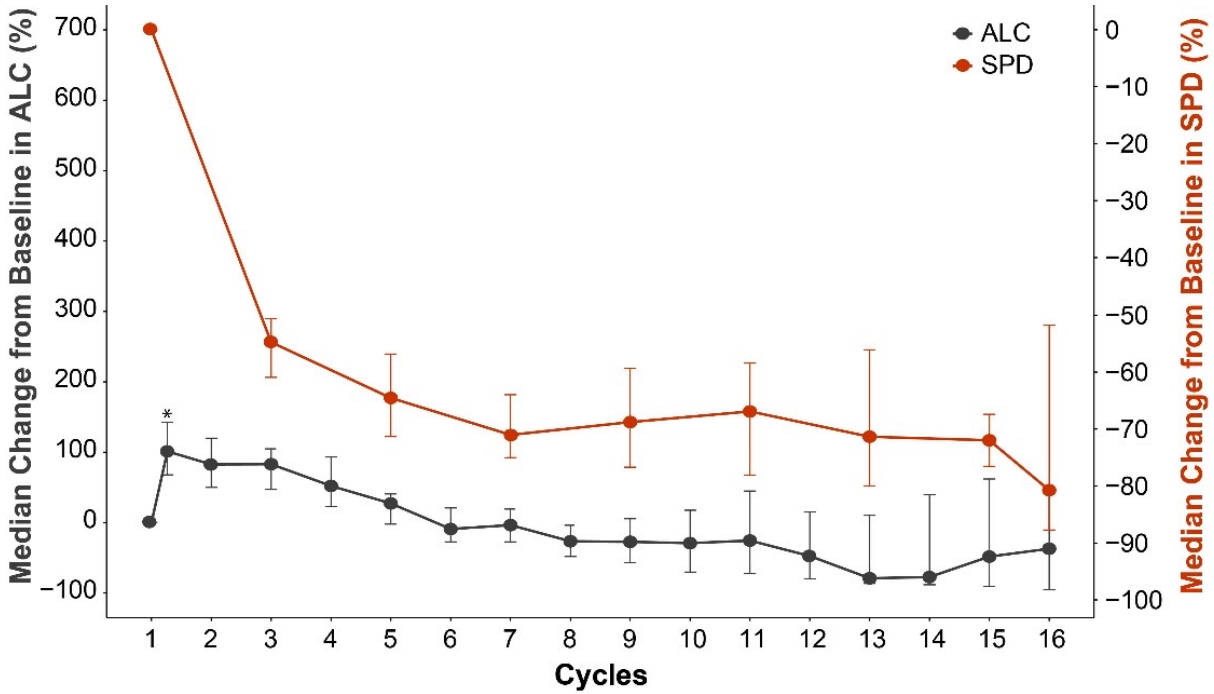
All doses and patients (n=323)								
	Treatment-emergent AEs, (≥10%), n (%)[a]						Treatment-related AEs, n (%)	
Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade		Grades 3/4	Any Grade
Fatigue	40 (12%)	22 (7%)	3 (1%)	-	65 (20%)		2 (<1%)	27 (8%)
Diarrhea	45 (14%)	10 (3%)	-	-	55 (17%)		-	28 (9%)
Contusion	37 (12%)	5 (2%)	-	-	42 (13%)		-	29 (9%)
AEs of special interest[b,c]								
Bruising	48 (15%)	5 (2%)	-	-	53 (16%)		-	37 (12%)
Rash	30 (9%)	5 (2%)	-	-	35 (11%)		-	18 (6%)
Arthralgia	13 (4%)	3 (1%)	-	-	16 (5%)		-	5 (2%)
Hemorrhage	10 (3%)	4 (1%)	1 (<1%)[d]	-	15 (5%)		-	5 (2%)
Hypertension	2 (<1%)	9 (3%)	4 (1%)	-	15 (5%)		-	4 (1%)
Atrial fibrillation/flutter	-	2 (<1%)[e]	-	-	2 (<1%)		-	-

No DLTs reported and MTD not reached
5 of 323 patients (1.5%) discontinued due to treatment-related AEs
200mg QD selected as recommended Phase 2 dose

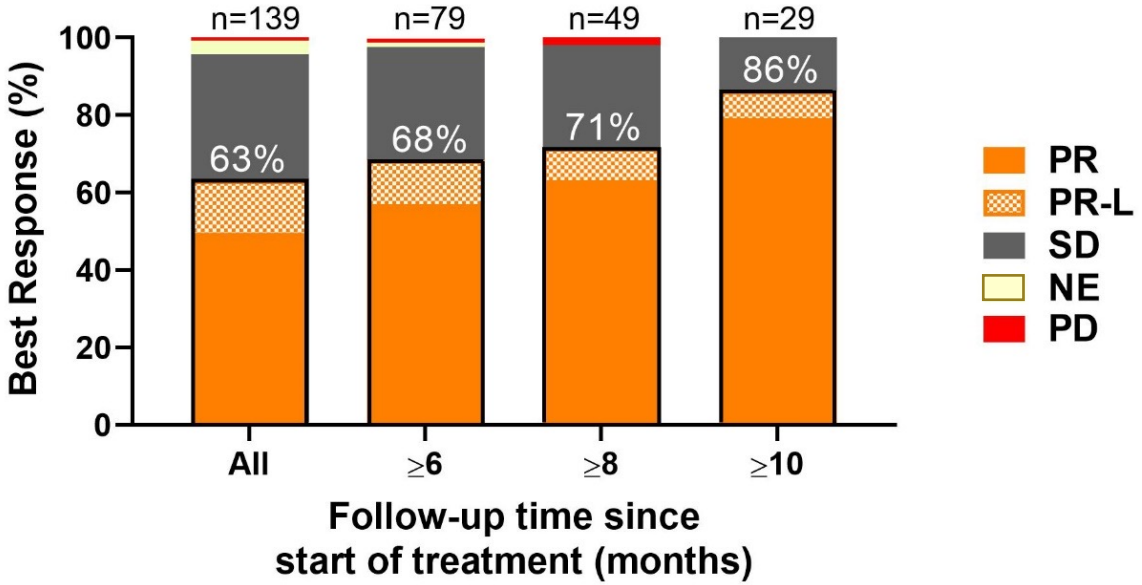
Data cutoff date of 27 September 2020. Total % may be different than the sum of the individual components due to rounding. [a]The AEs listed are the most common that occurred at any grade in at least 10% of the patients, regardless of attribution. [b]AEs of special interest are those that were previously associated with covalent BTK inhibitors. [c]Bruising includes contusion, petechia, ecchymosis and increased tendency to bruise. Hemorrhage includes hematoma, epistaxis, rectal hemorrhage, subarachnoid hemorrhage, upper gastrointestinal hemorrhage, vitreous hemorrhage and wound hemorrhage. Rash includes rash maculo-papular, rash, rash macular, rash erythematous, rash popular, rash pruritic and rash pustular. [d]Subarachnoid bleed sustained during a bicycle accident, considered by investigator as unrelated to LOXO-305. [e]Both events considered by investigators as unrelated to LOXO-305 due to a history of prior atrial fibrillation in each.

BRUIN: Pirtobrutinib Responses Deepen Over Time

Lymphocytosis Precedes Tumor Reduction and Resolves Over Time[a]

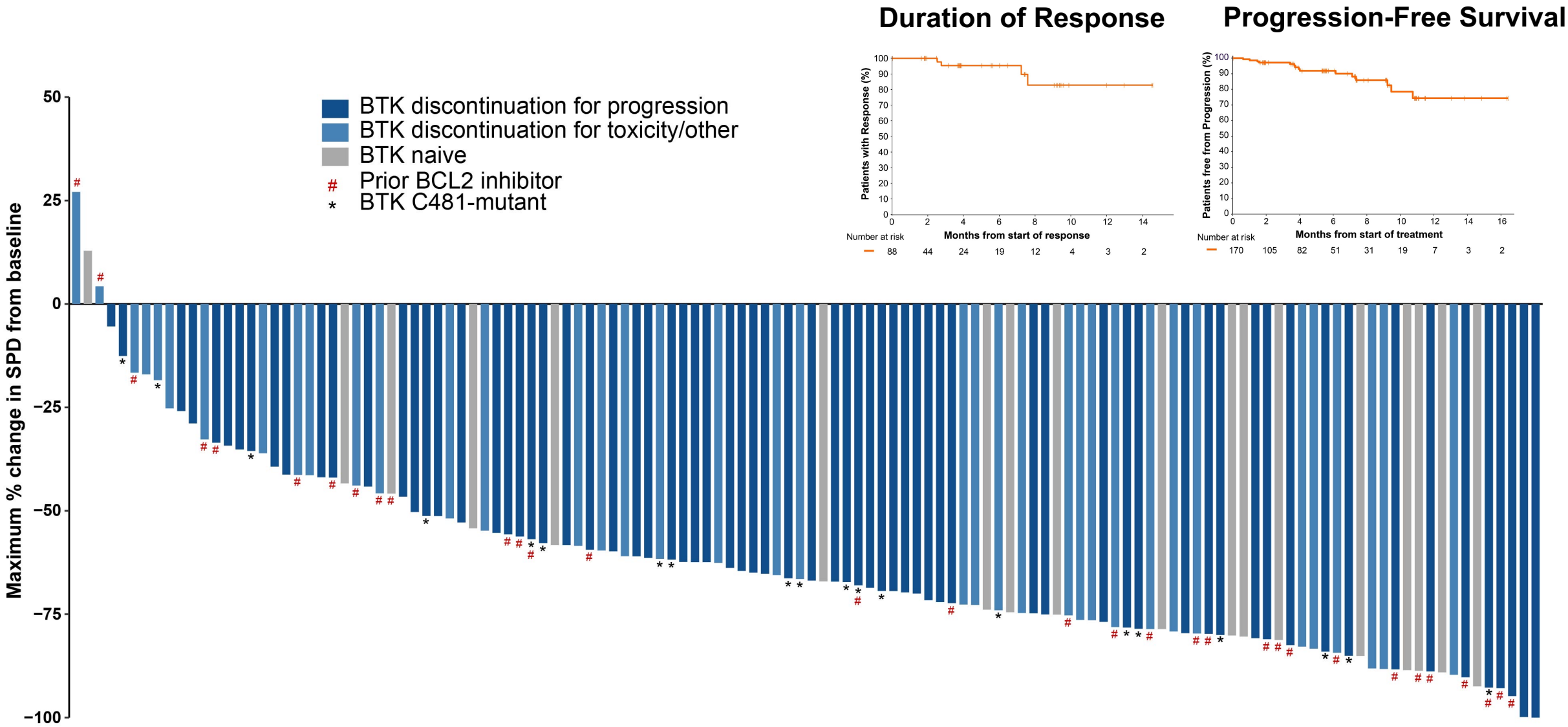


Overall Response Rate Increases Over Time[b]



Data cutoff date of 27 September 2020. [a]BTKi-induced lymphocytosis is defined as absolute lymphocyte count increasing ≥50% from baseline and ≥5x10^9/L. [b]Includes the efficacy-evaluable CLL/SLL patients at the time of data cutoff. Data at each timepoint includes the efficacy-evaluable CLL/SLL patients who had the opportunity to be followed for at least the indicated amount of time.

BRUIN: Efficacy of Pirtobrutinib in CLL/SLL



Duration of Response

Progression-Free Survival

Data cutoff date of 27 September 2020. Total % may be different than the sum of the individual components due to rounding. Data for 13 CLL/SLL patients are not shown in the waterfall plot due to 4 having no target lesions identified at baseline, 5 with no/incomplete post-baseline lesion measurements, and 4 discontinued prior to first post-baseline disease assessment.

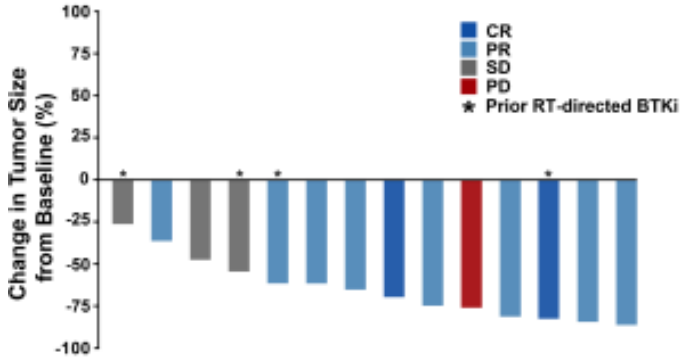
Phase I/II Trial of Pirtobrutinib in Richter's transformation

Table 1. Baseline characteristics

Characteristics	n=17
Median age, years (range)	64 (33-84)
Male, n (%) Female, n (%)	14 (82) 3 (18)
ECOG PS, n (%) 0 1 2	 8 (47) 7 (41) 2 (12)
Any *BTK* mutation status, n (%) Wildtype Unknown	 10 (59) 7 (41)
Bulky disease, n (%) < 5 cm ≥ 5 cm	 10 (59) 7 (41)
DLBCL RT histology	17 (100)
Median lines of prior systemic therapy, n (range)	6 (2-10)
Median lines of therapy for CLL prior to RT, n (range)	4 (1-9)
Median lines of prior RT-directed therapy, n (range)	2 (1-5)
All Prior therapies (CLL+RT-directed) BTK inhibitor BCL2 inhibitor	 14 (82) 10 (59)
Prior RT-directed systemic therapies, n (%) Chemotherapy Anti-CD20 antibody BTK inhibitor PD/PDL-1 immunotherapies mTOR inhibitor PI3K inhibitor Lenalidomide BCL2 inhibitor CAR-T	 17 (100) 17 (100) 6 (35) 5 (29) 4 (24) 3 (18) 3 (18) 3 (18) 1 (6)

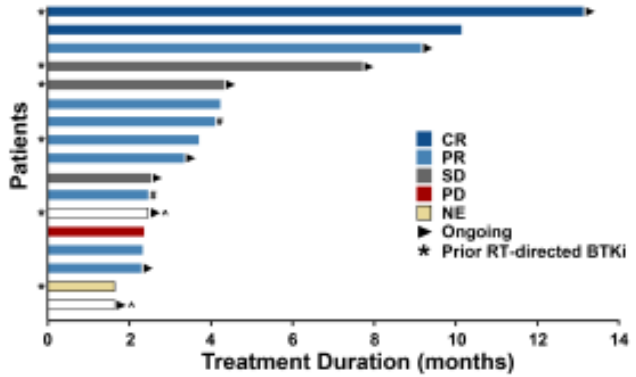
- Median time on treatment was 3.4 months (range 1.6-13.1+ months).

Fig 1. Best change in tumor size and response

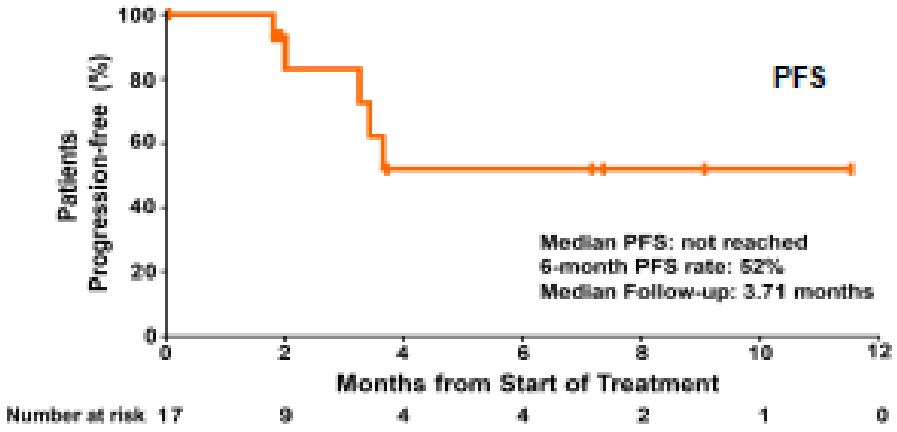


1 patient not shown due to discontinuation prior to first post- baseline tumor assessment.

Fig 2. Treatment duration and best response



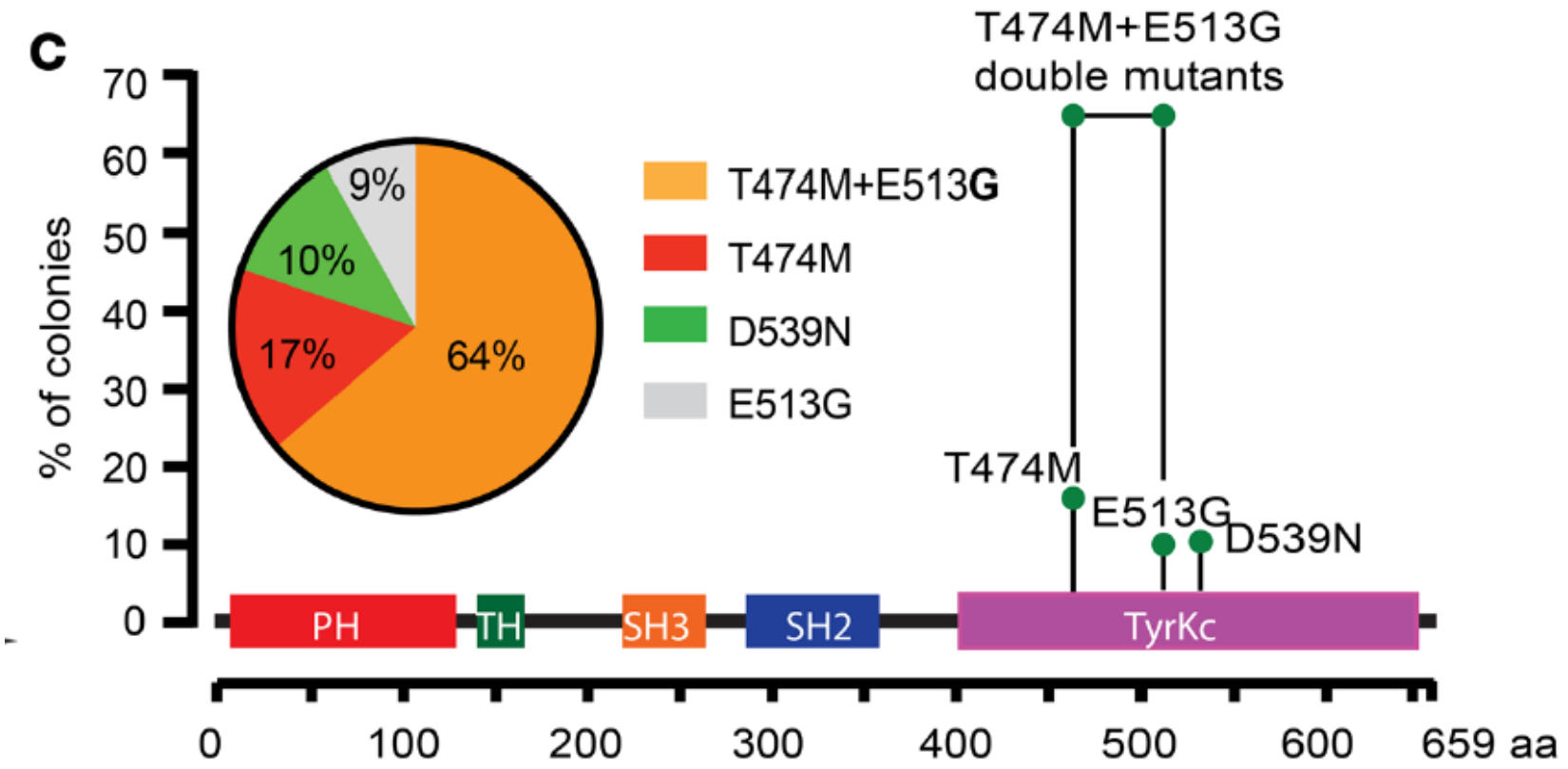
#Electively discontinued in response, to pursue transplant.
^2 patients were non-evaluable for efficacy (1 ongoing prior to first post-baseline assessment, 1 ongoing with incomplete post-baseline assessment).



ORR 67%, CR 13% (n=2)

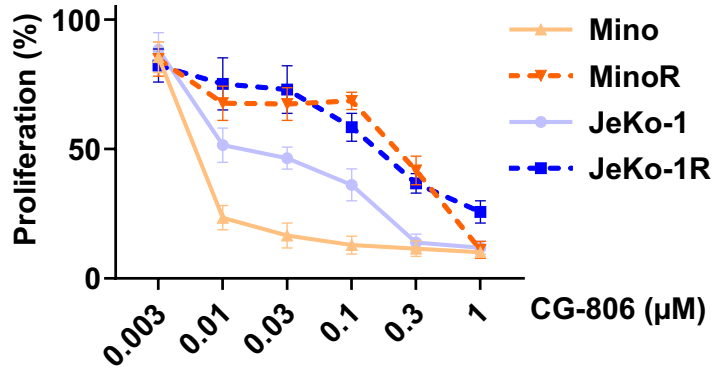
Mato et al, EHA 2021

Potential resistance to non-covalent BTKi

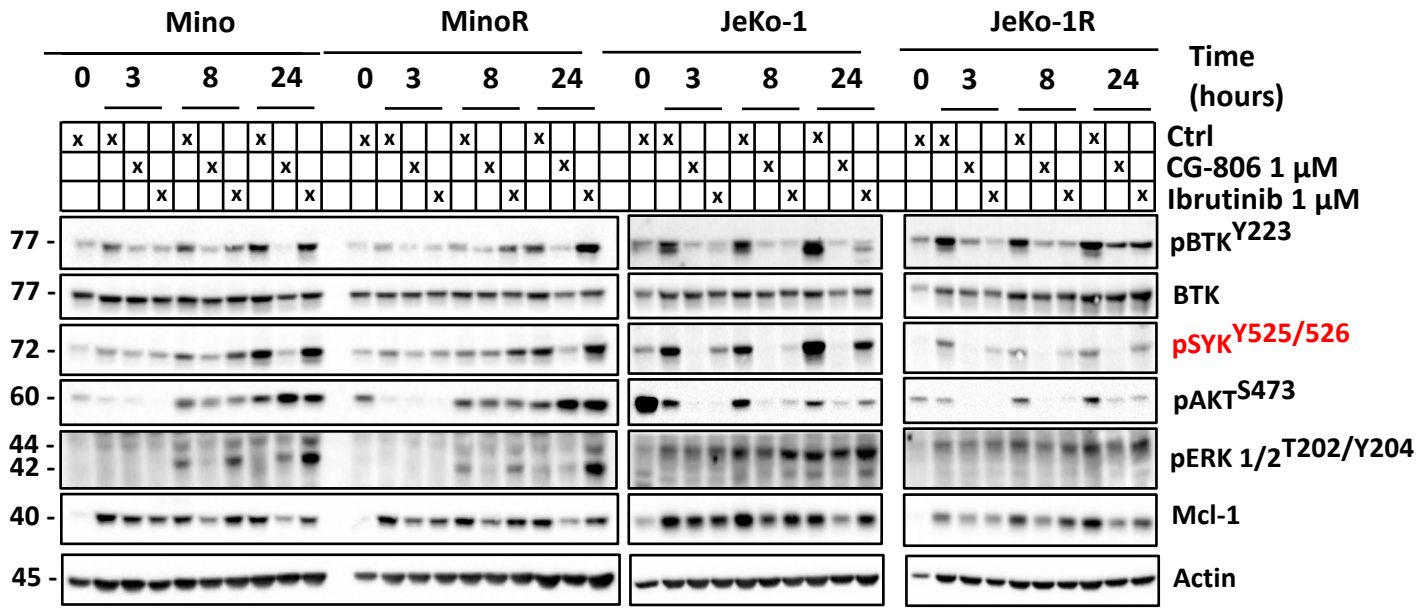


Wang S et al, JCI Insight 2019

Luxeptinib (CG-806) – a non-covalent BTK/SYK inhibitor



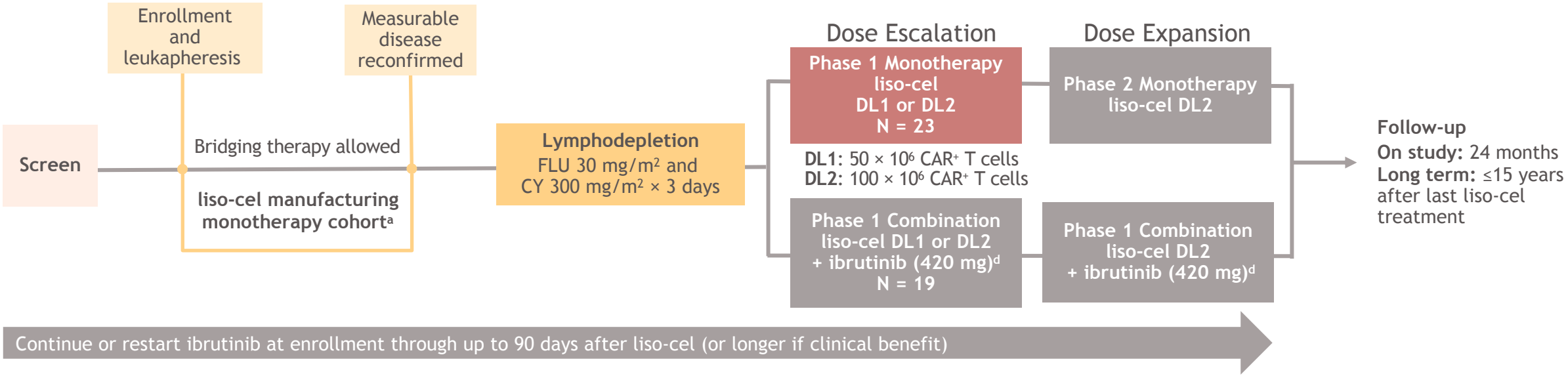
Stronger SYK, AKT, ERK and MCL-1 inhibition than ibrutinib in parental and ibrutinib-resistant Mantle cell lymphoma cells



Select ongoing Pirtobrutinib (LOXO-305) studies

- **Study of Pirtobrutinib Versus Investigator's Choice (IdelaR or BR) in Patients With CLL or SLL (BRUIN CLL-321**; NCT04666038)
  - CLL previously treated with covalent BTKi; PFS
- **A Trial of Pirtobrutinib Plus Venetoclax and Rituximab (PVR) Versus Venetoclax and Rituximab (VR) in Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) (BRUIN CLL-322;** NCT04965493**)**
  - CLL 1 prior therapy (=/- BTKi); PFS

TRANSCEND CLL 004 Phase 1/2 Study Design 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

Demographic and Baseline Disease Characteristics: monotherapy cohort

Characteristic	Monotherapy Cohort (N = 23)	BTKi Progression/Venetoclax Failure Subgroup[c] (n = 11)
Median age, y (range)	66 (50–80)	68 (59–76)
Male, n (%)	11 (48)	6 (55)
Median time since diagnosis, mo (range)	87.5 (30–209)	106 (30–209)
Bulky disease ≥5 cm, n (%)[a]	8 (35)	4 (36)
Median SPD, cm^2 (range)	25 (2–197)	41 (2—197)
Median BALL risk score[1] (range)	2 (0–3)	2 (0–3)
Median LDH, U/L (range)	235 (1–1956)	240 (1–1956)
Stage, n (%)		
Rai stage III/IV	15 (65)	7 (64)
Binet stage C	16 (70)	8 (73)
High-risk feature (any), n (%)	19 (83)	10 (91)
Del(17p)	8 (35)	4 (36)
TP53 mutated	14 (61)	8 (73)
Complex karyotype[b]	11 (48)	5 (45)
Median no. of lines of prior therapy (range)	4 (2–11)	5 (4–10)
Ibrutinib progression, n (%)	**17 (74)**	11 (100)
Ibrutinib intolerant, n (%)	6 (26)	0
Received bridging therapy, n (%)	17 (74)	8 (73)

[a]Defined as ≥1 lesion with longest diameter of >5 cm. [b]At least 3 chromosomal aberrations. [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. BALL, β_2 microglobulin, anemia, LDH, last therapy; SPD, sum of the product of perpendicular diameters.

1. Soumerai JD, et al. *Lancet Haematol*. 2019;6:e366-e374.

Siddiqi et al, ASH 2020

TRANSCEND CLL 004: Treatment-Emergent AEs, Cytokine Release Syndrome, and Neurological Events: monotherapy cohort

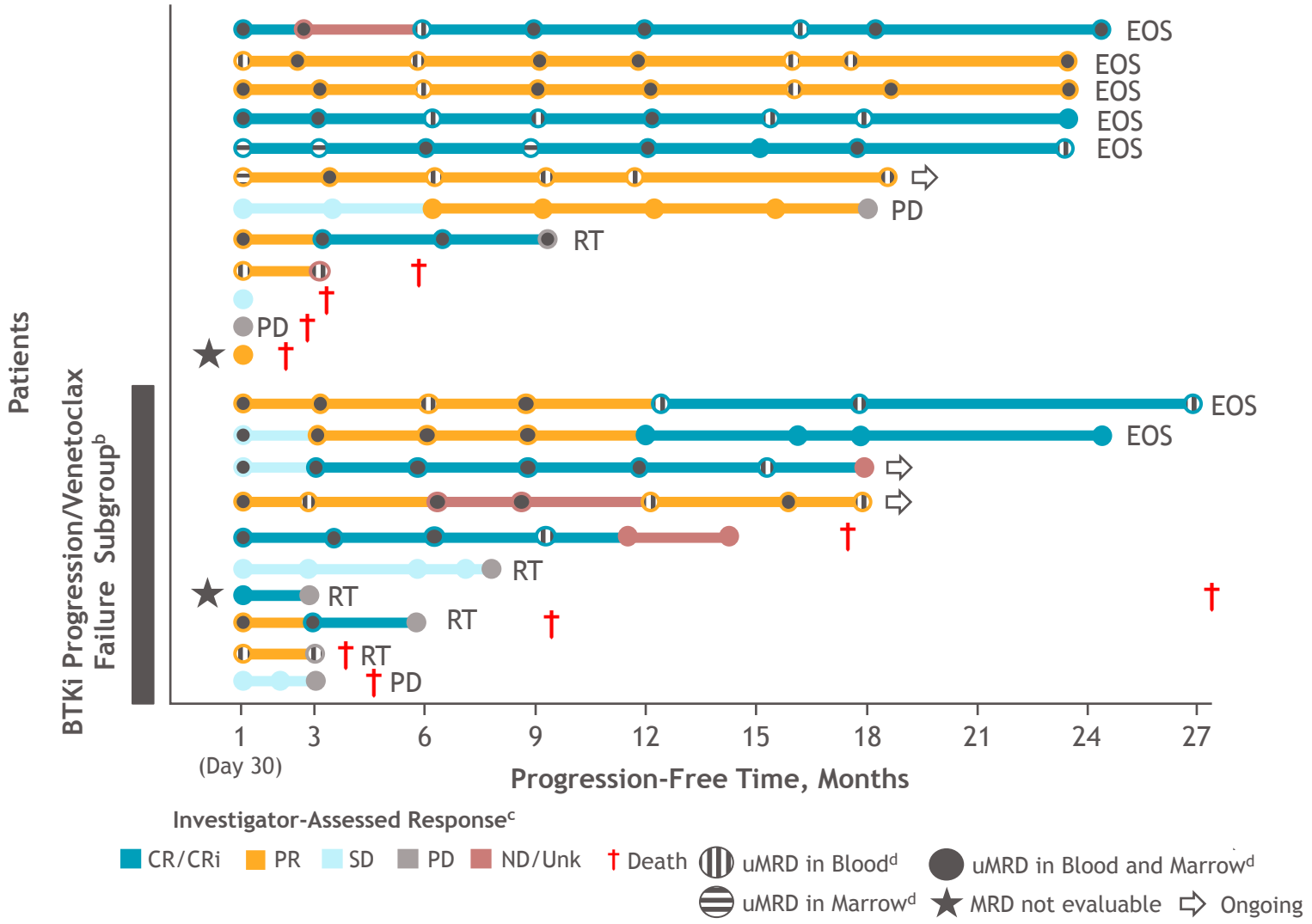
- Dose-limiting toxicities were reported for 2 patients at DL2, which resolved
- No late or delayed AEs of concern have emerged with longer follow-up

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

TRANSCEND CLL 004 – Patient Response at 24-Month Median Follow-Up: monotherapy

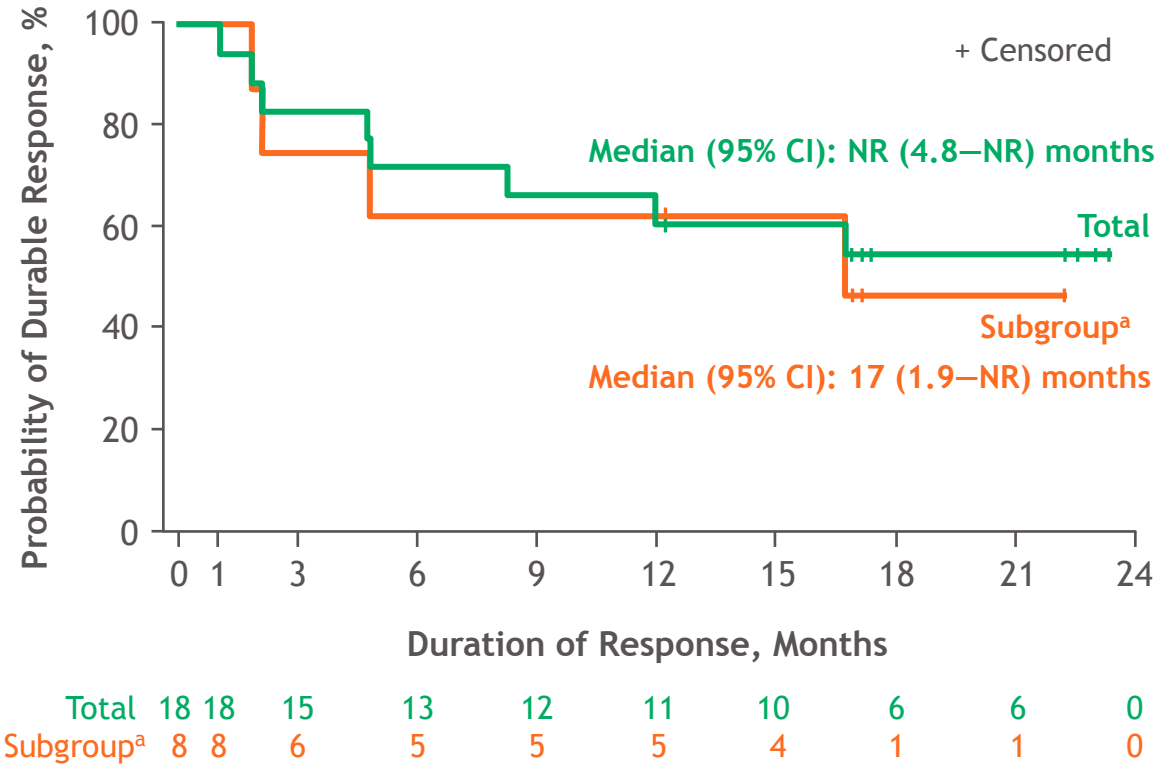


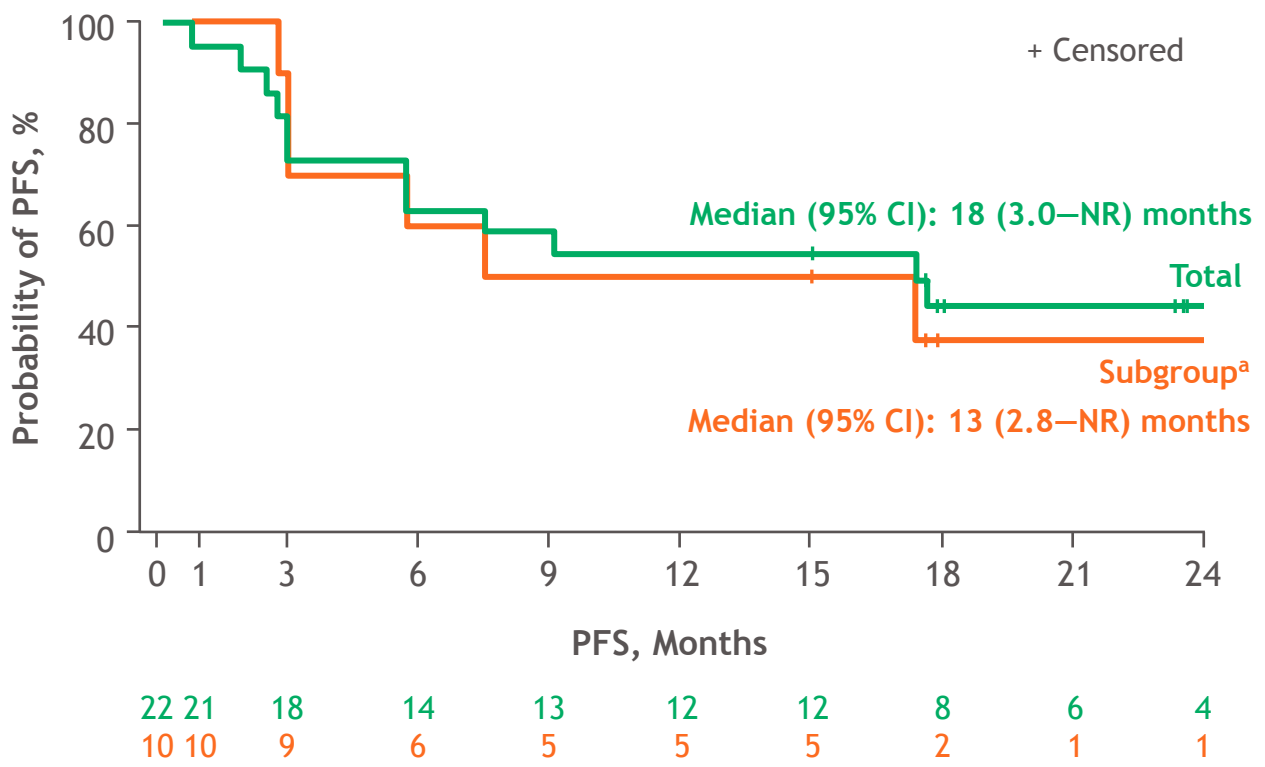
- ORR was 82% (CR/CRi, 46%; PR, 36%), with 68% (n = 15/22)[a] of patients achieving a rapid response within 30 days
- 27% (n = 6/22) of patients had a deepening of response
- Response was durable. At 12 months, 50% (n = 11/22) were in response and only 2 of these responders progressed beyond 12 months
- Richter's transformation (RT) the most common reason for progression
- Median PFS 18 months

[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.

Siddiqi et al, ASH 2020

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





[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

TRANSCEND CLL 004 – Treatment-Emergent AEs, Cytokine Release Syndrome, and Neurological Events: ibrutinib + CAR T cohort

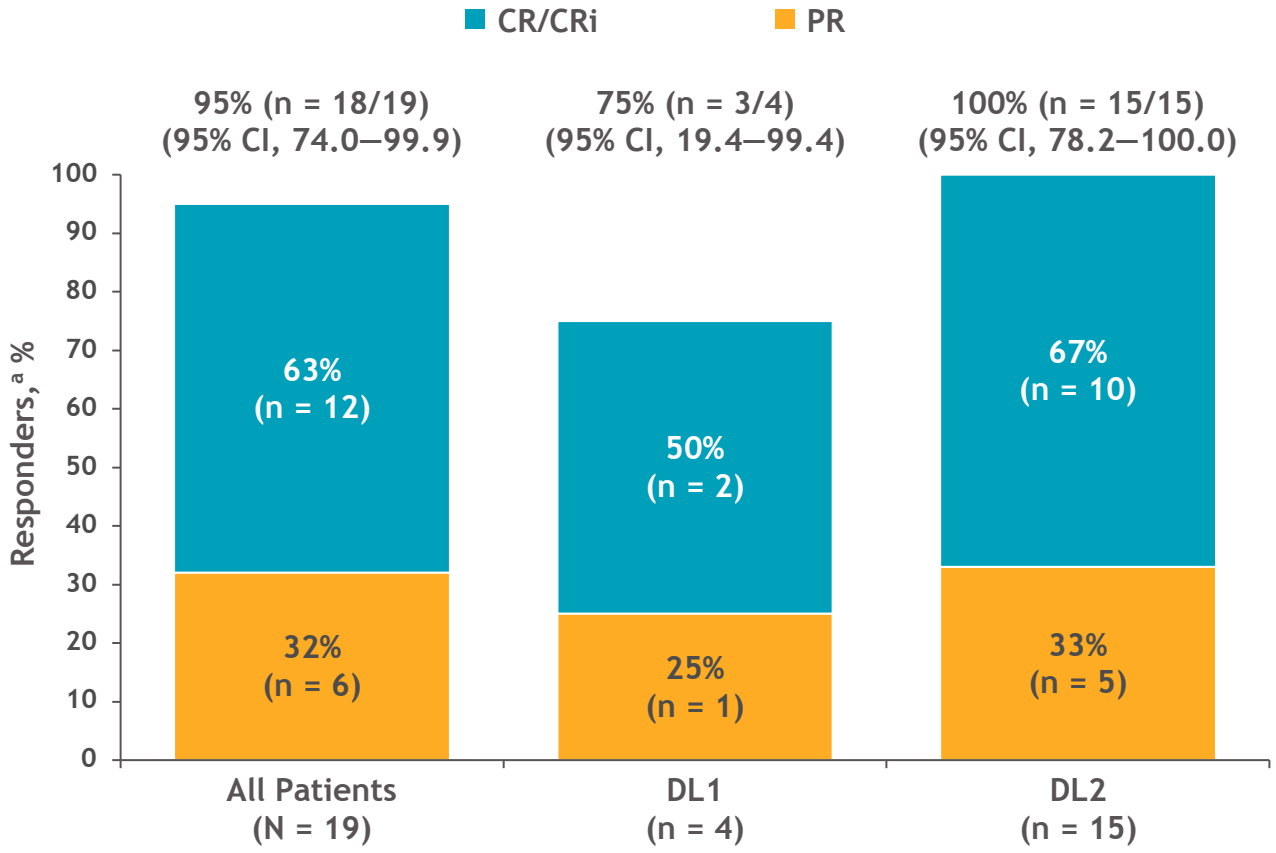
- The combination of liso-cel and ibrutinib was well tolerated, with no reported dose-limiting toxicities
- No grade 5 AEs or grade 4 CRS or NEs were reported

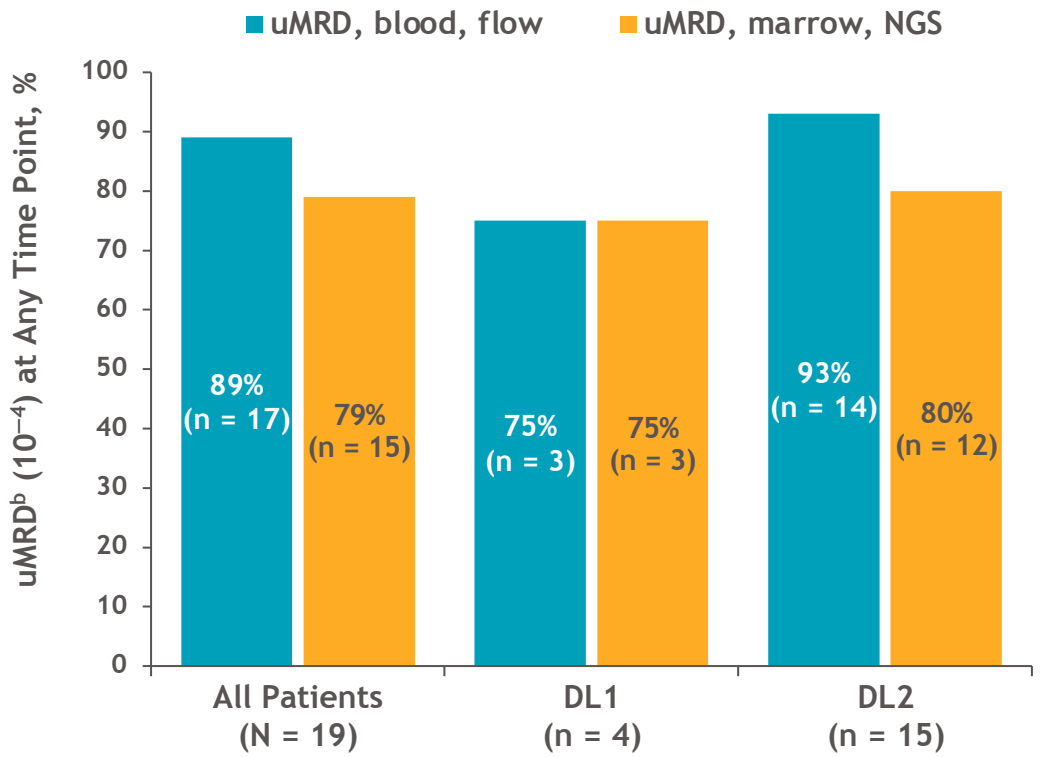
Parameter	Combination Cohort (N = 19)	DL1 + Ibrutinib (n = 4)	DL2 + Ibrutinib (n = 15)
Common grade 3/4 treatment-emergent AEs (TEAEs), n (%)	18 (95)	4 (100)	14 (93)
Neutropenia/neutrophil count decrease	17 (89)	3 (75)	14 (93)
Anemia	9 (47)	3 (75)	6 (40)
Febrile neutropenia	5 (26)	1 (25)	4 (27)
Cytokine 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).

Weirda et al, ASH 2020

Best Overall Response and uMRD (≤10^{-4}) at 10-Month Follow-Up: Ibrutinib + CAR T combination cohort (TRANSCEND CLL 004)





- 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.

Weirda et al, ASH 2020

Candidates for CAR T-cell therapy

- Double-refractory/intolerant patients (BTKi/BCL2)
- Single-refractory patients with high genetic risk
- Relatively fit with limited comorbidities (comorbidities predict inferior outcomes with CAR T cells

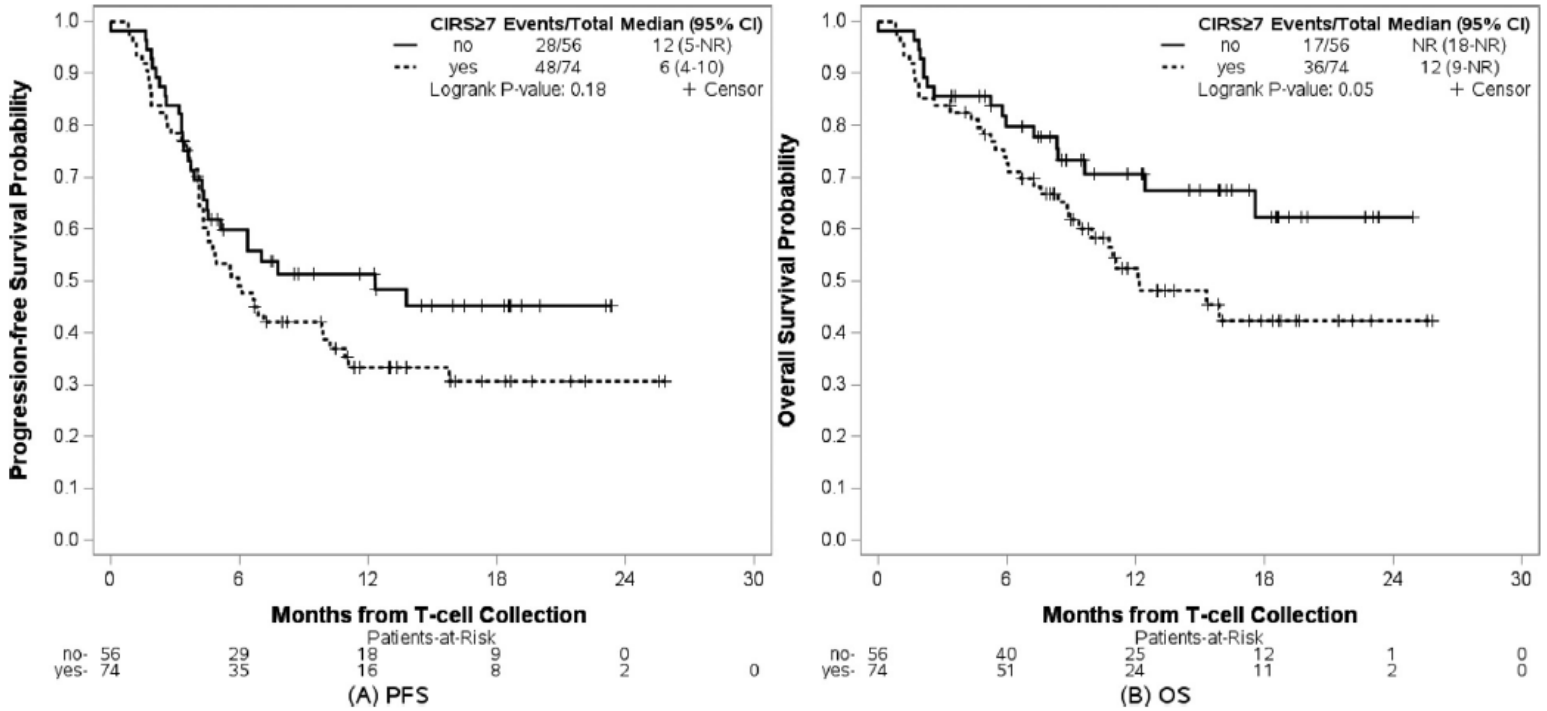


Figure 2. PFS and OS of patients with DLBCL treated with CAR-T therapy by CIRS ≥7.

Kittai & Danilov, TCT 2021

Some Novel/emerging targets

Targeted therapies:

- Mcl-1 (AMG-176, AZD5991)
- CDK9 (AZD4573, voruciclib, CYC065, VIP152)
- PROTACs
- Bcl-xL (AZD4320, navitoclax)

Antibodies:

- Bi-specific CD20 antibodies (mosunetuzumab, epcoritamab)
- Alternative antibodies
  - VAY-736 targeting BAFF-R
  - Tafasitamab targeting CD19
  - Cirmtuzumab targeting ROR1

CAR T-cell therapy

- Phase I/II trial of liso-cel in R/R CLL/SLL (NCT03331198)
- Phase I/II trial of PBCAR20A in R/R CLL/SLL (NCT04030195)

Clinical case

A 56-year-old woman is evaluated for CAR T-cell therapy

Concurrent comorbidities: DM type 2 (on oral meds), HTN

- Dec 2013 – diagnosed with CLL, del 17p, presents with B symptoms and progressive LAD
- June-Dec 2015 – **Bendamustine-Obinutuzumab x 6 cycles** achieving CR
- July 2017 – progressive lymphocytosis, started **Entospletinib+Obinutuzumab** achieving PR
- June 2018 - progressive lymphocytosis, started **ibrutinib** achieving PR
- July 2019 – progressed on ibrutinib with bulky lymphadenopathy and lymphocytosis
- August 2019 - Starts **Venetoclax+Rituximab**, achieving PR;
- May 2020 – develops AIHA, resolved with steroids+rituximab
- October 2020 – develops PE, starts on anticoagulation
    - Bone marrow biopsy: 50% CLL; 45,XX,-1,add(6)(q24),-9,inv(12)(p13q13),del(13)(q14q22),-17,add(18)(p11.2),+2mar[9]/45,sl,add(7)(q34),add(10)(p13)[14]/90~91,sdl1x2[2]

      NGS panel: *TP53* mutation 72%, no other abnormalities

January 12, 2021 – FluCY -> **Liso-cel**. Complications: Grade 3 CRS (receives Toci)

April 2021 – BMBX – normocellular bone marrow, no CLL. MRD negative