# Promising Investigational Agents and Strategies

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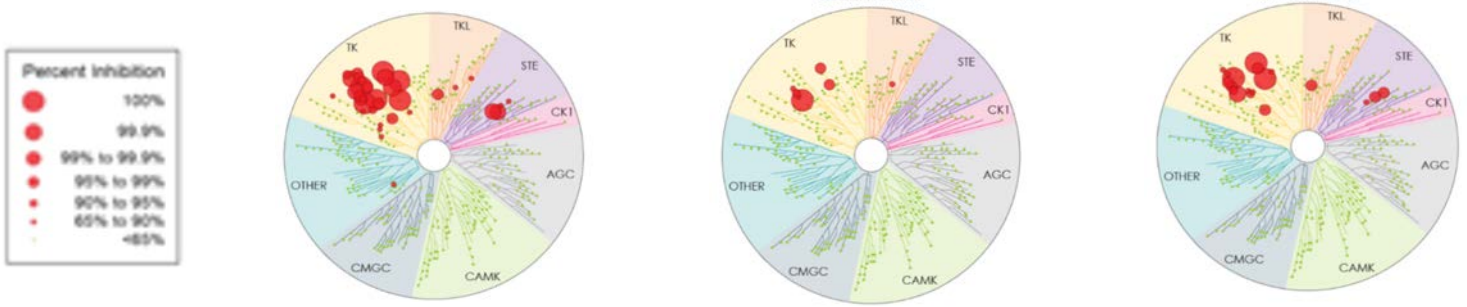
# BTK inhibitors: comparing kinome selectivity and *in vivo* activity

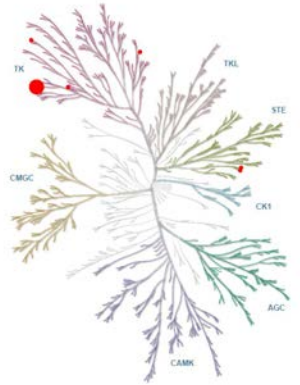
**Covalent**

**Ibrutinib** **Acalabrutinib** **Zanubrutinib**



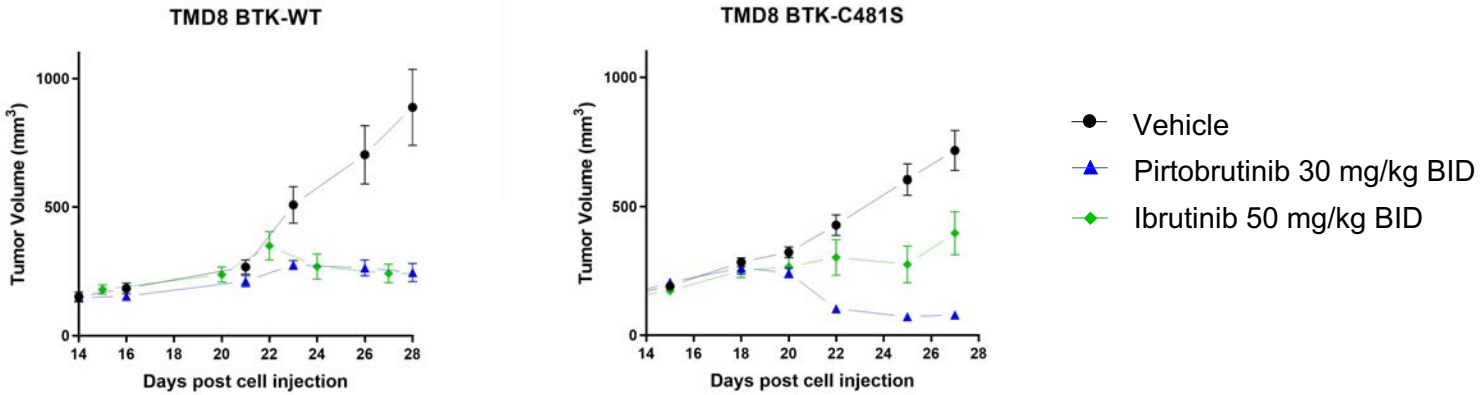

**Non-Covalent**

**Pirtobrutinib**




## Xenograft models

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




**Pirtobrutinib**

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

Kaptein A, et al. *Blood.* 2018;132(Supplement 1):1871. Mato et al, *Lancet*, 2021:397:892-901. Brandhuber BJ, et al. *Clin. Lymphoma Myeloma Leuk*. 2018.18:S216

# BRUIN: phase I/II study of Pirtobrutinib

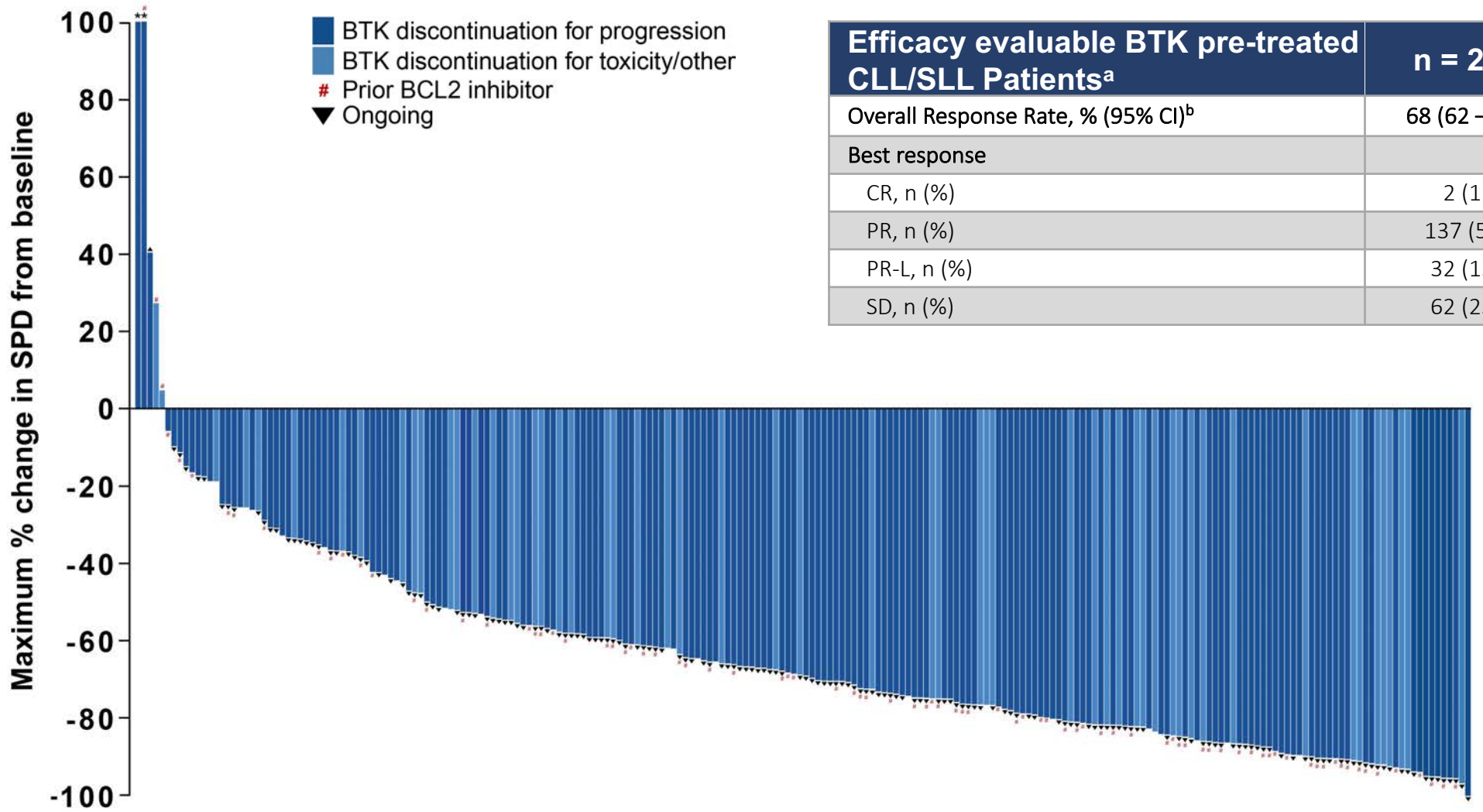
The most recent clinical update focused on CLL/SLL patients previously treated with BTK inhibitor

| Characteristics | N = 261 |
|---|---|
| Median age, years (range) | 69 (36-88) |
| Female, n (%) | 84 (32) |
| Male, n (%) | 177 (68) |
| ECOG PS[a], n (%) | |
| 0 | 138 (53) |
| 1 | 104 (40) |
| 2 | 19 (7) |
| Median number of prior lines of systemic therapy (range) | 3 (1-11) |
| Prior therapy, n (%) | |
| BTK inhibitor | 261 (100) |
| Anti-CD20 antibody | 230 (88) |
| Chemotherapy | 207 (79) |
| BCL2 inhibitor | 108 (41) |
| PI3K inhibitor | 51 (20) |
| CAR-T | 15 (6) |
| Stem cell transplant | 6 (2) |
| Allogeneic stem cell transplant | 5 (2) |
| Autologous stem cell transplant | 1 (<1) |
| Reason discontinued prior BTKi, n (%) | |
| Progressive disease | 196 (75) |
| Toxicity/Other | 65 (25) |

| Baseline Molecular Characteristics | |
|---|---|
| Mutation status, n (%) | |
| BTK C481-mutant | 89 (43) |
| BTK C481-wildtype | 118 (57) |
| PLCG2-mutant | 33 (16) |
| High Risk Molecular Features, n (%) | |
| 17p deletion | 51 (28) |
| TP53 mutation | 64 (37) |
| 17p deletion or TP53 mutation | 77 (36) |
| Both 17p deletion and TP53 mutation | 38 (27) |
| IGHV unmutated | 168 (84) |
| 11q deletion | 45 (25) |

Mato A, et al. *Blood*. 2021;136(Supplement 1):35-37

# Pirtobrutinib efficacy in BTK pre-treated CLL/SLL patients

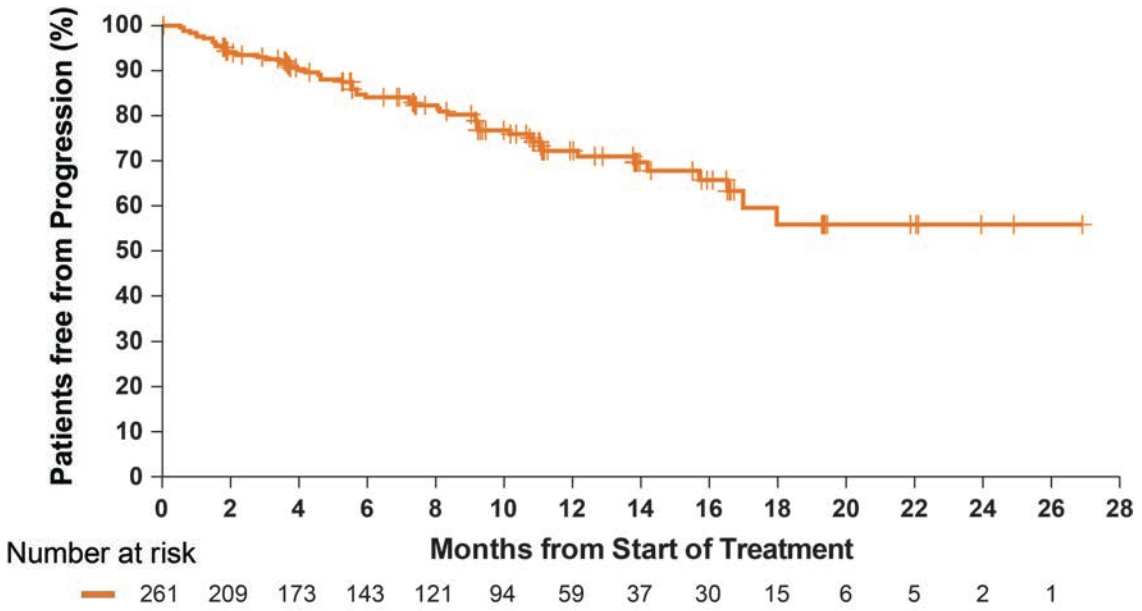



| Efficacy evaluable BTK pre-treated CLL/SLL Patients[a] | n = 252 |
|---|---|
| Overall Response Rate, % (95% CI)[b] | 68 (62 – 74) |
| Best response | |
| CR, n (%) | 2 (1) |
| PR, n (%) | 137 (54) |
| PR-L, n (%) | 32 (13) |
| SD, n (%) | 62 (25) |

Mato A, et al. *Blood*. 2021;136(Supplement 1):35-37; Mato AR et al. EHA 2022; Abstract S147.

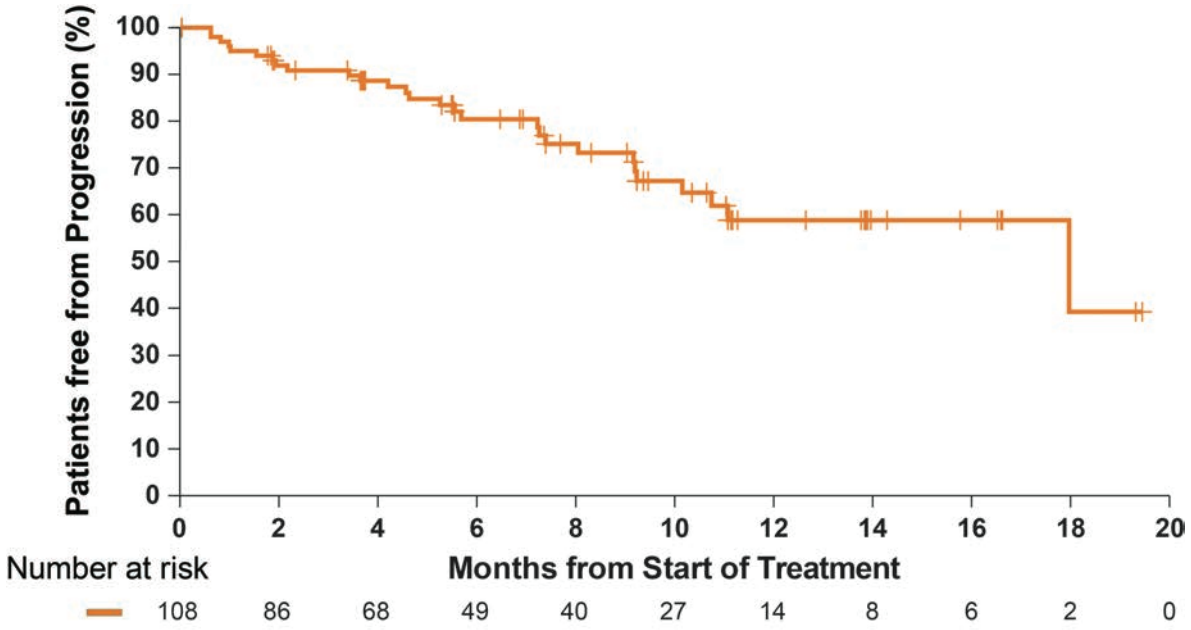
# Progression-free survival in BTK pre-treated CLL/SLL patients

**PFS in at least BTK pre-treated patients**
**Median prior lines = 3**




Median PFS: Not Estimable (95% CI: 17.0 months – Not Estimable)

**PFS in at least BTK and BCL2 pre-treated patients**
**Median prior lines = 5**

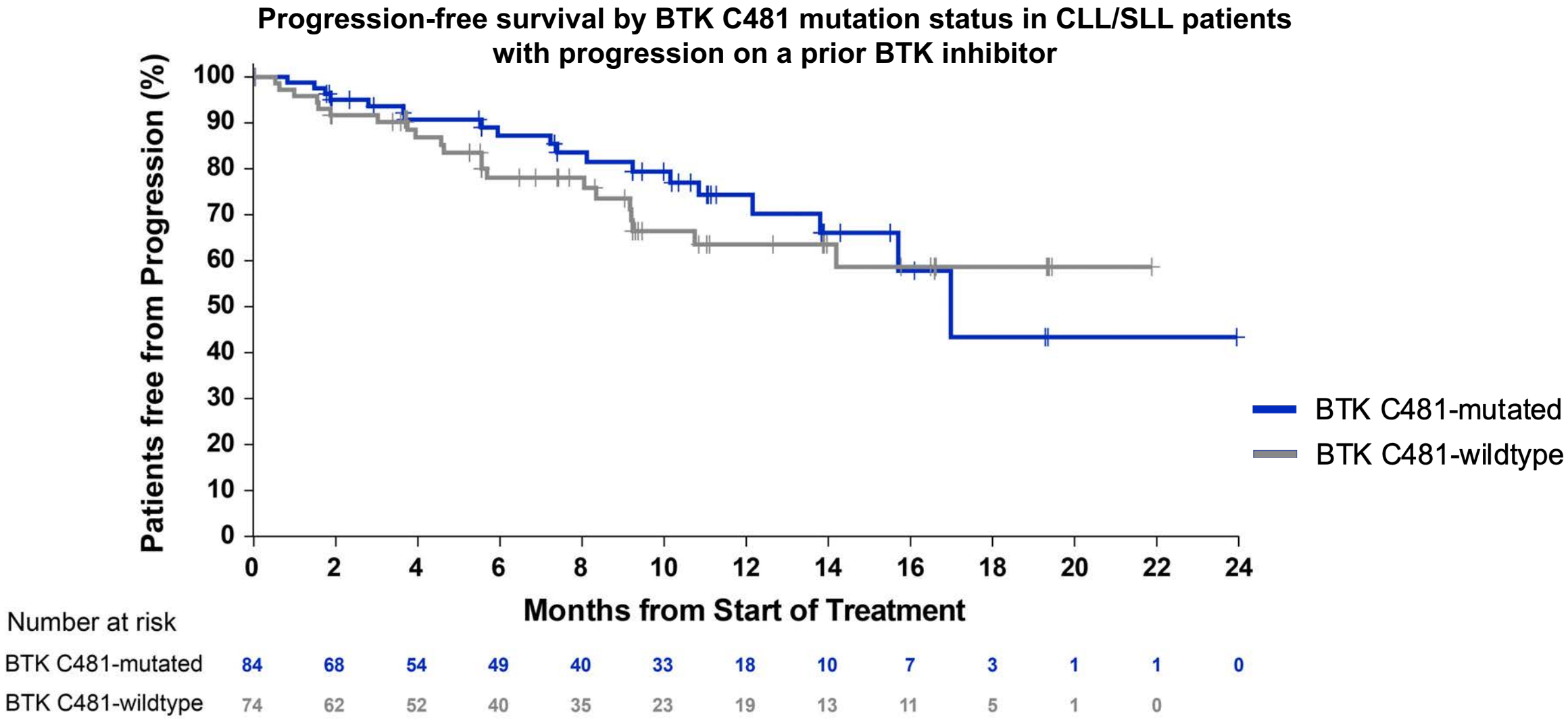



Median PFS: 18 months (95% CI: 10.7 months – Not Estimable)

- 74% (194/261) of BTK pre-treated patients remain on pirtobrutinib
- Median follow-up of 9.4 months (range, 0.3 – 27.4) for all BTK pre-treated patients

Mato A, et al. *Blood*. 2021;136(Supplement 1):35-37; Mato AR et al. EHA 2022; Abstract S147.

# BTK C481 mutation status is not predictive of Pirtobrutinib benefit




Mato A, et al. *Blood*. 2021;136(Supplement 1):35-37; Mato AR et al. EHA 2022; Abstract S147.

# Pirtobrutinib safety profile

| All doses and patients (n=618) | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Treatment-emergent AEs, (≥15%), % | | | | | Treatment-related AEs, % | |
| Adverse Event | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Any Grade | Grades 3/4 | Any Grade |
| Fatigue | 13% | 8% | 1% | - | 23% | 1% | 9% |
| Diarrhea | 15% | 4% | <1% | <1% | 19% | <1% | 8% |
| Neutropenia | 1% | 2% | 8% | 6% | 18% | 8% | 10% |
| Contusion | 15% | 2% | - | - | 17% | - | 12% |
| AEs of special interest | | | | | | | |
| Bruising | 20% | 2% | - | - | 22% | - | 15% |
| Rash | 9% | 2% | <1% | - | 11% | <1% | 5% |
| Arthralgia | 8% | 3% | <1% | - | 11% | - | 3% |
| Hemorrhage | 5% | 2% | 1%[g] | - | 8% | <1% | 2% |
| Hypertension | 1% | 4% | 2% | - | 7% | <1% | 2% |
| Atrial fibrillation/flutter | - | 1% | <1% | <1% | 2%[h] | - | <1% |

**No DLTs reported and MTD not reached**
**96% of patients received ≥1 pirtobrutinib dose at or above RP2D of 200 mg daily**
**1% (n=6) of patients permanently discontinued due to treatment-related AEs**

Mato A, et al. *Blood*. 2021;136(Supplement 1):35-37; Mato AR et al. EHA 2022; Abstract S147.

# ASH 2022: Pirtobrutinib in CLL

Saturday, 4:00 – 5:30 PM

347 (Oral). Efficacy of Pirtobrutinib, a Highly Selective, Non-Covalent (Reversible) BTK Inhibitor in Richter Transformation: Results from the Phase 1/2 BRUIN Study

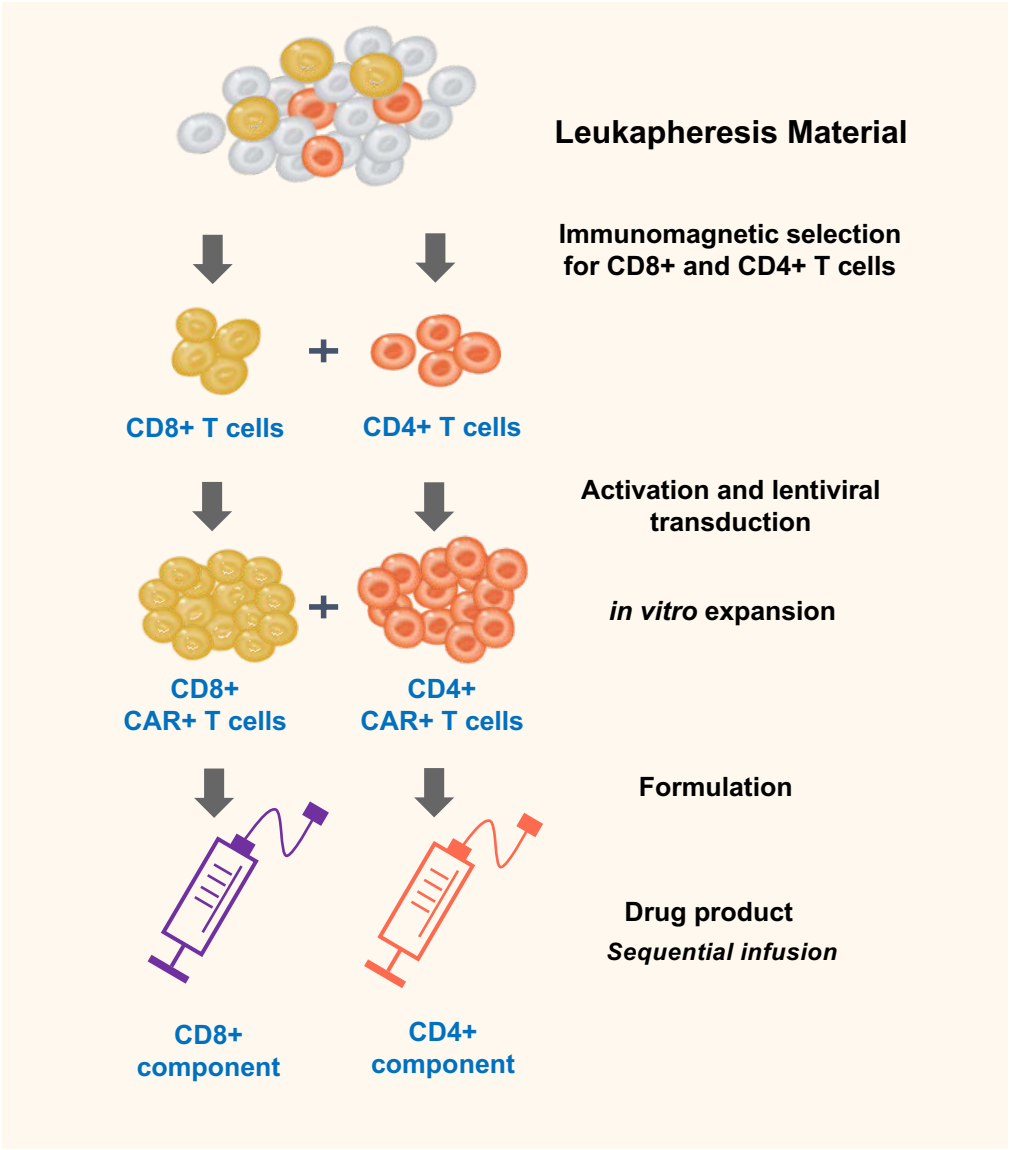
Saturday, 5:30 – 7:30 PM

1797 (Poster). Safety and Tolerability of Pirtobrutinib Monotherapy in Patients with B-Cell Malignancies Who Were Previously Intolerant to a Covalent BTK Inhibitor: Results from the Phase 1/2 BRUIN Study

Monday, 4:30 – 6:30 PM

961 (Oral). Efficacy of Pirtobrutinib in Covalent BTK-Inhibitor Pre-Treated Relapsed / Refractory CLL/SLL: Additional Patients and Extended Follow-up from the Phase 1/2 BRUIN Study

# TRANSCEND CLL 004: Liso-Cel in CLL




## *CD19-Directed, Defined Composition, 4-1BB CAR T Cell Product*

**CD8+ and CD4+ CAR+ T cell components are administered separately at equal target doses of CD8+ and CD4+ CAR+ T cells**

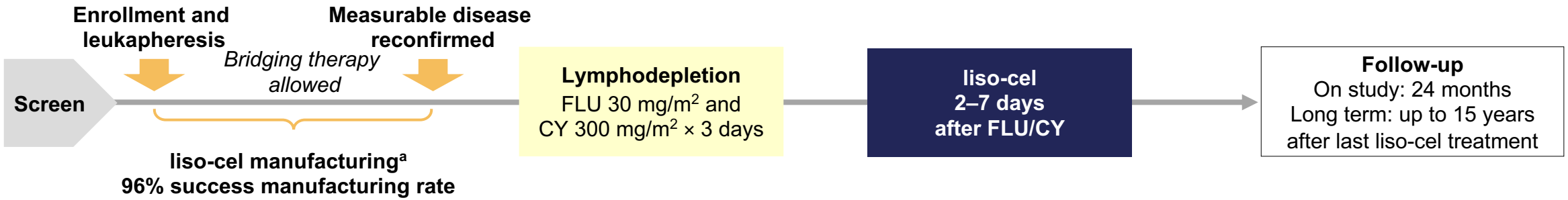
The defined composition of liso-cel results in:

- Consistent administered CD8+ and CD4+ CAR+ T cell dose
- Low variability in the CD8+/CD4+ ratio

Dose and ratio of CD8+ and CD4+ CAR+ T cells may influence the incidence and severity of CRS and neurological events

Siddiqi T, et al. *Blood*. 2019;134(Supplement 1):503. Turtle CJ, et al. *Sci Transl Med*. 2016;8(355):355ra116. DeAngelo DJ, et al. *J Immunother Cancer*. 2017;5(Suppl 2):116: Abstract P217. Neelapu SS, et al. *N Engl J Med*. 2017;377:2531–2544.

# TRANSCEND CLL 004 Study Design




## Key Eligibility

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

## Dose Escalation: mTPI-2 Design[d]

**28-day DLT period**

***Primary Objectives***

- Safety
- Determine recommended dose

***Exploratory Objectives***

- Antitumor activity
- Pharmacokinetic profile

| Dose Level | Dose | Evaluable (N=23) |
|---|---|---|
| 1 | 50 × $10^6$ CAR+ T cells | 9 |
| 2 | 100 × $10^6$ CAR+ T cells | 14 |

ClinicalTrials.gov identifier: NCT03331198.

[a]One patient received nonconforming product. [b]Failure defined as SD or PD as best response, or PD after previous response, or discontinuation due to intolerance (unmanageable toxicity). Ineligibility defined as requirement for full-dose anticoagulation or history of arrhythmia. [c]Complex cytogenetic abnormalities, del(17p), *TP53* mutation, or unmutated IGHV. [d]Guo W, et al. *Contemp Clin Trials.* 2017;58:23-33.

BTKi, Bruton tyrosine kinase inhibitor; CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; CY, cyclophosphamide; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; FLU, fludarabine; IGHV, immunoglobulin heavy-chain variable region; mTPI, modified toxicity probability interval for dose escalation; PD, progressive disease; SD, stable disease; SLL, small lymphocytic lymphoma.

Siddiqi T, et al. *Blood*. 2019;134(Supplement 1):503.

# Baseline Characteristics

| | All Patients (N=23) | Failed BTKi and Venetoclax (n=9) |
|---|---|---|
| **Age, years, median (range)** | 66 (49–79) | 68 (59–76) |
| **Male, n (%)** | 11 (48) | 4 (44) |
| **Time from diagnosis, months, median (range)** | 87.5 (30–209) | 145 (30–209) |
| **Bulky disease >5 cm, n (%)[a]** | 8 (35) | 4 (44) |
| **BALL risk score,[1] median (range)** | 2 (0–3) | 2 (0–3) |
| **SPD, $cm^2$, median (range)** | 25 (2–197) | 46 (2–197) |
| **LDH, U/L, median (range)** | 243 (119–634) | 245 (119–634) |
| **Received bridging therapy, n (%)** | 17 (74) | 7 (78) |
| **Stage, n (%)** | | |
| Rai stage III/IV | 15 (65) | 7 (78) |
| Binet stage C | 16 (70) | 7 (78) |
| **High-risk features (any), n (%)** | 19 (83) | 8 (89) |
| Del(17p) | 8 (35) | 2 (22) |
| *TP53* mutation | 14 (61) | 6 (67) |
| Complex karyotype[b] | 11 (48) | 3 (33) |
| **Lines of prior therapy, median (range)** | 5 (2–11) | 6 (5–10) |
| Prior ibrutinib, n (%) | 23 (100) | 9 (100) |
| Ibrutinib refractory/relapsed, n (%) | 21 (91) | 9 (100) |
| BTKi progression and failed venetoclax,[c] n (%) | 9 (39) | 9 (100) |

Siddiqi T, et al. *Blood*. 2019;134(Supplement 1):503.

# Treatment emergent AEs (≥20% all grades)

| | Any grade | Grade ≥3 | | |
|---|---|---|---|---|
| | **Total (n = 23)** | **Total (n = 23)** | **Dose level 1 (n = 9)** | **Dose level 2 (n = 14)** |
| Patients with any TEAE | 23 (100) | 22 (96) | 8 (89) | 14 (100) |
| Anemia | 19 (83) | 17 (74) | 6 (67) | 11 (79) |
| Cytokine release syndrome | 17 (74) | 2 (9) | 0 | 2 (14) |
| Thrombocytopenia | 17 (74) | 16 (70) | 4 (44) | 12 (86) |
| Neutropenia/Neutrophil count decrease | 16 (70) | 16 (70) | 5 (56) | 11 (79) |
| Leukopenia | 11 (48) | 10 (43) | 4 (44) | 6 (43) |
| Pyrexia | 10 (43) | 0 | 0 | 0 |
| Hypokalemia | 9 (39) | 0 | 0 | 0 |
| Diarrhea | 8 (35) | 0 | 0 | 0 |
| Hypophosphatemia | 8 (35) | 5 (22) | 0 | 5 (36) |
| Nausea | 8 (35) | 0 | 0 | 0 |
| Chills | 7 (30) | 0 | 0 | 0 |
| Headache | 7 (30) | 0 | 0 | 0 |
| Tremor | 7 (30) | 0 | 0 | 0 |
| Acute kidney injury | 6 (26) | 1 (4) | 1 (11) | 0 |
| Decreased appetite | 6 (26) | 0 | 0 | 0 |
| Febrile neutropenia | 6 (26) | 6 (26) | 0 | 6 (43) |
| Hypomagnesemia | 6 (26) | 0 | 0 | 0 |
| Hyponatremia | 6 (26) | 0 | 0 | 0 |
| Lymphopenia | 6 (26) | 6 (26) | 2 (22) | 4 (29) |
| Confusional state | 5 (22) | 2 (9) | 0 | 2 (14) |
| Encephalopathy | 5 (22) | 4 (17) | 1 (11) | 3 (21) |
| Hypogammaglobulinemia | 5 (22) | 0 | 0 | 0 |
| Insomnia | 5 (22) | 0 | 0 | 0 |

DLTs occurred in 2 patients receiving liso-cel at DL2

- Patient 1: grade 4 hypertension
- Patient 2: grade 3 encephalopathy, grade 3 muscle weakness, and grade 4 TLS

Nine deaths occurred

- 7 due to PD
- 1 patient with pneumonia, respiratory failure (2.5 mo after liso-cel)
- 1 patient with septic shock (>90 days after liso-cell)
- No deaths within 30 days of liso-cel administration

Siddiqi T, et al. *Blood*. 2022;139(12):1794-1806.

# CRS and neurologic events

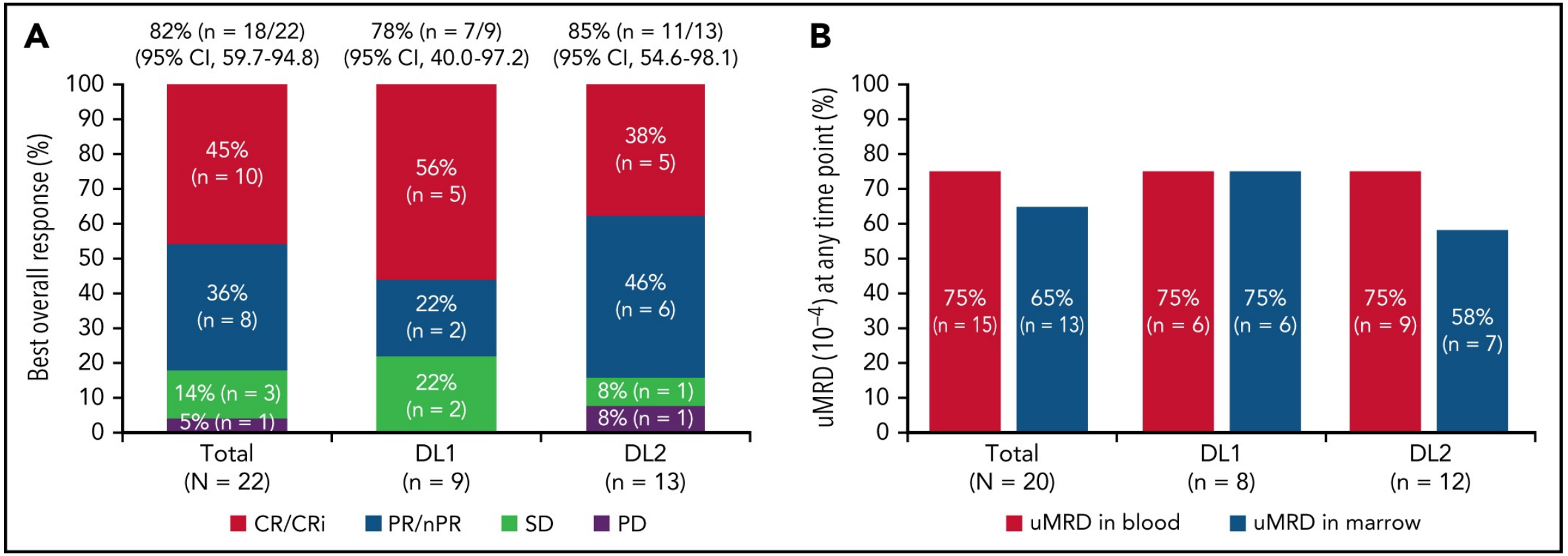
| | All Patients (N=23) | Dose level 1 (n = 9) | Dose level 2 (n = 14) |
|---|---|---|---|
| **CRS—any grade, n (%)** | 17 (74) | 7 (78) | 10 (71) |
| Median time to onset, days (range) | 3 (1-10) | 7 (1-10) | 2 (1-10) |
| Median time to resolution, days (range) | 12 (2-50) | 6 (2-30) | 12.5 (2-50) |
| Grade 3, n (%) | 2 (9) | 0 | 2 (14) |
| **NE[a]—any grade, n (%)** | 9 (39) | 2 (22) | 7 (50) |
| Median time to onset, days (range) | 4 (2-21) | 16 (11-21) | 4 (2-11) |
| Median time to resolution, days (range) | 20.5 (6-50) | 8.5 (6-11) | 29.5 (9-50) |
| Grade ≥3,[a] n (%) | 5 (22) | 2 (22) | 3 (21) |
| **Any CRS or NE, n (%)** | 18 (78) | 7 (78) | 11 (79) |
| **CRS only, n (%)** | 9 (39) | 5 (56) | 4 (29) |
| **NE only, n (%)** | 1 (4) | 0 | 1 (7) |
| **Tocilizumab and/or steroid use** | | | |
| Tocilizumab only | 6 (26) | 3 (33) | 3 (21) |
| Corticosteroids only | 1 (4) | 0 | 1 (7) |
| Both tocilizumab and corticosteroids | 8 (35) | 2 (22) | 6 (43) |
| Tocilizumab and/or corticosteroids | 15 (65) | 5 (56) | 10 (71) |

Siddiqi T, et al. *Blood*. 2022;139(12):1794-1806.

# Best overall response and undetectable MRD

Best Overall Response (n = 22 evaluable for efficacy)

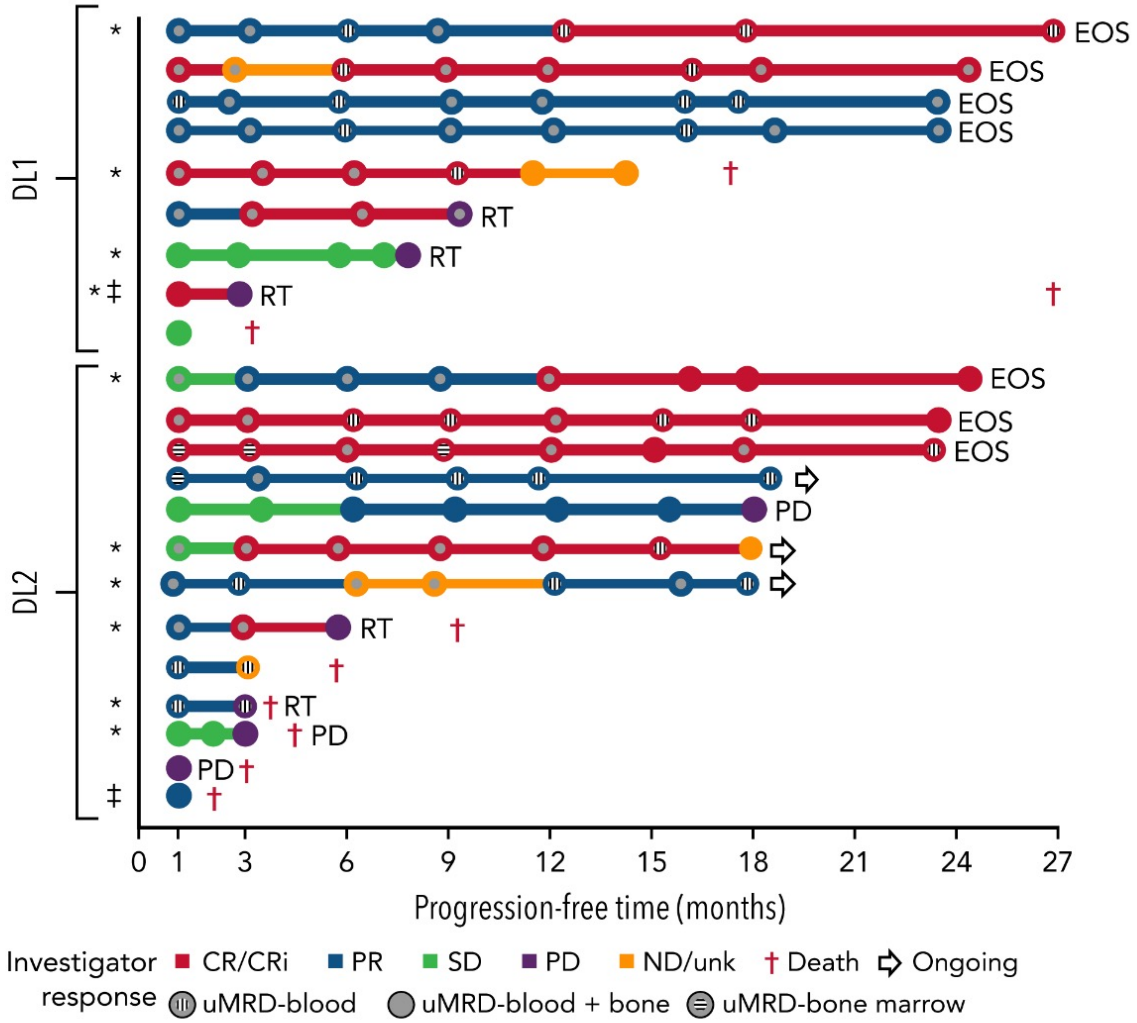
uMRD (n = 20 evaluable for MRD)



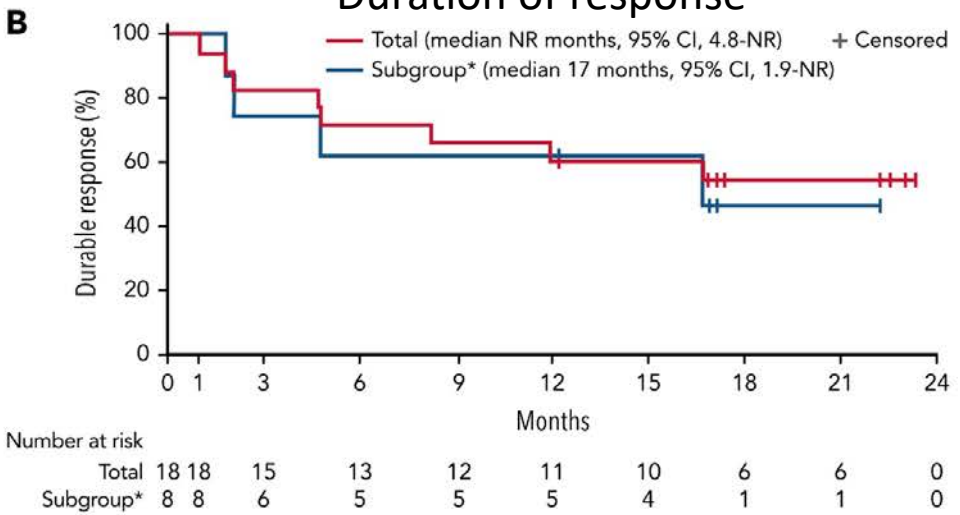

Median follow up = 24 months

Siddiqi T, et al. *Blood*. 2022;139(12):1794-1806.

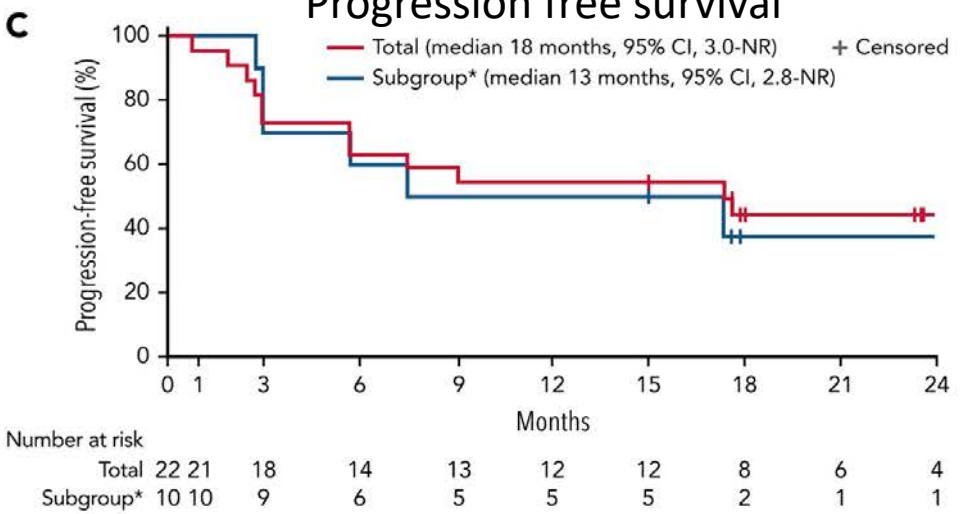
# Individual patient efficacy, duration of response, and progression free survival




Duration of response

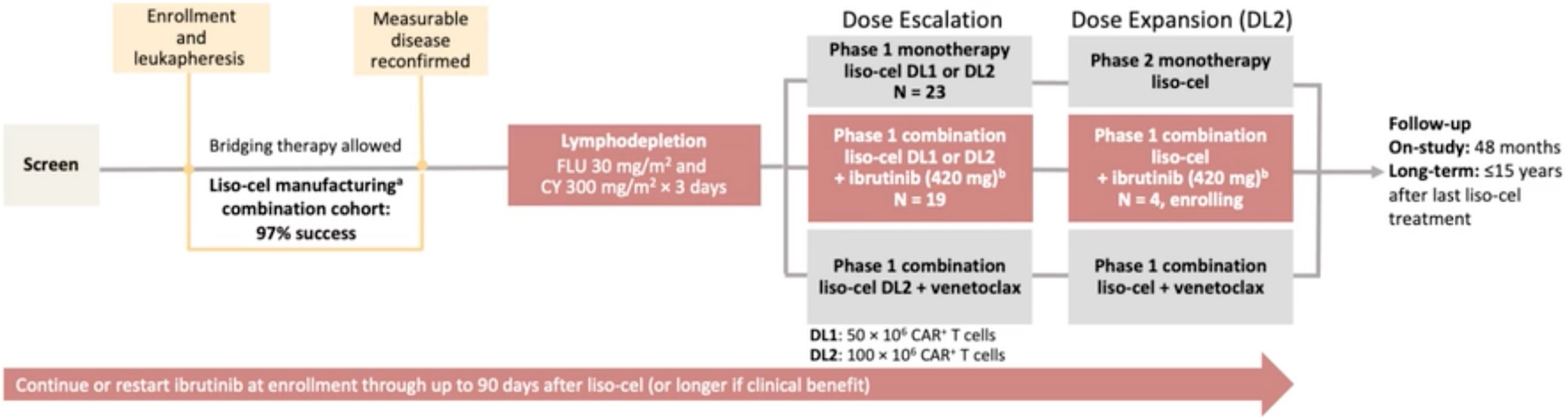



Progression free survival




Siddiqi T, et al. *Blood*. 2022;139(12):1794-1806.

# TRANSCEND CLL 004: Liso-cel + Ibrutinib




Patients were eligible if they had 1 or more:

- received ibrutinib and progressed at time of study enrollment
- high-risk features and received ibrutinib for ≥6 months with less than a complete response
- *BTK* or *PLCγ2* gene mutation, with or without progression on ibrutinib
- received prior ibrutinib with no contraindication to reinitiating ibrutinib

| Baseline Characteristics | N = 23 |
|---|---|
| **Age, median (range)** | 61 (50 – 77) |
| **High risk features** | |
| del17p | 9 (39%) |
| TP53 mutation | 8 (35%) |
| complex karyotype | 10 (43%) |
| **Prior lines of therapy, median (range)** | 4 (1-10) |
| Ibrutinib refractory | 23 (100%) |
| Venetoclax refractory | 12 (53%) |

Weirda B, et al. iwCLL 2021.

# Liso-cel + Ibrutinib Safety

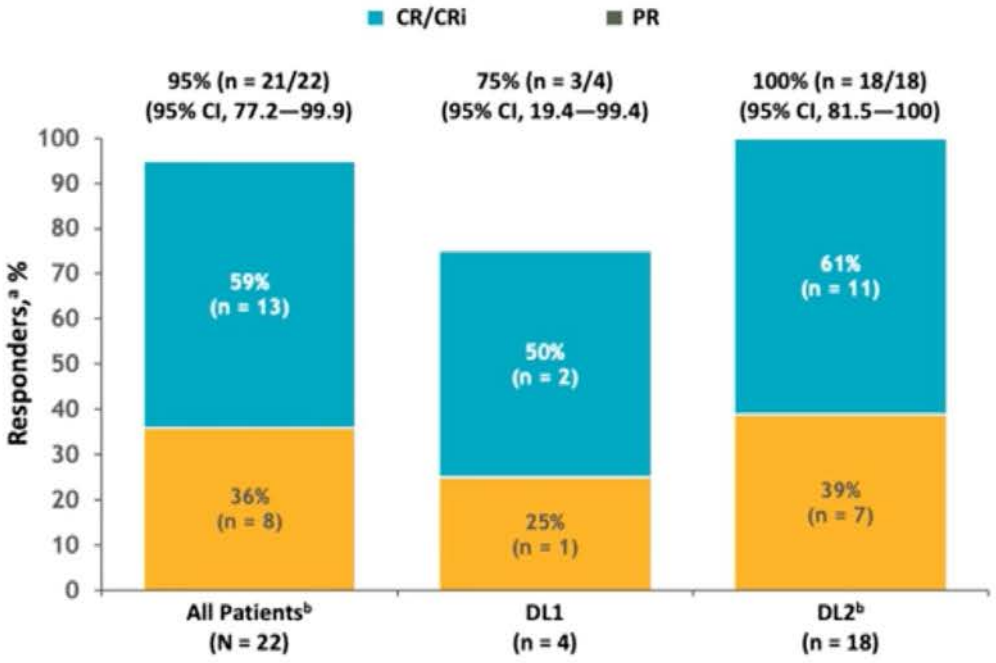
- The combination of liso-cel and ibrutinib was well tolerated, with no reported dose-limiting toxicities
- No grade 5 AEs or grade 4 or 5 cytokine release syndrome (CRS) or neurological events (NE) were reported

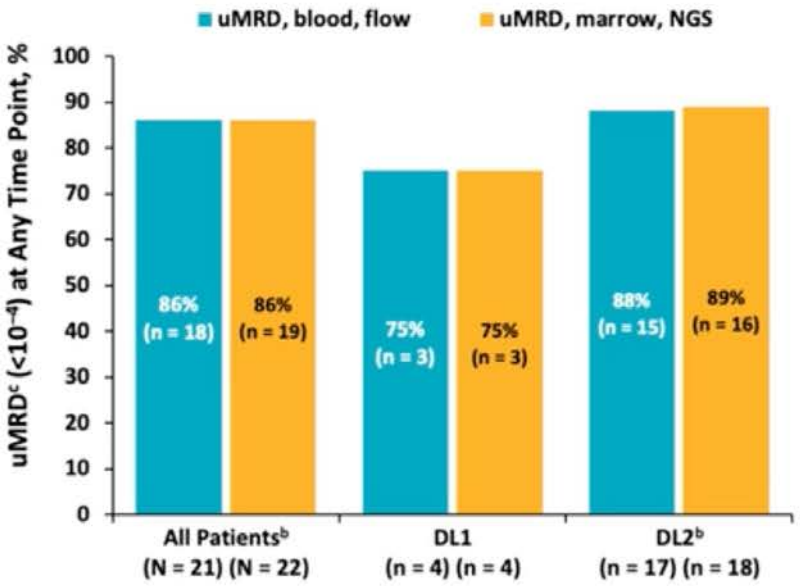
| Parameter | All Patients (N = 23) | DL1 + Ibrutinib (n = 4) | DL2 + Ibrutinib (n = 19) |
|---|---|---|---|
| **Common grade 3/4 treatment-emergent AEs (TEAEs), n (%)** | 22 (96) | 4 (100) | 18 (95) |
| Neutropenia/neutrophil count decrease | 20 (87) | 3 (75) | 17 (89) |
| Anemia | 10 (43) | 3 (75) | 7 (37) |
| Febrile neutropenia | 7 (30) | 1 (25) | 6 (32) |
| **CRS[a]** | | | |
| All-grade CRS, n (%) | 18 (78) | 4 (100) | 14 (74) |
| Median time to CRS onset, days (range) | 7 (1—13) | 8 (6—13) | 6.5 (1—11) |
| Median duration of CRS, days (range) | 5.5 (3—13) | 6.5 (4—7) | 5 (3—13) |
| Grades 1—2 CRS, n (%) | 17 (74) | 3 (75) | 14 (74) |
| Grade 3 CRS, n (%) | 1 (4) | 1 (25) | 0 |
| **NEs** | | | |
| All-grade NEs, n (%) | 7 (30) | 2 (50) | 5 (26) |
| Median time to NE onset, days (range) | 9 (5—13) | 9 (6—12) | 9 (5—13) |
| Median duration of NE, days (range) | 7 (1—10) | 8 (8—8) | 6 (1—10) |
| Grades 1—2 NEs, n (%) | 3 (13) | 2 (50) | 1 (5) |
| Grade 3 NEs,[b] n (%) | 4 (17) | 0 | 4 (21) |
| **Management of CRS and/or NEs, n (%)** | | | |
| Tocilizumab only | 3 (13) | 0 | 3 (16) |
| Corticosteroids only | 3 (13) | 2 (50) | 1 (5) |
| Tocilizumab and corticosteroids | 5 (22) | 1 (25) | 4 (21) |

Weirda B, et al. iwCLL 2021.

# Liso-cel + Ibrutinib Efficacy

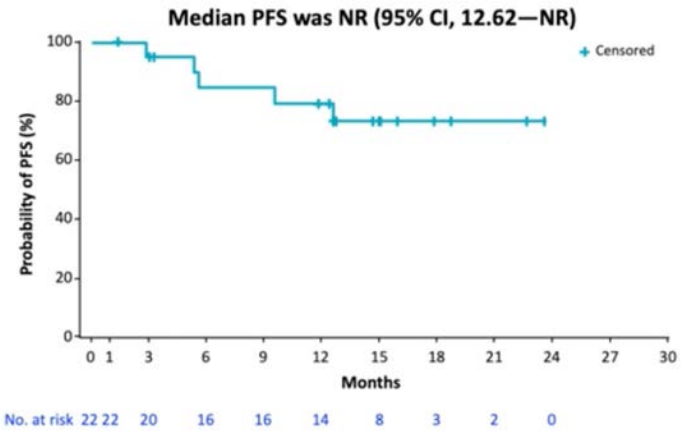
## Best Objective Response by iwCLL and uMRD ($<10^{-4}$)




### Progression Free Survival

Median follow up = 17 months




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

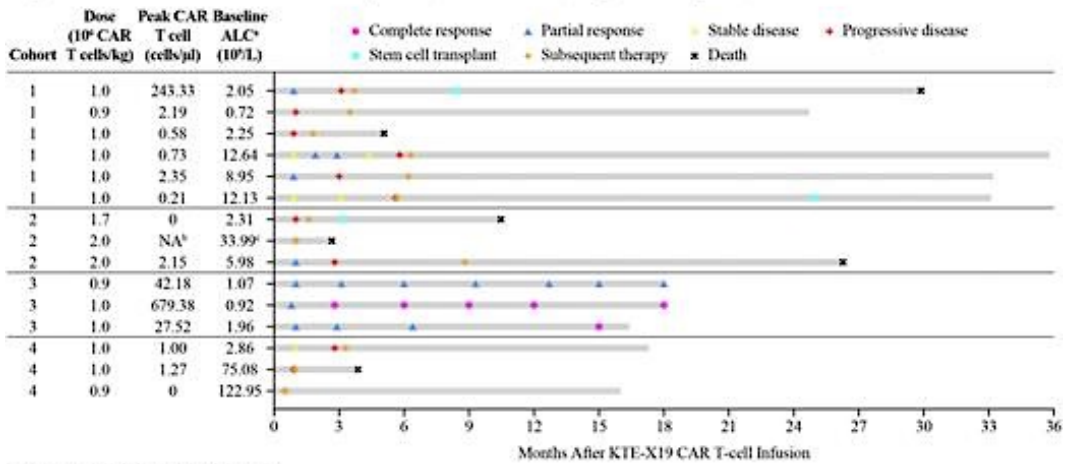
Weirda B, et al. iwCLL 2021.

# ZUMA-8: To be presented at ASH 2022 (Sunday, 6 – 8 PM, abstract 3319)

**Study Design:**

- Brexucabtagene autoleucel: CD-19 Autologous CAR T-cell
- Patients with relapsed/refractory CLL
  - ≥2 prior lines of therapy
  - Including a BTK inhibitor
- Conditioning: Fludarabine / Cyclophosphamide
- 2 dose levels
  - DL1: $1 \times 10^6$ CAR T cells/kg
  - DL2: $2 \times 10^6$ CAR T cells/kg

**Figure:** Patient-level Peak CAR T-cell Expansion, Baseline ALC, Objective Response, and Survival Over Time.




Gray bars indicate duration of follow-up.
*Baseline ALC data were based on central assessment, except for 1 patient in Cohort 2. †Peak CAR T-cell data were not available. ‡Based on local assessment.
ALC, absolute lymphocyte count; CAR, chimeric antigen receptor; NA, not available.

**Table:** ZUMA-8 Patient Characteristics and AE Summary.

| | Cohort 1 (low dose) n=6 | Cohort 2 (high dose) n=3 | Cohort 3 (low tumor burden) n=3 | Cohort 4 (post ibrutinib) n=3 | Overall N=15 |
|---|---|---|---|---|---|
| Median follow-up duration, months (range) | 35.8 (33.6–40.4) | 30.3 (29.9–30.6) | 18.2 (18.2–18.4) | 17.05 (15.5–17.9) | 30.3 (15.5–40.4) |
| **Baseline Characteristics** | | | | | |
| Median age, years (range) | 60.5 (53–68) | 61.0 (52–63) | 69.0 (56–79) | 67.0 (53–70) | 63.0 (52–79) |
| Male, n (%) | 3 (50) | 2 (67) | 3 (100) | 2 (67) | 10 (67) |
| ECOG PS 1, n (%) | 4 (67) | 1 (33) | 1 (33) | 2 (67) | 8 (53) |
| >3 prior therapy lines, n (%) | 6 (100) | 3 (100) | 1 (33) | 2 (67) | 12 (80) |
| 17p deletion, n (%) | 1 (17) | 1 (33) | 0 | 2 (67) | 4 (27) |
| Complex karyotype, n (%)[a] | 3 (50) | 3 (100) | 1 (33) | 0 | 7 (47) |
| Median tumor burden, $mm^2$ (range) | 7,026.0 (464.0–26,688.3) | 7,458.1 (2,140.4–9,715.0) | 625.0 (614.0–2,472.0) | 1,434.0 (786.0–2,308.5) | 2,308.50 (464.0–26,688.3) |
| Median CLL lymphocytes in bone marrow aspirate, % (range)[b] | 75.0 (0.1–93.5) | 86.4 (16.0–97.0) | 30.0 (5.0–40.0) | 91.0 (33.0–96.0) | 75.0 (0.1–97.0) |
| **AE Summary** | | | | | |
| Grade ≥3 AE, n (%) | | | | | |
| Any | 6 (100) | 3 (100) | 3 (100) | 3 (100) | 15 (100) |
| Treatment related | 4 (67) | 2 (67) | 2 (67) | 1 (33) | 9 (60) |
| CRS | | | | | |
| Any | 5 (83) | 2 (67) | 3 (100) | 2 (67) | 12 (80) |
| Grade ≥3 | 0 | 0 | 1 (33) | 0 | 1 (7) |
| NE | | | | | |
| Any | 6 (100) | 1 (33) | 3 (100) | 1 (33) | 11 (73) |
| Grade ≥3 | 2 (33) | 0 | 1 (33) | 0 | 3 (20) |

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# ASH 2022: Promising investigational agents in CLL

- **BTK Degraders**
  - 965. NX-2127-001, a First-in-Human Trial of **NX-2127**, a Bruton's Tyrosine Kinase-Targeted Protein Degrader, in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia and B-Cell Malignancies
- **Bispecific T cell Engagers**
  - 348. Subcutaneous **Epcoritamab** in Patients with Richter's Syndrome: Early Results from Phase 1b/2 Trial (EPCORE CLL-1)
- **Protein Kinase C β Inhibitor**
  - 963. Initial Results from a Phase 1/2 Dose Escalation and Expansion Study Evaluating **MS-553**, a Novel and Selective PKCβ Inhibitor, in Patients with CLL/SLL
- **ROR1**
  - 1810. First-in-Human Phase I Trial of a ROR1 Targeting Bispecific T Cell Engager (**NVG-111**) in Combination with Ibrutinib or As Monotherapy in Subjects with Relapsed Refractory Chronic Lymphocytic Leukaemia (CLL) and Mantle Cell Lymphoma (MCL)
- **New BCL2i**
  - 962. A Phase 1 Study with the Novel B-Cell Lymphoma 2 (Bcl-2) Inhibitor **Bgb-11417** As Monotherapy or in Combination with Zanubrutinib (ZANU) in Patients (Pts) with CLL/SLL: Preliminary Data
  - 964. **Lisaftoclax** (APG-2575) Safety and Activity As Monotherapy or Combined with Acalabrutinib or Rituximab in Patients (pts) with Treatment-Naïve, Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (R/R CLL/SLL): Initial Data from a Phase 2 Global Study

# Appendix

# Editorial Review

- Pharmacologic similarities and differences between the investigational noncovalent BTK inhibitor pirtobrutinib and covalent BTK inhibitors
  - Slide 2
- Updated results among patients with R/R CLL in the BRUIN study of pirtobrutinib
  - Slides 3-8
- Documented efficacy and safety of CAR T-cell therapies alone or combined with other systemic therapies among patient with R/R CLL (eg, TRANSCEND CLL 004, ZUMA-8)
  - Slides 9-19
- Other promising agents and strategies under investigation for CLL
  - Slide 20

# Appendix Slides – None