POST-SAN DIEGO 2024
Novità dal Meeting della Società Americana di Ematologia

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Bologna
Palazzo Re Enzo
13-15 Febbraio 2025

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3° SESSIONE – LEUCEMIA LINFATICA CRONICA:
Terapie di salvataggio

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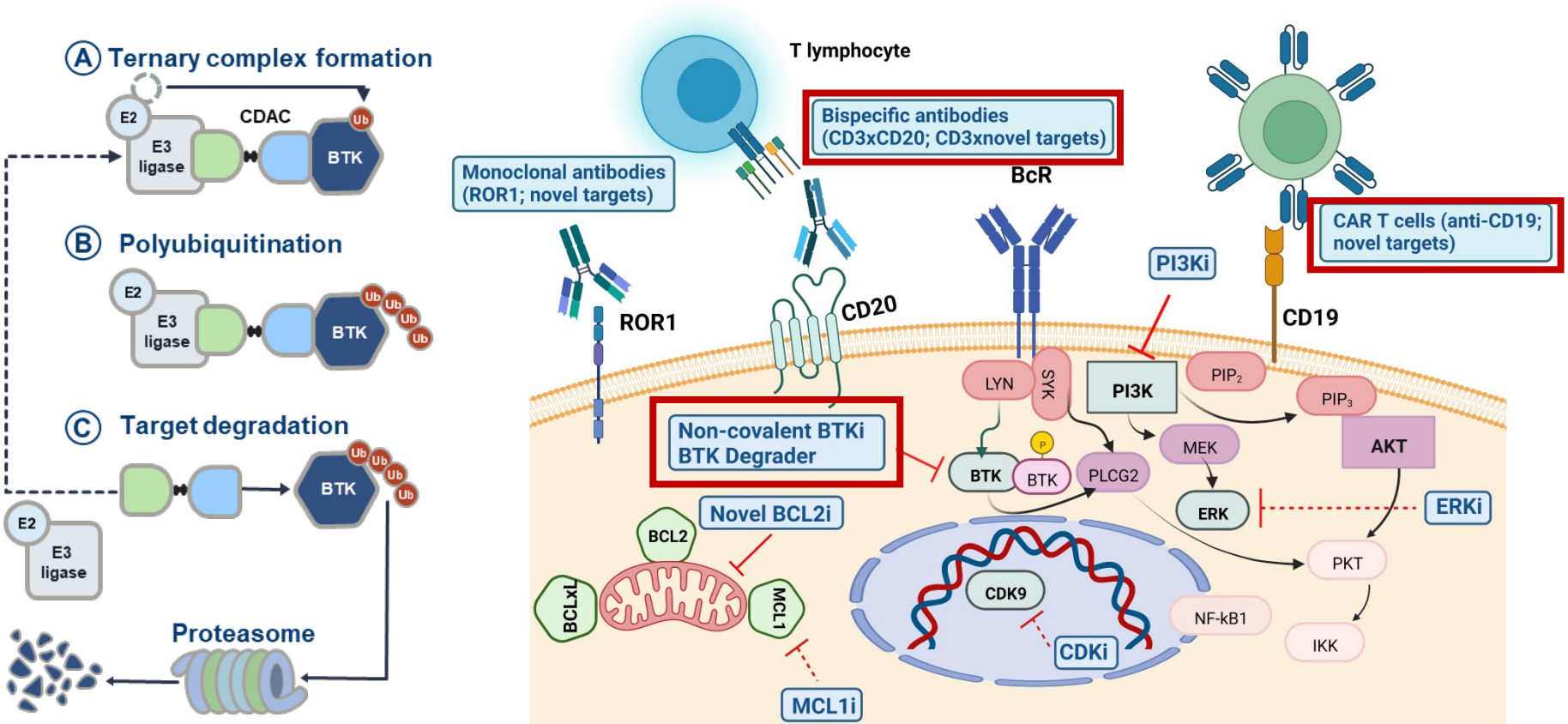
Disclosures of Lydia Scarfò

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
AbbVie			X			X	
AstraZeneca			X			X	
BeiGene			X			X	
J&J			X			X	
Lilly						X	
Merck			X				

Is there hope for the future?



Scarfò L., ASH Education Program 2022

CaDAnCe-101: Phase 1/2, Open-Label, Dose-Escalation/ Expansion Study in R/R B-Cell Malignancies

CaDAnCe-101 (BGB-16673-101, NCT05006716)

Key eligibility criteria for CLL/SLL

- Meets iwCLL 2018 criteria for treatment
- ≥2 prior therapies, including cBTKi if approved for disease
- ECOG PS 0-2 & adequate end-organ function

Key study objectives for part 1

- **Primary:** safety[c] and tolerability, MTD, and RP2D
- **Secondary:** PK, PD, and preliminary antitumor activity[d]

Part 1: Monotherapy dose finding[a]

Part 1a: Dose escalation
Selected R/R B-cell malignancies
(MZL, FL, MCL, **CLL/SLL**, WM, DLBCL, RT)
n≤72
Oral, QD, 28-day cycle[b]
Doses: 50 mg, 100 mg, 200 mg, 350 mg, 500 mg, 600 mg

Part 1b: Safety expansion
Selected R/R B-cell malignancies
(MZL, MCL, **CLL/SLL**, WM)
n≤120

Part 1c: Additional safety expansion
Selected R/R B-cell malignancies
(MZL, WM, RT, DLBCL, FL)
n≤100

Part 1d: Additional safety expansion
R/R CLL/SLL
n≤30

Part 1e: Additional safety expansion
Selected R/R B-cell malignancies (Japan only)
(MZL, FL, MCL, CLL/SLL, WM)
n=6-9

Part 1f: Monotherapy safety expansion
Selected BTK inhibitor–naive B-cell malignancies
(MZL, MCL, CLL/SLL, WM, RT)
n≤40

Determination of BGB-16673 RDFE

Phase 2

- **Cohort 1:** Post BTK inhibitor, R/R CLL/SLL
- **Cohort 2:** Post BTK inhibitor, R/R MCL
- **Cohort 3:** Post BTK inhibitor, R/R WM
- **Cohort 4:** Post BTK inhibitor, R/R MZL
- **Cohort 5:** R/R FL
- **Cohort 6:** R/R non-GCB DLBCL
- **Cohort 7:** Post BTK inhibitor, R/R RT

[a] Data from gray portions of the figure are not included in this presentation. [b] Treatment was administered until progression, intolerance, or meeting other criteria for treatment discontinuation. [c] Safety was assessed according to CTCAE v5.0 in all patients and iwCLL hematologic toxicity criteria in patients with CLL; DLTs were assessed during the first 4 weeks of part 1a. [d] Response was assessed per iwCLL 2018 criteria after 12 weeks in patients with CLL; response was assessed per Lugano criteria after 12 weeks in patients with RT.
GCB, germinal center B cell; RT, Richter transformation.

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Baseline Patient Characteristics

Heavily pretreated, with high-risk CLL features

	Total (N=60)
Age, median (range), years	70 (50-91)
Male, n (%)	39 (65.0)
ECOG PS, n (%)	
0	34 (56.7)
1	25 (41.7)
2	1 (1.7)
CLL/SLL risk characteristics at study entry, n/N with known status (%)	
Binet stage C	27/56 (48.2)
Unmutated IGHV	38/46 (82.6)
del(17p) and/or *TP53* mutation	40/60 (66.7)
Complex karyotype (≥3 abnormalities)	19/38 (50.0)

	Total (N=60)
Mutation status, n/N (%)	
BTK mutation present	18/54 (33.3)
PLCG2 mutation present	8/54 (14.8)
No. of prior lines of therapy, median (range)	4 (2-10)
Prior therapy, n (%)	
Chemotherapy	43 (71.7)
cBTK inhibitor	56 (93.3)
ncBTK inhibitor	13 (21.7)
BCL2 inhibitor	50 (83.3)
cBTK + BCL2 inhibitors	38 (63.3)
cBTK + ncBTK + BCL2 inhibitors	12 (20.0)
Discontinued prior BTK inhibitor due to PD, n/N (%)[a]	50/56 (89.3)

Data cutoff: September 2, 2024.

[a] Remaining 6 patients discontinued prior BTK inhibitor due to toxicity (n=3), treatment completion (2), and other (n=1).

cBTK, covalent BTK; ncBTK, noncovalent BTK.

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Safety Summary and All-Grade TEAEs in ≥10% of All Patients

- No atrial fibrillation
- No pancreatitis
- Major hemorrhage[b]: 3.3% (n=2; grade 1 subarachnoid hemorrhage [n=1] and grade 3 subdural hemorrhage [n=1])
- Febrile neutropenia: 1.7% (n=1; in the context of COVID-19 pneumonia and norovirus diarrhea)

	Total (N=60)	
Patients, n (%)	All Grade	Grade ≥3
Fatigue	18 (30.0)	1 (1.7)
Contusion (bruising)	17 (28.3)	0
Neutropenia[c]	15 (25.0)	13 (21.7)
Diarrhea	14 (23.3)	1 (1.7)
Anemia	11 (18.3)	0
Lipase increased[a]	10 (16.7)	2 (3.3)
Cough	9 (15.0)	0
Pneumonia	8 (13.3)	5 (8.3)
Pyrexia	8 (13.3)	0
Arthralgia	7 (11.7)	0
COVID-19	7 (11.7)	0
Dyspnea	7 (11.7)	0
Peripheral edema	7 (11.7)	0
Thrombocytopenia[d]	7 (11.7)	2 (3.3)
Amylase increased[a]	6 (10.0)	0
Nausea	6 (10.0)	0
Sinusitis	6 (10.0)	0

Median follow-up: 10.2 months (range, 0.3-26.4+).

[a] All events were lab findings and were transient, mostly occurring during the first 1-3 cycles of treatment, with no clinical pancreatitis. [b] Grade ≥3, serious, or any central nervous system bleeding. [c] Neutropenia combines preferred terms *neutrophil count decreased* and *neutropenia*. [d] Thrombocytopenia combines preferred terms *platelet count decreased* and *thrombocytopenia*.

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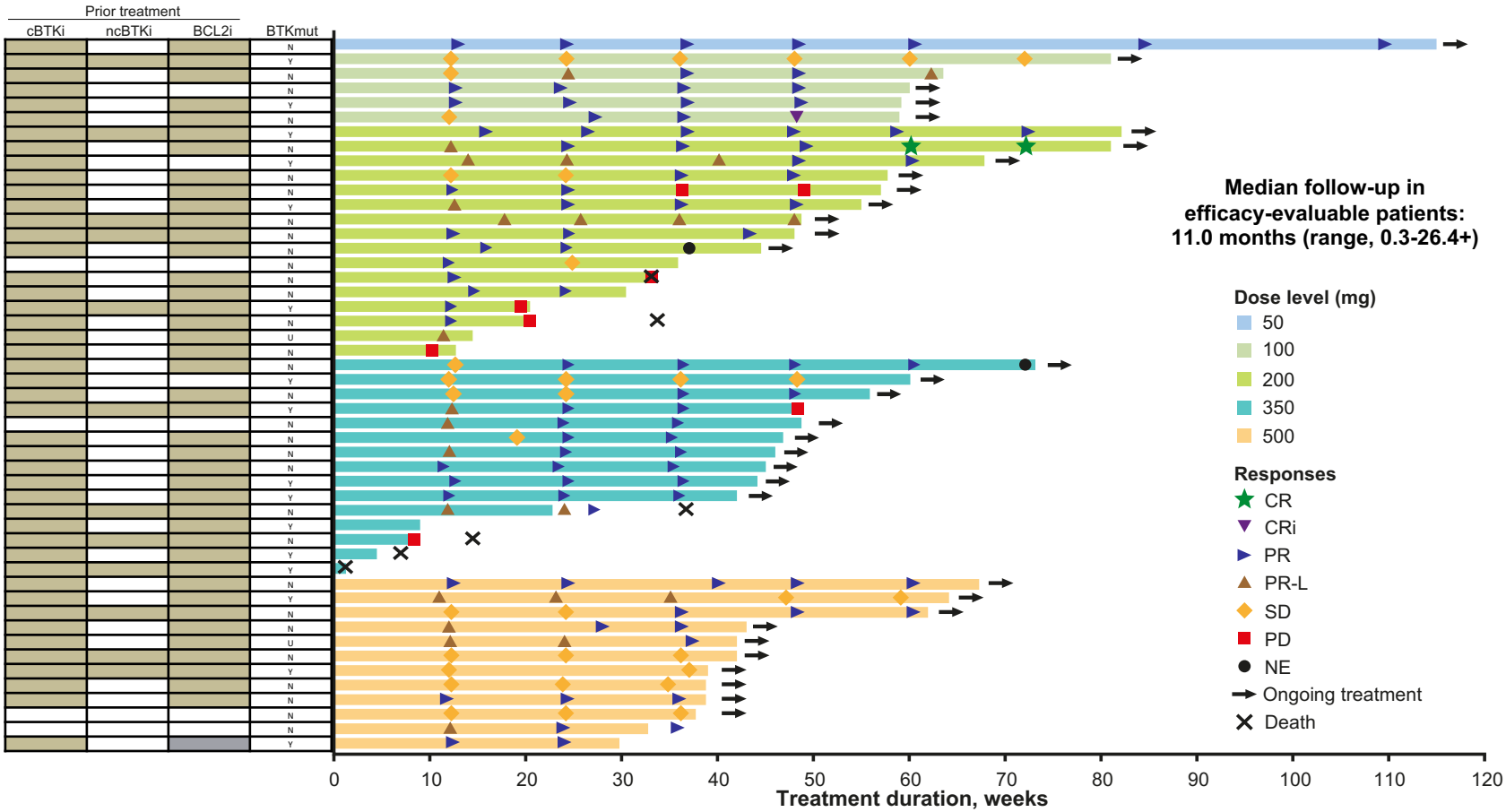
Treatment Duration and Response



Data cutoff: September 2, 2024. Efficacy-evaluable patients. First response assessment after 12 weeks.

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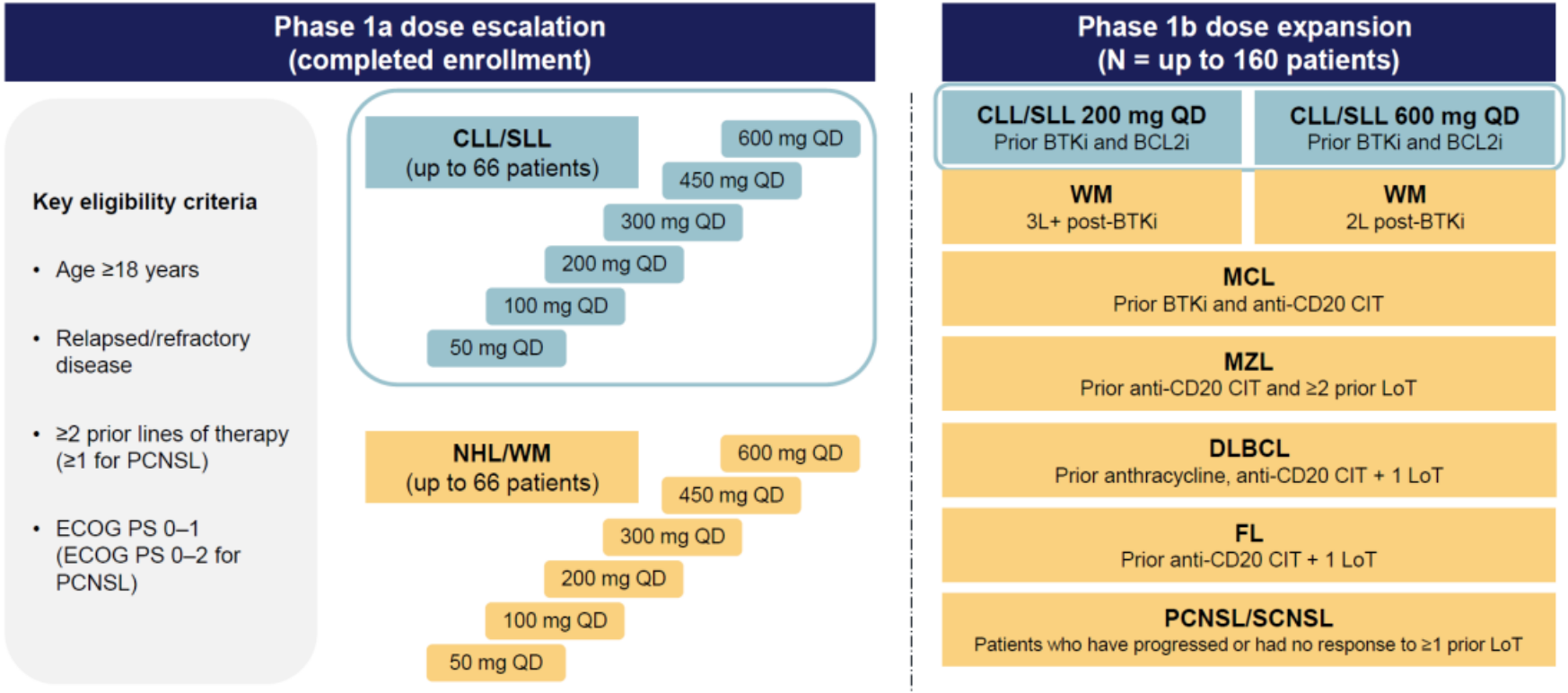
NX5948-301: Trial design



BCL2i, BCL2 inhibitor; **BTKi**, BTK inhibitor; **CIT**, chemo-immunotherapy; **CLL**, chronic lymphocytic leukemia; **DLBCL**, diffuse large B-cell lymphoma; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **FL**, follicular lymphoma; **LoT**, lines of treatment; **MCL**, mantle cell lymphoma; **MZL**, marginal zone lymphoma; **NHL**, non-Hodgkin's lymphoma; **PCNSL**, primary CNS lymphoma; **QD**, once daily; **SCNSL**, secondary CNS lymphoma; **SLL**, small lymphocytic lymphoma; **WM**, Waldenstrom's macroglobulinemia

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NX5948-301: Patient characteristics

Characteristics	Patients with CLL/SLL[a] (n=60)
ECOG PS, n (%)	
0	24 (40.0)
1	36 (60.0)
CNS involvement, n (%)	5 (8.3)
Median prior lines of therapy (range)	4.0 (1–12)
Previous treatments[b], n (%)	
BTKi	59 (98.3)
cBTKi	59 (98.3)
ncBTKi[c]	17 (28.3)
BCL2i	50 (83.3)
BTKi and BCL2i	49 (81.7)
CAR-T therapy	3 (5.0)
Bispecific antibody	4 (6.7)
PI3Ki	18 (30.0)
Chemo/chemo-immunotherapies (CIT)	43 (71.7)
Mutation status[d] (n=57), n (%)	
TP53	23 (40.4)
BTK	22 (38.6)
PLCG2	7 (12.3)
BCL2	6 (10.5)

[a]Baseline disease characteristics in CLL cohort were comparable to those in the overall population; [b]Patients could have received multiple prior treatments; [c]All patients who received ncBTKi have also previously received cBTKi; [d]Mutations presented here were centrally sequenced.

BCL2, B-cell lymphoma 2; **BCL2i**, BCL2 inhibitor; **BTK**, Bruton's tyrosine kinase; **BTKi**, BTK inhibitor; **cBTKi**, covalent BTKi; **CAR-T**, chimeric antigen receptor T-cell; **CLL**, chronic lymphocytic leukemia; **CNS**, central nervous system; **ECOG PS**, Eastern Cooperative Oncology Group (ECOG) performance status; **ncBTKi**, non-covalent BTKi; **PI3Ki**, phosphoinositide 3-kinase inhibitor; **PLCG2**, phospholipase C gamma 2; **SLL**, small lymphocytic lymphoma Data cutoff: 10 Oct 2024

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NX5948: Safety Profile

TEAEs, n (%)	Patients with CLL/SLL (n=60)			Overall population (N=125)		
	Any grade	Grade ≥3	SAEs	Any grade	Grade ≥3	SAEs
Purpura/contusion[a]	22 (36.7)	–	–	42 (33.6)	–	–
Fatigue[b]	16 (26.7)	–	–	29 (23.2)	2 (1.6)	–
Petechiae	16 (26.7)	–	–	28 (22.4)	–	–
Thrombocytopenia[c]	10 (16.7)	1 (1.7)	–	26 (20.8)	7 (5.6)	–
Rash[d]	14 (23.3)	1 (1.7)	1 (1.7)	24 (19.2)	2 (1.6)	1 (0.8)
Neutropenia[e]	14 (23.3)	11 (18.3)	–	23 (18.4)	18 (14.4)	–
Anemia	11 (18.3)	4 (6.7)	–	21 (16.8)	10 (8.0)	–
Headache	10 (16.7)	–	–	21 (16.8)	1 (0.8)	1 (0.8)
COVID-19[f]	10 (16.7)	–	–	19 (15.2)	2 (1.6)	2 (1.6)
Diarrhea	12 (20.0)	1 (1.7)	–	18 (14.4)	1 (0.8)	–
Cough	9 (15.0)	–	–	16 (12.8)	1 (0.8)	–
Pneumonia[g]	4 (6.7)	2 (3.3)	2 (3.3)	10 (8.0)	6 (4.8)	6 (4.8)
Lower respiratory tract infection	3 (5.0)	1 (1.7)	1 (1.7)	9 (7.2)	3 (2.4)	2 (1.6)
Fall	1 (1.7)	1 (1.7)	1 (1.7)	8 (6.4)	2 (1.6)	2 (1.6)
Hypertension	2 (3.3)	1 (1.7)	–	7 (5.6)	5 (4.0)	–
Hyponatremia	–	–	–	3 (2.4)	2 (1.6)	–
Pulmonary embolism	1 (1.7)	1 (1.7)	1 (1.7)	2 (1.6)	2 (1.6)	2 (1.6)
Subdural hematoma	1 (1.7)	–	1 (1.7)	2 (1.6)	1 (0.8)	2 (1.6)

- Tolerable safety profile consistent with prior disclosures
- 1 case of Grade 1 AFib in a CLL patient with pre-existing AFib
- 6 TEAEs resulted in drug discontinuation (1 CLL; 5 NHL)
- 2 Grade 5 AEs (1 pulmonary embolism; 1 case pending) deemed not related to NX-5948

[a]Purpura/contusion includes episodes of contusion or purpura; [b]Fatigue was transient; [c]Aggregate of 'thrombocytopenia' and 'platelet count decreased'; [d]Aggregate of 'rash' and 'rash maculopapular' and 'rash pustular'; [e]Aggregate of 'neutrophil count decreased' or 'neutropenia'; [f]Aggregate of 'COVID-19' and 'COVID-19 pneumonia'; [g]Aggregate of 'pneumonia' and 'pneumonia klebsiella'

AE, adverse event; **AFib**, atrial fibrillation; **CLL**, chronic lymphocytic leukemia; **NHL**, non-Hodgkin's lymphoma; **SAE**, serious adverse event; **SLL**, small lymphocytic lymphoma; **TEAE**, treatment emergent AE

Data cutoff: 10 Oct 2024

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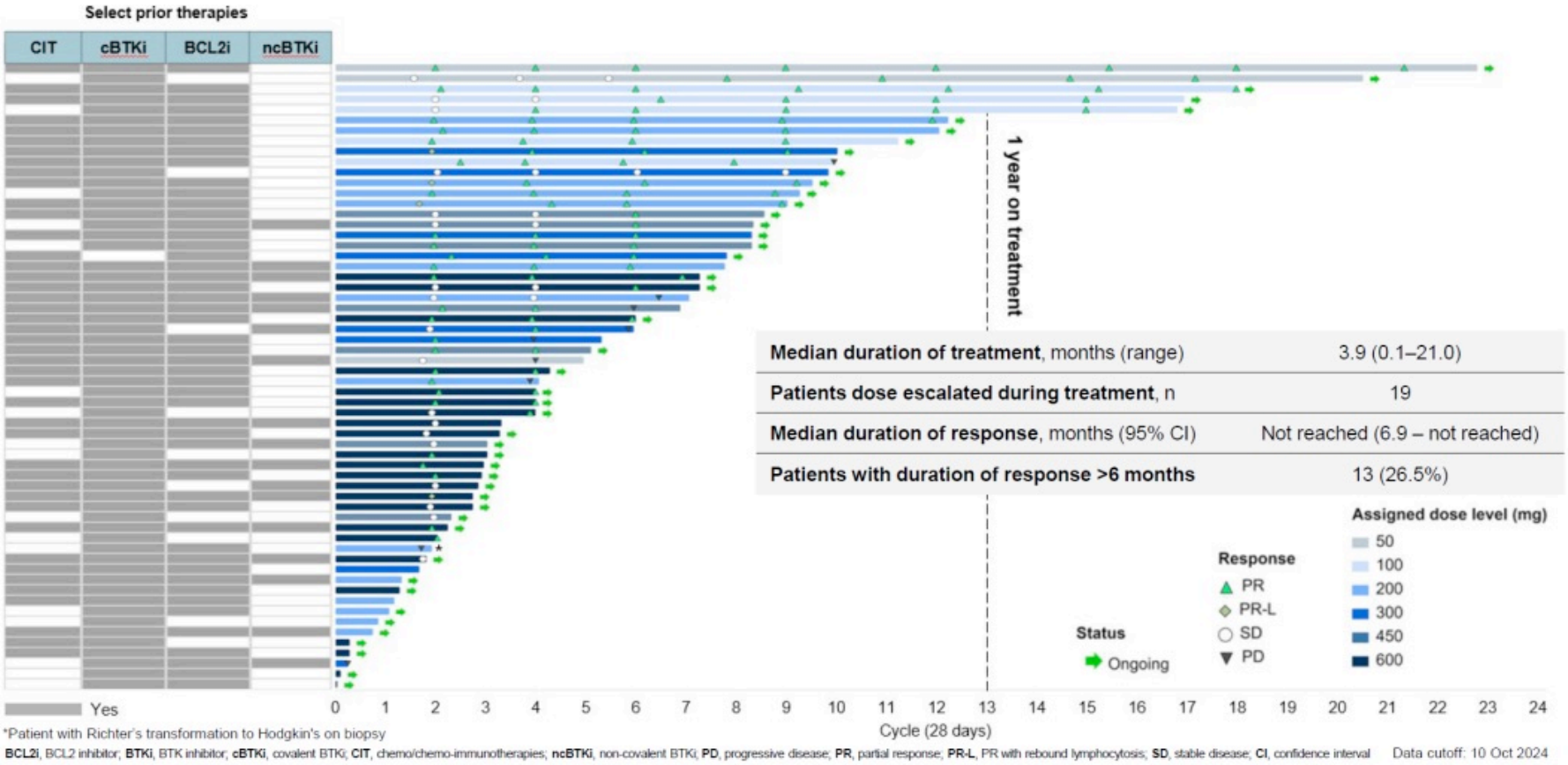
NX5948: Duration of treatment



*Patient with Richter's transformation to Hodgkin's on biopsy

BCL2i, BCL2 inhibitor; **BTKi**, BTK inhibitor; **cBTKi**, covalent BTKi; **CIT**, chemo/chemo-immunotherapies; **ncBTKi**, non-covalent BTKi; **PD**, progressive disease; **PR**, partial response; **PR-L**, PR with rebound lymphocytosis; **SD**, stable disease; **CI**, confidence interval Data cutoff: 10 Oct 2024 10

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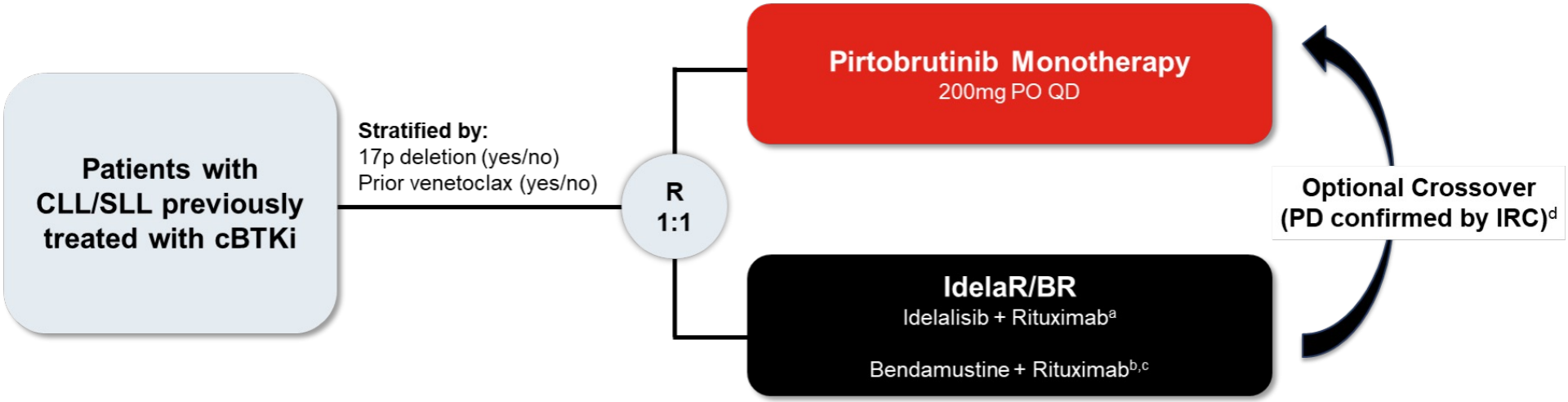
BRUIN CLL-321: Study Design



Key Eligibility

- Age ≥18
- ECOG PS 0-2
- Confirmed CLL/SLL requiring treatment per iwCLL 2018
- **Prior cBTKi required**
- **No limit on prior lines of therapy**
- **Prior history of atrial fibrillation allowed**

Key Endpoints

- **Primary Endpoint: PFS assessed by IRC**
- PFS assessed by investigator
- Event-Free Survival
- Time to Next Treatment
- Overall survival
- Safety

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BRUIN CLL-321: Baseline characteristics

Characteristics	Pirtobrutinib n=119	IdelaR/BR n=119
Median age, years (range)	66 (42-90)	68 (42-85)
Male, n (%)	83 (70)	83 (70)
Region, n (%)		
North America	24 (20)	39 (33)
Europe	76 (64)	63 (53)
Asia	14 (12)	15 (13)
Australia	5 (4)	2 (2)
Histology, n (%)		
CLL	109 (92)	108 (91)
SLL	10 (8)	11 (9)
ECOG PS, n (%)		
0-1	107 (90)	114 (96)
2	12 (10)	5 (4)
Rai stage[a], n (%)		
0-II	58 (49)	62 (52)
III-IV	56 (47)	54 (45)
High-risk molecular features (Central Lab), n/n available (%)		
17p deletion and/or *TP53* mutation	51/94 (54)	53/98 (54)
IGHV unmutated	90/97 (93)	74/93 (80)
Complex karyotype[b]	53/74 (72)	44/75 (59)
Molecular Characteristics, n/n available (%)		
BTK C481S	37/99 (37)	36/94 (38)
PLCγ2	15/99 (15)	11/94 (12)

Characteristics	Pirtobrutinib n=119	IdelaR/BR n=119
Median lines of prior systemic therapy, n (range)	3 (1-13)	3 (1-11)
Prior therapy, n (%)		
cBTKi	119 (100)	119 (100)
Ibrutinib	100 (84)	106 (89)
Acalabrutinib	17 (14)	20 (17)
Zanubrutinib	10 (8)	7 (6)
Other[c]	5 (4)	3 (3)
>1 Prior cBTKi	17 (14)	18 (15)
BCL2 inhibitor[d]	60 (50)	62 (52)
Chemotherapy	81 (68)	83 (70)
Anti-CD20 Antibody	86 (72)	83 (70)
PI3K inhibitor	11 (9)	11 (9)
Immunomodulator	2 (2)	3 (3)
Autologous Stem Cell Transplant	1 (1)	0 (0)
Allogeneic Stem Cell Transplant	2 (2)	1 (1)
Reason for any prior cBTKi discontinuation[e], n (%)		
Disease progression	85 (71)	87 (73)
Toxicity	20 (17)	22 (18)
Other	14 (12)	8 (7)

Poor prognosis (e.g., >50% del(17p) and/or *TP53 mutation* and complex karyotype) and heavily pre-treated population (e.g., 33% received ≥ 4 prior lines of therapy, ~50% received prior BCL2i)

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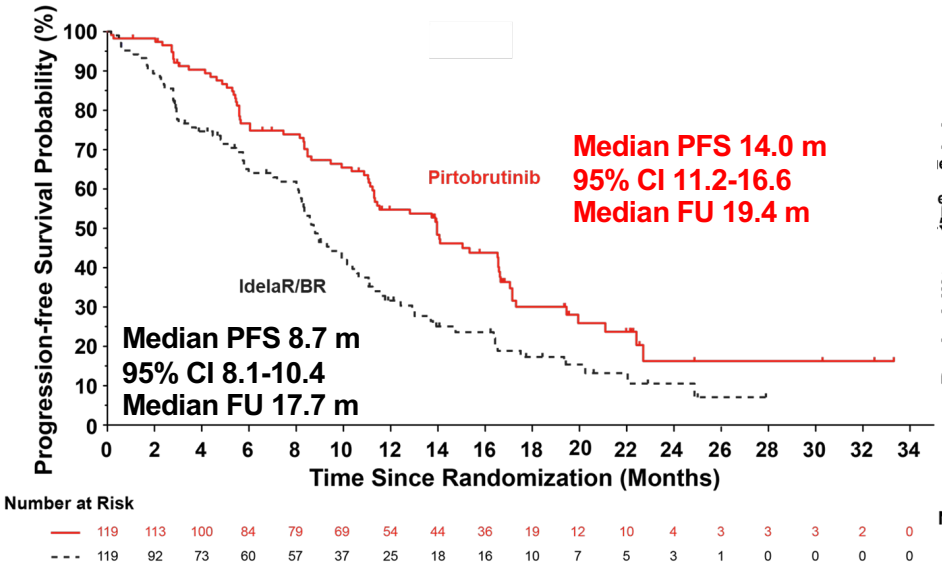
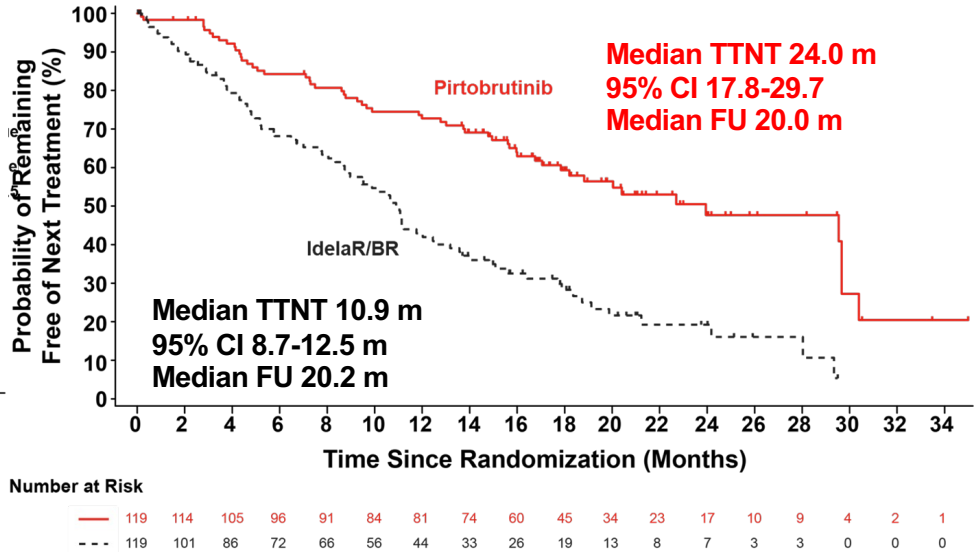
BRUIN CLL-321: IRC-Assessed PFS (Primary Endpoint) and TTNT or Death

IRC-Assessed PFS



HR 0.54 (0.39-0.75), p = 0.0002

TTNT or Death



HR 0.37 (0.25-0.52), p < 0.0001

Cross-over rate: 50/66 (76%) → OS follow-up limited and confounded by high rate of post-progression crossover

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BRUIN CLL-321: Safety Exposure Adjusted Incidence Rate

Treatment-Emergent Adverse Event (Any Grade)	Pirtobrutinib (n=116) IR[a]	IdelaR or BR (n=109) IR[a]	IRR (95% CI)[b]	p-value[c]
Infections[d]	94.5	125.5	0.75 (0.53-1,07)	0.11
Pneumonia[e]	20.4	19.5	1.04 (0.54-2.03)	0.90
COVID-19	11.1	33.4	0.33 (0.17-0.65)	0.001
Anemia	18.5	30.3	0.61 (0.33-1.12)	0.11
Neutropenia[f]	26.4	66.5	0.40 (0.25-0.64)	<0.001
Cough	14.3	30.8	0.47 (0.25-0.88)	0.02
Diarrhea	15.3	63.7	0.24 (0.14-0.42)	<0.001
Pyrexia	11.1	52.4	0.21 (0.11-0.40)	<0.001
Fatigue	9.5	34.2	0.28 (0.14-0.55)	<0.001
Nausea	9.8	38.3	0.26 (0.13-0.51)	<0.001
Vomiting	5.8	29.6	0.19 (0.08-0.44)	<0.001
ALT increased	2.8	33.6	0.08 (0.03-0.25)	<0.001
Weight decreased	2.8	28.5	0.10 (0.03-0.29)	<0.001

When adjusting for exposure, the incidence rates of TEAEs was lower with pirtobrutinib than with IdelaR/BR

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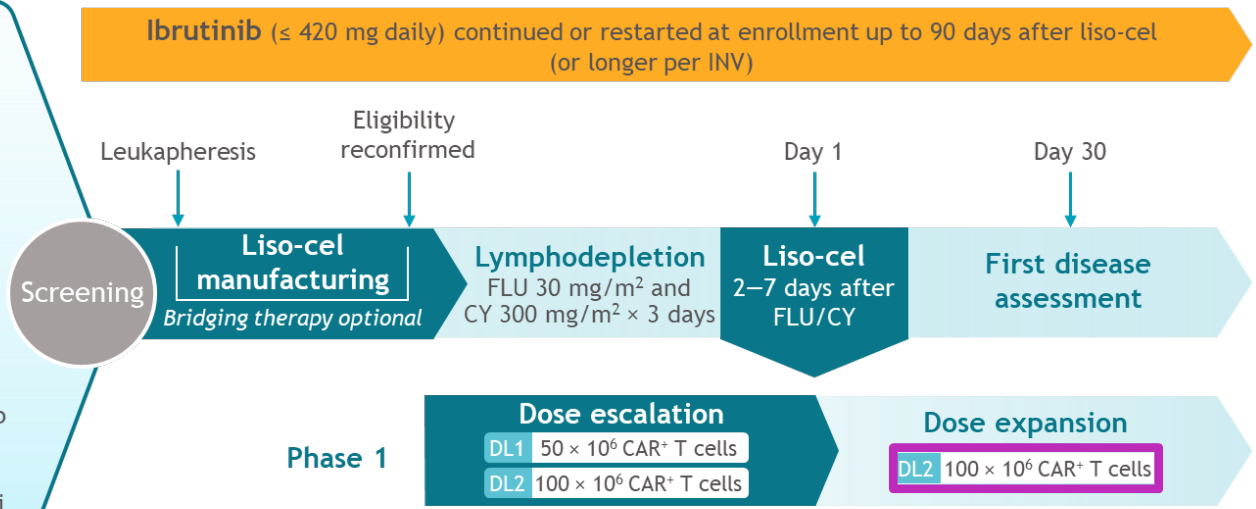
TRANSCEND 004 Ibrutinib cohort: Study Design

Key eligibility criteria for liso-cel plus ibrutinib cohort

- Age ≥ 18 years
- R/R CLL/SLL
- ECOG PS 0–1
- Adequate organ function
- No active CNS involvement
- No Richter transformation
- Met ≥ 1 of the following:
  - Receiving BTKi with progression at study entry
  - High-risk features with < CR after ≥ 6 mo on BTKi
  - *BTK*/*PLCγ2* mutation[a] ± ibrutinib progression
  - Prior BTKi with no contraindications to restart BTKi
- Progression on BTKi and received prior venetoclax (per amendment 5)



Follow-up

On-study:
24 or 48 months
LTFU study (NCT03435796):
up to 15 years after liso-cel infusion

Primary endpoint (at DL2)
CR/CRi rate per iwCLL 2018 by INV assessment

Secondary endpoints
Safety (DL1 + DL2); ORR, DOR, DOCR, time to response, time to CR/CRi, PFS, OS, and uMRD4[b] rate in blood at DL2

Exploratory analyses
uMRD4[b] rate in marrow, cellular kinetics (CAR T cell expansion and persistence)

[a]Per local laboratory assessment; [b]MRD was assessed by next-generation sequencing using a clonoSEQ assay. Undetectable MRD was defined as < 1 CLL cell per 10,000 leukocytes at ≥ 1 time point after infusion (uMRD4). CY, cyclophosphamide; DOR, duration of response; DOCR, duration of continued CR after initial CR; FLU, fludarabine; INV, investigator; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; LTFU, long-term follow-up; uMRD4, undetectable minimal residual disease at < 1 in 10^{-4} leukocytes.

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TRANSCEND 004 Ibrutinib cohort: Baseline Characteristics

	DL2 + ibrutinib set (n = 51)	Total liso-cel + ibrutinib combination set (n = 56)
Median (range) age, y	65 (44–77)	65 (44–77)
Median (range) prior lines of systemic therapy	**5 (1–13)**	**5 (1–13)**
≤ 3 prior therapies, n (%)	19 (37)	20 (36)
Prior BTKi, n (%)	51 (100)	56 (100)
Prior venetoclax, n (%)	39 (76)	42 (75)
Prior BTKi and venetoclax, n (%)	39 (76)	42 (75)
BTKi progression/venetoclax failure,[a] n (%)	**28 (55)**	**31 (55)**
High-risk cytogenetics, n (%)	50 (98)	55 (98)
Del(17p)	23 (45)	25 (45)
Mutated *TP53*	23 (45)	24 (43)
Unmutated IGHV	37 (73)	39 (70)
Complex karyotype[b]	25 (49)	29 (52)
Bulky disease (≥ 5 cm) per INV before LDC,[c] n (%)		
Yes	18 (35)	18 (32)
Unknown	4 (8)	5 (9)
Median (range) SPD per INV before LDC,[d] cm^2	29 (1–218)	27 (1–218)
LDH ≥ ULN before LDC, n (%)	22 (43)	24 (43)
Received bridging therapy (in addition to ibrutinib),[e] n (%)	13 (25)	16 (29)

- Median (range) ibrutinib exposure was 34 days (15–188) before and 95 days (6–1517) after liso-cel in the total combination-treated set
- Liso-cel was manufactured for 63/65 (97%) patients in the leukapheresed set
  - Median (range) time from leukapheresis to liso-cel availability was 25 (17–79) days (n = 62)

[a]Includes patients who progressed on a BTKi and met 1 of the following criteria: 1) discontinued venetoclax due to disease progression or intolerability and the patient's disease met indications for further treatment per iwCLL 2018 criteria or 2) failed to achieve an objective response within 3 months of initiating therapy; [b]At least 3 chromosomal aberrations; [c]At least 1 lesion with a longest diameter ≥ 5 cm; [d]Forty-seven patients at DL2 and 51 patients in the total combination-treated set had SPD measurements; [e]Included other anticancer therapies in addition to concurrent ibrutinib treatment given for disease control during liso-cel manufacturing. IGHV, immunoglobulin heavy-chain variable region; LDC, lymphodepleting chemotherapy; SPD, sum of the product of perpendicular diameters.

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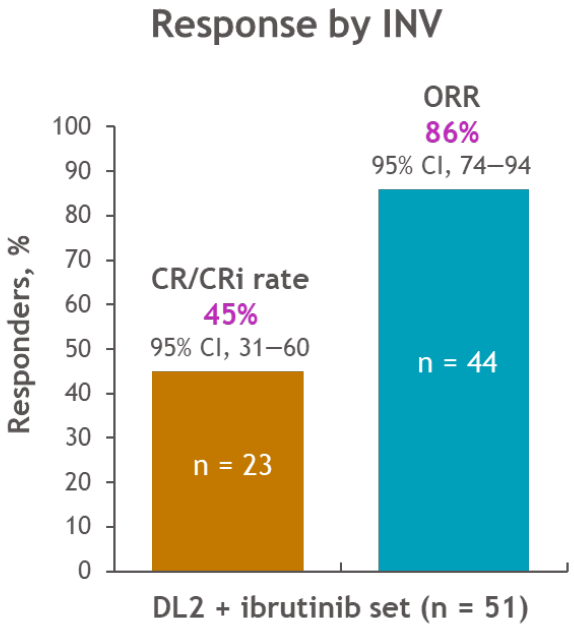
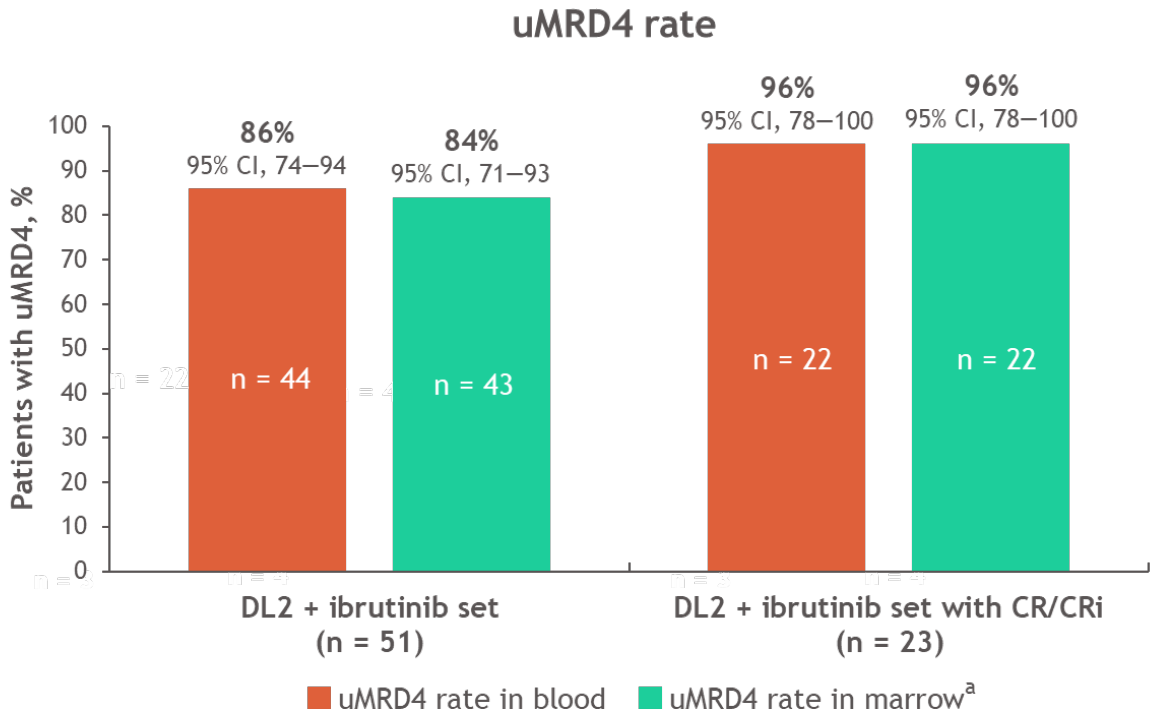
TRANSCEND 004 Ibrutinib cohort: Response and MRD

Median (IQR) on study follow-up: 24.8 m (14.2-34.6)
Median (range) time to first response: 1 m (0.9-6.0)
Median (range) time to CR/CRi: 3 m (0.9-12.1)





[a]Forty-nine patients (22 with CR/CRi) were evaluable for MRD in marrow.

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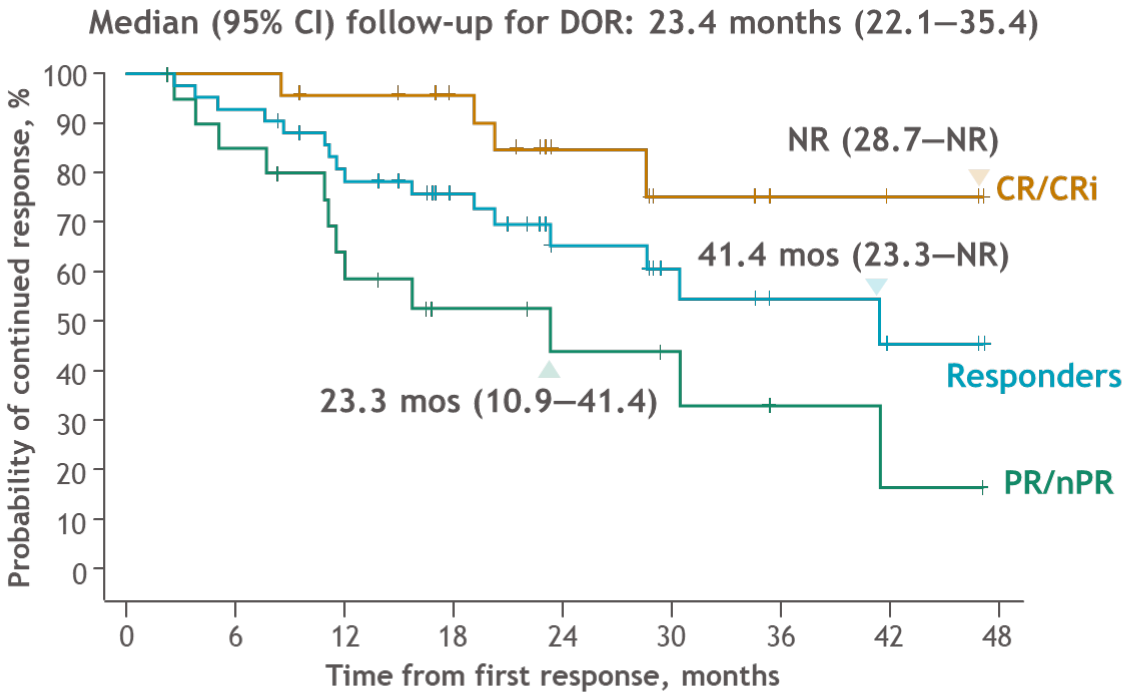
TRANSCEND 004 Ibrutinib cohort: DOR by best response at DL2



	% continued response (95% CI)	
	12 months	24 months
Responders (n = 44)	79 (63—88)	65 (47—79)
Patients with CR/CRi (n = 23)	96 (73—99)	85 (60—95)

- All 17 patients ongoing in the study at data cutoff were responders (CR/CRi, n = 13; PR/nPR, n = 4)

Data on KM curves are expressed as median (95% CI). No formal landmarking analyses were conducted. NR, not reached.

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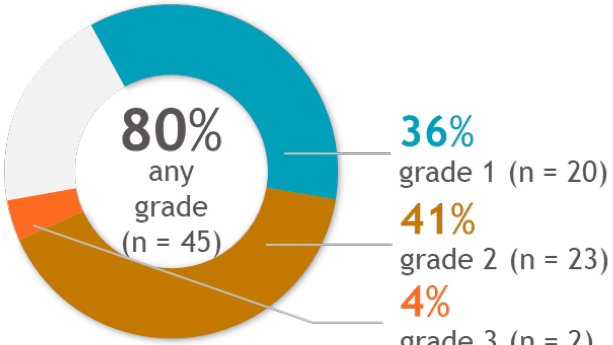
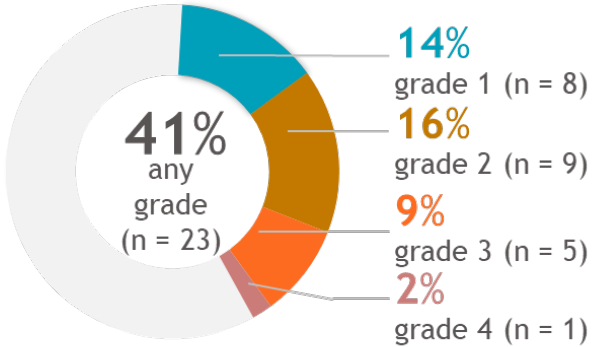
TRANSCEND 004 Ibrutinib cohort: Safety

CRS[a,b]



No grade 4 or 5 events

NEs[a,c]



No grade 5 events

	Total combination-treated set (n = 56)
Median (range) days to CRS onset	7 (1–14)
Median (range) days to CRS resolution	5 (2–18)
Received tocilizumab and/or corticosteroids for CRS and/or NE, n (%)	33 (59)

	Total combination-treated set (n = 56)
Median (range) days to NE onset	8 (1–15)
Median (range) days to NE resolution	8 (1–362)
Received tocilizumab and/or corticosteroids for CRS and/or NE, n (%)	33 (59)

[a]Summed percentages for grouped grades within each graph may not equal the any-grade percentage due to rounding; [b]CRS was graded based on Lee 2014 criteria; [c]NEs were defined as -INV-identified neurological AEs related to liso-cel.

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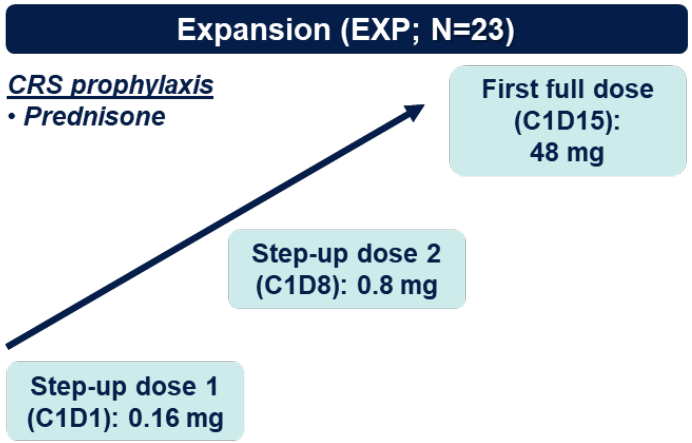
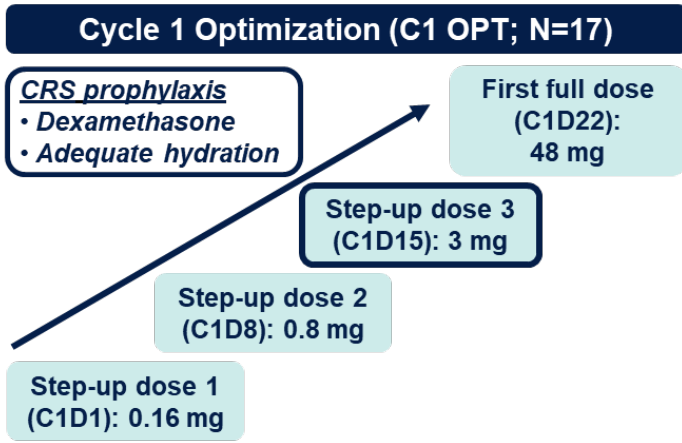
EPCORE 101: study design

Key inclusion criteria

- $CD20^+$ R/R CLL
- ≥2 prior lines of systemic therapy
- ECOG PS 0–2
- Measurable disease with ≥5×10^9/L B lymphocytes (expansion only)
- No prior allogeneic HSCT



Data cutoff: May 28, 2024
Median follow-up: 22.8 months



Data cutoff: May 28, 2024
Median follow-up: 2.9 months

- **Primary endpoint (EXP):** Overall response rate
- **Primary endpoint (C1 OPT):** Incidence and severity of CRS, ICANS, and clinical TLS
- **Key secondary endpoints (EXP):** CR rate, time to response, MRD (PBMCs using the clonoSEQ® assay), and safety/tolerability

- To ensure patient safety and better characterize CRS, inpatient monitoring was required for at least 24 hours after each epcoritamab dose in C1

ClinicalTrials.gov: NCT04623541; EudraCT: 2023-504828-25.

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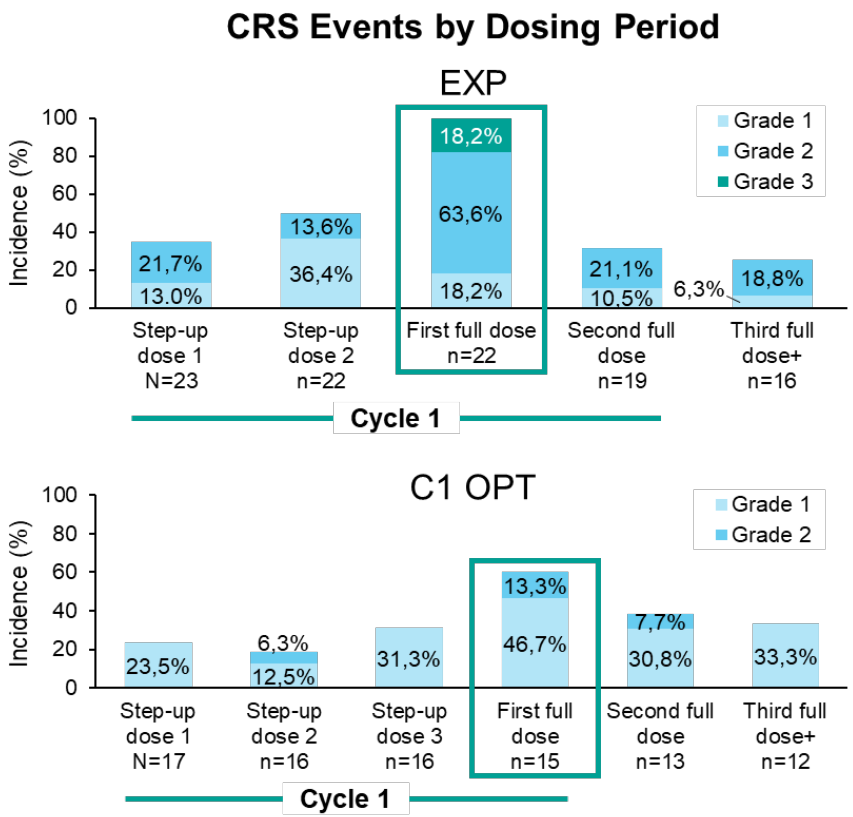
EPCORE 101: Safety Optimization

	EXP N=23	C1 OPT N=17
CRS, n (%)	**22 (96)**	**14 (82)**
Grade 1	2 (9)	12 (71)
Grade 2	16 (70)	2 (12)
Grade 3	4 (17)	0
Treated with tocilizumab, n (%)	20 (87)	6 (35)
Leading to treatment discontinuation, n (%)	**0**	**0**
CRS resolution, n/n (%)	22/22 (100)	14/14 (100)
Median time to resolution, days (range)	3 (1–16)	3.5 (1–7)
ICANS, n (%)	**3 (13)**	**0**
Grade 1	1 (4)	0
Grade 2	2 (9)	0
Clinical TLS, n (%)	**1 (4)**	**0**
Grade 2	1 (4)	0



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EPCORE 101: Efficacy data

Response, n (%)	EXP mFU: 22.8 months					C1 OPT mFU: 2.9 months
	Full Analysis Set N=23	Response Evaluable n=21	*TP53* Aberration n=15	*IGHV* Unmutated n=16	Double Exposed[a] n=19	Response Evaluable n=10
Overall response[b]	**14 (61)**	**14 (67)**	**10 (67)**	**10 (63)**	**10 (53)**	**6 (60)**
Complete response	9 (39)	9 (43)	5 (33)	7 (44)	7 (37)	1 (10)
Partial response	5 (22)	5 (24)	5 (33)	3 (19)	3 (16)	5 (50)
Stable disease	4 (17)	4 (19)	2 (13)	3 (19)	4 (21)	2 (20)
Progressive disease	1 (4)	1 (5)	1 (7)	0	1 (5)	1 (10)

- With limited follow-up, the C1 OPT regimen does not appear to affect epcoritamab efficacy
- uMRD4 in PBMCs was observed in most responders, including all patients with CR who were tested for MRD

EXP MRD Negativity, n/n (%)[c]	uMRD4	uMRD6[d]
Overall response[b]	9/12 (75)	8/12 (67)
Complete response	7/7 (100)	6/7 (86)
Partial response	2/5 (40)	2/5 (40)
Full analysis set	9/23 (39)	8/23 (35)

Four patients (*TP53* aberration, n=2; *IGHV* unmutated, n=3; double exposed, n=4) in EXP and 1 in C1 OPT shown above were not evaluable or had no assessment, including 3 in EXP (*TP53* aberration, n=2; *IGHV* unmutated, n=2; double exposed, n=3) and 1 in C1 OPT who died without postbaseline assessment. [a]Patients previously treated with both a BTK inhibitor and a BCL-2 inhibitor. [b]Response assessment according to iwCLL criteria. [c]Patients evaluated for MRD had at least 1 on-treatment MRD result and were not MRD negative at baseline. MRD was only evaluated in patients with CR or PR. [d]Two of 3 evaluated patients had uMRD6 in bone marrow at or shortly after the first CR assessment. mFU, median follow-up.

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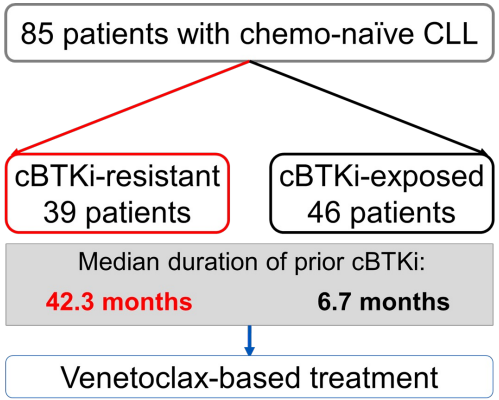
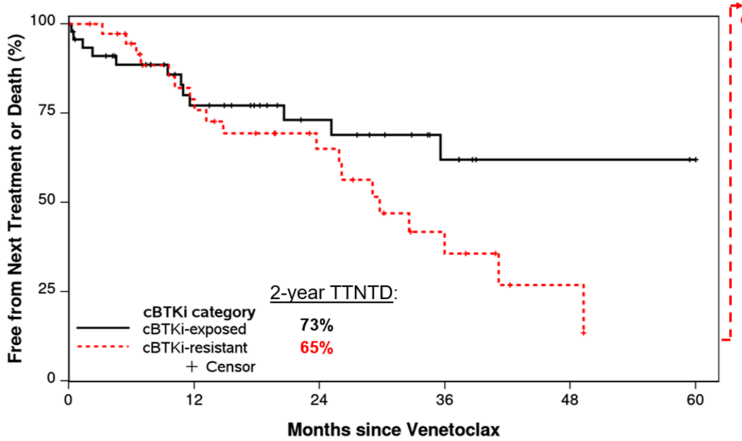
Outcomes with Venetoclax-Based Treatment in Patients with Covalent Bruton Tyrosine Kinase Inhibitor (cBTKi)-Treated, Chemotherapy-Naïve Chronic Lymphocytic Leukemia (CLL): An International Retrospective Study



Parameter		Number (%) or Median [IQR]
Total patients		**85**
Age, years		69 [62, 77]
Males		59 (69)
Prior lines of therapy		1 [1, 2]
	Prior anti-CD20 mAb	32 (38)
	Two prior cBTKi	8 (9)
Combination with anti-CD20 mAb	Rituximab	45 (53)
	Obinutuzumab	27 (32)
	None/Venetoclax Monotherapy	13 (15)
***IGHV* status*, n=56**	Unmutated	46 (82)
Complex karyotype*, n=37	Complex (≥3 abnormalities)	15 (41)
***TP53* disruption*, n=73**	Present (Abnormal)	33 (45)



cBTKi-resistant (n=39)

Median TTNTD:
30 months

2-year TTNTD estimates by anti-CD20 mAb combo

- Venetoclax monotherapy (n=5): **53%**
- Venetoclax + rituximab (n=30): **62%**
- Venetoclax + obinutuzumab (n=4): **100%**

Total Cohort

- TTNTD: only ***TP53* disruption with HR 2.23** (95% CI 1.02-4.87; P=0.04)
- OS: only older age with HR 1.05 (P=0.02)

cBTKi-Resistant Subgroup

- TTNTD: only ***TP53* disruption with HR 6.68** (95% CI 1.51-29.46; P=0.01)
- OS: only ***TP53* disruption with HR 7.95** (95% CI 1.02-61.97; P=0.04)

Hampel P, ASH2024, abs #1856 poster presentation

Thank you

Prof Paolo Ghia

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BANDO RICERCA FINALIZZATA 2018
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