Duvelisib

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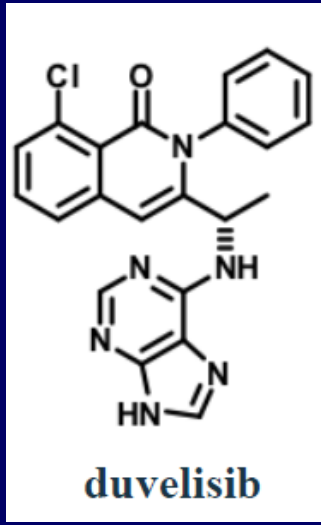
Duvelisib: Novel Dual PI3K-δ (DELTA), -γ (GAMMA) Inhibitor



duvelisib

- **Selective for PI3K over other protein and lipid kinases**
- **Orally bioavailable**

Inhibition measures for duvelisib (-δ/γ inhibitor) and idelalisib (-δ inhibitor):

δ (delta)	duvelisib	idelalisib
Biochemical Activity (KD)	23 pM	273 pM
Cellular Activity (IC50) RAJI cells stimulated with anti-IgM	0.36 nM	4.9 nM

γ (gamma)	duvelisib	idelalisib
Biochemical Activity (KD)	243 pM	85,700 pM
Cellular Activity (IC50) RAW264.7 cells stimulated with C5a	19.6 nM	520 nM

- Duvelisib has been extensively characterized across biochemical binding, cellular,
  and whole blood assays as a –delta/ –gamma dual inhibitor
- Characterization of idelalisib by the same assays confirms idelalisib as a –delta selective inhibitor, analogous to what has been reported by Gilead

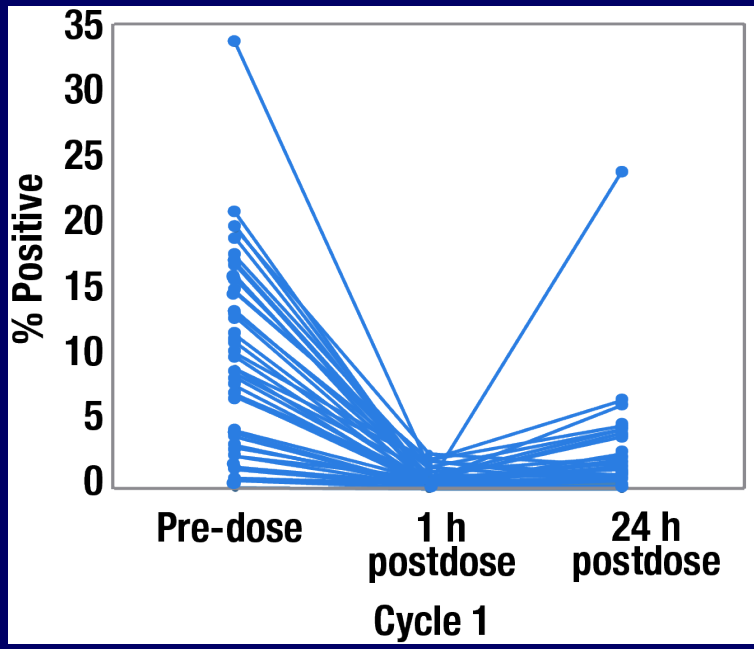
Winkler et al. , Chemistry & Biology. 2013;20:1-11

Study IPI-145-02 Design: Focus on CLL

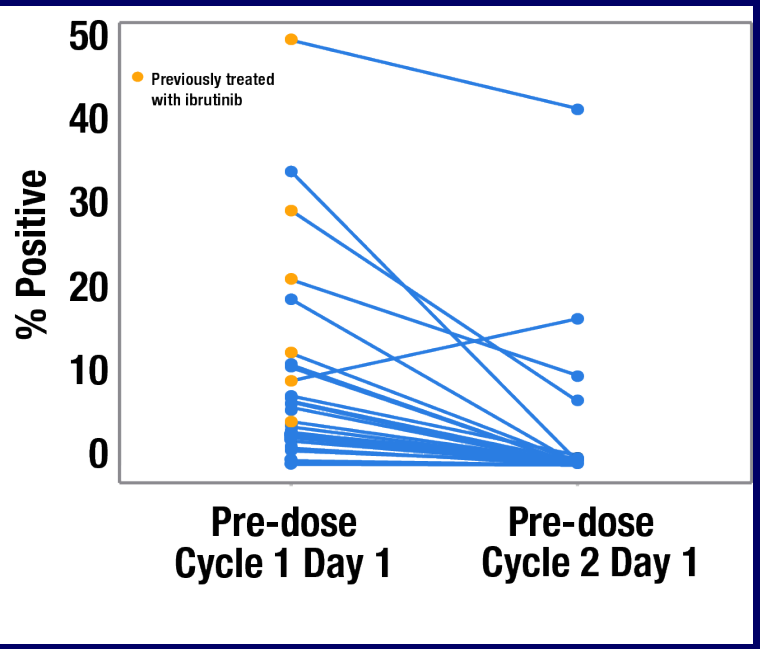
- Objectives – maximum tolerated dose (MTD), pharmacokinetics (PK), pharmacodynamics (PD), safety, and efficacy in patients with advanced hematologic malignancies
- 25 mg BID selected for phase 3 development based on early clinical activity (Flinn et al, ASH 2013)
- 55 R/R CLL/SLL pts received duvelisib BID in 28-day cycles
  - Response criteria per iwCLL 2008
  - AEs per CTCAE v 4.03
  - PD markers: pAKT and Ki67 in CLL cells, serum cytokines & chemokines
  - Prior treatment with a Bruton's tyrosine kinase inhibitor (BTKi) allowed

Pharmacodynamics & Mechanism of Action Studies: pAKT (S473) and Ki67 Measurements in CLL Cells

pAKT (S473) Percent Positive in CLL Cells*(n=41)

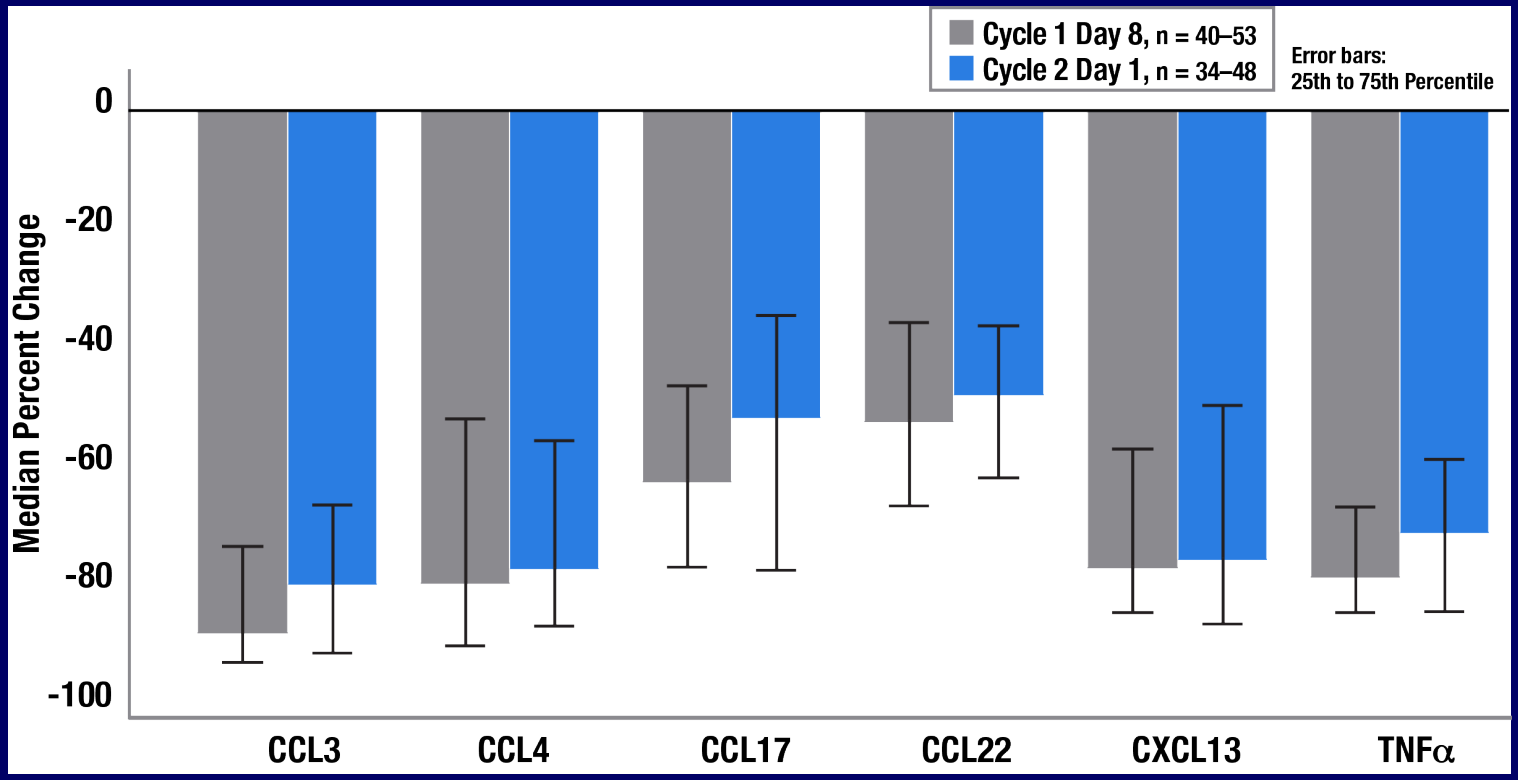


Ki67 Percent Positive in CLL Cells* (n=29)



- Rapid inhibition of pAKT (S473) following duvelisib
- Inhibition of CLL proliferation (Ki67) following 1 cycle of duvelisib, with near complete inhibition in pts not previously treated with BTKi

Change in Key Serum Chemokines and Cytokines



- Evidence of pharmacodynamic modulation of chemokines/cytokines that support the malignant B-cell microenvironment

Study Patients

Demographics	25 mg BID* (N=31)	All Doses (N=55)
Age (years), median (range)	66 (42, 82)	66 (42, 82)
Prior therapies, median (range)	5 (1,11)	4 (1, 11)
Rai Stage ≥ 3, n (%)	18 (64.3)	33 (60.0)
ECOG score, 0 / 1 / 2 / missing, n	8 / 20 / 2 / 2	12 / 38 / 3 / 2
Bulky lymphadenopathy (> 5 cm lesion), n (%)	13/31 (42)	24/51 (47)
Organomegaly, n %	8/26 (31)	13/48 (42)
ALC x10^3/μL, median (range)	14 (0.6, 233)	13 (0.6, 280)
Grade 4 cytopenia, n %	3 (9.7)	8 (14.5)
Prior ibrutinib treatment, n %	2 (6)	6 (11)
Risk Factors		
Unmutated *IGHV*, n (%)	20/23 (87)	31/35 (89)
TP53 mutation/17p deletion, n (%)	15/29 (52)	26/50 (52)

* *Includes 1 pt dosed at 8 mg BID, and 2 pts dosed at 15 mg BID*

All TEAEs (> 20% Overall) & Grade 3/4 (N = 55)

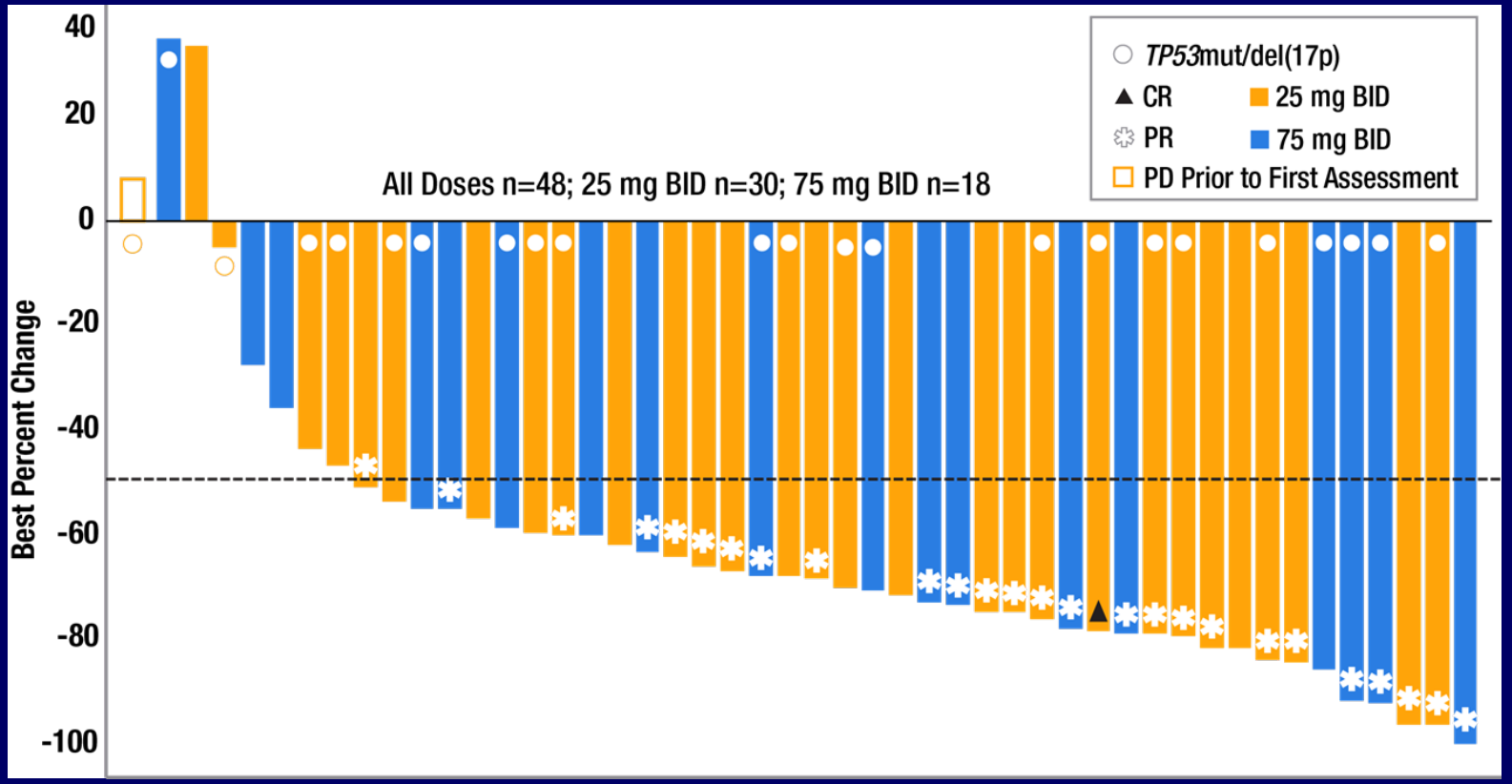
AE (preferred term)	Overall n (%)	Grade 3 n (%)	Grade 4 n (%)
Neutropenia	29 (53)	10 (18)	13 (24)
Rash (combined)	25 (46)	1 (2)	1 (2)
Diarrhea	24 (44)	5 (9)	0
Cough	21 (38)	0	0
Fatigue	21 (38)	4 (7)	1 (2)
Pneumonia (combined)	20 (36)	13 (24)	1 (2)
ALT/AST increase	16 (29)	4(7)	1 (2)
Anemia	16 (29)	9 (16)	1 (2)
Pyrexia	15 (27)	2 (4)	0
Nausea	14 (26)	1 (2)	0
Decreased Appetite	13 (24)	1 (2)	0
Thrombocytopenia	12 (22)	2 (4)	8 (15)

Rash (combined) = any preferred terms associated with rash within Skin and Subcutaneous Tissue Disorders SOC;
Pneumonia (combined) = all preferred terms of lung inflammation due to infectious or non-infectious etiologies

TEAEs Leading to Treatment Discontinuation

AE (Preferred term)	n
Pneumonia (combined)	7
Diarrhea	2
Stomatitis	2
ALT/AST	1
Cold-type hemolytic anemia	1
Colitis	1
Metabolic acidosis	1
Hand-foot syndrome	1
Polyarthritis	1
Pruritis	1
Squamous cell carcinoma	1

Maximum Lymph Node Reduction



- 25/30 (83%) pts at 25 mg BID with baseline CT scan achieved a nodal response (≥ 50% reduction in measurable area of disease)

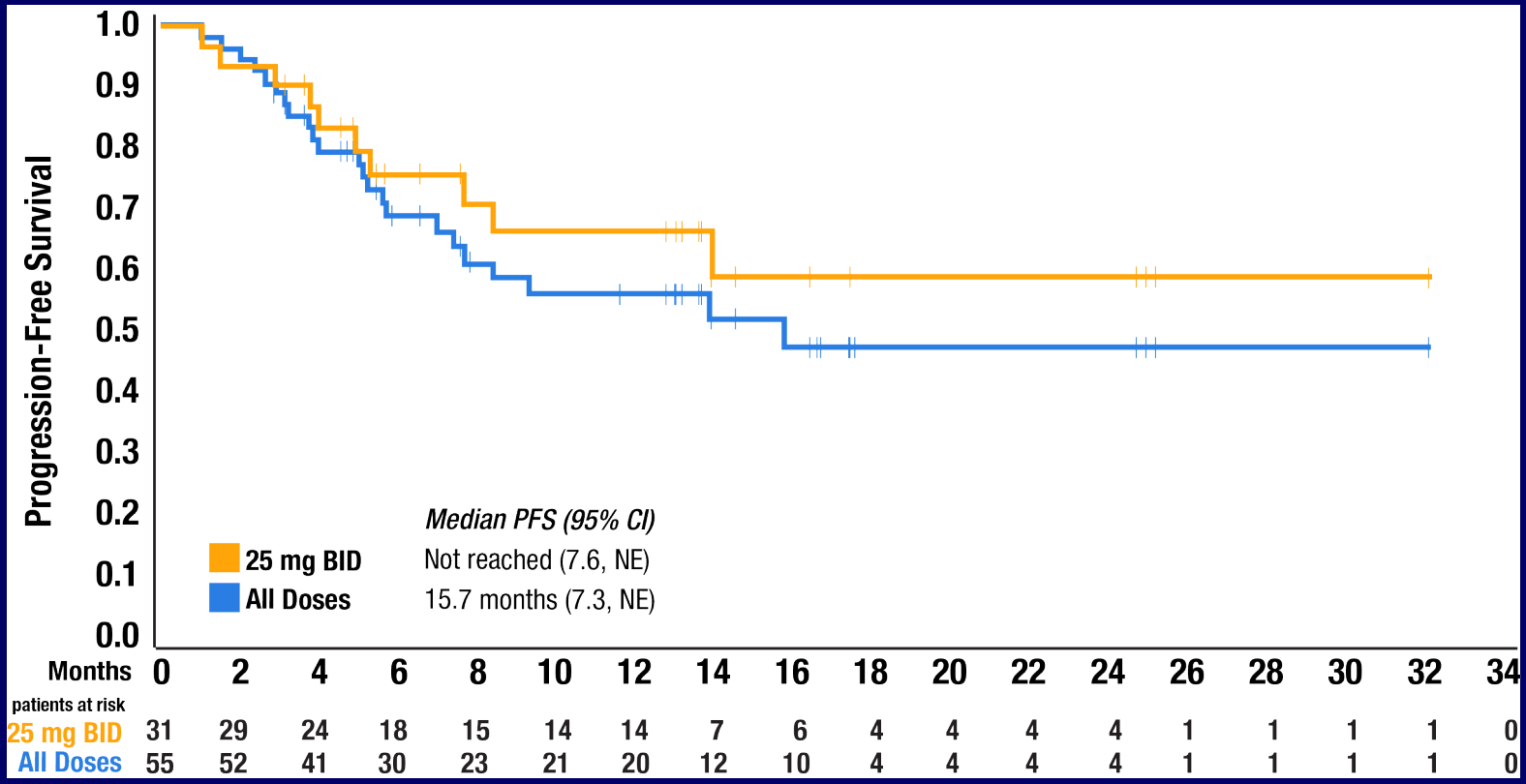
Best Overall Response (ORR) per iwCLL

Population	n	CR n (%)	PR n (%)	SD* n (%)	PD n (%)	ORR n (%)
All Doses	52	1 (2)	29 (56)	21 (40)	1 (2)	30 (58)
25 mg BID	30	1 (3)	16 (53)	12 (40)	1 (3)	17 (57)
Unmutated *IGHV*	20	1 (5)	11 (55)	8 (40)	0	12 (60)
*TP53*mut/del(17p)	15	1 (7)	6 (40)	7 (48)	1 (7)	7 (48)
Previous BTKi	6	0	1 (17)	5 (83)	0	1 (17)

Table includes efficacy evaluable pts only = at least one response assessment or PD without a response assessment
** Stable disease includes pts with PR + lymphocytosis*

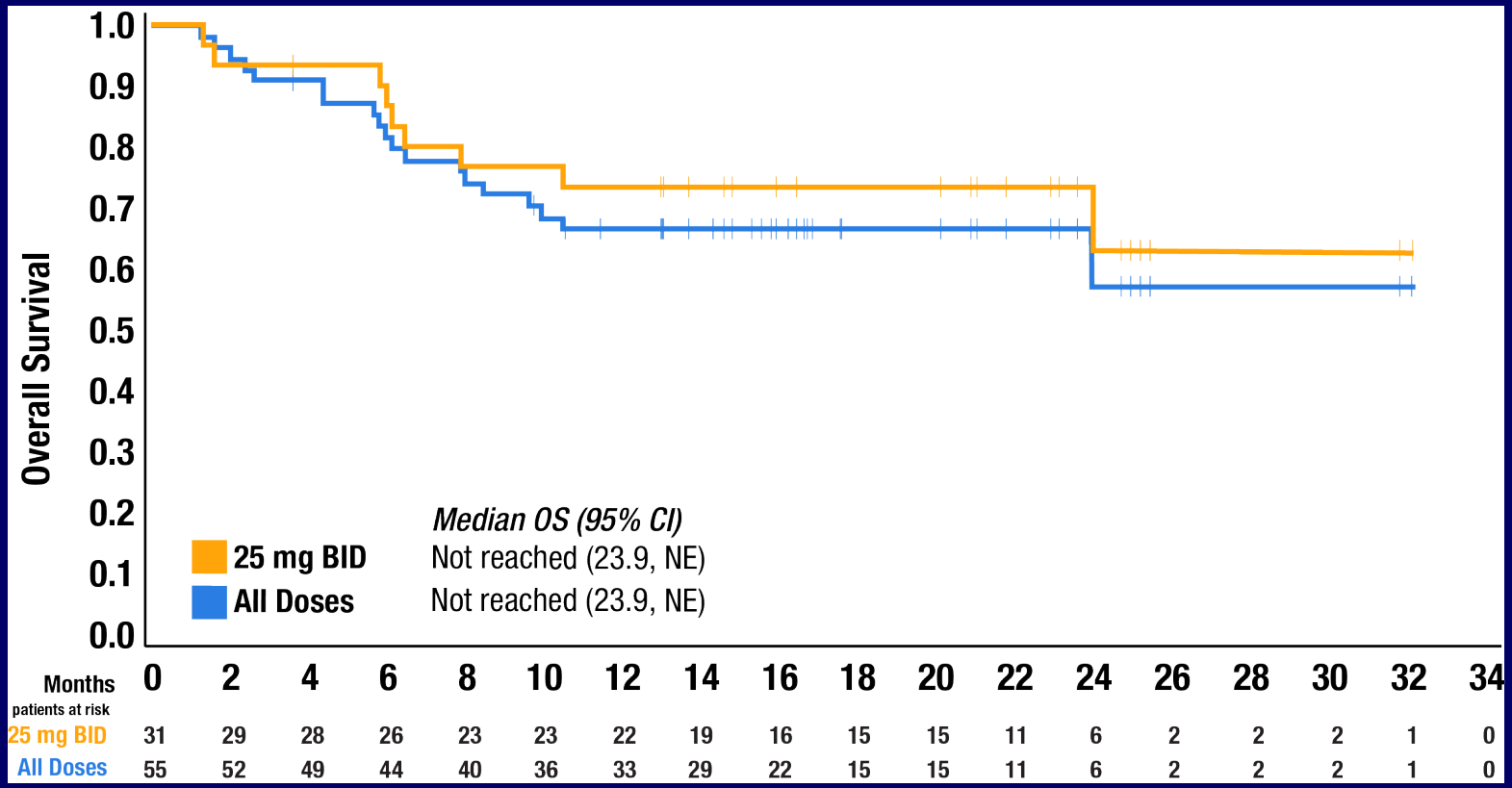
- **57% ORR by iwCLL at 25 mg BID, including 1 CR**
- **Median time to iwCLL response = 1.9 months**

Progression-Free Survival



- Median PFS at 25 mg BID not reached
  - 66% progression-free at 12 months
  - 59% progression-free at 24 months

Overall Survival (OS)



- Median OS at 25 mg BID not reached
  - 74% survival at 12 months
  - 63% survival at 24 months

Study IPI-145-02 Design

»TN CLL Expansion Cohort (n=18)

- Duvelisib 25 mg BID in 28-day cycles
- TN CLL pts enriched for high-risk status:
  - TP53mutation/17p-deletion; *and/or*
  - ≥ 65 years old
  - Response criteria per iwCLL 2008

Study Patients

Demographics	TN CLL (N = 18)
Age (years), median (range)	74 (49, 83)
Years from initial diagnosis, median (range)	3 (0, 9)
Rai Stage ≥3, n (%)	8 (47)*
ECOG Score, 0 / 1, n	8 / 10
Bulky lymphadenopathy (> 5 cm lesion), n (%)	1 (6)
Splenomegaly, n (%)	8 (44)
Hepatomegaly, n (%)	1 (6)
Grade 4 cytopenia, n (%)	2 (11)
ALC X 10^3/μL, median (range)	54 (2, 204)
Risk Factors	
≥ 65 years, n (%)	15 (83)
TP53 mutation/17p deletion, n (%)	10 (56)

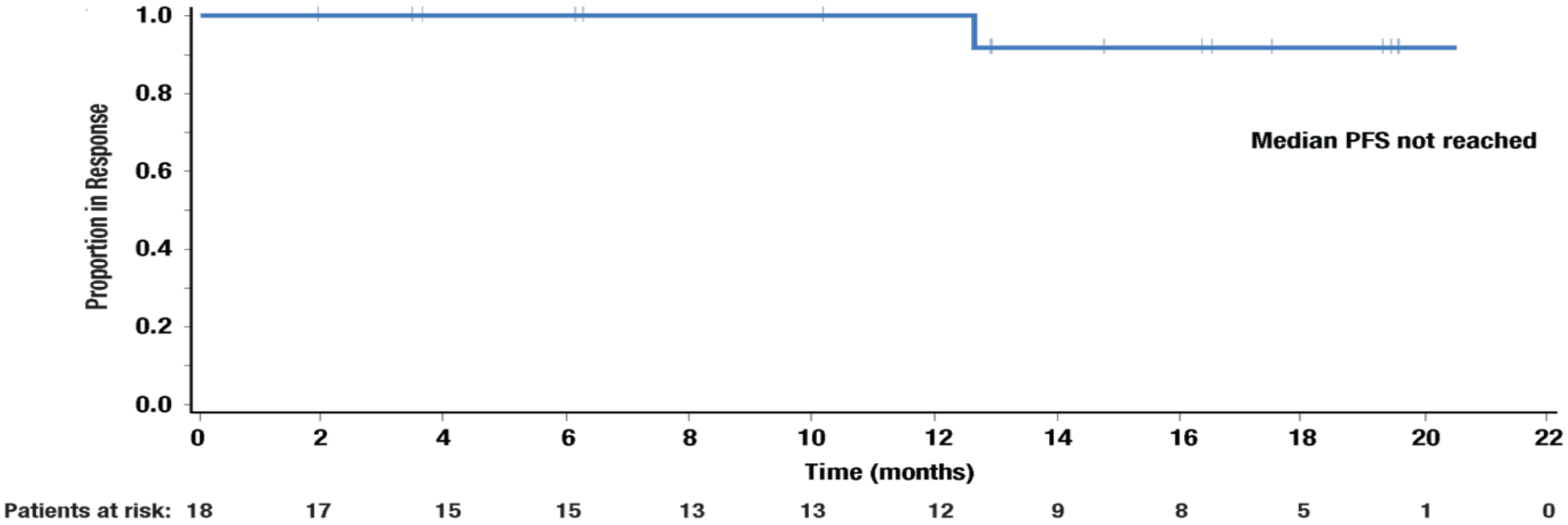
Best Overall Response (ORR) per iwCLL

Population *	n	CR n (%)	PR n (%)	SD n (%)	PD n (%)	ORR n (%)
TN CLL	17	0	15 (88)	2 (12)	0	15 (88)
P53 mutation/17p(del)	9	0	8 (89)	1 (11)	0	8 (89)

* 1 pt with TP53 mutation/17p-deletion withdrew consent prior to the first efficacy assessment (C3D1), and was not in the efficacy evaluable population

- Median time to iwCLL response = 3.7 months
- 7 of 15 (47%) responses occurred by the first assessment (Cycle 3 Day 1)

Progression-Free Survival



- Median PFS not reached
  - PFS rate 100% at 12 months and 92% at 18 months
- 1 pt progressed at Cycle 13

All AEs (>25% Overall) and Grade 3/4 (N = 18)

AE (preferred term)*	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)
Diarrhea	14 (78)	4 (22)	0
Rash (combined)**	9 (50)	2 (11)	0
Cough	8 (44)	0	0
Neutropenia/Neutrophil count decreased	8 (44)	1 (6)	5 (28)
Peripheral edema	8 (44)	0	0
Fatigue	7 (39)	1 (6)	0
Nausea	7 (39)	1 (6)	0
Pyrexia	6 (33)	0	0
ALT/AST increased	5 (28)	3 (17)	0
Anemia/Hemoglobin decreased	5 (28)	1 (6)	0
Dizziness	5 (28)	0	0

* >1 AE may have occurred in a single pt.
** Rash (combined) = any PT associated w/ rash w/in Skin and Subcutaneous Tissue Disorders SOC

SAEs and AEs Leading to Treatment Discontinuation

SAEs in > 1 Patient

SAE (preferred term)*	n
Diarrhea	3
Colitis	2
Dehydration	2
Pneumonia	2
Pneumonitis	2

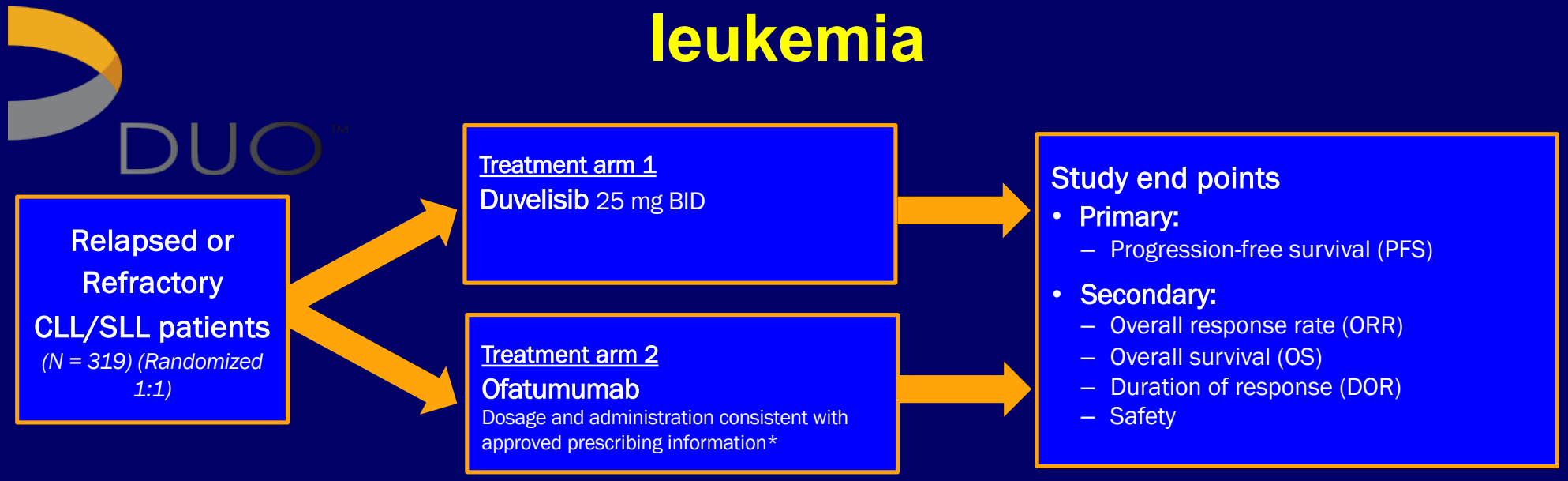
- 13 pts with an SAE(s)
  - 9 pts remained on duvelisib
- No SAEs resulted in death

AEs Leading to Treatment Discontinuation

Pt	AE (Grade)	Week *
1	ALT/AST increased (G3); dehydration (G3); spinal stenosis (G3)	9
2	Arthritis (G2)	11
3	Pneumonitis (G3)	20
4	Colitis (G3)	36
5	Diarrhea (G1)	47
6	Colitis (G1) and stomatitis (G3)	53

* Date of pt discontinuation from study drug

DUO™: Phase 3 study of Duvelisib in relapsed/refractory Chronic lymphocytic leukemia



✓ First Phase 3 trial showing PI3K inhibitor monotherapy efficacy in CLL/SLL

* 8 weekly infusions, starting with an initial IV dose of 300 mg ofatumumab on Day 1 followed by 7 weekly doses of 2,000 mg. Thereafter, 2,000 mg ofatumumab monthly for 4 months.

Baseline Characteristics and Prognostic Features

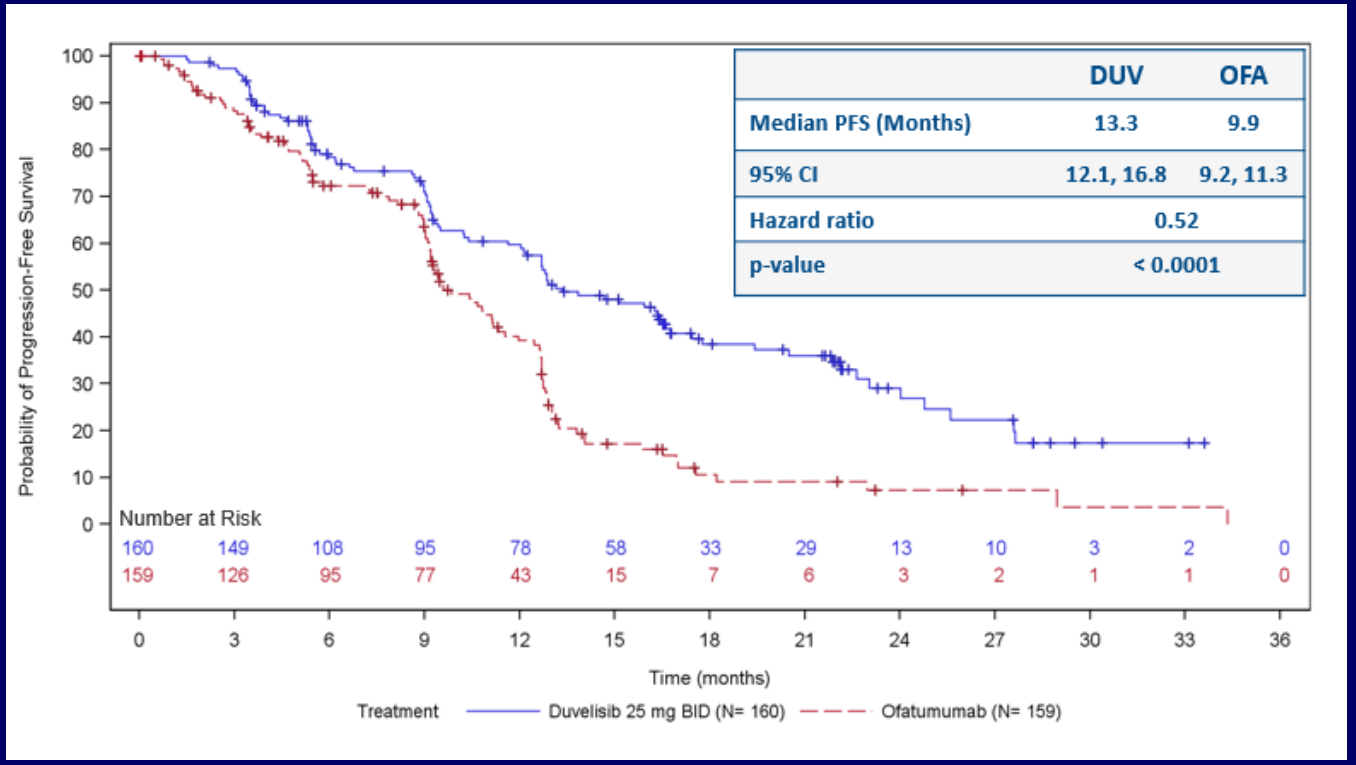
Characteristic	DUV N = 160	OFA N = 159
CLL/SLL, %	97 / 3	99 / 1
Median age (range), years	69 (39-90)	69 (39-89)
Number of Prior Regimens (range)	2 (1-10)	2 (1-8)
ECOG PS 2, %	7	10
Rai stage ≥ 3 / Binet Stage C, %	56 / 41	56 / 34
Bulky disease (≥ 5 cm target lesion), %	46	45
Grade 4 Cytopenia(s), %	11	11
Molecular features (per central laboratory), %		
17p deletion	21	28
TP53 mutation	20	18
17p deletion and/or *TP53* mutation	**31**	**33**
Unmutated IGHV	69	73
ZAP70 Positive (≥ 20%)	54	52

Prior Anticancer Regimens

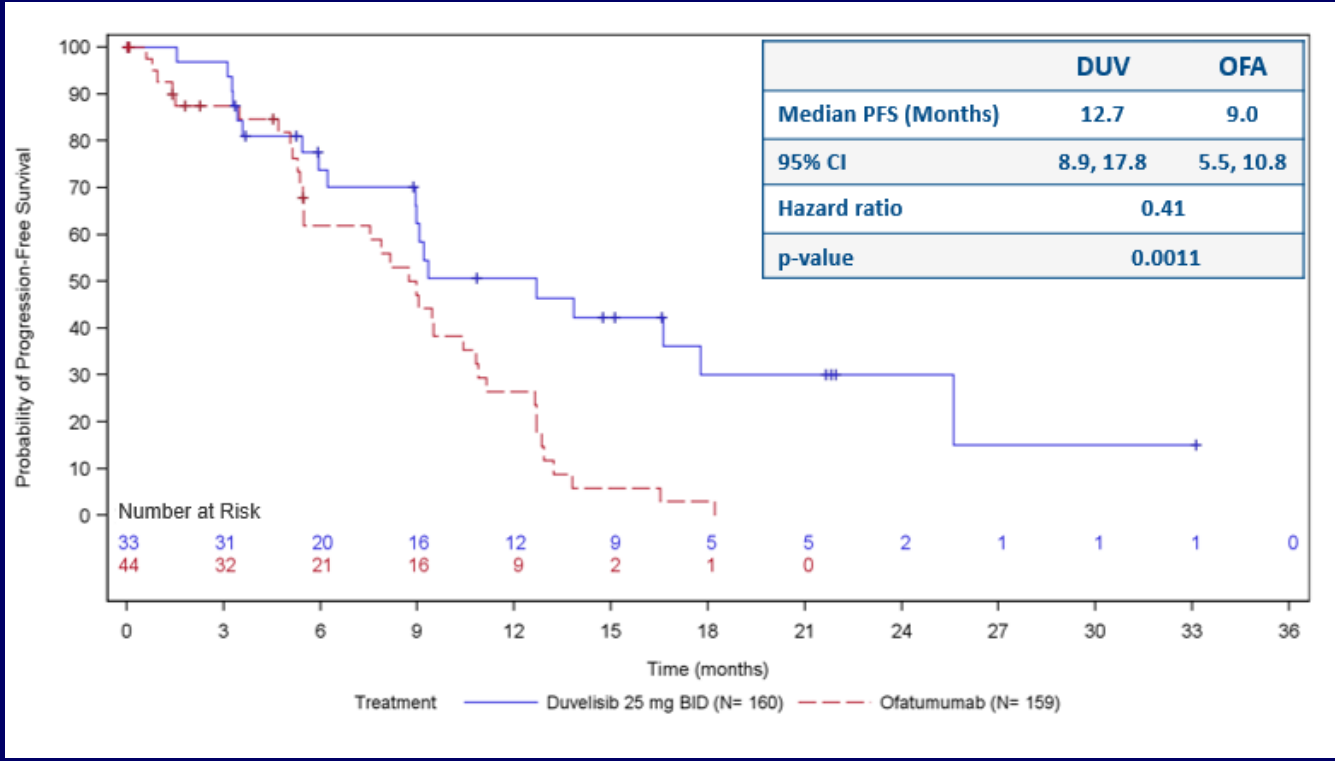
Characteristic	DUV N = 160	OFA N = 159
Median prior therapies (range)	2 (1-10)	2 (1-8)
Median months from prior therapy (range)	22 (1-149)	18 (1-106)
Purine Analog, %	60	71
Alkylator, %	93	95
Cyclophosphamide	59	70
Chlorambucil	39	32
Bendamustine	37	38
Monoclonal antibody, %	78	83
Rituximab	77	82
Ofatumumab	2	3
Obinutuzumab	1	2
Alemtuzumab	8	3

DUO Met Primary Endpoint of PFS

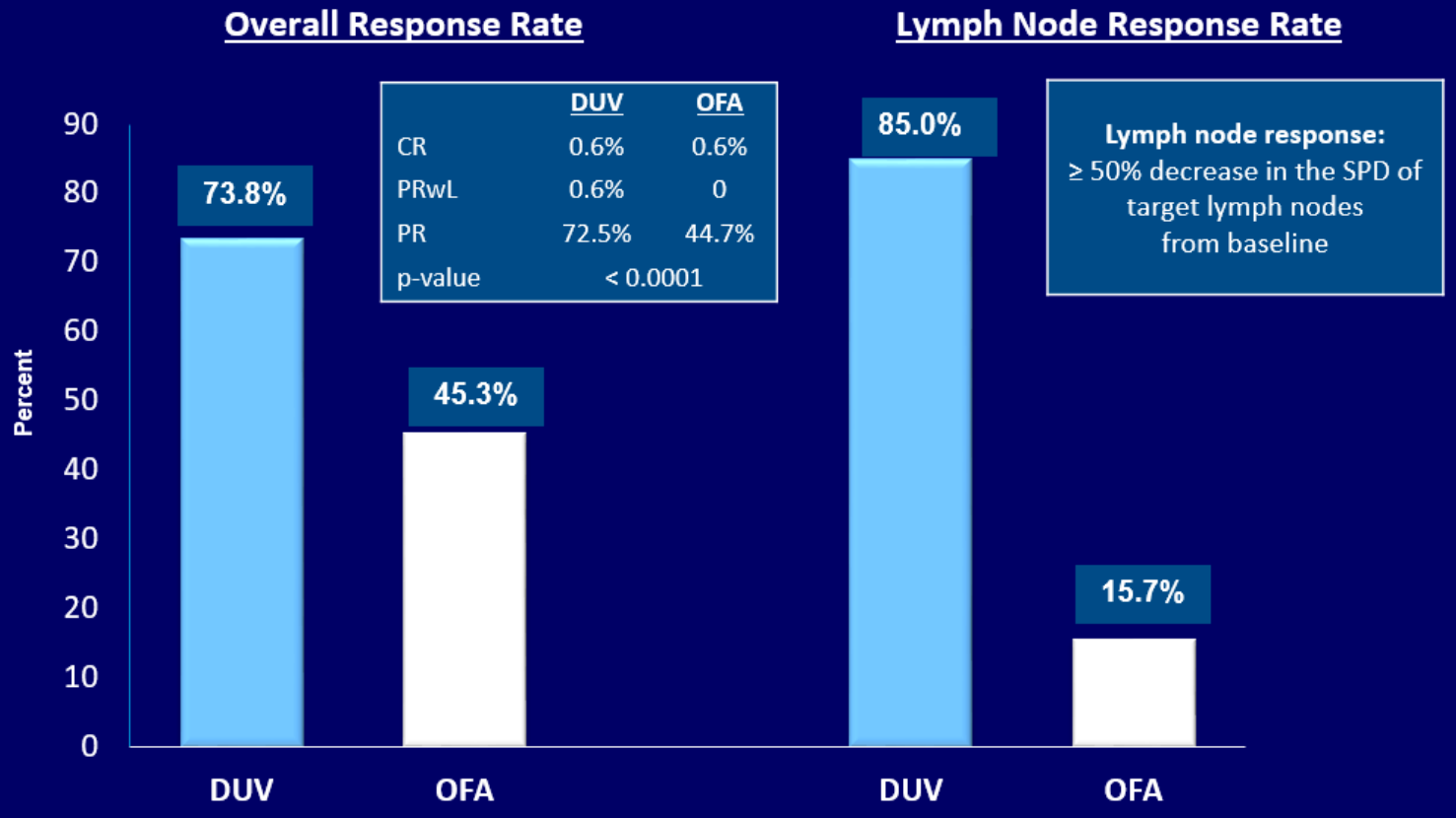
Significantly Longer Median PFS with Duvelisib per IRC



Significantly Longer PFS with Duvelisib in Patient with 17p Deletion per IRC

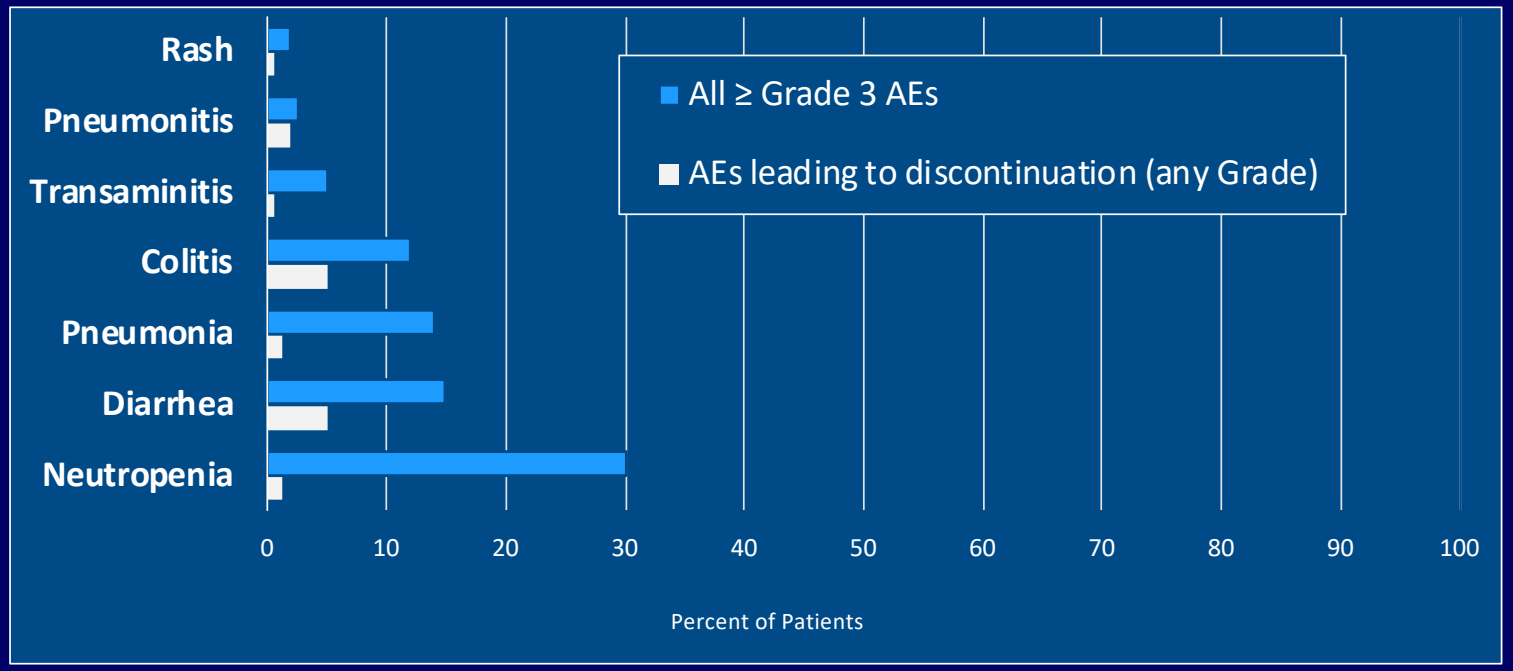


Significantly Higher ORR with Duvelisib per IRC



- ORR in patients with **17p deletion**: duvelisib 70% vs OFA 43% (p=0.0182)

Adverse Events of Special Interest Infrequently Led to Duvelisib Discontinuation



- Severe opportunistic infections (6%): bronchopulmonary aspergillosis (n=4), fungal infection (n=2), PJP (n=2)*, and cytomegalovirus colitis (n=1)
  - No severe Herpes zoster infections
- Treatment-related AEs leading to death (n=4): general health deterioration (n=1); pneumonia staphylococcal (n=2); sepsis (n=1)

* Neither patient on prophylaxis at the time of the event

Study Design: Phase 1 Duvelisib + Rituximab or Rituximab/Bendamustine

Arm 1 (N = 27)	
Duvelisib	25 mg* PO BID continuously until progression/intolerable toxicity
Rituximab	375 mg/m^2 IV, d1 qw x 4 for 2 cycles

→ Cohort A: CD20+ CLL
At least 1 prior anticancer therapy

→ Cohort B: CD20+ NHL
At least 1 prior anticancer therapy

Arm 2 (N = 19)	
Duvelisib	25 mg* PO BID continuously until progression/intolerable toxicity
Bendamustine	90 mg/m2 IV d1,2 up to 6 cycles (NHL) 70 mg/m2 IV d1,2 up to 6 cycles (CLL)
Rituximab	375 mg/m^2 IV, d1 up to 6 cycles

→ Cohort A: CD20+ CLL
At least 1 prior anticancer therapy

→ Cohort B: CD20+ NHL
At least 1 prior anticancer therapy

*25 mg duvelisib is the dose expansion dose; other tested doses were 50 mg (7 patients, 4 on arm 1 and 3 on arm 2) and 75 mg
(3 patients on arm 1) BID. There were no DLTs, but a concurrent Phase 1 study showed no efficacy benefit of duvelisib doses higher than 25 mg BID.

Flinn, I. *Am J Hematol*. 2019;1-10

Baseline Patient Characteristics

	Duvelisib + Rituximab (N = 27)	Duvelisib + Bendamustine + Rituximab (N = 19)	Total (N = 46)
Median Age, years (range)	70 (40-78)	64 (44-83)	66.5 (40-83)
Age, N (%)			
≥ 65 years	16 (59.3)	9 (47.4)	25 (54.3)
≥ 18-64 years	11 (40.7)	10 (52.6)	21 (45.7)
Sex, N (%)			
Male	12 (44.4)	12 (63.2)	24 (52.2)
Female	15 (55.6)	7 (36.8)	22 (47.8)
Race, N (%)			
Caucasian	25 (92.6)	18 (94.7)	43 (93.5)
Asian	0	1 (5.3)	1 (2.2)
Other	1 (3.7)	0	1 (2.2)
Unknown	1 (3.7)	0	1 (2.2)
ECOG PS, N (%)			
0	13 (48.1)	9 (47.4)	22 (47.8)
1	14 (51.9)	7 (36.8)	21 (45.7)
2	0	1 (5.3)	1 (2.2)
Missing	0	2 (10.5)	2 (4.3)
Disease Category, N (%)			
CD20+ CLL	11 (40.7)	6 (31.6)	17 (37.0)
CD20+ B-Cell Lymphoma	16 (59.3)	13 (68.4)	29 (63.0)
Follicular	11 (40.7)	4 (21.1)	15 (32.6)
DLBCL	2 (7.4)	7 (36.8)	9 (19.6)
Mantle Cell	2 (7.4)	0	2 (4.3)
Other	1 (3.7)	2 (10.5)	3 (6.5)
Median Number Prior Regimens* (range)	3 (1-7)	2 (1-5)	2 (1-7)

***Prior regimens include chemotherapies and monoclonal antibody treatments.**

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Most Common Adverse Events (≥ 20% of Patients)

Preferred Term, N (%)	Duvelisib + Rituximab N = 27		Duvelisib + Bendamustine + Rituximab (N = 19)		Total (N = 46)	
	All grades	≥ Grade 3	All grades	≥ Grade 3	All grades	≥ Grade 3
Subjects with any TEAE	27 (100)	24 (88.9)	19 (100)	16 (84.2)	46 (100)	40 (87.0)
Neutropenia	13 (48.1)	12 (44.4)	8 (42.1)	7 (36.8)	21 (47.7)	19 (41.3)
Fatigue	12 (44.4)	0	7 (36.8)	1 (5.3)	19 (41.3)	1 (2.2)
Rash	11 (40.7)	5 (18.5)	8 (42.1)	4 (21.1)	19 (41.3)	9 (19.6)
Diarrhea	11 (40.7)	4 (14.8)	6 (31.6)	2 (10.5)	17 (37.0)	6 (13.0)
Pruritus	9 (33.3)	0	4 (21.1)	0	13 (28.3)	0
Cough	6 (22.2)	0	5 (26.3)	0	11 (23.9)	0
Nausea	7 (25.9)	0	4 (21.1)	0	11 (23.9)	0
Alanine Aminotransferase Increase	6 (22.2)	2 (7.4)	4 (21.1)	1 (5.3)	10 (21.7)	3 (6.5)
Pyrexia	7 (25.9)	1 (3.7)	3 (15.8)	0	10 (21.7)	1 (2.2)
Anemia	4 (14.8)	1 (3.7)	5 (26.3)	1 (5.3)	9 (19.9)	2 (4.3)
Aspartate Aminotransferase Increased	5 (18.5)	1 (3.7)	4 (21.1)	0	9 (19.6)	1 (2.2)
Thrombocytopenia	3 (11.1)	1 (3.7)	5 (26.3)	2 (10.5)	8 (17.4)	3 (6.5)
Vomiting	4 (14.8)	0	4 (21.1)	0	8 (17.4)	0
Headache	3 (11.1)	0	4 (21.1)	0	7 (15.2)	0
Upper Respiratory Tract Infection	6 (22.2)	0	1 (5.3)	0	7 (15.2)	0
Arthralgia	2 (7.4)	1 (3.7)	4 (21.1)	0	6 (13.0)	1 (2.2)

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SAEs, Dose Modifications, and Discontinuations

- Nine patients (19.6%) experienced at least 1 SAE that was related to duvelisib (7 patients [25.9%] in Arm 1 and 2 patients [10.5%] in Arm 2), of which 2, Grade 5 pneumonia and Grade 5 cardiac arrest, resulted in death
- 37 patients had dose interruptions and 24 with dose reductions
- 11 patients discontinued treatment due to an AE
  - SAEs: colitis, acute lung injury, rash
  - AEs: *C difficile*, anemia, diarrhea, maculopapular rash, neutrophil count decreased/colitis/diarrhea, increased AST/increased ALT, rash/increased AST/increased ALT, and pruritus/local swelling

AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; SAE = serious adverse event.

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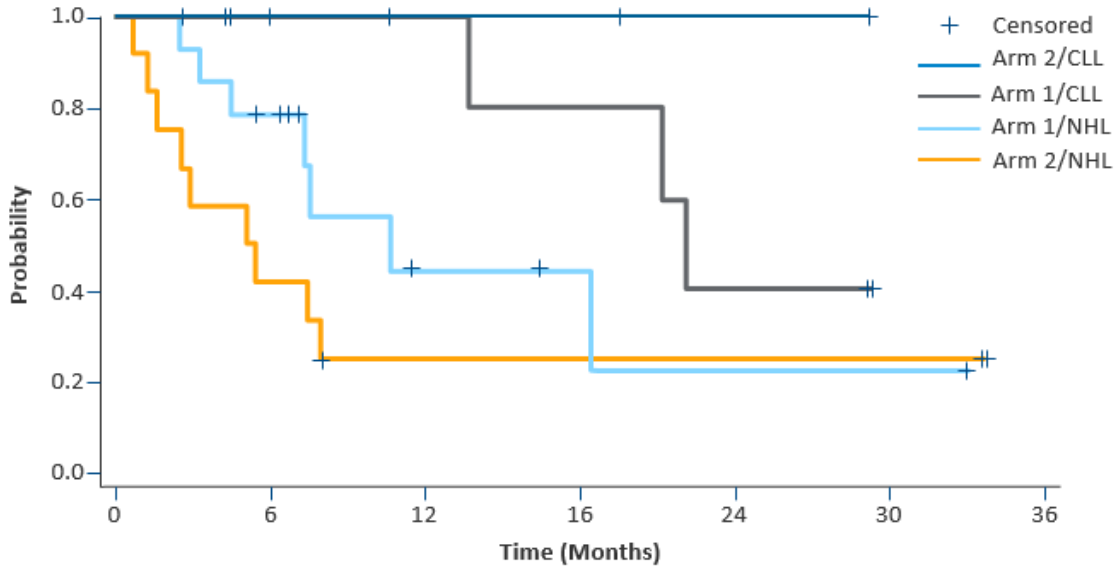
Survival Outcomes

Progression-Free Survival by Treatment Arm and Disease



- Arm 1 = duvelisib + rituximab
- Arm 2 = duvelisib + bendamustine + rituximab

	Arm 1 CLL	Arm 1 NHL	Arm 2 CLL	Arm 2 NHL	All Patients
Median PFS, months (95% CI)	22.1 (13.7, NA)	10.7 (4.5, NA)	NA (NA, NA)	5.3 (1.2, NA)	13.7 (7.4, NA)
Median OS, months (95% CI)	NR	NR	NR	9.1 (2.6,NR)	NR

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NA = not applicable; NR = not reached.

Summary of Best Response and ORR in Evaluable Patients

Parameter, N (%)	Duvelisib + Rituximab (Arm 1)			Duvelisib + Bendamustine + Rituximab (Arm 2)			All Evaluable Patients
	CLL[a] (n = 9)	NHL[b] (n = 14)	Total (n = 23)	CLL[a] (n = 4)	NHL[b] (n = 12)	Total (n = 16)	N = 39
ORR (CR + PR)	8 (88.9)	10 (71.4)	18 (78.3)	3 (75.0)	7 (58.3)	10 (62.5)	28 (71.8)
Best Overall Response							
CR	0	3 (21.4)	3 (13.0)	1 (25.0)	2 (16.7)	3 (18.8)	6 (15.4)
PR	8 (88.9)	7 (50.0)	15 (65.2)	2 (50.0)	5 (41.7)	7 (43.8)	22 (56.4)
SD	1 (11.0)	3 (21.4)	4 (17.4)	0	1 (8.3)	1 (6.3)	5 (12.8)
PD	0	0	0	0	2 (16.7)	2 (12.5)	2 (5.1)
NE	0	1 (7.1)	1 (4.3)	1 (25.0)	2 (16.7)	3 (18.8)	4 (10.3)
Median Duration of Response	15.1 mo	5.0 mo	NA	16.9 mo	6.2 mo	NA	NA

[a]Response assessed per Hallek criteria.
[b]Response assessed per Cheson criteria.

CR = complete response; NA = not applicable; NE = not evaluable; ORR = overall response rate; PD = progressive disease; PR = partial response; SD = stable disease.

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A Phase IB/II Study of Duvelisib in Combination with FCR (DFCR) For Frontline Therapy for Younger CLL Patients

DFCR

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A Phase IB/II Investigator Initiated Study of Duvelisib + FCR (DFCR) For Younger Previously Untreated Patients with CLL

Endpoints

Primary

- Rate of CR with BM MRD negativity 2 mo. post FCR completion

Secondary

- Clinical response: ORR, CR, PR, PFS, EFS, and remission duration
- Rates of best response and best BM and PB MRD-negativity
- Safety/Tolerability
- Association of established CLL prognostic factors (e.g. FISH cytogenetics, *IGHV*, *TP53* and *NOTCH1* mutation) with clinical response

Exploratory

- Association of novel prognostic factors such as BH3 profiling with response
- Comparison of MRD assessment by 4-color flow cytometry vs. Adaptive clonoSEQ assay

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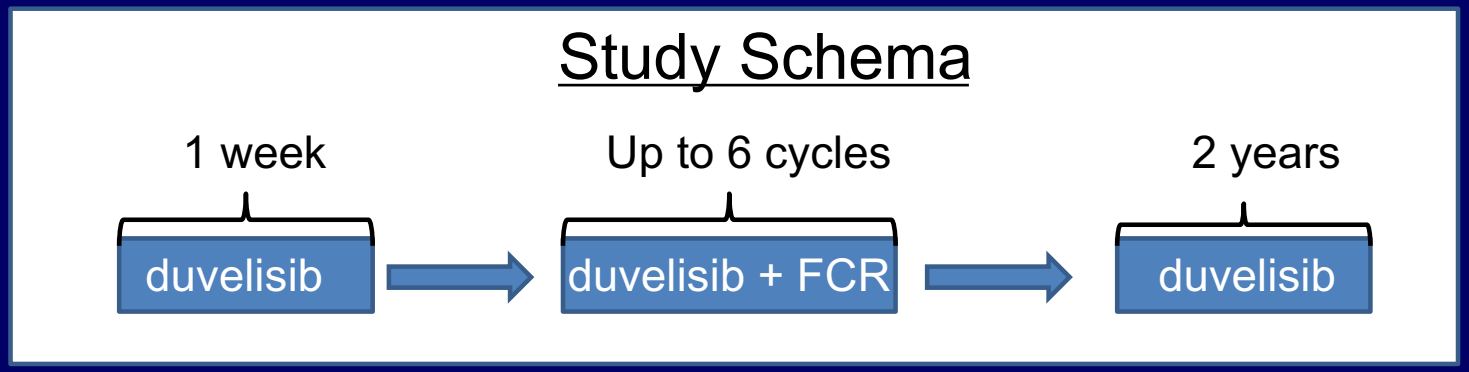


G-CSF and PJP/HSV/VZV prophylaxis mandatory for all patients

- A standard 3 + 3 phase Ib design with 2 dose levels of duvelisib with monthly cycles
- 25 mg qd (starting level) and 25 mg bid, then a phase II expansion cohort
- Standard toxicity assessments by CTCAE v4.03 and 2008 IW-CLL
- Response evaluations by 2008 IW-CLL: after 3 cycles, 2 mo. after final FCR, then q6 mo.
- All CRs were confirmed with CT and bone marrow biopsy
- MRD: assessed by 4-color flow cytometry (sensitivity 10^{-4})

Baseline Patient Characteristics (Fully Enrolled, N=32)

- Median age at enrollment: 55 years (range 45-65)
- Male: 69%
- FISH[#]:

del (17p)*	del(11q)	Trisomy 12	del(13q)	Del(6q)	Normal
n=3 (9%)	n=8 (25%)	n=7 (22%)	n=14 (44%)	n=3 (9%)	N=6 (19%)
#some patients had >1 FISH abnormality, *all with complex karyotype					

- *IGHV*: 18/32 (56%) unmutated, ZAP-70: 19/31 (61%) pos.
- Somatic Mutations: *TP53* mut without del(17p) n=2, *NOTCH1* mut n=1
- Median β2M: 4.0 mg/L (range 2.2-8.1)
- 41% with Rai stage III/IV disease
- Median of 80% bone marrow involvement (range 0-95%)
- Baseline counts (median, range):
  - WBC: 97 K/uL (2.7-595)
  - Hgb: 11 g/dl (5.8-15.9)
  - Plts: 115 K/uL (19-377)

Safety Analysis (N=32)

- Only 1 DLT in dose escalation (Gr 3 febrile neutropenia at 25 mg qd)
- RP2D of duvelisib given with FCR: 25 mg bid

All grade hematologic toxicity:
-neutropenia: 59% (50% gr 3/4)
-thrombocytopenia: 65% (34% gr 3/4)
-anemia: 38% (16% gr 3/4)

All grade immune-mediated toxicities:
-transaminitis: (34%, 28% gr 3/4)
-inflammatory arthritis: (9%, all gr2)
-colitis: (6%, 1 gr2, 1 gr3)
-pericarditis and pancreatitis: (3%, gr2)

Other all grade non-heme toxicities:

- nausea: (72%, all gr1/2)
- fatigue (69%, 3% gr3)
- fever (53%, all gr1/2)
- diarrhea (47%, 3% gr3)

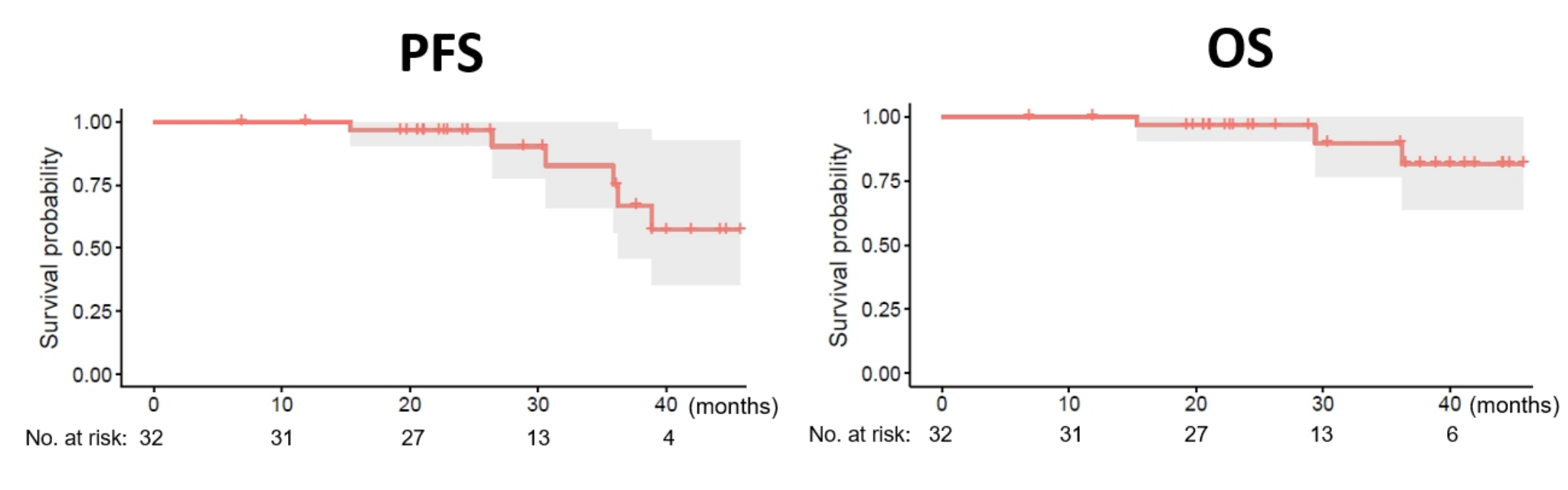
DFCR Primary Efficacy Analysis (31 patients evaluable for 1° endpoint)

	C4D1	Primary Endpoint (2 mo. post-FCR)	Best Response
ORR	**94%** (29/31)	**94%** (29/31)	**94%** (29/31)
PR	**74%** (23/31)	**68%** (21/31)	**42%** (13/31)
CR/CRi	**19%** (6/31)	**26%** (8/31)	**52%** (16/31)
CR with BM MRD neg.	**13%** (4/31)	**26%** (8/31)*	**55%** (16/29)
BM MRD neg.	**54%** (15/28)	**67%** (18/27)	**76%** (22/29)

- All patients who achieved CR at primary endpoint also were BM MRD neg.
- 53% (10/19) of PR patients were BM MRD neg. at primary endpoint, most w/ LN <2.5 cm
- Responses deepened with duvelisib maintenance

*primary endpoint

DFCR: Survival Analyses



- With a median follow-up of 24.5 months (range 6.9-46):
  - 2 year PFS and OS: 97%

DFCR: Conclusions

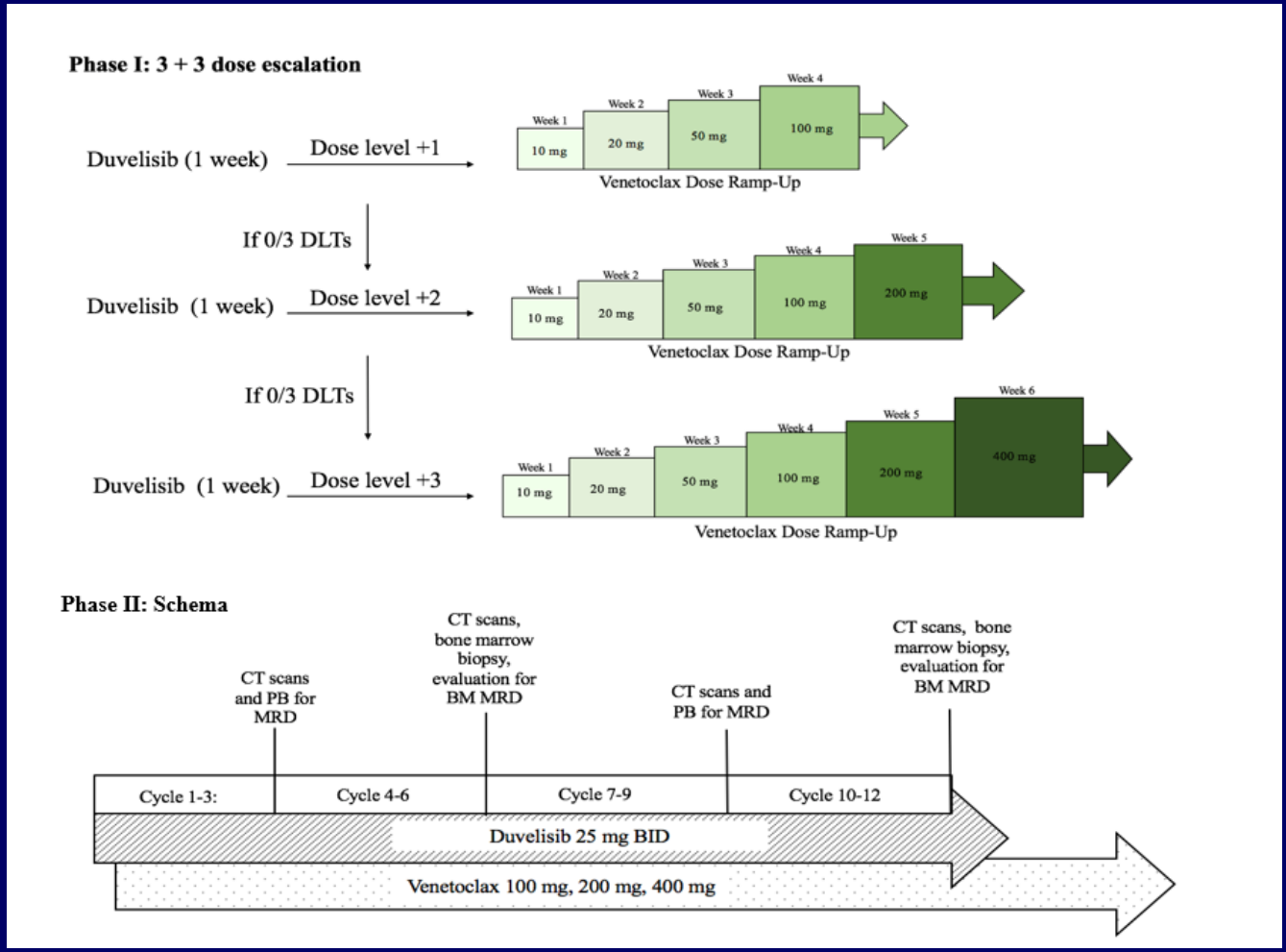
- Rate of best BM MRD neg. of 76% is significantly higher than historical data with FCR and similar to the ibrutinib + FCR regimen (Davids et al., ASH, 2017)

- High rates of BM MRD neg. were observed even in higher risk CLL such as unmutated *IGHV*, and responses deepened on duvelisib maintenance

- DFCR toxicities are comparable to duvelisib and FCR individually, with infectious, immune-mediated toxicities, and secondary malignancies observed

- DFCR is an effective regimen for the initial therapy of younger, fit CLL patients who desire a time-limited therapy with potential for long term remission

A Phase I/II Investigator-Initiated Study of Duvelisib + Venetoclax in Patients with R/R CLL/SLL



PI: Davids, DFCI