SUPPLEMENTAL MATERIALS

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Analysis of Patient Cytokine Profiles

Serum protein assessments were made using Luminex® xMAP technology (Luminex Corp., Austin, TX) as previously described.[1] The 24 chemokines, cytokines, and growth factors evaluated were: CCL1, CCL15, CCl17, CCL19, CCL22, CCL3, CCL4, CXCL10, CXCL11, CXCL13, CXCL5, CXCL9, IL10, IL12P40, IL12P70, IL15, IL16, IL2RA, IL6, MMP12, TNFA, TPO, TRAIL, VEGFD. For statistical analysis, P-value were determined from a one sample students t-test under the null hypothesis where the percentage change equals to 0, per treatment arm based on log-transformed values. A Bonferroni-Holm adjustment was applied for 24 multiple comparisons.

Supplemental Tables

Table S1. Prior Anticancer Therapies

Prior Treatments	Duvelisib (N=160)	Ofatumumab (N=159)
Median prior anticancer therapies (range)	2 (1-10)	2 (1-8)
Patients receiving ≥ 3 prior therapies, n (%)	50 (31.3)	55 (34.6)
Purine Analog, n (%)	96 (60.0)	113 (71.1)
Alkylator, n (%)	148 (92.5)	151 (95.0)
Chlorambucil	62 (38.8)	51 (32.1)
Bendamustine	59 (36.9)	61 (38.4)
Cyclophosphamide	95 (59.4)	111 (69.8)
Monoclonal antibody (CD20), n (%)	125 (78.1)	132 (83.0)
Ofatumumab	3 (1.9)	4 (2.5)
Rituximab	123 (76.9)	131 (82.4)
Obinutuzumab	1 (0.6)	3 (1.9)
Alemtuzumab, n (%)	12 (7.5)	4 (2.5)

Table S2. Overall Response Rate by Blinded IRC Assessment

Best Overall Response	Duvelisib (N=160) n (%)	Ofatumumab (N=159) n (%)	P-value[a]
Overall Response Rate (ORR) (CR, CRi, PR, or PRwL)	118 (73.8)	72 (45.3)	< 0.0001
95% Confidence Interval	(66.9, 80.6)	(37.5, 53.0)	
Odds Ratio (95% Confidence Interval)	3.50 (2.16, 5.65)		
ORR without PRwL (CR, CRi, or PR)	117 (73.1)	72 (45.3)	< 0.0001
95% Confidence Interval	(66.3, 80.0)	(37.5, 53.0)	
Odds Ratio (95% Confidence Interval)	3.37 (2.09, 5.43)		
CR	1 (0.6)	1 (0.6)	
CRi[b]	0	0	
PR	116 (72.5)	71 (44.7)	
PRwL	1 (0.6)	0	
SD	34 (21.3)	63 (39.6)	
PD	2 (1.3)	10 (6.3)	
Other[c]	6 (3.8)	14 (8.8)	

Abbreviations: CR = complete response; CRi = complete response with incomplete marrow recovery; IRC = Independent Review Committee; ORR = overall response rate; PD = progressive disease; PR = partial response; PRwL = partial response with lymphocytosis; SD = stable disease.

Note: Percentages are based on the number of intent-to-treat patients in each treatment group. The overall response is determined using the best overall response from the blinded IRC.

[a] One-sided stratified Cochran-Mantel-Haenszel test to compare duvelisib 25 mg BID versus ofatumumab using randomization strata, as randomized.

[b] CRi applies to patients with a diagnosis of CLL only.

[c] Other includes responses of Unknown due to missing, incomplete, or inadequate data; No Evidence of Disease if radiological and clinical data indicate no disease involvement; and Not Evaluable if no target lesions were identified at Baseline and the radiological and clinical data at post-Baseline does not support the disease response of PD or Unknown.

Table S3. Serious Adverse Events in ≥ 2% of Patients

Serious Adverse Events	Duvelisib (n=158)	Ofatumumab (n=155)
	n (%)	n (%)
Any SAE	115 (73)	50 (32)
Hematologic SAEs		
Febrile neutropenia	10 (6)	3 (2)
Nonhematologic SAEs		
Pneumonia	23 (15)	5 (3)
Colitis	19 (12.0)	1 (1)
Diarrhoea	16 (10)	1 (1)
Pyrexia	7 (4)	1 (1)
Pneumonitis	6 (4)	0
Bronchitis	5 (3)	1 (1)
General physical health deterioration	4 (3)	0
Renal failure acute	4 (3)	2 (1)
Gastroenteritis	4 (3)	1 (1)
Toxic skin eruption	4 (3)	0
Bronchopulmonary aspergillosis	3 (2)	0
Pneumocystis jirovecii pneumonia	3 (2)	0
Pneumonia pseudomonas aeruginosa	3 (2)	0
Sepsis	3 (2)	1 (1)
Upper respiratory tract infection	3 (2)	0
Pulmonary embolism	3 (2)	2 (1)
Infusion related reaction	0	3 (2)

Abbreviations: SAE = serious adverse event.

Table S4. All Adverse Events Leading to Deaths

Deaths	Duvelisib (n=158)	Ofatumumab (n=155)
	n (%)	n (%)
Any AE leading to death	19 (12)[a]	7 (5)
Bronchopulmonary aspergillosis	2 (1)	0
Haemorrhagic stroke	2 (1)	0
Pneumonia staphylococcal	2 (1)	0
Bronchitis	1 (1)	0
Cardiac failure	1 (1)	0
Chronic obstructive pulmonary disease	1 (1)	0
Death	1 (1)	0
Enterococcal sepsis	1 (1)	0
Escherichia sepsis	1 (1)	0
General physical health deterioration	1 (1)	0
Mental impairment	1 (1)	0
Multi-organ failure	1 (1)	0
Pneumonia bacterial	1 (1)	0
Pneumonia pseudomonas aeruginosa	1 (1)	0
Pseudomonal sepsis	1 (1)	0
Sepsis	1 (1)	0
Septic shock	1 (1)	0
Sudden death	1 (1)	0
Disease progression	0	2 (1)
Hepatic failure	0	1 (1)
Fall	0	1 (1)
Glioblastoma multiforme	0	1 (1)
Squamous cell carcinoma	0	1 (1)
Renal failure acute	0	1 (1)

Abbreviations: AE = adverse event

[a] Two patients were reported as having 2 AEs leading to death

Supplemental Figures

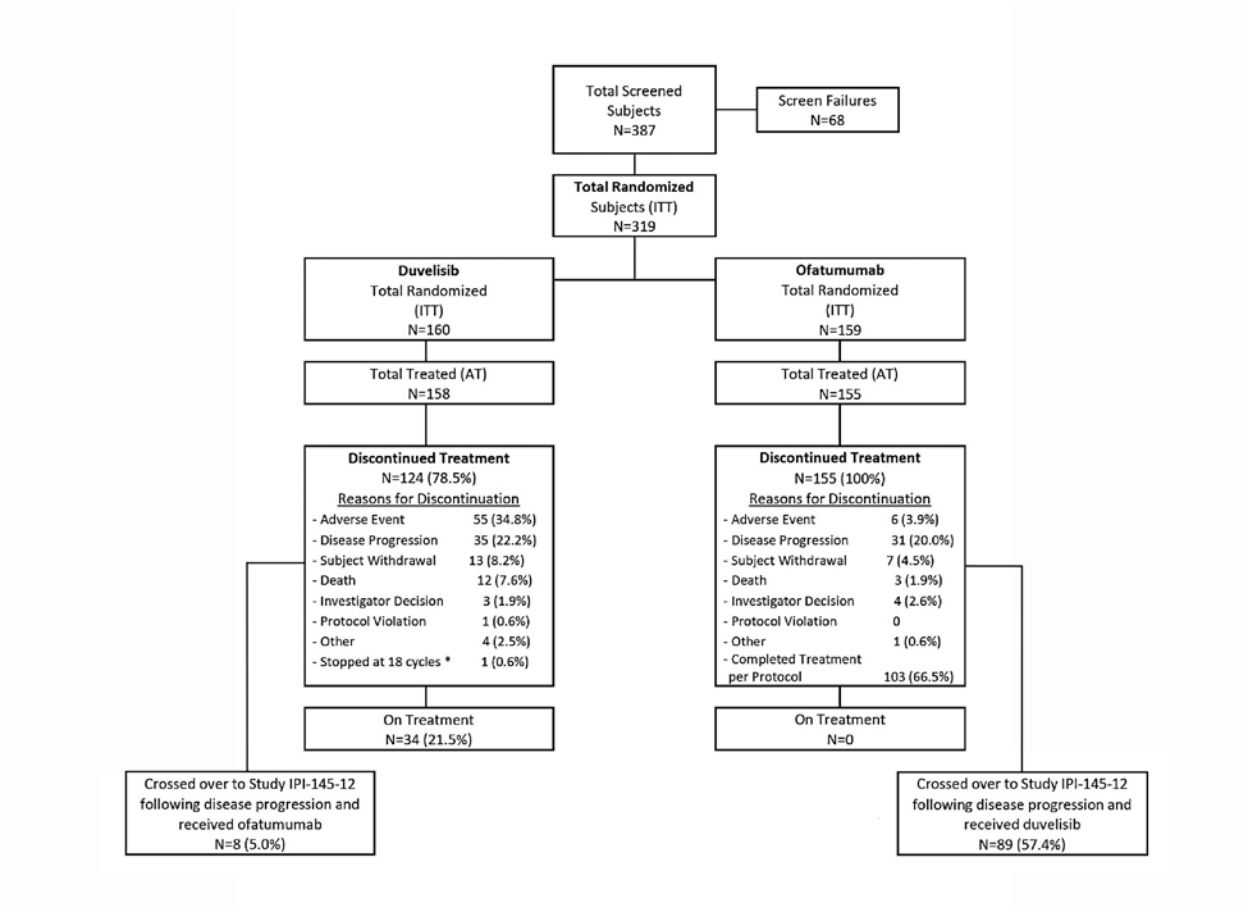

Figure S1. Disposition of DUO study patients. At the time of the data cut, 34 patients remained on duvelisib and no patients remained on ofatumumab. Eight patients on the duvelisib arm who had disease progression voluntarily crossed over to receive ofatumumab on separate extension study IPI-145-12, and 89 patients who had disease progression on the ofatumumab arm opted to crossover to receive duvelisib in the extension study.

*Patients who had achieved a sustained response (> 3 months) at 18 months were allowed to discontinue treatment, as per study protocol. Abbreviations: AT = all-treated; ITT = intent-to-treat.

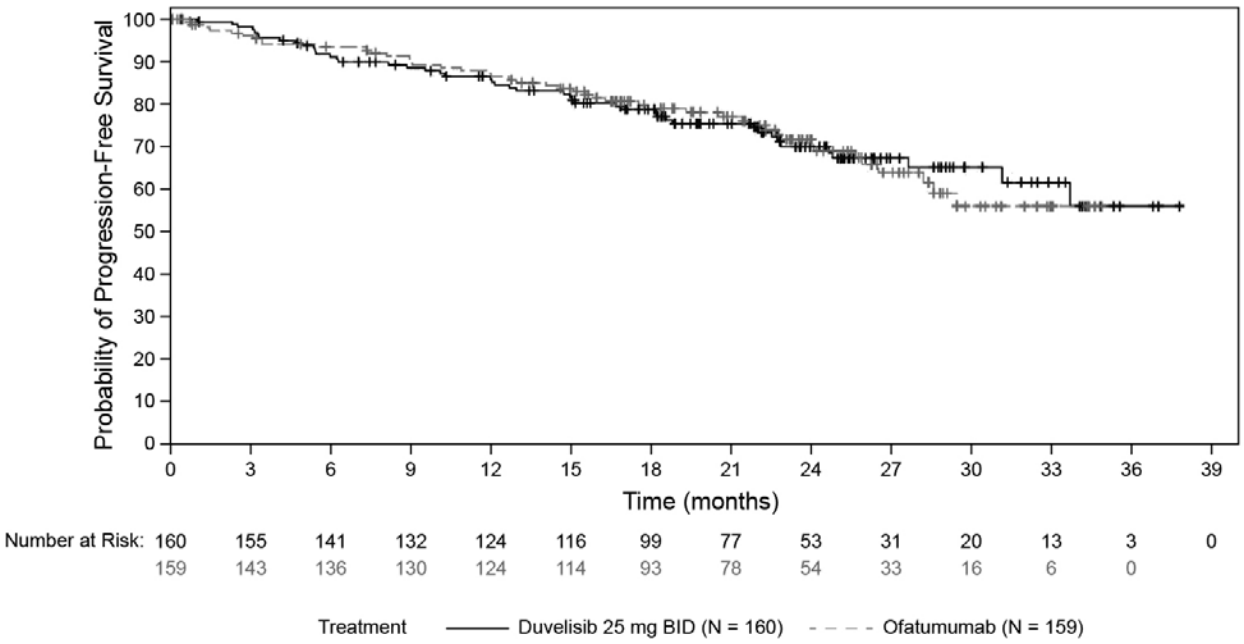

Figure S2. Kaplan-Meier plot of overall survival in the total CLL/SLL population receiving duvelisib or ofatumumab monotherapy. OS was not statistically different with either treatment. The estimated probability of survival at 12 months was 86% for both duvelisib and ofatumumab-treated patients. Median OS was not evaluable in either study arm. Abbreviations: BID = twice daily; CLL = chronic lymphocytic leukemia; OS = overall survival; SLL = small lymphatic lymphoma.

Supplemental References

1. Flinn IW, O'Brien S, Kahl B, et al. Duvelisib, a novel oral dual inhibitor of PI3K-delta,gamma, is clinically active in advanced hematologic malignancies. *Blood*. 2018;131(8):877-887.