

Supplementary Table 1: Key Diagnostic information and prior treatment lines

Key diagnostic Information (15/3/2017)	<ul style="list-style-type: none"> • Baseline full blood count: Hb 137 g/L, WCC 46 x 10⁹/L, Lymphocyte count 43 x 10⁹/L, Platelets 147 x 10⁹/L • Morphology: small to medium size lymphocytes with intensely basophilic cytoplasm, nucleoli and characteristic cytoplasmic blebbing • Immunophenotyping: dominant CD8 positive lymphocytic population positive for: CD2, CD3, CD5, CD7 (strong), TCR alpha/beta. Negative for CD19, CD4, CD25, CD57, CD56, TCR gamma/delta. • Cytogenetics analysis by fluorescent <i>in situ</i> hybridization: T-cell receptor alpha/delta (<i>TRA/TRD</i>) (chromosome 14q11.2) rearrangement in 57/100 cells; <i>ATM</i> (chromosome 11q22.3) deletion in 189/200 cells) 									
Chemotherapy regimen	Dose	Frequency	Start date	End date	Duration (days)	Total cycles	Initial FBC (10 ⁹ /L)	Best response FBC (10 ⁹ /L)	Best ORR	Toxicities (Grade 3+)
Alemtuzumab IV	30 mg	three times a week	26/07/2017	10/10/2017	76	11	Hb 125 g/L WCC 64 Lymph 51 Plt 21	Hb 86 g/L WCC 89 Lymph 86 Plt 19	refractory disease	N/A
Alemtuzumab IV	30 mg	five times a week	11/10/2017	17/11/2017	37	5	Hb 106 g/L WCC 99 Lymph 95 Plt 50	Hb 87 g/L WCC 81 Lymph 78 Plt 21	refractory disease	N/A
Pentostatin*	4 mg/m ²	every 14 days	24/11/2017	16/02/2018	84	6	Hb 99 g/L WCC 86 Lymph 8 Plt 46	Hb 105 g/L WCC 71 Lymph 68 Plt 73	refractory disease	N/A
Fludarabine Mitoxantrone Dexamethasone	25 mg/m ² 12 mg/m ² 20 mg	day 1-3 every 4 weeks day 1 every 4 weeks day 1-5 every 4 weeks	24/03/2018	09/05/2018	46	2	Hb 88 g/L WCC 81 Lymph 80 Plt 9	Hb 78 g/L WCC 53 Lymph 49 Plt 12	refractory disease	febrile neutropenia-grade 3
Venetoclax	20 mg escalated to 800 mg	Daily	10/05/2018	28/08/2018	111	N/A	Hb 69 g/L WCC 60 Lymph 61 Plt 6	Hb 87 g/L WCC 22 Lymph 21 Plt 3	Minor WCC response in peripheral blood Refractory disease otherwise	Grade 2 diarrhea and Grade 4 neutropenia at 800 mg od

Abbreviations: FBC full blood count; Hb: haemoglobin, WCC: white cell count; Plt: platelet count; Lymph: lymphocyte count; ORR: overall response rate; IV: intravenous; mg: milligrams

Supplementary Table 2: Full blood count during venetoclax dose escalation phase

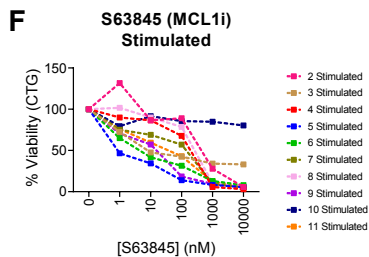
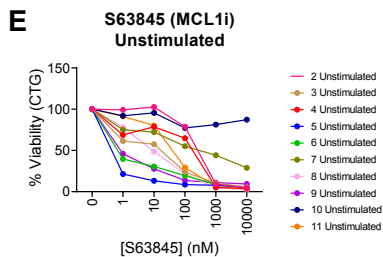
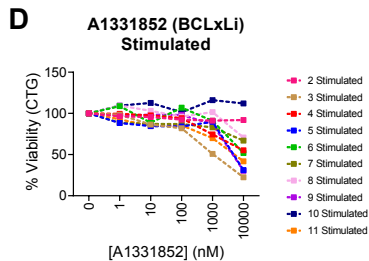
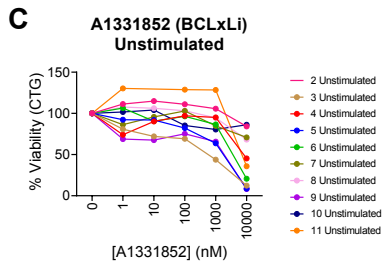
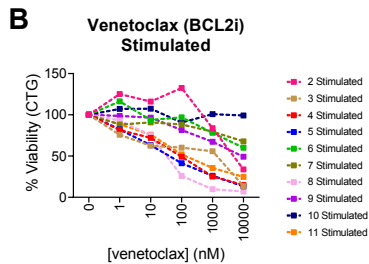
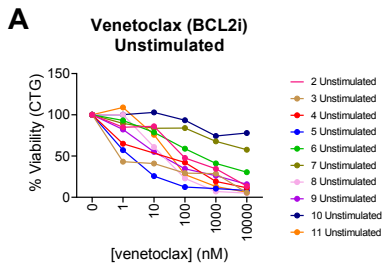
Venetoclax Dose	Day	Hemoglobin (g/L)	White cell count (WCC) (10⁹/L)	Platelet count (10⁹/L)
20 mg o.d.	1	69	61.36	6
50 mg o.d.	5	76	122.22	7
100 mg o.d.	8	84	147.67	7
200 mg o.d.	12	88	117.81	6
400 mg o.d.	15	95	99.16	6
600 mg o.d.	20	81	97.07	5
800 mg o.d.	29	89	45.38	4
800 mg o.d.	39 (WCC nadir)	87	22.47	3

Supplementary Figure 1. In Vitro sensitivity to BH3 mimetics in T-PLL patient samples.

PBMCs isolated from 10 T-PLL patients were incubated with different concentrations of venetoclax (A,B) , S63845 (C,D) or A1331852 (E,F) with and without stimulation by IL-2, IL-4 and CD40L for 24h before analysis of cell viability using CellTiterGlo. Experiments were performed in triplicate and data shown are mean. (G) Calculated EC50 for each sample.

Supplementary Figure 2. Synergistic interaction between BCL2 and MCL1 inhibition in unstimulated samples.

(A-J) Cells isolated from 10 T-PLL patients were treated with different concentrations of venetoclax and S63845 in combination without cytokine stimulation for 24h before analysis of cell viability using CellTiterGlo. Experiments were performed in triplicate and data shown are mean. Combination index (CI) values < 1 indicate synergy.



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	EC50 (nM)					
	venetoclax		A1331852		S63845	
	Unstimulated	Stimulated	Unstimulated	Stimulated	Unstimulated	Stimulated
2	159.50	5540.00	>10,000	13.42	231.80	475.80
3	<1	232.60	2874.00	1323.00	7.53	32.97
4	13.20	83.91	7204.00	981.70	87.71	163.70
5	1.47	47.69	>10,000	>10,000	<1	0.79
6	453.90	>10,000	>10,000	1504.00	<1	5.44
7	45030.00	>10,000	1037.00	>10,000	286.60	54.73
8	21.09	33.58	3660.00	>10,000	9.31	238.60
9	28.87	7979.00	1581.00	3044.00	<1	9.72
10	>10,000	>10,000	64.65	>10,000	>10,000	>10,000
11	39.18	206.80	>10,000	>10,000	40.56	25.41

