

Supplementary materials

BMI1-Inhibitor PTC596 in Combination with MCL1 Inhibitor S63845 or MEK Inhibitor Trametinib in the Treatment of Acute Leukemia

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A)

Drug	Dose	Effect
PTC596 [nM]	100	0.95
	200	0.85
	400	0.68
APR246 [nM]	10	0.98
	20	0.96
S63845 [nM]	25	0.71
	50	0.59
Trametinib [nM]	10	0.97
	100	0.93
PKC412 [nM]	50	0.78
	100	0.73
HDM201 [nM]	50	0.87
	100	0.78
CI [nM]	50	0.71
	100	0.55

B)

CI Data for Non-Constant Combo:
PTC596+APR246

Dose P	Dose A	Effect	CI
100	10	0.85	0.96
200	10	0.72	0.95
400	10	0.5	0.91
100	20	0.7	0.99
200	20	0.62	1.08
400	20	0.45	1.07

CI Data for Non-Constant Combo:
PTC596+PKC412

Dose P	Dose PKC	Effect	CI
100	50	0.66	0.45
200	50	0.53	0.39
400	50	0.39	0.49
100	100	0.58	0.37
200	100	0.5	0.39
400	100	0.3	0.38

CI Data for Non-Constant Combo:
PTC596+S63845

Dose P	Dose S	Effect	CI
100	25	0.51	0.41
200	25	0.44	0.43
400	25	0.38	0.57
100	50	0.42	0.42
200	50	0.35	0.39
400	50	0.32	0.54

CI Data for Non-Constant Combo:
PTC596+HDM201

Dose P	Dose HDM	Effect	CI
100	50	0.78	0.85
200	50	0.67	0.77
400	50	0.49	0.74
100	100	0.7	0.90
200	100	0.63	0.89

CI Data for Non-Constant Combo:
PTC596+Trametinib

Dose P	Dose T	Effect	CI
100	10	0.72	0.29
200	10	0.6	0.41
400	10	0.42	0.51
100	100	0.68	0.26
200	100	0.55	0.36
400	100	0.4	0.49

CI Data for Non-Constant Combo:
PTC596+CI

Dose PTC	Dose CI	Effect	CI
100	50	0.65	1.01
200	50	0.62	1.11
400	50	0.58	1.34
100	100	0.58	1.33
200	100	0.56	1.41
400	100	0.52	1.54

Figure S1. Combination index (CI) MOLM-13. (A) Input of dose-effect values of cell viability in MOLM-13 cells treated with PTC596 and other targeted compounds or conventional induction therapy (CI, nM) and (B) output of combination index values as calculated on CompuSyn software.

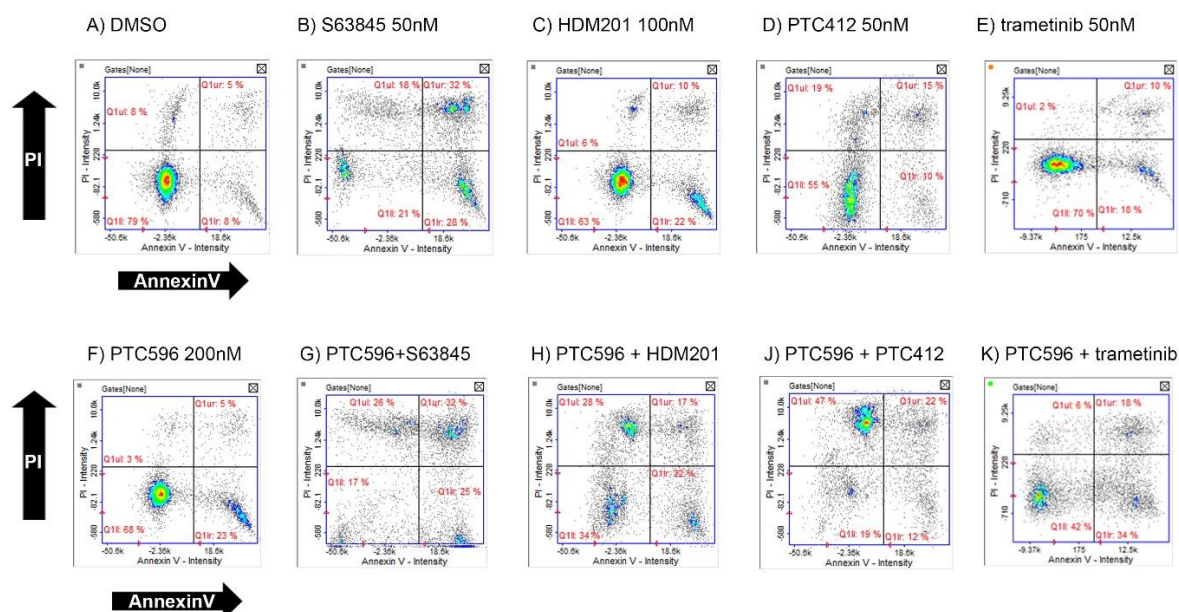


Figure S2. Imaging cytometry in MOLM-13 cells treated for 20 hrs with targeted compounds alone A) mock-treated, B) S63845, C) HDM201, D) PTC412, E) trametinib, F) PTC596, G) PTC596 and in combination G) PTC596 and S62834, H) PTC596 and HDM201, J) PTC596 and PTC412, K) PTC596 and trametinib, showing induction of apoptosis and cell death using annexinV and PI staining.

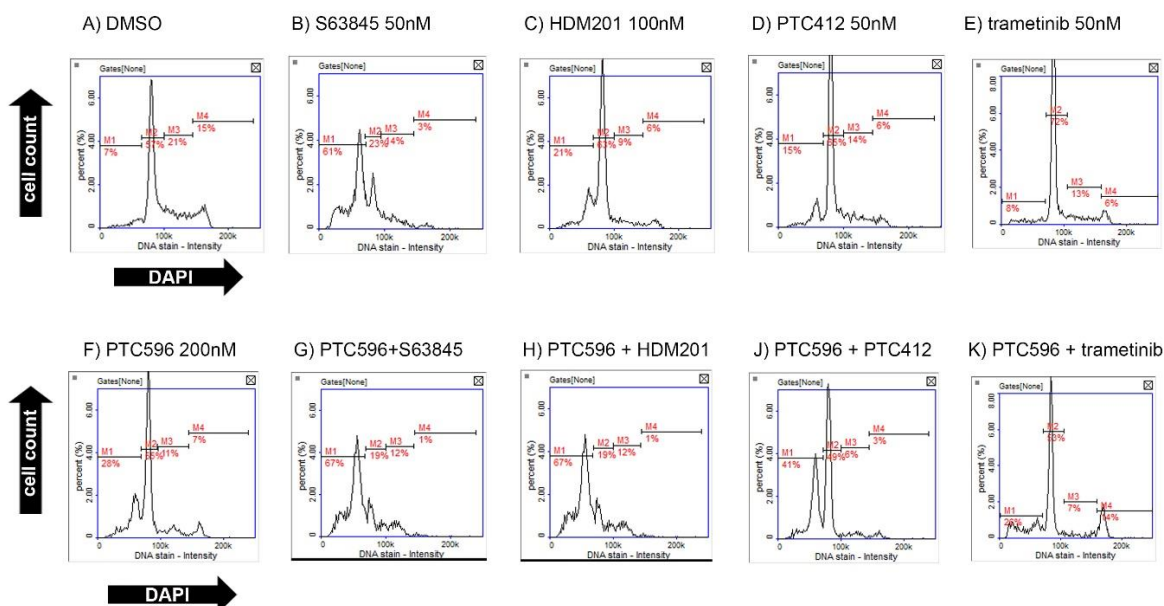


Figure S3. Imaging cytometry in MOLM-13 cells treated for 20 hrs with targeted compounds alone A) mock-treated, B) S63845, C) HDM201, D) PTC412, E) trametinib, F) PTC596, G) PTC596 and in combination G) PTC596 and S62834, H) PTC596 and HDM201, J) PTC596 and PTC412, K) PTC596 and trametinib, showing induction of cell cycle arrest and cell death (subG1 fraction) using DAPI staining.