

Identification of Clinically Achievable Combination Therapies in Childhood Rhabdomyosarcoma – Supplementary Figures

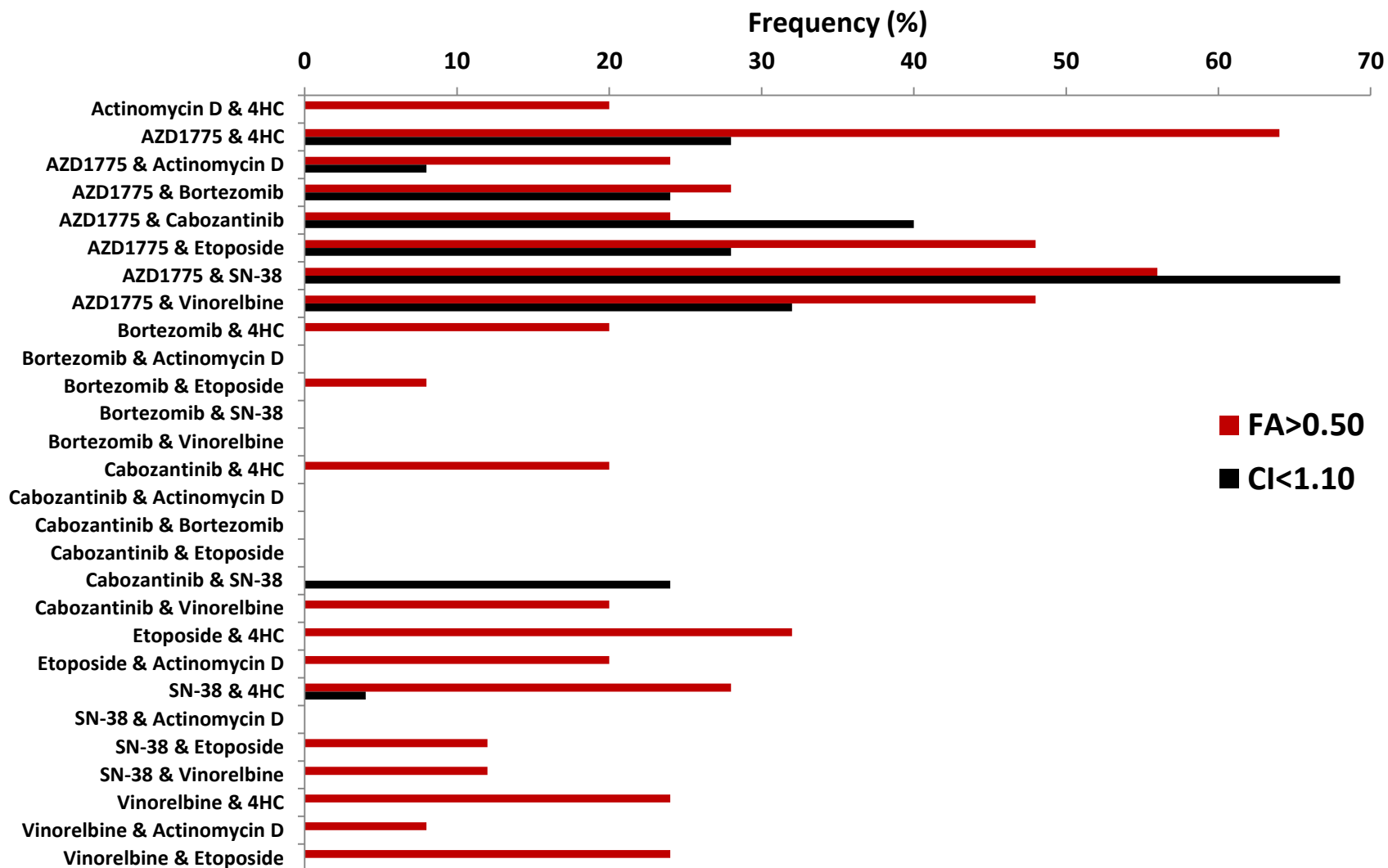
Elliot Kahen^{1*}, Diana Yu^{1*}, Douglas Harrison², Justine Clark¹, Pooja Hingorani³, Christopher Cubitt^{1,3} and Damon Reed^{1,4,5,6}

*equal contribution

¹Sunshine Project and Translational Research Lab, ⁴Chemical Biology and Molecular Medicine Program, ⁵Sarcoma Department, ⁶Adolescent and Young Adult Program; H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida; ²Division of Pediatrics, MD Anderson Cancer Center, Houston, TX; ³Center for Cancer and Blood Disorders, Phoenix Children's Hospital, Phoenix, Arizona

Corresponding author: damon.reed@moffitt.org

Supplemental Fig 2: Frequency graph showing all two-drug combinations that demonstrated FA>0.50 and CI<1.10



Agents	Mechanism		Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average		Agents	Mechanism		Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average			
	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI	FA	CI		Tx1	Tx2	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI	FA	CI
Actinomycin D	4HC	Alky/ator	Alky/ator	2	5000	0.893	3.94	0.999	0.10	0.999	0.95	0.998	1.02	1.00 ± 0.05	0.69 ± 1.68	AZD1775	4HC	Wee I	Alky/ator	500	5000	0.996	1.07	1.000	0.03	1.000	0.69	1.000	5.00	1.00 ± 0.00	1.91 ± 2.24
				2500	0.650	5.00	0.998	0.07	0.381	3.00	0.452	4.93	0.61 ± 0.28	2.67 ± 2.31	2500					0.934	1.37	1.000	0.03	0.996	0.60	0.996	0.78	1.00 ± 0.03	0.47 ± 0.55		
				1250	0.614	5.00	0.491	5.00	0.212	5.00	0.359	5.00	0.35 ± 0.17	5.00 ± 0.00	1250					0.891	1.14	0.830	1.11	0.905	0.78	0.978	0.91	0.90 ± 0.06	0.93 ± 0.17		
				625	0.622	5.00	0.450	5.00	0.229	5.00	0.327	5.00	0.34 ± 0.17	5.00 ± 0.00	625					0.867	0.99	0.815	0.86	0.883	0.59	0.978	0.73	0.89 ± 0.07	0.73 ± 0.17		
				313	0.642	5.00	0.417	5.00	0.178	5.00	0.314	5.00	0.30 ± 0.20	5.00 ± 0.00	313					0.862	0.87	0.833	0.64	0.853	0.55	0.981	0.61	0.89 ± 0.07	0.60 ± 0.14		
				1	5000	0.836	4.22	0.999	0.09	0.999	0.96	0.998	1.01	1.00 ± 0.08	0.69 ± 1.82					1	5000	0.996	1.06	1.000	0.02	1.000	0.63	1.000	0.61	1.00 ± 0.00	0.42 ± 0.43
		2500	0.596	5.00	0.998	0.07	0.501	1.73	0.364	3.66	0.62 ± 0.27	1.82 ± 2.16	2500	0.879	1.46		1.000	0.02	0.973	0.85	0.964	1.12	0.98 ± 0.05	0.66 ± 0.62							
		1250	0.552	5.00	0.429	5.00	0.202	4.17	0.193	4.78	0.27 ± 0.18	4.63 ± 0.39	1250	0.823	1.09		0.763	1.15	0.796	0.84	0.866	1.25	0.81 ± 0.04	1.08 ± 0.18							
		625	0.556	5.00	0.315	5.00	0.173	5.00	0.201	4.24	0.23 ± 0.17	4.75 ± 0.38	625	0.811	0.80		0.742	0.81	0.689	0.72	0.845	1.09	0.76 ± 0.07	0.87 ± 0.16							
		313	0.573	5.00	0.298	5.00	0.166	5.00	0.169	4.61	0.21 ± 0.19	4.87 ± 0.20	313	0.798	0.68		0.715	0.65	0.654	0.62	0.847	0.97	0.74 ± 0.09	0.74 ± 0.16							
		0.5	5000	0.796	3.90	0.999	0.10	0.999	0.95	0.998	0.98	1.00 ± 0.10	0.68 ± 1.66	0.5	5000		0.993	1.20	1.000	0.04	1.000	0.40	1.000	0.58	1.00 ± 0.00	0.34 ± 0.49					
		2500	0.489	5.00	0.997	0.08	0.534	1.50	0.214	3.38	0.58 ± 0.33	1.95 ± 2.15	2500	0.737	1.75		0.985	2.20	0.888	1.09	0.841	1.40	0.91 ± 0.10	0.90 ± 0.66							
	1250	0.443	5.00	0.402	5.00	0.129	5.00	0.069	5.00	0.20 ± 0.19	5.00 ± 0.00	1250	0.716	1.08	0.700	1.21	0.534	1.01	0.482	1.72	0.57 ± 0.12	1.31 ± 0.32									
	625	0.380	5.00	0.280	5.00	0.002	5.00	0.078	4.31	0.12 ± 0.18	4.77 ± 0.35	625	0.645	0.85	0.647	0.84	0.361	0.93	0.528	1.29	0.51 ± 0.13	1.02 ± 0.21									
	313	0.404	5.00	0.247	5.00	0.013	5.00	0.054	5.00	0.10 ± 0.18	5.00 ± 0.00	313	0.599	0.74	0.564	0.71	0.267	0.95	0.545	1.10	0.46 ± 0.15	0.92 ± 0.19									
	0.25	5000	0.726	3.98	0.998	0.11	0.999	0.95	0.996	1.05	1.00 ± 0.14	0.70 ± 1.69	0.25	5000	0.986	1.38	0.990	0.37	1.000	0.61	1.000	5.00	1.00 ± 0.01	1.99 ± 2.15							
	2500	0.426	5.00	0.998	0.06	0.329	1.84	0.145	2.89	0.49 ± 0.37	1.60 ± 2.06	2500	0.654	1.77	1.000	0.03	0.639	1.40	0.801	1.26	0.81 ± 0.17	0.90 ± 0.76									
	1250	0.291	5.00	0.398	3.83	0.072	5.00	0.033	4.45	0.17 ± 0.17	4.43 ± 0.56	1250	0.602	1.08	0.662	1.24	0.384	1.01	0.279	1.59	0.44 ± 0.18	1.28 ± 0.26									
	625	0.203	5.00	0.245	5.00	-0.017	5.00	0.042	3.41	0.09 ± 0.13	4.47 ± 0.79	625	0.423	0.94	0.545	0.94	0.094	1.42	0.334	1.10	0.32 ± 0.19	1.15 ± 0.23									
	313	0.229	5.00	0.170	5.00	-0.051	5.00	0.023	4.66	0.05 ± 0.13	4.89 ± 0.17	313	0.287	0.99	0.413	0.81	0.049	1.79	0.283	1.04	0.25 ± 0.15	1.21 ± 0.43									
	0.125	5000	0.697	3.64	0.999	0.10	0.998	1.00	0.998	0.96	1.00 ± 0.15	0.69 ± 1.53	0.125	5000	0.980	1.51	1.000	0.01	1.000	0.60	1.000	5.00	1.00 ± 0.01	1.87 ± 2.23							
	2500	0.379	5.00	0.997	0.08	0.495	1.45	0.101	2.57	0.53 ± 0.37	1.37 ± 2.08	2500	0.623	1.72	0.990	0.18	0.941	0.91	0.734	1.22	0.89 ± 0.17	0.77 ± 0.64									
	1250	0.211	5.00	0.406	2.93	0.011	5.00	0.019	3.62	0.15 ± 0.19	3.85 ± 1.04	1250	0.476	1.10	0.601	1.39	0.423	0.85	0.181	1.38	0.40 ± 0.18	1.21 ± 0.26									
	625	0.146	5.00	0.237	5.00	-0.001	5.00	0.054	1.72	0.10 ± 0.10	3.91 ± 1.64	625	0.264	0.95	0.505	0.95	0.114	0.88	0.172	1.00	0.26 ± 0.17	0.94 ± 0.05									
313	0.162	5.00	0.110	5.00	-0.027	5.00	-0.001	5.00	0.03 ± 0.09	5.00 ± 0.00	313	0.149	1.01	0.380	0.74	0.057	0.95	0.115	0.99	0.18 ± 0.14	0.89 ± 0.12										
Actinomycin D	AZD1775	Wee I	Alky/ator	2	0.861	3.38	0.749	1.04	0.788	0.64	0.960	1.22	0.83 ± 0.09	0.97 ± 1.23	AZD1775	Bortezomib	Wee I	Proteasome	500	10	0.861	1.07	0.723	1.33	0.721	1.27	0.973	0.88	0.81 ± 0.12	1.16 ± 0.21	
				0.5	0.836	2.58	0.747	0.89	0.737	0.75	0.970	0.85	0.82 ± 0.11	0.83 ± 0.88					0.5	6.67	0.873	0.90	0.753	1.04	0.783	0.90	0.983	0.63	0.84 ± 0.10	0.86 ± 0.17	
				1	0.854	1.47	0.776	0.70	0.727	0.75	0.977	0.65	0.83 ± 0.11	0.70 ± 0.39					1	4.45	0.872	0.83	0.771	0.87	0.818	0.70	0.988	0.49	0.86 ± 0.09	0.69 ± 0.17	
				0.25	0.863	1.04	0.811	0.56	0.785	0.58	0.983	0.53	0.86 ± 0.09	0.56 ± 0.24					0.25	2.97	0.871	0.78	0.755	0.85	0.826	0.61	0.988	0.47	0.86 ± 0.10	0.64 ± 0.17	
				0.125	0.863	0.88	0.752	0.73	0.820	0.49	0.983	0.50	0.85 ± 0.10	0.58 ± 0.19					0.125	1.98	0.874	0.74	0.786	0.71	0.815	0.59	0.989	0.42	0.86 ± 0.09	0.57 ± 0.14	
				250	2	0.689	5.00	0.517	4.69	0.571	0.99	0.496	5.00	0.53 ± 0.09					3.56 ± 1.96	250	10	0.783	0.93	0.481	1.65	0.496	1.45	0.882	1.15	0.62 ± 0.20	1.42 ± 0.32
		1	0.642	5.00	0.493	3.32	0.510	1.01	0.359	5.00	0.45 ± 0.12	3.11 ± 1.89	1	6.67		0.776	0.82	0.481	1.40	0.530	1.12	0.893	0.95	0.63 ± 0.20	1.16 ± 0.25						
		0.5	0.518	5.00	0.324	5.00	0.277	2.26	0.233	5.00	0.28 ± 0.13	4.09 ± 1.37	0.5	4.45		0.794	0.69	0.530	1.08	0.569	0.89	0.900	0.83	0.67 ± 0.18	0.93 ± 0.16						
		0.25	0.357	5.00	0.390	2.91	0.232	2.31	0.183	5.00	0.27 ± 0.10	3.41 ± 1.40	0.25	2.97		0.798	0.62	0.445	1.23	0.601	0.73	0.912	0.72	0.65 ± 0.21	0.89 ± 0.27						
		0.125	0.313	5.00	0.541	0.93	0.245	1.88	0.148	5.00	0.31 ± 0.17	2.60 ± 1.11	0.125	1.98		0.793	0.60	0.558	0.83	0.549	0.76	0.918	0.66	0.67 ± 0.18	0.75 ± 0.10						
		125	2	0.638	5.00	0.356	5.00	0.509	0.97	0.535	3.92	0.47 ± 0.12	3.30 ± 1.91	125		10	0.441	1.41	0.459	1.26	0.228	1.88	0.507	1.86	0.40 ± 0.12	1.67 ± 0.31					
		1	0.582	5.00	0.250	5.00	0.457	0.85	0.494	2.70	0.40 ± 0.14	2.85 ± 2.01	1	6.67		0.484	1.11	0.219	1.89	0.185	1.78	0.517	1.56	0.31 ± 0.17	1.74 ± 0.35						
	0.5	0.470	5.00	0.228	5.00	0.248	1.86	0.537	1.70	0.34 ± 0.16	2.85 ± 1.86	0.5	4.45	0.515	0.92	0.186	1.85	0.210	1.40	0.546	1.30	0.31 ± 0.19	1.52 ± 0.38								
	0.25	0.476	5.00	0.213	5.00	0.244	1.36	0.527	1.36	0.33 ± 0.16	2.57 ± 2.10	0.25	2.97	0.501	0.82	0.157	1.63	0.209	1.25	0.577	1.11	0.33 ± 0.20	1.33 ± 0.32								
	0.125	0.485	3.20	0.262	4.65	0.274	0.93	0.515	1.21	0.35 ± 0.13	2.26 ± 1.75	0.125	1.98	0.506	0.81	0.092	2.75	0.235	1.04	0.595	1.00	0.31 ± 0.23	1.60 ± 0.90								
	62.5	2	0.695	5.00	0.511	4.34	0.561	0.58	0.520	3.56	0.53 ± 0.09	2.83 ± 1.95	62.5	10	0.159	2.04	0.246	1.59	0.005	5.00	0.164	2.69	0.14 ± 0.10	3.09 ± 1.52							
	1	0.627	5.00	0.418	5.00	0.512	0.48	0.372	2.93	0.43 ± 0.11	2.80 ± 2.15	1	6.67	0.158	1.79	0.094	2.29	0.007	5.00	0.148	2.33	0.08 ± 0.07	3.21 ± 1.45								
	0.5	0.505	5.00	0.327	5.00	0.324	0.87	0.251	2.54	0.30 ± 0.11	2.80 ± 2.02	0.5	4.45	0.174	1.50	0.048	3.03	0.003	5.00	0.161	1.91	0.07 ± 0.08	3.31 ± 1.57								
	0.25	0.365	5.00	0.289	5.00	0.286	0.73	0.187	2.16	0.25 ± 0.07	2.63 ± 2.13	0.25	2.97	0.139	1.67	0.038	3.17	0.010	5.00	0.160	1.69	0.07 ± 0.07	3.29 ± 1.58								
	0.125	0.284	5.00	0.502	0.49	0.268	0.59																								

Agents	Mechanism		Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average		Agents	Mechanism		Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average	
	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI	FA	CI		Tx1	Tx2	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI
AZD1775	SN-38	Wee1	Topo I	5	0.916	0.55	0.920	0.29	0.935	0.37	0.990	0.38	0.95 ± 0.03	0.35 ± 0.11	AZD1775	Vinorelbine	Wee1	Microtubule	4	0.911	1.18	0.920	1.04	0.829	0.47	0.994	0.30	0.91 ± 0.07	0.61 ± 0.43
				2	0.893	0.63	0.910	0.30	0.880	0.51	0.987	0.44	0.93 ± 0.05	0.42 ± 0.14					2	0.894	0.99	0.883	0.93	0.815	0.51	0.992	0.35	0.90 ± 0.07	0.60 ± 0.31
				1.25	0.871	0.72	0.886	0.36	0.858	0.50	0.987	0.43	0.91 ± 0.06	0.43 ± 0.15					1	0.880	0.88	0.867	0.73	0.795	0.55	0.991	0.36	0.88 ± 0.08	0.55 ± 0.22
				0.625	0.867	0.72	0.867	0.40	0.837	0.51	0.989	0.39	0.90 ± 0.07	0.43 ± 0.15					0.5	0.862	0.86	0.858	0.60	0.790	0.56	0.988	0.42	0.88 ± 0.08	0.53 ± 0.19
				0.313	0.862	0.73	0.839	0.48	0.827	0.50	0.986	0.44	0.88 ± 0.07	0.47 ± 0.13					0.25	0.852	0.85	0.833	0.59	0.776	0.60	0.988	0.41	0.87 ± 0.09	0.53 ± 0.18
				5	0.869	0.48	0.841	0.30	0.836	0.68	0.931	0.62	0.87 ± 0.04	0.53 ± 0.17					4	0.890	1.15	0.880	1.37	0.802	0.28	0.988	0.26	0.89 ± 0.08	0.63 ± 0.58
	2.5	0.838	0.51	0.792	0.35	0.783	0.61	0.912	0.66	0.83 ± 0.06	0.54 ± 0.14	2	0.869	0.87		0.880	0.78	0.786	0.29	0.988	0.23	0.88 ± 0.08	0.43 ± 0.33						
	1.25	0.820	0.52	0.757	0.38	0.720	0.59	0.903	0.67	0.79 ± 0.08	0.55 ± 0.12	1	0.841	0.73		0.831	0.68	0.747	0.34	0.984	0.26	0.85 ± 0.10	0.42 ± 0.24						
	0.625	0.807	0.52	0.754	0.37	0.663	0.59	0.903	0.66	0.77 ± 0.10	0.54 ± 0.12	0.5	0.832	0.61		0.790	0.58	0.734	0.35	0.978	0.30	0.83 ± 0.10	0.41 ± 0.16						
	0.313	0.800	0.52	0.633	0.57	0.626	0.59	0.908	0.63	0.72 ± 0.14	0.59 ± 0.04	0.25	0.827	0.53		0.793	0.44	0.738	0.35	0.980	0.27	0.84 ± 0.10	0.35 ± 0.11						
	5	0.799	0.52	0.718	0.36	0.773	0.83	0.693	1.05	0.73 ± 0.05	0.75 ± 0.31	4	0.847	1.44		0.896	1.10	0.582	0.36	0.934	0.57	0.80 ± 0.16	0.68 ± 0.49						
	2.5	0.778	0.44	0.637	0.39	0.695	0.71	0.571	1.18	0.63 ± 0.09	0.76 ± 0.36	2	0.688	1.95		0.791	1.25	0.367	0.76	0.802	1.03	0.65 ± 0.20	0.51 ± 0.51						
1.25	0.741	0.43	0.629	0.34	0.561	0.75	0.537	1.12	0.58 ± 0.09	0.74 ± 0.35	1	0.526	2.20	0.469	2.62	0.203	1.57	0.611	1.51	0.43 ± 0.18	1.90 ± 0.53								
0.625	0.727	0.40	0.615	0.33	0.514	0.62	0.583	0.94	0.57 ± 0.09	0.63 ± 0.28	0.5	0.494	1.60	0.323	2.65	0.184	1.45	0.553	1.37	0.35 ± 0.17	1.82 ± 0.60								
0.313	0.636	0.52	0.450	0.52	0.369	0.77	0.588	0.90	0.47 ± 0.12	0.73 ± 0.19	0.25	0.513	1.10	0.151	4.00	0.181	1.27	0.548	1.16	0.29 ± 0.21	2.14 ± 1.41								
5	0.697	0.72	0.580	0.49	0.776	0.74	0.407	1.57	0.59 ± 0.16	0.93 ± 0.48	4	0.740	2.56	0.874	1.30	0.521	0.30	0.906	0.62	0.77 ± 0.17	0.74 ± 1.00								
2.5	0.628	0.64	0.563	0.35	0.674	0.66	0.304	1.48	0.51 ± 0.17	0.83 ± 0.49	2	0.473	4.16	0.714	1.74	0.320	0.66	0.632	1.64	0.56 ± 0.17	1.35 ± 1.49								
1.25	0.646	0.41	0.526	0.30	0.521	0.70	0.321	1.09	0.46 ± 0.13	0.69 ± 0.35	1	0.361	3.54	0.445	2.61	0.205	1.08	0.451	1.87	0.37 ± 0.11	1.85 ± 1.05								
0.625	0.576	0.42	0.512	0.26	0.310	0.96	0.323	0.93	0.38 ± 0.13	0.71 ± 0.36	0.5	0.281	2.88	0.170	4.94	0.191	0.86	0.428	1.32	0.26 ± 0.12	2.37 ± 1.84								
0.313	0.337	0.83	0.246	0.60	0.107	2.01	0.257	1.02	0.20 ± 0.10	1.21 ± 0.62	0.25	0.286	1.77	0.192	2.48	0.194	0.67	0.446	0.92	0.28 ± 0.12	1.36 ± 0.83								
5	0.598	1.06	0.485	0.61	0.789	0.65	0.363	1.44	0.55 ± 0.18	0.90 ± 0.39	4	0.809	1.68	0.817	1.93	0.447	0.34	0.838	0.95	0.70 ± 0.19	1.07 ± 0.72								
2.5	0.564	0.70	0.474	0.38	0.723	0.49	0.277	1.17	0.49 ± 0.19	0.68 ± 0.35	2	0.449	4.36	0.630	2.40	0.163	2.44	0.320	4.85	0.37 ± 0.20	3.23 ± 1.28								
1.25	0.540	0.47	0.431	0.29	0.535	0.58	0.202	1.05	0.39 ± 0.16	0.64 ± 0.32	1	0.207	5.00	0.155	5.00	0.034	5.00	0.120	5.00	0.10 ± 0.07	5.00 ± 0.00								
0.625	0.513	0.35	0.437	0.21	0.261	0.99	0.189	0.84	0.30 ± 0.15	0.68 ± 0.38	0.5	0.133	5.00	-0.057	5.00	0.010	5.00	0.102	5.00	0.02 ± 0.09	5.00 ± 0.00								
0.313	0.221	0.95	0.151	0.61	0.039	4.41	0.130	0.91	0.11 ± 0.08	1.98 ± 1.80	0.25	0.130	3.56	-0.058	5.00	0.001	5.00	0.084	3.72	0.01 ± 0.08	4.57 ± 0.79								
Bortezomib	4HC	Proteasome	Allylator	5000	0.968	1.90	1.000	0.03	1.000	0.77	0.999	0.84	1.00 ± 0.02	0.54 ± 0.77	Bortezomib	Actinomycin D	Proteasome	Allylator	2	0.562	5.00	0.398	5.00	0.187	5.00	0.300	5.00	0.30 ± 0.16	5.00 ± 0.00
				2500	0.402	2.52	1.000	0.05	0.876	1.43	0.699	1.73	0.86 ± 0.26	1.07 ± 1.03					1	0.466	5.00	0.271	5.00	0.026	5.00	0.224	4.82	0.21 ± 0.14	4.94 ± 0.09
				1250	0.358	1.61	0.554	2.18	0.091	2.41	0.073	2.91	0.24 ± 0.23	2.50 ± 0.54					0.5	0.232	5.00	0.150	5.00	-0.039	5.00	0.086	5.00	0.07 ± 0.12	5.00 ± 0.00
				625	0.209	1.31	0.454	1.76	0.026	2.69	0.053	2.71	0.18 ± 0.20	2.39 ± 0.70					0.25	0.058	5.00	0.167	5.00	-0.058	5.00	0.061	4.40	0.06 ± 0.09	4.80 ± 0.30
				313	0.131	1.15	0.333	1.62	0.014	2.81	0.063	2.32	0.14 ± 0.14	2.25 ± 0.74					0.125	0.029	5.00	0.233	5.00	-0.046	5.00	0.050	3.55	0.08 ± 0.12	4.52 ± 0.72
				5000	0.959	1.93	1.000	0.03	0.793	2.58	1.000	0.68	0.93 ± 0.10	1.09 ± 1.16					2	0.585	5.00	0.353	5.00	0.171	5.00	0.273	5.00	0.27 ± 0.18	5.00 ± 0.00
	2500	0.361	2.42	1.000	0.06	0.798	1.44	0.541	1.75	0.78 ± 0.28	1.08 ± 0.99	1	0.485	5.00		0.255	5.00	0.094	5.00	0.137	5.00	0.16 ± 0.18	5.00 ± 0.00						
	1250	0.342	1.43	0.521	2.10	0.139	1.75	0.013	3.66	0.22 ± 0.22	2.50 ± 0.99	0.5	0.230	5.00		0.053	5.00	-0.051	5.00	-0.024	5.00	-0.01 ± 0.13	5.00 ± 0.00						
	625	0.178	1.12	0.349	1.89	0.018	2.19	0.004	4.51	0.12 ± 0.16	2.86 ± 1.46	0.25	0.031	5.00		0.076	5.00	-0.050	5.00	-0.026	5.00	0.00 ± 0.06	5.00 ± 0.00						
	313	0.101	0.94	0.232	1.68	0.005	2.71	-0.002	5.00	0.08 ± 0.11	3.13 ± 1.77	0.125	0.020	5.00		0.233	5.00	-0.029	5.00	-0.028	5.00	-0.01 ± 0.03	5.00 ± 0.00						
	5000	0.958	1.88	1.000	0.03	1.000	5.00	1.000	0.75	1.00 ± 0.02	1.93 ± 2.19	2	0.583	5.00		0.394	5.00	0.194	5.00	0.277	5.00	0.29 ± 0.17	5.00 ± 0.00						
	2500	0.375	2.26	1.000	0.02	0.673	1.51	0.576	1.53	0.75 ± 0.26	1.02 ± 0.94	1	0.466	5.00		0.246	5.00	0.115	5.00	0.152	5.00	0.17 ± 0.16	5.00 ± 0.00						
1250	0.318	1.33	0.464	2.22	0.142	1.47	0.021	2.52	0.21 ± 0.19	2.07 ± 0.58	0.5	0.240	5.00	0.069	5.00	-0.054	5.00	0.011	5.00	0.01 ± 0.13	5.00 ± 0.00								
625	0.207	0.92	0.316	1.84	0.037	1.42	0.023	1.89	0.13 ± 0.14	1.72 ± 0.45	0.25	0.065	5.00	0.125	5.00	-0.052	5.00	-0.038	5.00	0.01 ± 0.08	5.00 ± 0.00								
313	0.066	0.83	0.191	1.63	0.036	1.13	-0.002	5.00	0.07 ± 0.08	2.59 ± 1.93	0.125	0.040	5.00	0.042	5.00	-0.015	5.00	-0.055	5.00	-0.01 ± 0.05	5.00 ± 0.00								
5000	0.930	2.08	0.976	0.68	1.000	0.47	1.000	0.70	0.99 ± 0.03	0.62 ± 0.74	2	0.603	5.00	0.425	5.00	0.202	5.00	0.269	5.00	0.30 ± 0.18	5.00 ± 0.00								
2500	0.496	2.11	1.000	0.03	0.776	1.30	0.474	1.53	0.75 ± 0.28	0.95 ± 0.88	1	0.476	5.00	0.322	5.00	0.093	5.00	0.136	5.00	0.18 ± 0.18	5.00 ± 0.00								
1250	0.319	1.24	0.449	2.19	0.189	1.21	0.010	2.49	0.22 ± 0.19	1.96 ± 0.66	0.5	0.266	5.00	0.128	5.00	-0.049	5.00	0.006	5.00	0.03 ± 0.14	5.00 ± 0.00								
625	0.148	0.89	0.332	1.62	0.055	1.04	0.016	1.61	0.13 ± 0.14	1.42 ± 0.38	0.25	0.080	5.00	0.044	5.00	-0.039	5.00	-0.012	5.00	0.00 ± 0.05	5.00 ± 0.00								
313	0.056	0.72	0.228	1.28	0.059	0.75	-0.018	5.00	0.09 ± 0.10	2.34 ± 2.06	0.125	0.052	5.00	0.144	5.00	-0.013	5.00	-0.036	5.00	0.03 ± 0.08	5.00 ± 0.00								
5000	0.956	1.84	1.000	0.04	1.000	5.00	1.000	0.71	1.00 ± 0.02	1.92 ± 2.20	2	0.591	5																

Agents		Mechanism		Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average		Agents	Mechanism	Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average						
Tx1	Tx2	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI	FA	CI	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI	FA	CI					
Bortezomib	Vinorelbine	Proteasome	Microtubule	10	4	0.764	2.51	0.853	1.88	0.435	1.02	0.667	2.81	0.65 ± 0.18	1.90 ± 0.79	Cabozantinib	4HC	TKI	Allyl/ator	2000	5000	0.993	1.18	1.000	0.03	1.000	5.00	1.000	0.44	1.00 ± 0.00	1.82 ± 2.27			
					2	0.325	5.00	0.636	2.88	0.029	5.00	0.223	5.00	0.30 ± 0.25	4.29 ± 1.06						2500	0.383	2.37	1.000	0.02	0.997	0.56	0.927	0.86	0.97 ± 0.30	0.48 ± 1.01			
					1	0.087	5.00	0.381	3.90	-0.015	5.00	0.084	5.00	0.15 ± 0.17	4.63 ± 0.55						1250	0.337	1.47	0.501	1.86	0.431	1.40	0.286	1.44	0.41 ± 0.10	1.57 ± 0.21			
					0.5	0.057	5.00	0.207	4.57	-0.015	5.00	0.094	5.00	0.10 ± 0.09	4.86 ± 0.22						625	0.209	1.23	0.367	1.45	0.142	3.04	0.283	1.09	0.26 ± 0.10	1.86 ± 0.90			
				0.25	0.035	5.00	0.223	2.70	-0.024	5.00	0.056	5.00	0.09 ± 0.11	4.23 ± 1.15	313					0.150	1.13	0.222	1.39	0.119	3.33	0.299	0.85	0.21 ± 0.08	1.86 ± 1.12					
				6.67	4	0.732	2.77	0.856	1.71	0.463	0.70	0.661	2.65	0.66 ± 0.16	1.69 ± 0.96					5000	0.965	1.71	1.000	5.00	1.000	5.00	1.000	5.00	1.000	5.00	1.000	0.32	1.00 ± 0.02	5.00 ± 1.65
					2	0.259	5.00	0.575	3.34	0.035	5.00	0.122	5.00	0.24 ± 0.24	4.45 ± 0.83					2500	0.359	2.23	1.000	0.02	0.968	0.82	0.907	0.89	0.96 ± 0.30	0.58 ± 0.92				
					1	0.062	5.00	0.173	5.00	-0.003	5.00	-0.008	5.00	0.05 ± 0.08	5.00 ± 0.00					1250	0.301	1.31	0.439	2.10	0.256	1.50	0.133	1.82	0.28 ± 0.13	1.81 ± 0.35				
					0.5	0.037	5.00	0.046	5.00	-0.010	5.00	-0.017	5.00	0.01 ± 0.04	5.00 ± 0.00					625	0.183	0.97	0.364	1.35	0.035	5.00	0.104	1.76	0.17 ± 0.14	2.70 ± 1.85				
				0.25	0.045	5.00	0.157	3.21	-0.021	5.00	-0.028	5.00	0.04 ± 0.09	4.40 ± 0.90	313					0.056	1.17	0.247	1.07	0.030	5.00	0.126	1.26	0.13 ± 0.10	2.44 ± 1.92					
				4.45	4	0.735	2.64	0.854	1.65	0.449	0.56	0.659	2.52	0.65 ± 0.17	1.58 ± 0.96					5000	0.982	1.46	1.000	0.01	1.000	5.00	1.000	0.62	1.00 ± 0.01	1.88 ± 2.23				
					2	0.291	5.00	0.592	3.00	0.055	5.00	0.149	5.00	0.27 ± 0.23	4.33 ± 1.00					2500	0.421	2.00	1.000	0.02	0.940	0.91	0.848	0.97	0.93 ± 0.26	0.63 ± 0.81				
					1	-0.008	5.00	0.170	5.00	-0.005	5.00	0.014	5.00	0.06 ± 0.09	5.00 ± 0.00					1250	0.277	1.23	0.408	2.23	0.183	1.38	0.059	2.23	0.22 ± 0.15	1.95 ± 0.54				
					0.5	-0.040	5.00	0.092	5.00	-0.008	5.00	-0.015	5.00	0.02 ± 0.06	5.00 ± 0.00					625	0.163	0.83	0.378	1.24	0.001	5.00	0.048	2.06	0.14 ± 0.17	2.77 ± 1.88				
				0.25	-0.051	5.00	0.097	4.60	-0.017	5.00	-0.037	5.00	0.01 ± 0.07	4.87 ± 1.20	313					0.061	0.77	0.359	0.68	-0.001	5.00	0.024	3.65	0.13 ± 0.17	3.11 ± 1.15					
				2.97	4	0.731	2.64	0.860	1.52	0.444	0.46	0.658	2.44	0.65 ± 0.17	1.47 ± 1.00					5000	0.828	2.52	1.000	5.00	1.000	5.00	1.000	5.00	1.000	5.00	1.000	0.09	1.00 ± 0.09	5.00 ± 2.14
					2	0.272	5.00	0.587	2.96	0.047	5.00	0.086	5.00	0.24 ± 0.25	4.32 ± 1.02					2500	0.340	2.12	1.000	0.02	0.929	0.93	0.872	0.94	0.93 ± 0.30	0.63 ± 0.86				
					1	0.010	5.00	0.173	5.00	0.003	5.00	-0.007	5.00	0.06 ± 0.09	5.00 ± 0.00					1250	0.313	1.12	0.493	1.76	0.195	1.11	0.032	2.32	0.24 ± 0.19	1.73 ± 0.58				
					0.5	-0.058	5.00	0.023	5.00	-0.001	5.00	-0.006	5.00	0.01 ± 0.03	5.00 ± 0.00					625	0.176	0.72	0.282	1.60	-0.004	5.00	0.014	3.56	0.10 ± 0.14	3.39 ± 1.93				
				0.25	-0.059	5.00	0.132	3.23	-0.012	5.00	-0.032	5.00	0.03 ± 0.09	4.41 ± 0.89	313					0.082	0.53	0.130	1.55	-0.018	5.00	-0.019	5.00	0.03 ± 0.07	3.85 ± 2.32					
				1.98	4	0.745	2.42	0.856	1.53	0.449	0.38	0.670	2.25	0.66 ± 0.17	1.39 ± 0.93					5000	0.880	2.52	1.000	5.00	1.000	0.68	1.000	0.69	1.00 ± 0.06	2.12 ± 2.04				
					2	0.286	5.00	0.604	2.71	0.092	5.00	0.151	5.00	0.28 ± 0.23	4.24 ± 1.15					2500	0.360	2.05	0.999	0.03	0.925	0.94	0.762	1.05	0.90 ± 0.29	0.67 ± 0.83				
					1	0.026	5.00	0.174	5.00	-0.009	5.00	0.024	5.00	0.06 ± 0.08	5.00 ± 0.00					1250	0.310	1.09	0.388	2.31	0.180	1.02	0.065	5.00	0.19 ± 0.17	2.78 ± 1.86				
					0.5	0.028	5.00	0.053	5.00	0.025	5.00	-0.022	5.00	0.02 ± 0.04	5.00 ± 0.00					625	0.141	0.72	0.279	1.60	0.017	5.00	0.009	3.14	0.09 ± 0.14	3.25 ± 1.88				
0.25	-0.072	5.00	0.014	5.00	-0.023	5.00	-0.036	5.00	-0.01 ± 0.04	5.00 ± 0.00	313	0.065	0.49	0.152	1.33	-0.025	5.00	-0.048	5.00	0.03 ± 0.09	3.78 ± 2.39													
Cabozantinib	Actinomycin D	TKI	Allyl/ator	2000	2	0.615	5.00	0.393	5.00	0.249	5.00	0.396	4.64	0.35 ± 0.15	4.88 ± 0.18	Cabozantinib	Bortezomib	TKI	Proteasome	2000	10	0.103	1.89	0.386	1.10	0.112	4.60	0.282	1.88	0.26 ± 0.14	2.53 ± 1.53			
					1	0.553	5.00	0.249	5.00	0.220	4.35	0.346	2.94	0.27 ± 0.15	4.10 ± 0.97						6.67	0.093	1.68	0.217	1.21	0.101	4.54	0.287	1.47	0.20 ± 0.09	2.41 ± 1.56			
					0.5	0.354	5.00	0.192	5.00	0.151	5.00	0.308	1.99	0.22 ± 0.10	4.00 ± 1.51						4.45	0.118	1.31	0.152	1.23	0.080	5.00	0.265	1.33	0.17 ± 0.08	2.52 ± 1.86			
					0.25	0.130	5.00	0.224	5.00	0.046	5.00	0.283	1.45	0.18 ± 0.10	3.82 ± 1.78						2.97	0.072	1.57	0.139	1.09	0.112	3.66	0.268	1.14	0.17 ± 0.08	1.96 ± 1.22			
				0.125	0.073	5.00	0.313	2.30	0.104	5.00	0.328	0.90	0.25 ± 0.13	2.73 ± 2.05	1.98					0.079	1.40	0.130	1.01	0.097	4.08	0.265	1.03	0.16 ± 0.08	2.04 ± 1.48					
				1000	2	0.601	5.00	0.354	5.00	0.199	5.00	0.324	5.00	0.29 ± 0.17	5.00 ± 0.00					10	0.044	1.94	0.323	1.10	0.026	5.00	0.105	3.03	0.15 ± 0.14	3.04 ± 1.69				
					1	0.521	5.00	0.235	5.00	0.163	5.00	0.212	4.24	0.20 ± 0.16	4.75 ± 0.38					6.67	0.026	2.00	0.122	1.37	0.010	5.00	0.072	3.34	0.07 ± 0.05	3.24 ± 1.61				
					0.5	0.299	5.00	0.084	5.00	-0.019	5.00	0.144	3.38	0.07 ± 0.13	4.46 ± 0.81					4.45	0.070	1.08	0.000	5.00	0.019	5.00	0.093	2.31	0.04 ± 0.04	4.10 ± 1.97				
					0.25	0.096	5.00	0.224	5.00	-0.035	5.00	0.085	3.47	0.09 ± 0.11	4.49 ± 0.77					2.97	0.005	3.84	0.019	2.78	0.003	5.00	0.084	2.25	0.04 ± 0.04	3.34 ± 1.22				
				0.125	0.062	5.00	0.008	5.00	0.005	5.00	0.105	2.08	0.04 ± 0.05	4.03 ± 1.46	1.98					0.027	1.40	0.109	0.73	0.019	5.00	0.075	2.32	0.07 ± 0.04	2.68 ± 1.88					
				500	2	0.607	5.00	0.373	5.00	0.196	5.00	0.277	5.00	0.28 ± 0.18	5.00 ± 0.00					10	0.046	1.47	0.248	1.19	0.009	5.00	0.018	5.00	0.09 ± 0.11	3.73 ± 2.12				
					1	0.499	5.00	0.220	5.00	0.146	5.00	0.173	4.69	0.18 ± 0.16	4.90 ± 0.16					6.67	0.034	1.27	0.041	2.00	0.021	5.00	0.007	5.00	0.02 ± 0.01	4.00 ± 1.97				
					0.5	0.309	5.00	0.071	5.00	-0.028	5.00	0.064	5.00	0.04 ± 0.14	5.00 ± 0.00					4.45	0.005	2.34	-0.012	5.00	-0.001	5.00	-0.007	5.00	-0.01 ± 0.01	5.00 ± 1.33				
					0.25	0.048	5.00	0.012	5.00	-0.050	5.00	0.004	5.00	-0.01 ± 0.04	5.00 ± 0.00					2.97	0.022	1.04	-0.044	5.00	0.014	5.00	0.001	5.00	-0.01 ± 0.03	5.00 ± 1.98				
				0.125	0.011	5.00	-0.026	5.00	-0.014	5.00	0.018	5.00	-0.01 ± 0.02	5.00 ± 0.00	1.98					0.023	0.89	0.086	0.60	0.024	3.93	0.015	5.00	0.04 ± 0.03	3.18 ± 2.19					
				250	2	0.583	5.00	0.362	5.00	0.180	5.00	0.271	5.00	0.27 ± 0.17	5.00 ± 0.00					10	0.047	1.25	0.248	1.14	0.009	5.00	-0.027	5.00	0.08 ± 0.12	3.71 ± 2.20				
					1	0.497	5.00	0.306	5.00	0.120	5.00	0.165	4.68	0.20 ± 0.17	4.89 ± 0.16					6.67	0.039	0.96	0.016	2.67	0.000	5.00	-0.037	5.00	-0.01 ± 0.03	4.22 ± 1.97				
					0.5	0.294	5.00	0.054	5.00	-0.023	5.00	0.032	5.00	0.02 ± 0.14	5.00 ± 0.00					4.45	0.015	1.02	0.006	3.27	0.008	5.00	-0.039	5.00	-0.01 ± 0.02	4.42 ± 1.89				
					0.25	0.119	5.00	0.155	5.00	-0.062	5.00	-0.026	5.00	0.02 ± 0.11	5.00 ± 0.00					2.97	0.029	0.63	0.025	1.18	0.010	4.80	0.030	5.00	0.00 ± 0.03	3.66 ± 2.32				
				0.125	0.010	5.00	0.051	5.00	-0.018	5.00	0.006	5.00	0.01 ± 0.03	5.00 ± 0.00	1.98					0.016	0.67	-0.043	5.00											

Agents		Mechanism		Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average		Agents		Mechanism		Conc (ng/ml)		RD		SMS-CTR		RH30		RH41		Average	
Tx1	Tx2	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI	FA	CI	Tx1	Tx2	Tx1	Tx2	Tx1	Tx2	FA	CI	FA	CI	FA	CI	FA	CI	FA	CI
Cabozantinib	Vinorelbine	TKI	Microtubule	2000	4	0.647	3.92	0.804	2.10	0.584	0.46	0.853	0.80	0.75 ± 0.13	1.12 ± 1.57	Etoposide	4HC	Topo II	Alkylator	5000	5000	0.903	2.73	0.999	0.09	0.999	1.00	0.998	1.00	1.00 ± 0.05	0.70 ± 1.10
					2	0.431	4.80	0.635	2.38	0.382	0.99	0.735	0.87	0.58 ± 0.17	1.42 ± 1.83						2500	0.592	5.00	0.998	0.06	0.999	1.84	0.842	0.91	0.98 ± 0.19	0.94 ± 2.16
					1	0.270	5.00	0.411	2.89	0.495	1.86	0.238	0.86	0.38 ± 0.12	2.04 ± 1.61						1250	0.617	5.00	0.622	2.76	0.895	2.90	0.981	3.55	0.79 ± 0.15	3.07 ± 1.02
					0.5	0.149	5.00	0.273	2.75	0.158	2.88	0.387	1.28	0.27 ± 0.11	2.30 ± 1.53						625	0.625	5.00	0.549	3.51	0.878	3.04	0.855	2.97	0.76 ± 0.16	3.17 ± 0.94
					0.25	0.147	3.22	0.285	1.46	0.145	2.88	0.331	1.10	0.25 ± 0.10	1.81 ± 1.04						313	0.637	4.90	0.494	4.69	0.870	3.09	0.856	2.81	0.74 ± 0.18	3.53 ± 1.07
					4	0.731	2.60	0.822	1.85	0.557	0.30	0.783	1.24	0.72 ± 0.12	1.13 ± 0.97						5000	0.910	2.25	0.999	0.09	0.996	1.17	0.998	0.96	1.00 ± 0.04	0.74 ± 0.89
		2	0.390	5.00	0.605	2.63	0.240	1.51	0.421	3.11	0.42 ± 0.15	2.42 ± 1.46	2500	0.458	4.82			0.999	0.05	0.933	1.31	0.927	1.13	0.95 ± 0.25	0.83 ± 2.07						
		1	0.146	5.00	0.294	4.51	0.097	5.00	0.219	4.24	0.20 ± 0.09	4.58 ± 0.98	1250	0.455	3.95			0.469	3.14	0.679	2.64	0.363	5.00	0.50 ± 0.13	3.59 ± 1.03						
		0.5	0.072	5.00	0.213	3.49	0.044	5.00	0.148	3.85	0.13 ± 0.08	4.11 ± 0.78	625	0.445	3.64			0.396	3.44	0.658	2.52	0.416	5.00	0.49 ± 0.12	3.65 ± 1.02						
		0.25	0.045	5.00	0.104	4.04	0.041	5.00	0.139	2.53	0.09 ± 0.05	3.86 ± 1.17	313	0.491	2.74			0.378	3.26	0.600	2.90	0.421	5.00	0.47 ± 0.10	3.72 ± 1.04						
		4	0.768	2.11	0.829	1.76	0.563	0.19	0.722	1.69	0.70 ± 0.11	1.21 ± 0.85	5000	0.877	2.34			0.999	0.09	0.999	0.94	0.998	0.96	1.00 ± 0.06	0.66 ± 0.93						
		2	0.382	5.00	0.620	2.45	0.194	1.66	0.299	5.00	0.37 ± 0.18	3.10 ± 1.66	2500	0.434	2.93			0.998	0.05	0.756	1.53	0.928	0.91	0.89 ± 0.25	0.83 ± 1.13						
	1	0.124	5.00	0.262	5.00	0.056	5.00	0.122	5.00	0.15 ± 0.09	5.00 ± 0.00	1250	0.401	1.98	0.590		1.48	0.305	2.80	0.132	5.00	0.34 ± 0.19	3.09 ± 1.55								
	0.5	0.048	5.00	0.077	5.00	0.035	5.00	0.062	5.00	0.06 ± 0.02	5.00 ± 0.00	625	0.358	1.77	0.349		2.14	0.135	5.00	0.150	5.00	0.21 ± 0.12	4.05 ± 1.76								
	0.25	0.032	5.00	0.055	5.00	0.040	5.00	0.058	5.00	0.05 ± 0.01	5.00 ± 0.00	313	0.350	1.57	0.413		1.04	0.050	5.00	0.150	5.00	0.20 ± 0.17	3.68 ± 2.14								
	4	0.784	1.91	0.831	1.73	0.545	0.16	0.683	2.01	0.69 ± 0.13	1.30 ± 0.87	5000	0.884	2.27	0.999		0.09	0.999	0.95	0.998	0.96	1.00 ± 0.06	0.66 ± 0.90								
	2	0.370	5.00	0.615	2.49	0.157	2.65	0.213	5.00	0.33 ± 0.21	3.38 ± 1.40	2500	0.404	2.19	0.998		0.05	0.827	1.15	0.888	0.94	0.90 ± 0.26	0.71 ± 0.88								
	1	0.108	5.00	0.203	5.00	0.038	5.00	0.066	5.00	0.10 ± 0.07	5.00 ± 0.00	1250	0.359	1.33	0.426		2.19	0.114	2.45	0.082	5.00	0.21 ± 0.17	3.21 ± 1.58								
	0.5	0.046	5.00	0.077	5.00	0.008	5.00	0.020	5.00	0.04 ± 0.03	5.00 ± 0.00	625	0.185	1.60	0.301		1.81	0.026	5.00	0.078	5.00	0.13 ± 0.12	3.94 ± 1.90								
	0.25	-0.001	5.00	-0.008	5.00	0.014	5.00	0.025	5.00	0.01 ± 0.02	5.00 ± 0.00	313	0.095	2.97	0.208		1.88	0.018	5.00	0.052	5.00	0.09 ± 0.08	3.96 ± 1.55								
	4	0.779	1.96	0.829	1.75	0.527	0.15	0.692	1.93	0.68 ± 0.13	1.28 ± 0.87	5000	0.852	2.41	0.999		0.08	0.999	0.97	0.998	0.96	1.00 ± 0.07	0.67 ± 0.96								
	2	0.330	5.00	0.625	2.38	0.142	3.18	0.184	5.00	0.32 ± 0.22	3.52 ± 1.32	2500	0.400	2.01	0.998		0.05	0.676	1.28	0.733	1.10	0.80 ± 0.25	0.81 ± 0.81								
	1	0.091	5.00	0.137	5.00	0.025	5.00	0.062	5.00	0.07 ± 0.05	5.00 ± 0.00	1250	0.327	1.14	0.481		1.82	0.158	1.18	0.089	1.90	0.24 ± 0.18	1.63 ± 0.41								
	0.5	0.019	5.00	0.059	5.00	0.004	5.00	0.004	5.00	0.02 ± 0.03	5.00 ± 0.00	625	0.161	0.95	0.307		1.52	0.035	1.69	0.080	1.59	0.14 ± 0.12	1.60 ± 0.33								
0.25	0.023	5.00	0.039	5.00	0.032	5.00	-0.001	5.00	0.02 ± 0.02	5.00 ± 0.00	313	0.096	1.01	0.180	1.45	0.057	0.99	0.027	4.26	0.09 ± 0.07	2.23 ± 1.57										
Etoposide	Actinomycin D	Topo II	Alkylator	5000	2	0.779	5.00	0.545	5.00	0.887	2.61	0.921	1.96	0.78 ± 0.17	3.19 ± 1.59	SN-38	4HC	Topo I	Alkylator	5000	5000	0.996	1.01	1.000	5.00	1.000	0.64	1.000	0.65	1.00 ± 0.00	2.10 ± 2.12
					1	0.707	5.00	0.525	5.00	0.866	3.07	0.908	1.93	0.77 ± 0.17	3.33 ± 1.52						2500	0.652	2.23	0.987	0.21	0.988	0.72	0.895	1.03	0.96 ± 0.16	0.65 ± 0.86
					0.5	0.692	5.00	0.540	3.75	0.861	3.18	0.892	2.08	0.76 ± 0.16	3.00 ± 1.22						1250	0.579	1.85	0.602	1.60	0.860	0.90	0.469	1.41	0.64 ± 0.17	1.30 ± 0.40
					0.25	0.647	5.00	0.510	4.25	0.855	3.30	0.885	2.14	0.75 ± 0.18	3.23 ± 1.24						625	0.576	1.45	0.544	1.15	0.849	0.68	0.460	1.11	0.62 ± 0.17	0.98 ± 0.32
					0.125	0.647	5.00	0.582	2.24	0.856	3.29	0.867	2.50	0.77 ± 0.15	2.68 ± 1.24						313	0.560	1.34	0.544	0.76	0.843	0.56	0.476	0.91	0.62 ± 0.16	0.75 ± 0.33
					2	0.679	5.00	0.445	5.00	0.614	2.89	0.751	3.02	0.60 ± 0.13	3.64 ± 1.18						5000	0.994	1.15	1.000	5.00	1.000	5.00	1.000	0.69	1.00 ± 0.00	3.56 ± 2.36
		1	0.604	5.00	0.430	5.00	0.566	3.29	0.596	4.41	0.53 ± 0.08	4.23 ± 0.81	2500	0.547	2.31			1.000	5.00	0.944	0.96	0.868	1.01	0.94 ± 0.20	2.32 ± 1.89						
		0.5	0.549	5.00	0.388	5.00	0.566	3.20	0.560	4.41	0.50 ± 0.09	4.20 ± 0.85	1250	0.484	1.74			0.571	1.59	0.780	0.90	0.295	1.41	0.55 ± 0.20	1.30 ± 0.37						
		0.25	0.503	5.00	0.378	4.65	0.560	3.21	0.545	4.33	0.49 ± 0.08	4.06 ± 0.77	625	0.459	1.41			0.524	1.01	0.755	0.66	0.291	1.06	0.52 ± 0.19	0.91 ± 0.31						
		0.125	0.486	5.00	0.389	3.32	0.594	2.81	0.483	5.00	0.49 ± 0.08	3.71 ± 1.14	313	0.476	1.10			0.434	0.83	0.579	0.51	0.267	0.96	0.49 ± 0.20	0.76 ± 0.25						
		2	0.620	5.00	0.520	4.00	0.251	5.00	0.471	4.85	0.41 ± 0.16	4.62 ± 0.48	5000	0.982	1.46			1.000	5.00	1.000	0.59	1.000	0.64	1.00 ± 0.01	2.07 ± 2.09						
		1	0.562	5.00	0.372	5.00	0.184	5.00	0.277	5.00	0.28 ± 0.16	5.00 ± 0.00	2500	0.467	2.29			1.000	5.00	0.936	0.95	0.759	1.12	0.90 ± 0.24	2.36 ± 1.87						
	0.5	0.427	5.00	0.237	5.00	0.081	5.00	0.191	5.00	0.17 ± 0.14	5.00 ± 0.00	1250	0.404	1.60	0.575		1.49	0.682	0.89	0.157	1.47	0.47 ± 0.23	1.28 ± 0.32								
	0.25	0.299	5.00	0.177	5.00	-0.014	5.00	0.217	5.00	0.13 ± 0.13	5.00 ± 0.00	625	0.388	1.18	0.475		1.04	0.636	0.65	0.111	1.33	0.41 ± 0.22	1.01 ± 0.29								
	0.125	0.233	5.00	0.164	5.00	-0.016	5.00	0.182	5.00	0.11 ± 0.11	5.00 ± 0.00	313	0.418	0.83	0.545		0.48	0.617	0.52	0.125	1.02	0.43 ± 0.22	0.67 ± 0.26								
	2	0.590	5.00	0.476	5.00	0.134	5.00	0.398	4.66	0.34 ± 0.19	4.89 ± 0.17	5000	0.958	1.77	1.000		5.00	1.000	5.00	1.000	0.71	1.00 ± 0.02	3.57 ± 2.21								
	1	0.518	5.00	0.438	4.37	0.035	5.00	0.205	5.00	0.23 ± 0.22	4.79 ± 0.32	2500	0.393	2.30	0.999		0.04	0.938	0.93	0.633	1.21	0.86 ± 0.28	0.72 ± 0.93								
	0.5	0.309	5.00	0.199	5.00	-0.092	5.00	0.108	5.00	0.07 ± 0.17	5.00 ± 0.00	1250	0.372	1.38	0.475		1.89	0.535	0.94	0.069	1.62	0.36 ± 0.21	1.48 ± 0.41								
	0.25	0.106	5.00	0.091	5.00	-0.036	5.00	0.080	5.00	0.04 ± 0.07	5.00 ± 0.00	625	0.399	0.81	0.481		0.96	0.424	0.76	0.064	1.20	0.32 ± 0.19	0.97 ± 0.20								
	0.125	0.072	5.00	0.178	5.00	0.007	5.00	0.050	5.00	0.08 ± 0.07	5.00 ± 0.00	313	0.383	0.60	0.346		0.77	0.359	0.70	0.052	1.10	0.25 ± 0.16	0.86 ± 0.22								
	2	0.577	5.00	0.437	5.00	0.138	5.00	0.330																							

Detailed Drug Information - Alias, Mechanism, Source, and Concentrations

Agent	Alias or Trade Name	Target of Inhibition // Mechanism	Vendor	Product #	MW (g/mol)	Concentrations in Synergy (5x5) Experiments		
						Top Conc (ng/ml)	% of Cmax	Dilution Factor
4HC	4-Hydroxy Cyclophosphamide	DNA Crosslinking // DNA Damage	US Biological	H9015	293.1	5000	72	2.0
Actinomycin D	Dactinomycin / Cosmegen®	DNA intercalation // Inhibits RNA/DNA synth	Sigma-Aldrich	A9415	1255.4	1.0	1.0	2.0
AZD1775	MK1775	WEE1 // CDK1 activation	Selleck	S1525	500.6	500	61	2.0
Bortezomib	Velcade®	Proteasome	Sequoia	SRP02310b	384.2	10	8.0	1.5
Cabozantinib	XL184	Tyrosine Kinases (c-Met; VEGFR2)	Selleck	S1119	501.5	2000	100	2.0
Etoposide	VP-16	Topoisomerase II // DNA Damage	Selleck	S1225	588.6	5000	25	4.0
SN-38	Irinotecan metabolite	Topoisomerase IB // DNA Damage	Sequoia	SRP02075e	392.4	5.0	17	2.0
Vinorelbine	Navelbine®	Microtubule polymerization // Anti-mitotic	Selleck	S4269	1079.1	4.0	3.0	2.0

Supplemental Table S2: Drug information table

Cell Line Information

Line	Histology	Source	Commercial Source
RD	Embryonal	Gift from Dr. Calvin K. Lee (Moffitt)	ATCC® CCL-136™
SMS-CTR	Embryonal	Gift from Dr. Calvin K. Lee (Moffitt)	Not Commercially Available
RH30	Alveolar	Children's Oncology Group (COG)	Not Commercially Available
RH41	Alveolar	Children's Oncology Group (COG)	Not Commercially Available

Supplemental Table S3: Cell line information table