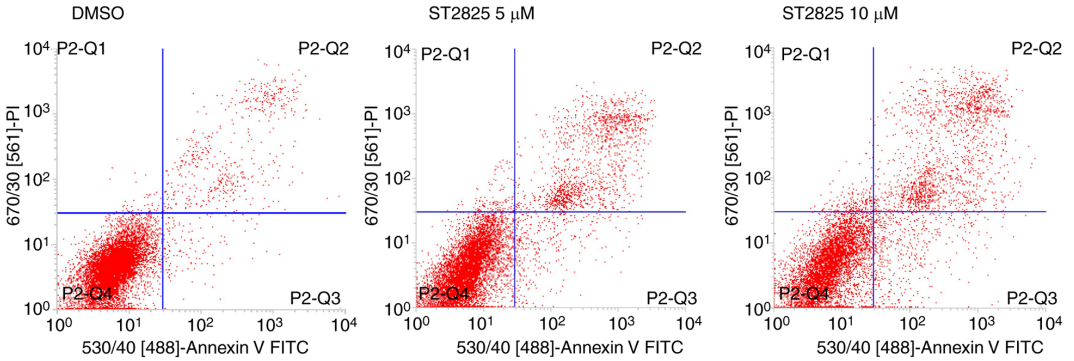
Figure S1. Apoptosis in diffuse large B-cell lymphoma cells treated with ST2825 or DMSO, detected using flow cytometry following annexin V/propidium iodide staining.

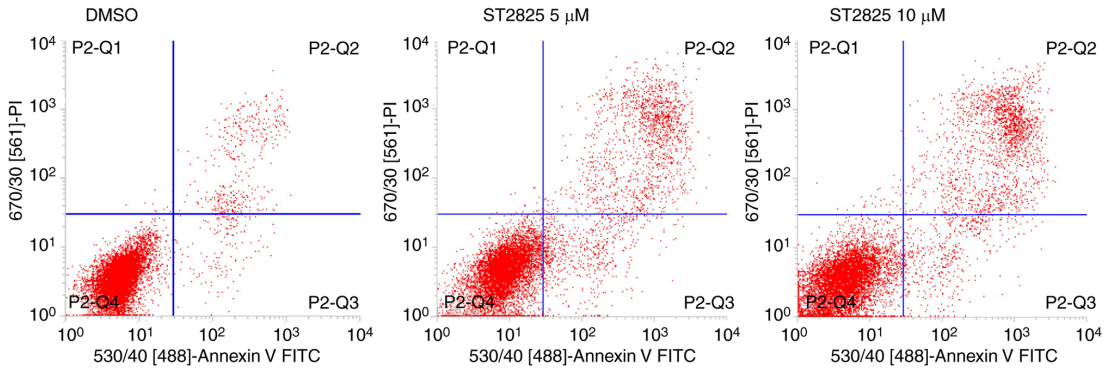
A OCI-LY10

%	DMSO	ST2825 5 μM	ST2825 10 μM
Necrosis (Q1)	0.46	1.26	1.90
Late apoptosis (Q2)	5.25	14.99	18.16
Early apoptosis (Q3)	1.31	3.62	5.15
Living cells (Q4)	92.98	80.13	74.79



B TMD8

%	DMSO	ST2825 5 μM	ST2825 10 μM
Necrosis (Q1)	0.09	0.21	0.35
Late apoptosis (Q2)	4.10	15.16	18.83
Early apoptosis (Q3)	1.55	6.94	5.01
Living cells (Q4)	94.26	77.69	75.81



C SU-DHL-4

%	DMSO	ST2825 5 μM	ST2825 10 μM
Necrosis (Q1)	0.38	0.16	0.21
Late apoptosis (Q2)	6.88	5.76	7.92
Early apoptosis (Q3)	1.69	1.74	2.74
Living cells (Q4)	91.05	92.34	89.13

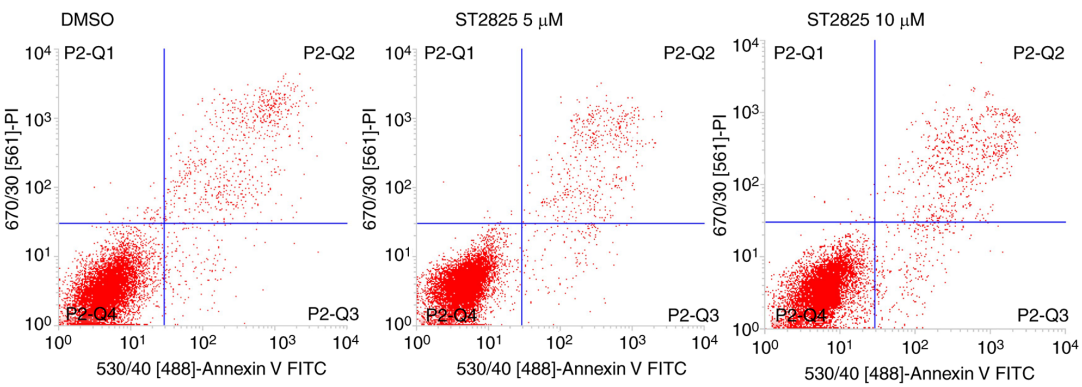


Figure S2. Synergistic effects of BTK inhibitor and myddosome assembly inhibitor on TMD8 cells. (A, B) TMD8 cells were treated for 72 h with ibrutinib, ST2825 or both, at the indicated doses, followed by a WST-1 assay. Inhibition at varying dosimetries for the inhibitor of BTK (ibrutinib) and MYD88 (ST2825) are depicted with (A) heat maps and (B) line graphs. (C) Synergism was evaluated via CI analysis, and the CI values of TMD8 cells at varying dosimetries for ibrutinib and ST2825 are demonstrated via heat maps. (D) Relative NF-κB luciferase activity was measured, following treatment of the TMD8 cells for 12 h with the indicated concentrations of ibrutinib, ST2825 or both. Statistical analysis by one-way ANOVA with Tukey's post hoc test. Data are presented as the mean ± standard error of the mean from three independent experiments. **P<0.01. BTK, Bruton's tyrosine kinase; MYD88, myeloid differentiation primary response gene 88; CI, combination index; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells.

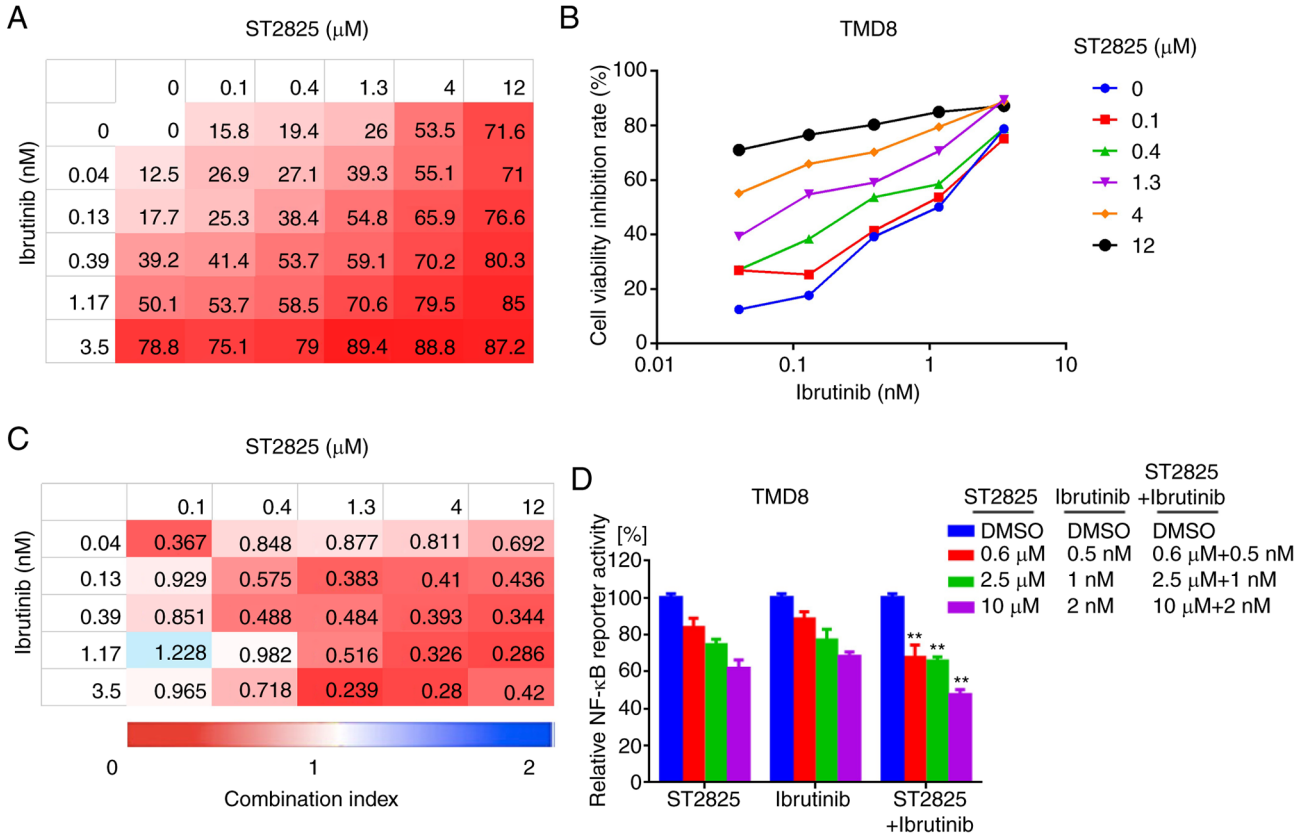


Figure S3. Synergistic effects of BCL-2 inhibitor and myddosome assembly inhibitor on TMD8 cells. (A, B) TMD8 cells were treated for 72 h with ABT-199, ST2825 or both, at the indicated doses, followed by a WST-1 assay. Inhibition at varying dosimetries for the inhibitor of BCL-2 (ABT-199) and MYD88 (ST2825) in TMD8 cells is depicted with (A) heat maps and (B) line graphs. (C) Synergism was evaluated via CI analysis, and the CI values of TMD8 cells at varying dosimetries for ABT-199 and ST2825 are demonstrated via heat maps. (D) Apoptotic cell populations (annexin V-positive) of TMD8 cells were analyzed via flow cytometry, following treatment for 48 h with the vehicle, ST2825 (10 μM), ABT-199 (1 μM) or combination treatment. Statistical analysis by one-way ANOVA with Tukey's post hoc test. Data are presented as the mean ± standard deviation. *P<0.05. BCL-2, B-cell lymphoma-2; MYD88, myeloid differentiation primary response gene 88; CI, combination index.

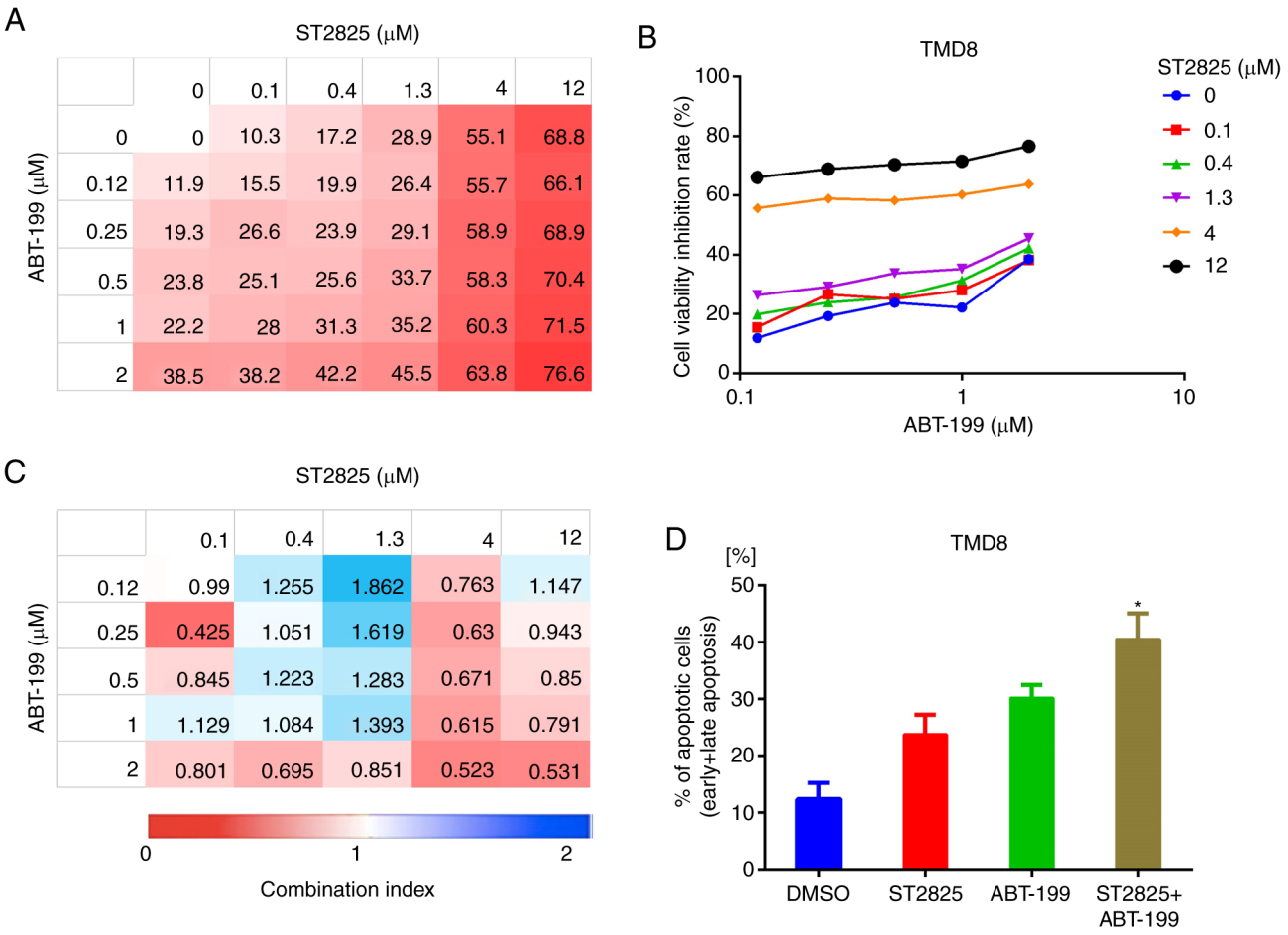
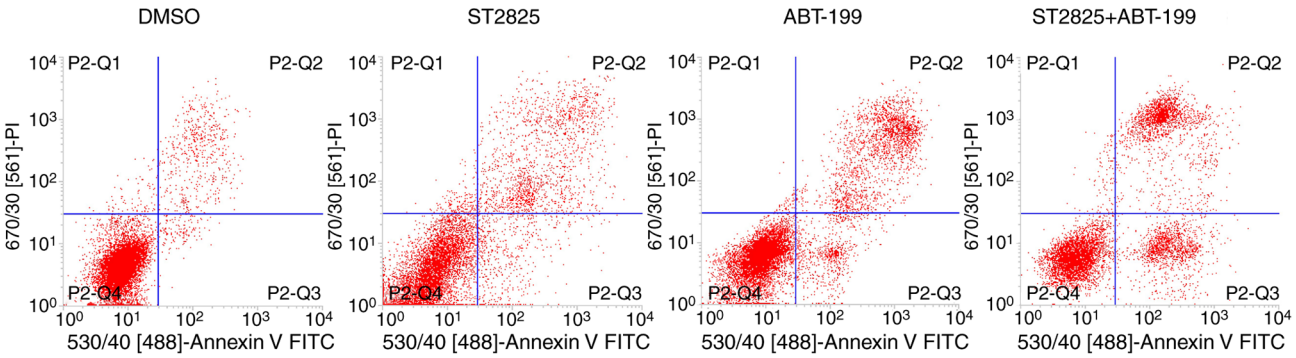


Figure S4. Combination treatment with ST2825 and ABT-199 increases apoptosis. (A, B) Apoptotic cell population (annexin V-positive) of (A) OCI-LY10 or (B) TMD8 cells, analyzed by flow cytometry following treatment for 48 h with the vehicle, ST2825 (10 μM), ABT-199 (1 μM) or combination treatment.

A OCI-LY10

%	DMSO	ST2825	ABT-199	ST2825+ABT-199
Necrosis (Q1)	1.25	1.67	1.13	1.36
Late apoptosis (Q2)	5.91	15.92	20.68	24.62
Early apoptosis (Q3)	2.79	5.44	7.67	16.94
Living cells (Q4)	90.05	76.97	70.52	57.08



B TMD8

%	DMSO	ST2825	ABT-199	ST2825+ABT-199
Necrosis (Q1)	1.59	2.27	3.61	2.12
Late apoptosis (Q2)	7.95	15.21	21.03	22.73
Early apoptosis (Q3)	4.77	7.81	6.74	17.56
Living cells (Q4)	85.69	74.71	68.62	57.59