

Figure S1. Efficacy of anti-S1P agents, the results of lentiviral shRNA and the synergic effect of antiS1P agents and carfilzomib. Fingolimod, SKI-I and ABC294640 inhibited the growth of multiple myeloma cell lines, (A) MM1S and (B) MM1R at 1 and 2.5 μ M. * P <0.05 vs. control and other concentration groups. ABC294640 exerted an inhibitory effect on RPMI8226; however, a higher concentration was required (25 μ M) to approach the same inhibition level as the other two agents. (C) Knockdown of the SphK1 and S1PR1 gene expression by shRNA. (D) Knockdown of the SphK1 and S1PR1 protein expression by shRNA in immunoblotting. (E) shRNA-mediated knockdown of S1PR1 or SphK1 induced caspase activity, and the addition of car enhanced the activity. * P <0.05. (F) Anti-S1P agents enhanced the growth inhibition of carfilzomib for MM cell lines. * P <0.05 carfilzomib 2 nM or 5 nM alone vs. carfilzomib 2 nM or 5 nM plus anti-S1P agent. car, carfilzomib; S1PR, sphingosine 1-phosphate receptor; shRNA, short hairpin RNA; SK, sphingosine kinase; SK1, sphingosine kinase 1.

