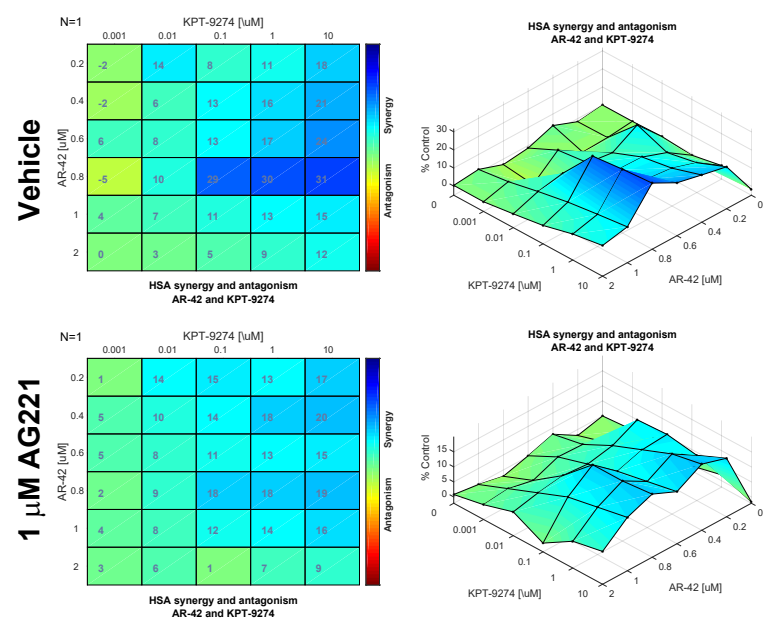
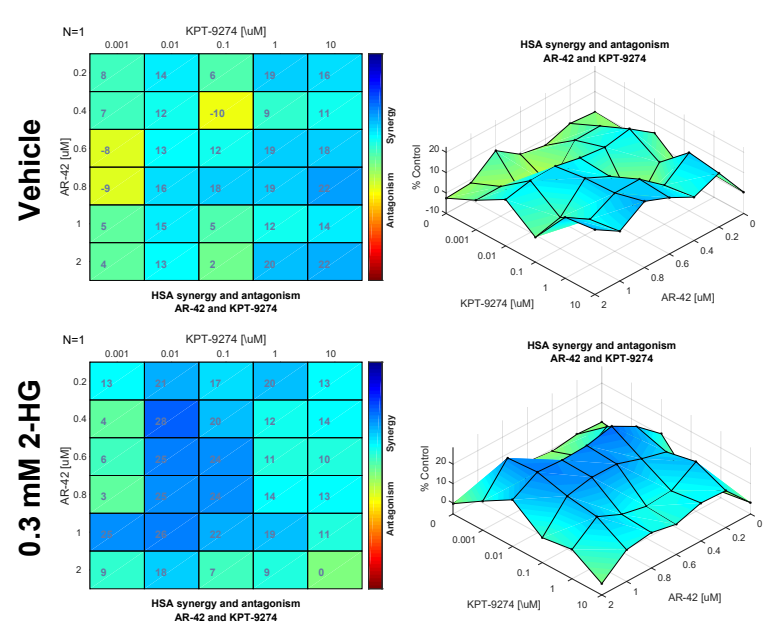


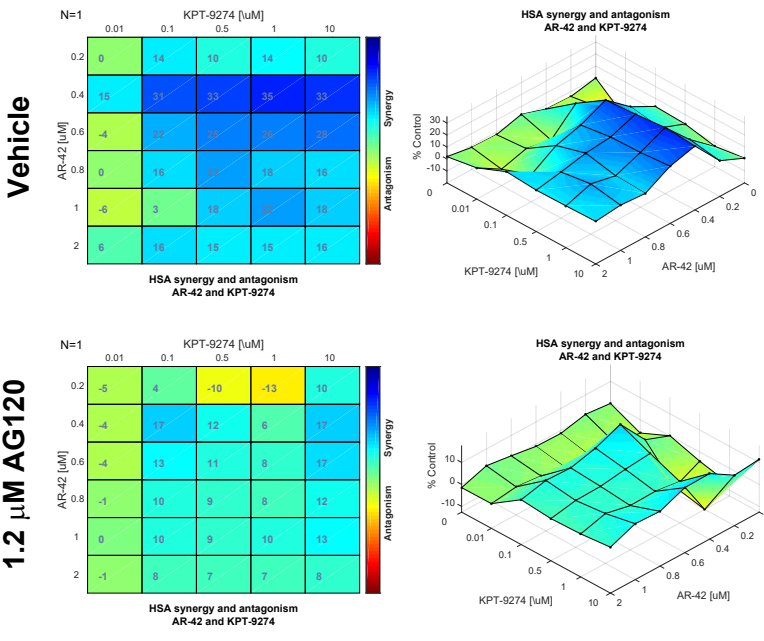
A IDH2^{mut} TF-1



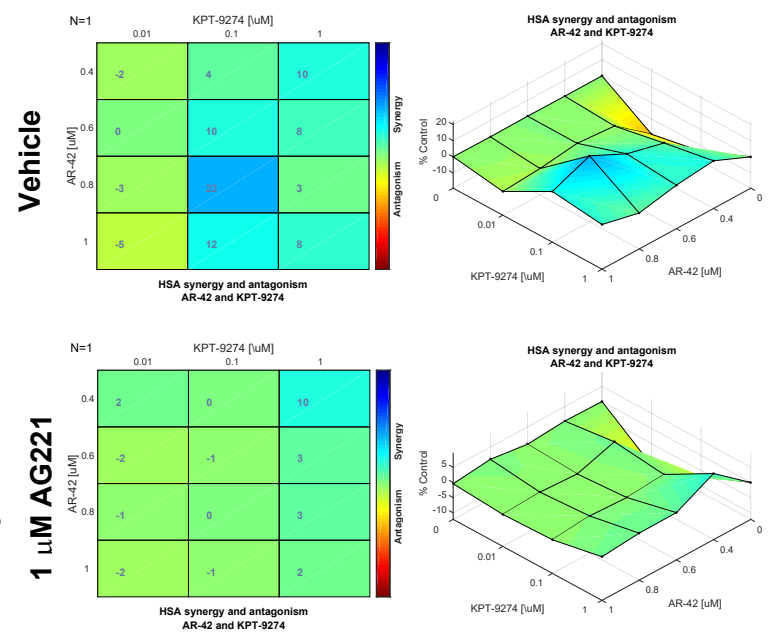
B IDH2^{WT} TF-1



C IDH1^{mut} patient#8



D IDH2^{mut} patient#9



Supplementary Figure S4. Mutant IDH1/2 enhances AR-42/KPT-9274 combination sensitivity in a 2-HG-dependent manner. **A)** AG221 treatment prevents drug combination sensitivity on IDH2-mutant TF-1 cells. IDH2-mutant TF-1 cells were pre-treated with 1 μ M AG221 for 48 hours before being subject to pairwise drug combination treatment. **B)** 2-HG treatment enhances AR-42/KPT-9274 sensitivity. IDH2-WT TF-1 cells were exposed to 0.3 mM octyl-2HG (Sigma-Aldrich, St. Louis, MO) or DMSO control for 24 hours before being treated with drug combination. **C-D)** Inhibitions of mutant IDH1 and IDH2 reverse the vulnerability of IDH1-mutant and IDH2-mutant patient cells to drug combination. IDH1-mutant and IDH2-mutant patient cells were incubated with 1.2 μ M AG120 and 1 μ M AG221, respectively before AR-42/KPT-9274 treatments at indicated doses in the presence of cytokines. Cell viability was examined with MTS assays and synergy matrix and surface plots were generated with Combenefit.