Figure S7

(a) Graph showing the effect of GDC-0994 and Cobimetinib on HCT116 CRC, KRAS\(^{G13D}\) cells. The graph displays the percentage of growth inhibition (%TI) against different dosages of GDC-0994 and Cobimetinib. The data points are color-coded to represent the tested doses, with trend lines indicating the %TI trend.

(b) Table showing the %TI for different combinations of GDC-0994 and Cobimetinib. The table includes dosages for both drugs at various concentrations, with asterisks indicating significant differences. The table notes that all combinations were tolerated and that bold text signifies >15% BW loss.

\(^{*}p<0.05\)

Bold red text >15% BW loss
Supplemental Figure 7. Cobimetinib and GDC-0994 demonstrate dose-dependent combination activity when dosed on a daily or intermittent schedule in the HCT116 xenograft tumor model. (a) HCT116 \((\text{KRAS}^{G13D},\text{colorectal})\) tumor xenograft bearing animals were dosed orally (PO) for 21 days with cobimetinib on a daily basis (QD, left panel) or a twice weekly schedule (BIW, right panel) in combination with GDC-0994 PO, QD at the indicated dose levels (blue circles, n=5/group) and %TGI was calculated relative to a vehicle control (n=10). Data were used to generate two-drug contour plots where observed %TGI was used to inform missing dose combinations (%TGI levels indicated in red and %TGI trend lines shown in yellow). Inward curved trend lines indicate greater than additive combination activity. (b) Summary data for the two-drug contour studies depicted above with measured %TGI at each dose combination. Dose combinations resulting in improved %TGI relative to each single agent are indicated (Student’s t test, * p<0.05). Dose combinations where combinations were considered intolerable are indicated in bold red.