

Fig.S8A. Rapamycin only partially reverses resistance in BT-40TramR xenografts with acquired resistance to trametinib. Trametinib resistant BT-40TramR xenografts had been treated with 7 cycles of trametinib therapy.

Left panel: Growth of BT-40 trametinib resistant xenografts in untreated mice;
 Center panel: Growth of BT-40TramR xenografts in mice treated with trametinib (1 mg/kg daily);
 Right panel: Growth of BT-40TramR xenografts in mice treated with trametinib (1 mg/kg daily) combined with rapamycin (5 mg/kg daily x 5 for 6 consecutive weeks). Each curve represents growth of an individual tumor.

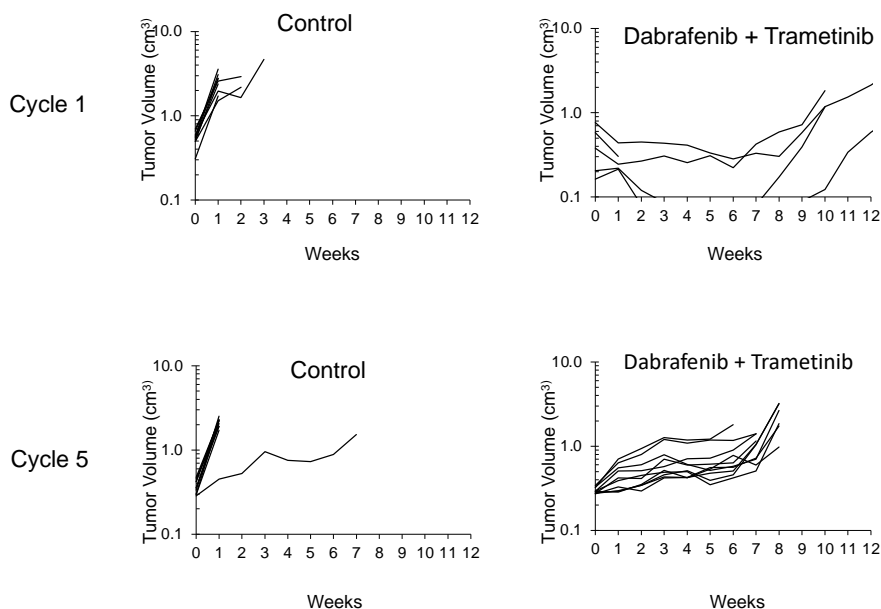


Fig. S8B. Development of resistance to the dabrafenib + trametinib combination.

Mice bearing subcutaneous BT-40 tumors were treated with a combination of dabrafenib (30 mg/kg daily PO) and trametinib (1 mg/kg daily PO) for 42 days. Tumor volumes were derived from weekly caliper measurements. Resistance was developed using the strategy shown in Fig.S5A. Event-free Survival (EFS) for Cycle 1 was 75.35 ± 10.05 days, and for Cycle 5 EFS was 48.8 ± 5.3 days ($P < 0.01$).

