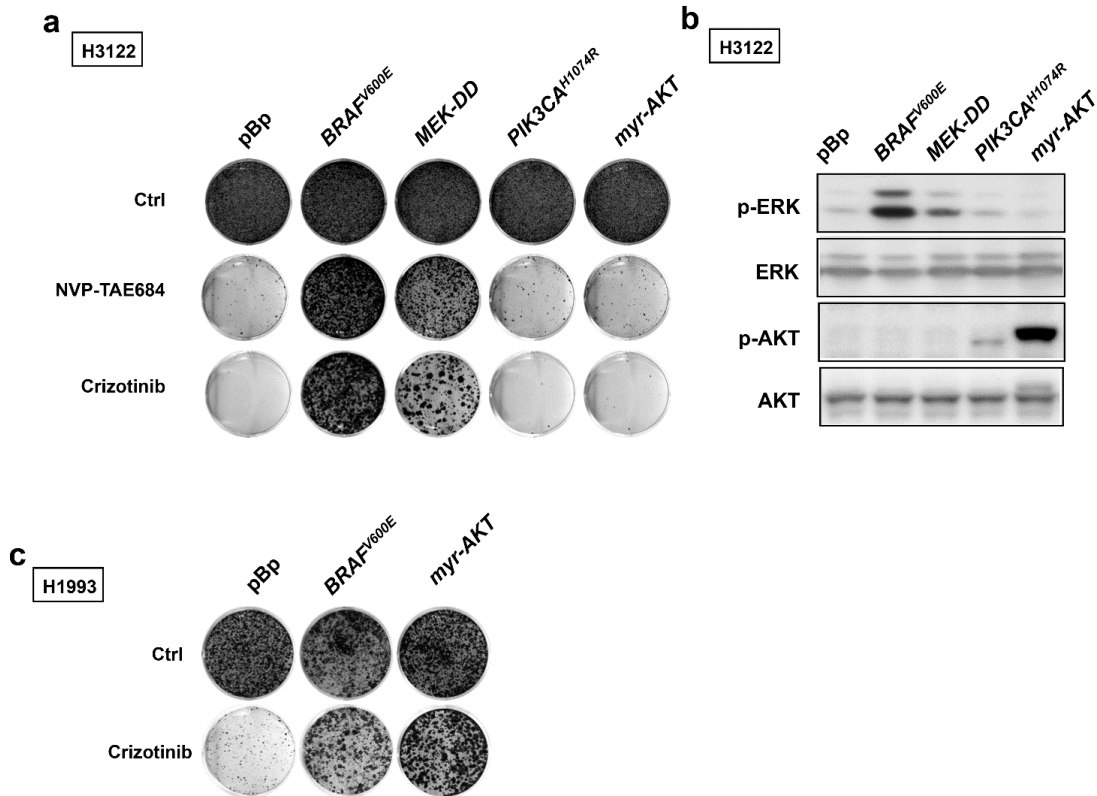


Figure S4



Supplementary information, Figure S4 MAPK/ERK activation is sufficient to confer resistance to MET and ALK inhibitors in NSCLCs, whereas AKT activation results in resistance to only MET inhibition.

(A) MAPK/ERK activation is sufficient to confer resistance to ALK inhibitors in NSCLC cells harboring *EML4-ALK* translocation. H3122 cells expressing pBp control or active alleles of these signalling components of MAPK/ERK and PI3K/AKT cascades (pBpBRAF^{V600}, pBp MEK-DD, pBpPIK3CA^{H1074R} or pBp-*myr-AKT*) were cultured in the absence or presence of 300 nM crizotinib. The cells were fixed, stained and photographed after 14 (untreated) and 21 (treated) days. **(B)** Western blotting analysis of H3122 cells expressing active alleles of these signalling components of MAPK/ERK and PI3K/AKT cascades. H3122 cells expressing pBp control, pBpBRAF^{V600}, pBp

MEK-DD, pBpPIK3CA^{H1074R} or pBp-*myr-AKT* were harvested and protein lysates were subjected to immunoblot analysis for the indicated proteins. (C) Activation of ERK or AKT is sufficient to confer resistance to MET inhibition in *MET*-amplified NSCLC cells. H1993 cells expressing pBp control, pBpBRAF^{V600E} or pBp-*myr-AKT*, were cultured in the absence or presence of 300 nM crizotinib. The cells were fixed, stained with crystal violet and photographed after 14 (untreated) and 21 (treated) days.