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Supplementary Figure Legends:

Supplementary Figure 1 Different EML4-ALK variants elicit similar proliferation rates

Ba/F3 cells expressing the indicated *EML4-ALK* fusion variants were plates at equal concentrations. Cell numbers were counted on each of the following four days. Each data point represents the mean of three triplicate measurements, error bars indicate SEM.

Supplementary Figure 2 ALK phosphorylation levels after inhibitor treatment

A NIH3T3 cells expressing the indicated *EML4-ALK* cDNAs were treated with increasing concentrations of crizotinib for 1h. Whole cell lysates were prepared and analyzed for pALK, pAKT, pERK, ALK and actin protein levels by immunoblotting. Black arrows indicate the respective fusion variant (upper and lower) or unspecific bands (middle).

C Whole cell lysates of NIH3T3 cells stably expressing *EML4-ALK v1* and *v3a* were treated with different concentrations of crizotinib for 1h. Levels of ALK, AKT and ERK phosphorylation were determined by immunoblotting. Actin was used as loading control. Black arrows indicate the respective fusion variant.

Supplementary Figure 3 Schematic representation of *EML4-ALK variants 1*, *2*, *3a* and *3b*

Protein domains of the indicated EML4-ALK variants are shown, the breakpoint between EML4 and ALK is indicated with a black arrow. The additional 33-bp sequence derived from intron 6 of *EML4* that differentiates *v3b* from *v3a* is shown as a gray box.

Supplementary Figure 4 TAE684 induced ALK protein degradation

NIH3T3 cells expressing the indicated *EML4-ALK* cDNAs were treated with 1µM TAE684 or DMSO. After 24h of treatment, lysates were prepared and analyzed for ALK and Actin protein levels by immunoblotting.

Supplementary Figure 5 Protein stability of *EML4-ALK* variants

NIH3T3 cells expressing the indicated *EML4-ALK* variants were treated with DMSO or 100µg/ml cycloheximide for 24h. Whole cell lysates were prepared and stained for total ALK levels by immunoblotting (left). Signal intensities of three independent experiments were analyzed using ImageJ software. Average signal ratios of DMSO/CHX are shown for each *EML4-ALK* variant, error bars indicate SEM (right).

Supplementary Figure 6 HSP90 inhibitor sensitivity of *EML4-ALK variants 2* and *3a*

Ba/F3 cells expressing the indicated *EML4-ALK* variants were treated with increasing concentrations of AUY922. Viability was determined after 72 hours of treatment by measurements of cellular ATP content, expressed as a function of compound dose relative to DMSO-treated controls.

Supplementary Figure 7 Bortezomib sensitivity of *EML4-ALK* variants

Ba/F3 cells expressing the indicated *EML4-ALK* variants were treated with increasing concentrations of bortezomib. Viability was determined after 72 hours of treatment by measurements of cellular ATP content, expressed as a function of compound dose relative to DMSO-treated controls.