Supplementary Material for

The ALK inhibitor ceritinib overcomes crizotinib resistance in non-small cell lung cancer

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Supplementary Figure Legend

Figure S1: Ceritinib impacts the growth of crizotinib naïve *EML4-ALK* wild-type cells. A) Ceritinib is selective to *ALK* translocated cell lines**.** A panel of tumor cell lines was treated with ceritinib for 3 days. The viable cells were measured by Cell-Titer-Glo. B) Initial and final body weight of mice treated with ceritinib or crizotinib for 14 days corresponding to Figure 1E experiment. C) Nude mice bearing MGH006 primary explants from a crizotinib naïve patient sample harboring *EML4-ALK* wild-type were treated with ceritinib 25 mg/kg. Tumor volumes are presented as mean +- SD (n= 5).

Figure S2: Cell survival assay of H3122 CR1, MGH021-4 and MGH045 cells following treatment with Crizotinib or ceritinib. (A-C) H3122 CR1 (A), MGH021-4 (B), and MGH045 (C) cells were treated with the indicated doses of crizotinib or ceritinib for 72 hours. After the incubation, the cell survival was assayed by Cell-Titer-Glo.

Figure S3: Cell survival assay of Ba/F3 cells following treatment with Crizotinib or ceritinib. Ba/F3 cells harboring *EML4-ALK* wild-type, L1196M, G1269A, S1206Y, I1171T, C1156Y, G1202R, 1151T-ins, L1152P or F1174C mutations were treated with the indicated doses of crizotinib or ceritinib for 48 hr. After the incubation, the cell survival was assayed by Cell-Titer-Glo.

Figure S4: Development of crizotinib resistant H2228 xenograft tumor models. SCID beige mice bearing H2228 tumors were treated with 50 mg/kg crizotinib once daily for 11 days, then at 75 mg/kg once daily for 10 days before the dose was increased to 100 mg/kg once daily. Tumors that stopped responding to and continued to grow on 100 mg/kg crizotinib treatment were considered resistant and harvested for sequencing. The tumor volume in 3 animals from the resistant model development studies are shown as the representative of the 80 animals in the studies.