Table S1. Cell viability of Ba/F3 cells overexpressing *EGFR* Exon20ins treated with poziotinib and amivantamab and antiproliferative potency in mutant over WT *EGFR*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Ba/F3 (EGFR)** | **Poziotinib (IC50, nM)** | **Amivantamab (IC30, mg/ml)** | **Potency (WT/mutant)** | |
| WT | 0.8 | 0.9 | Poziotinib | Amivantamab |
| V769\_D770insASV | 1.3 | 0.6 | 0.62 | 1.42 |
| D770delinsGY | 0.8 | 0.2 | 1.00 | 5.41 |
| H773\_V774insH | 10.4 | 0.1 | 0.07 | 12.96 |
| Y764\_V765insHH | 6.0 | 1.5 | 0.13 | 0.61 |
| D770\_N771insSVD | 1.5 | 1.4 | 0.53 | 0.64 |

**Table S2. Characteristics of PDC/PDO/PDX models.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Models** | ***EGFR* Exon20ins mutations** | **Prior treatment history** | **Co-occurring mutations** |
| DFCI-127 | P772\_H773insPNP | pemetrexed/carboplatin/bevacizumab  docetaxel. | ATR (I774fs), CREBBP (S893L), TP53 (D61fs) |
| DFCI-58 | H773\_V774insNPH | None | ATR (I774fs), ATM (L2307F), TP53 (H179Y), JAK3 (P151R) |
| YU-1163 | S768\_D770dup | pemetrexed/cisplatin | TP53 (R280T), DNMT3A (E863K), APC (S1148C), APC (R2660T), KMT2C (K2797fs) |
| YUO-036 | A767\_V769dup | afatinib/poziotinib  gemcitabine/carboplatin  pemetrexed | TP53 (R273L), GNAS (A280T) |
| YUO-029 | S768\_D770dup | pemetrexed/cisplatin | DNMT3A (E863K), APC (S1148C), TP53 (R280T) |
| YHIM-1029 | D770\_N771insG | pemetrexed/cisplatin  gefitinib/docetaxel/  vinorelbine/gemcitabine | FANCD2 (A1149V), KMT2C (G315C), WIF1 (V82L), TP53 (H178Q), STK11 (P281L), STK11 (F354L) |