

Legend to Supplemental Figures

Supplemental Figure 1. *MET* is not overexpressed in tumors which display *KRAS* mutations as a mechanism of secondary resistance to EGFR targeted monoclonal antibodies.

At relapse from anti-EGFR therapy, we collected tumor samples from three patients (#5, #6 and #7), in which *KRAS* mutations became detectable after treatment. Immunohistochemical staining for *MET* was negative in all three cases.

Supplemental Figure 2. Schematic representation of the PCR based strategy used to detect the locus-specific rearrangement associated to *MET* amplification in samples from patient #2

Regional detail (chr7:85,000,000-130,000,000) of the sequencing depth (y-axis) from the whole genome sequencing performed on Patient #2 (post Pmab); three distinct loci show an increased depth, including the region harbouring the *MET* oncogene (around position chr7:116,000,000). The lower scheme shows the positions and orientations of the primers used to detect both the rearranged and wild-type chromosome.

Supplemental Figure 3. Schematic representation of the PCR based strategy used to detect the locus-specific rearrangement associated to *MET* amplification in samples from patient #3 and identification of *MET* amplification in circulating tumor DNA during anti-EGFR therapy.

A. Regional detail (chr7:114,000,000-119,000,000) of the sequencing depth (y-axis) from the whole genome sequencing performed on Patient #3 (post Cmap); the entire region shows an increased depth, including the region harbouring the *MET* oncogene (around position chr7:116,000,000). The lower scheme shows the positions and orientations of the primers used to detect both the rearranged and wild-type chromosome. **B.** DNA electrophoresis of PCR products obtained using primers designed to detect the presence of the *MET* associated amplified rearrangement on Chromosome 7. The lower band corresponds to an 81 bp tumor-specific PCR product which is positive only when the re-arrangement is present. A control assay detecting the wild-type locus generated an amplicon of 103 bp (upper band) is also shown.

Supplemental Figure 4. Ectopic expression of MET in cetuximab sensitive DIFI and LIM1215 cell lines.

Western Blot analysis to evaluate the expression and phosphorylation of MET and MET kinase dead (MET KD) or the expression of KRAS upon lentiviral transduction of the corresponding vectors in DIFI and LIM1215 cell lines.

Supplemental Figure 5. Schematic representation of the scoring system applied to assess MET protein expression by immunohistochemistry