Supplemental Material for

Molecular heterogeneity and receptor co-amplification drive resistance to targeted therapy in *MET*-amplified esophagogastric cancer

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Supplemental Material:

Supplemental Figures

Supplemental Tables

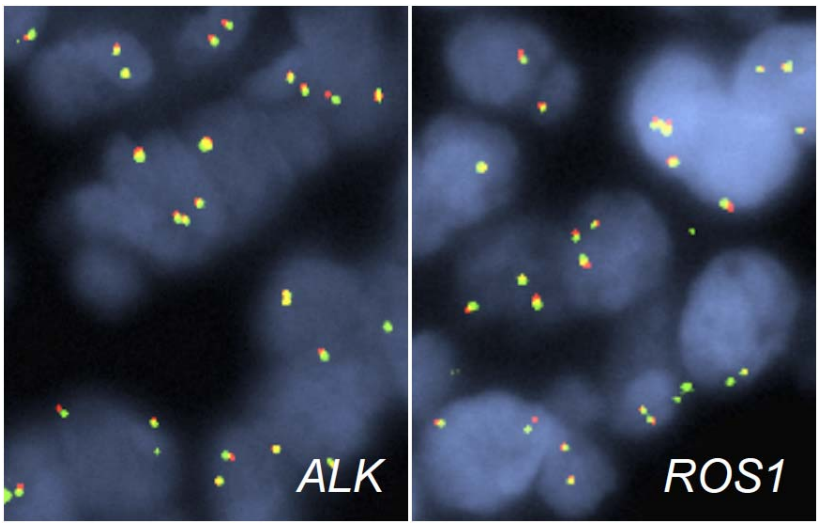

Figure S1: Absence of *ALK* or *ROS1* rearrangements in tumor tissue from Patient #3. Clinical testing by break-apart FISH assay shows lack of *ALK* or *ROS1* rearrangements in tumor tissue from Patient #3, as evidenced by the consistent close proximity of the green and red probes flanking each gene.

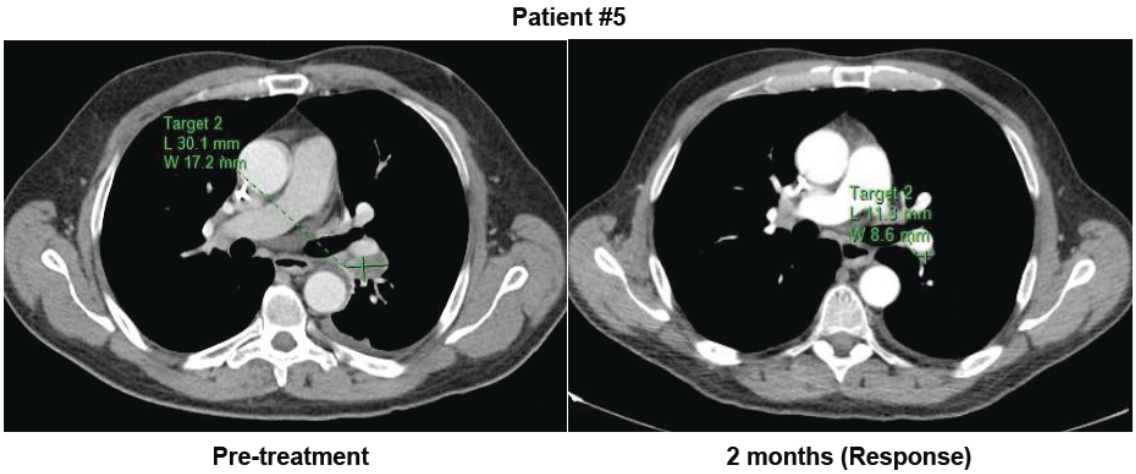

Figure S2: CT images for Patient #5. CT images obtained pre-treatment and at the time of partial response after two months of AMG337 therapy. One of the patients target lymph nodes and associated RECIST measurements are shown in green.

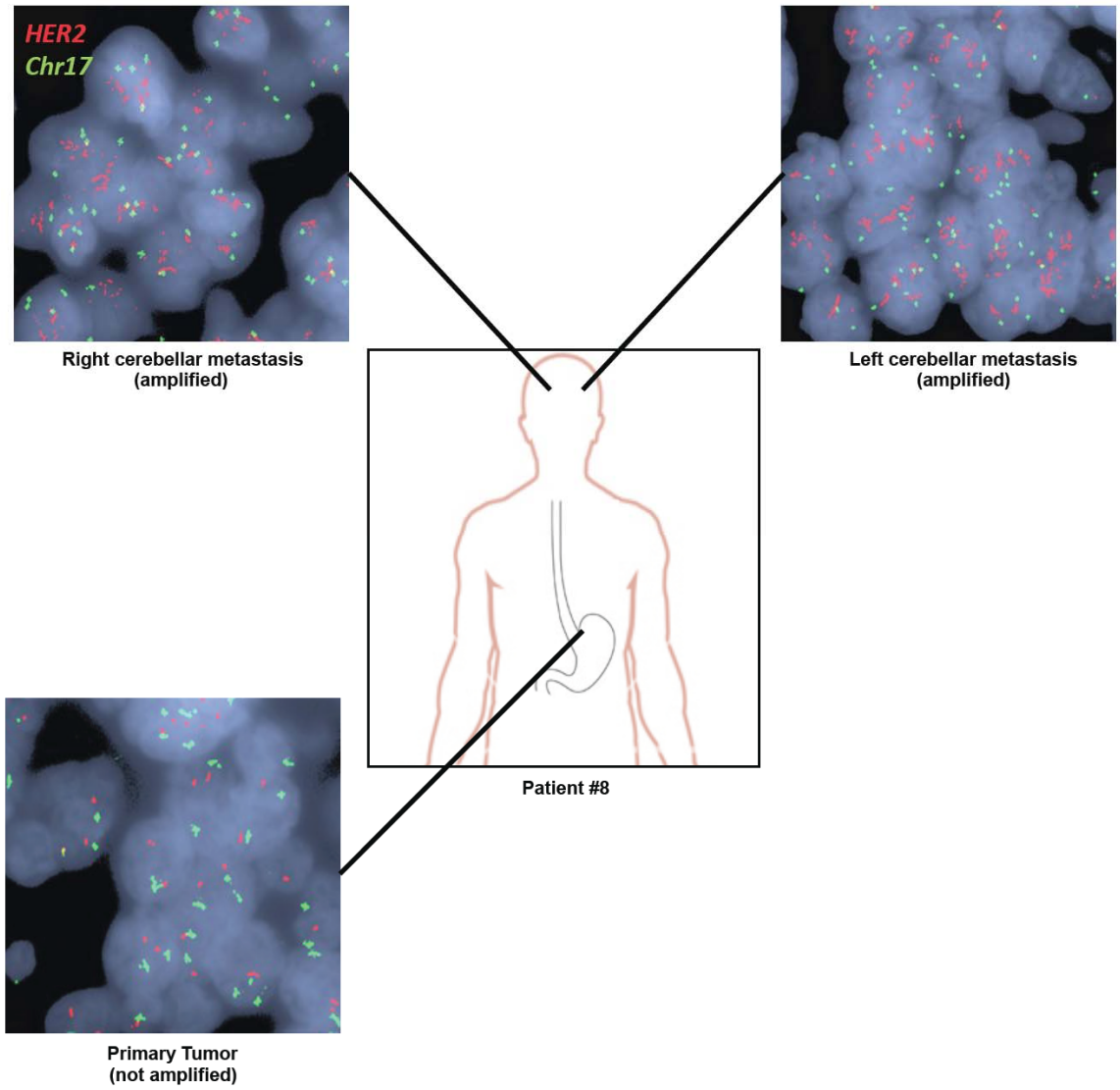

Figure S3: Interlesional molecular heterogeneity in a *HER2*-amplified EGC patient.

FISH analysis for *HER2* (red) with chromosome 17 control (green) for three tumor specimens obtained from Patient #8.

40 GENE PANEL	
AKT1	IDH1
ALK	IDH2
APC	KIT
BRAF	KRAS
CDH1	MAP2K1
CDKN2A	MET
CTNNB1	NOTCH
DDR2	NRAS
EGFR	PDGFRA
ERBB2	PIK3CA
ESR1	PIK3R1
FBXW7	PTEN
FGFR1	RET
FGFR2	ROS1
FGFR3	SMAD4
FOXL2	SMO
GNA11	STK11
GNAQ	TERTprmt
GNAS	TP53
HRAS	VHL

Table S1: 40 gene clinical targeted exome sequencing panel. Mutational profiling was performed in the Massachusetts General Hospital Molecular Pathology Department using the institution's standard clinical next-generation sequencing platform covering these 40 cancer-related genes.

Tumor specimen	*KRAS*^{G12D} Mutant Events	*KRAS* Wild-type Events	*KRAS* Total Events	*KRAS*^{G12D} (% abundance variant allele)
Pre-treatment	0	1405	1405	0/1405 (0%)
Post-progression	228	1825	2053	228/2053 (11.1%)

Table S2: Emergence of *KRAS*^{G12D} mutation in Patient #1 by ddPCR. High-sensitivity ddPCR for the *KRAS*^{G12D} allele was performed on the patient's pre-treatment tumor biopsy and on a post-progression tumor biopsy of the same lesion. The number of individual mutant or wild-type events detected and the percent abundance of the variant allele is shown for each specimen.

Patient #	Initial biopsy site	Status of initial biopsy	Status of Primary	TTP (months)
11	primary	*MET* amp	*MET* amp	36.0 (ongoing)
1	primary	*MET* amp	*MET* amp	24.0
12	primary	*MET* amp	*MET* amp	4.9 (ongoing)
2	primary	*MET* amp *HER2* amp	*MET* amp *HER2* amp	0.9
4	metastasis	*MET* amp	*MET* non-amp	0.8
5	metastasis	*MET* amp	*MET* non-amp	2.5

Table S3: Time to progression on MET inhibitor therapy. The time to progression (TTP) in months for each patient on AMG337 is shown. The original site of biopsy (metastatic vs. primary) is indicated, and the gene amplification status of the original biopsy and the primary tumor is shown.