Supplemental Information

Supplemental Table 1. Clinical Characteristics of the *MET*-amplified subgroup (Case No. 1-10) and four patients with *MET*-amplified tumors who received crizotinib (Cr1-4).

Case No.	Age, Sex	Tumor	Stage	Histology (G:CN)	Treatment	Outcome	Pertinent History	GERD/PPI	BE	HP	Smoking	Drinking
1	70, F	E, mid	IIIA (pT3N1)	AdCa (>10)	CXRT (Carb/FU)	DOD 452dpd	HTN,RA, OA,DP	+/+	-	N/A	40py	<1/day
2	68, M	E, distal	IIIA (cT3N1)	AdCa (>2.5)	CXRT (Cis/FU)	DOD 188dpd	CAD,UC, PSO	+/+	+	N/A	60py	none
3*	65, M	E, distal	IV (M1)	AdCa (>5)	Palliative	DOD 29dpd	HTN,DM, Gout	+/+	+	N/A	40py	heavy
4	44, M	GEJ	IV (M1)	AdCa (>2.5)	FU	DOD 215 dpd	PCKD,WT, OC,Gout,	+/+	-	-	Never	<1/day
5	33, M	GEJ	IV (M1)	AdCa (3.5)	Irinotecan	DOD 239 dpd	AR	+/+	-	-	15py	3/day
6	83, F	GEJ	I (pT1)	AdCa (4.2)	N/A	Alive 473 dpd, HGDx3	IDDM, HTN,NP	+/+	+	-	Never	<1/day
7	71, M	G	IV (M1)	AdCa (4.7)	Palliative	DOD 47 dpd	UTI,CC	+/+	-	-	55py	<1/day
8	61, M	G	IV (M1)	MAC (5.1)	Irinotecan/Cisplatin	DOD 123 dpd	HTN,HepA ,PE,BPH	+/+	-	-	No	2/day
9	72, M	G	IV (M1)	DTAC (3.2)	Irinotecan/Cisplatin	DOD 244 dpd	HTN,AEE	+/+	-	N/A	No	<1/day
10	59, M	G	IV (M1)	AdCa (>10)	Irinotecan/Cisplatin	Lost to F/U at 142 dpd	HTN,OA	-/-	-	N/A	No	<1/day
Cr1	62, M	G	IV (M1)	AdCa (3.3 focal)	Capecitabine/Cisplatin	DOD	GU+SGE	-/-	-	-	N/A	N/A
Cr2	51, M	G	IV (M1)	AdCa (>5)	Capecitabine/Cisplatin/Paclitaxel	DOD	N/A	-/-	-	-	12.5py	+
Cr3	57, M	GEJ	IIIA (pT3N1)	AdCa (>5)	Neoadj. ECF	PD	PE	+/+	+	N/A	37py	none
Cr4	52, M	GEJ	IIIA (pT3N1)	AdCa (>5)	CXRT +Crizotinib	DOD 492 dpd	DM2, TrigN, PE	+/+	+	+	30py	2/day

Abbreviations: +, positive/present; -, negative/absent; *, patient with low-level EGFR amplification (G:CN ~2.5); AdCa, Adenocarcinoma; AEE, arterial embolus with embolectomy; AR, allergic rhinitis; BE, Barrett's esophagus/intestinal metaplasia; BPH, benign prostatic hypertrophy; CAD, coronary artery disease; Carb, Carboplatin; CC, chronic constipation; CXRT, pre-operative chemo-radiation; DM2, diabetes mellitus type 2; DOD, died of disease; DP, depression; dpd, days post diagnosis; DTAC, diffuse-type adenocarcinoma; E, esophageal; ECF, epirubicin, cisplatin, 5-fluorouracil; F, female; FU, 5-fluorouracil; (G:CN), gene-to-copy number ratio with copies too numerous to count assigned >10; GEJ, gastroesophageal junction; GERD, gastroesophageal reflux disease; GU, gastric ulcer; HepA, hepatitis A; HGDx3, high-grade dysplasia on 3 subsequent biopsies; HP, *Helicobacter pyloris*; HTN, hypertension; IDDM, insulin dependent diabetes mellitus; M, male; MAC, mucinous adenocarcinoma; N/A, not applicable/available; NP, neuropathy; OA, osteoarthritis; OC, osteochondroma, PCKD, polycystic kidney disease; PD, progressive disease; PE, pulmonary embolism; PPI, proton pump inhibitor; PSO, psoriasis; py, pack-years; RA, rheumatoid arthritis; SGE, subtotal gastrectomy; TrigN, trigeminal neuralgia; tu, tumor; UC, ulcerative colitis; UTI, urinary tract infections; WT, Wilms tumor.

Supplemental Table 2. Clinicopathologic Characteristics of Patients with Gastro Esophageal Cancer by Location.

	Esophageal (E; N=222)		Junctional (J; N=97)		Gastric (G; N=170)		*P*		
Characteristics	No.	%	No.	%	No.	%	E v. G	J v. G	E v. J
Age, years							0.87	0.49	0.32
Median	64		62		66				
Range	36-89		22-93		30-96				
Sex							<0.0001	<0.0001	0.42
Male	181	82	83	86	103	61			
Female	41	18	14	14	67	39			
Pathology							<0.0001	<0.0001	0.004
Adeno									
Intestinal	190	86	88	91	92	54			
Diffuse	6	3	8	8	65	39			
(Signet-ring cell)	(6)				(37)	(22)			
Mixed					4	2			
Mucinous	1	0.5			4	2			
Medullary			1	1	1	1			
Adenosquamous	1	0.5							
Squamous	21	9							
Neuroendocrine	3	1			4	2			
Differentiation							<0.0001	0.008	0.36
Well	12	5	5	5	9	5.4			
Moderate	123	56	44	45	43	25			
Poor	84	38	47	49	117	69			
Undifferentiated	3	1	1	1	1	0.6			
Stage*							<0.0001	0.004	0.17
0	28	13	4	4	4	2			
I	26	12	12	12	31	18			
II	41	18	23	24	21	12			
III	58	26	30	31	33	20			
IV	69	31	28	29	81	48			

*Staging including sub-categories for esophageal and gastric lesions is provided in Fig. 2.

Note: Comparison of clinicopathologic characteristics demonstrates that esophageal (E) and junctional (J) carcinomas are more similar to each other rather than to gastric carcinoma (G). *P*-values derived from Fisher's exact test for dichotomous variables, or χ^2 for pathology, differentiation and stage comparisons (taking all categories into account).

Supplemental Table 3. Amplification frequency by anatomic site

	MET		*EGFR*		*HER2*		*MET+EGFR+HER2*		TN	
	No.	%	No.	%	No.	%	No.	%	No.	%
Esophageal (E) N=222	3	1.3	18	8	30	13.5	51	23	171	77
Junctional (J) N=97	3	3	1	1	10	10	14	14	83	85
E + J N=319	6	1.9	19	6	40	12.5	65	20	254	80
Gastric (G) N=170	4	2.3	4	2.4	5	2.9	13	8	157	92
E + J + G N=489	10	2	23	4.7	45	9.2	78	16	411	84

Note: We separated esophageal (E, prior Siewert type I[1,2]) from junctional (J, Type II) from gastric (G, Type III) carcinomas to allow comparison with prior datasets. Although prior guidelines subsumed J+G as 'gastric' [3], here we subsumed E+J as 'esophageal' according to current recommendations [4,5].

Abbreviations: TN, triple negative (no *MET*/*EGFR*/*HER2* amplification).

Supplemental References

1. Siewert JR, Stein HJ: Adenocarcinoma of the gastroesophageal junction: classification, pathology and extent of resection. Dis Esophagus 9:173-82, 1996
2. Siewert JR, Stein HJ: Classification of adenocarcinoma of the oesophagogastric junction. Br J Surg 85:1457-9, 1998
3. American Joint Committe on Cancer. Digestive system., AJCC Cancer Staging Manual 6th edn. New York, Springer, 2002, pp 91-103
4. American Joint Committee on Cancer, Chapter 10. Esophagus and esophagogastric junction, AJCC Cancer Staging Manual 7th edn. New York, Springer, 2009, pp 129-144
5. Sobin LH, Compton CC: TNM seventh edition: What's new, what's changed: communication from the International Union Against Cancer and the American Joint Committee on Cancer. Cancer 116:5336-9

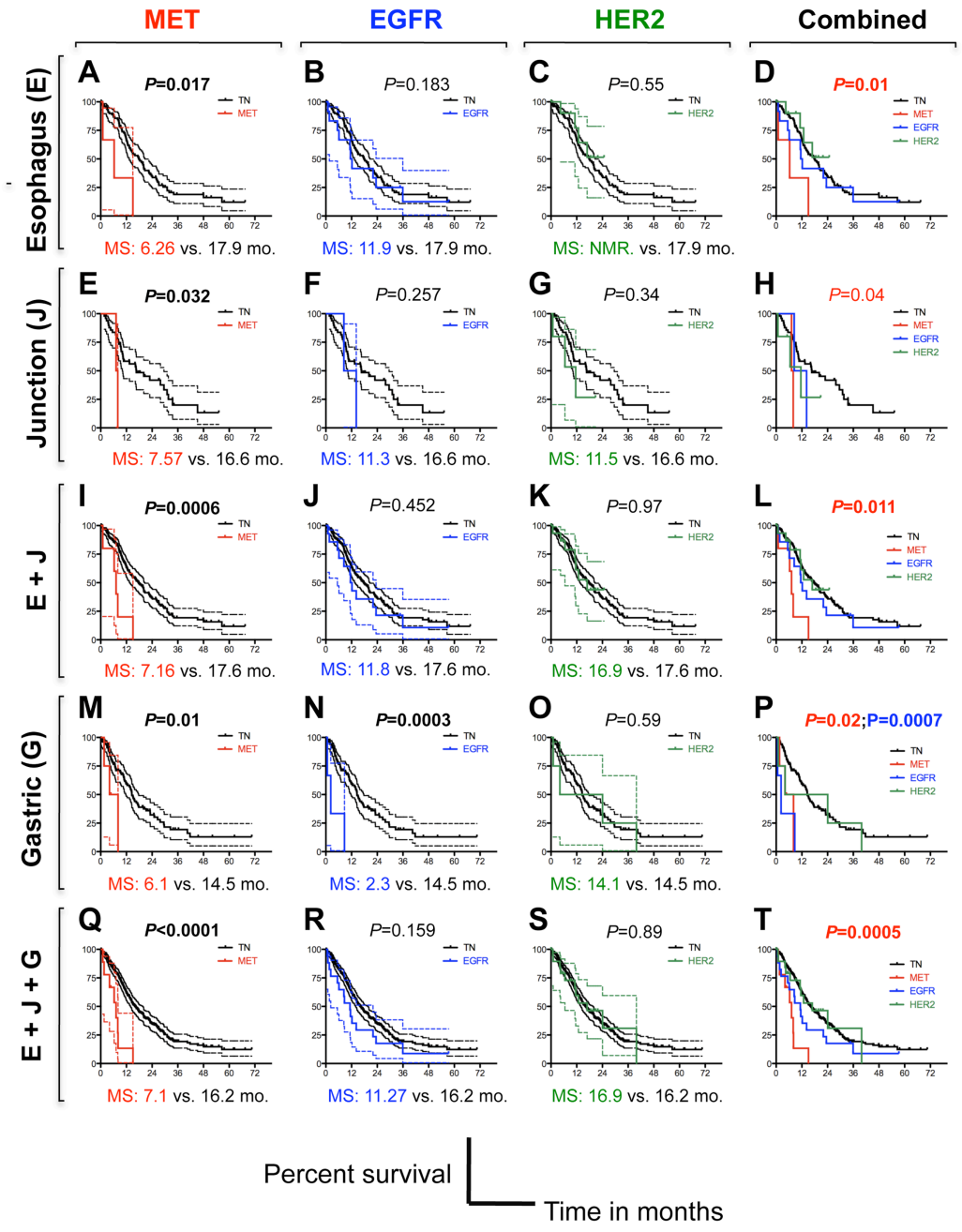
Supplemental Table 4. Statistical Comparison of Survival Times between Stage III vs. Stage IV Tumors by Location and Genotype.

	MET			*EGFR*			*HER2*			TN		
	III	IV	*P*	III	IV	*P*	III	IV	P	III	IV	*P*
E, MS (in mo.)	10.6	0.96	0.157	16.7	11.7	0.46	NMR	16.9	0.518	25.9	11.9	<0.0001
N=127(38); n(cens.)	2(0)	1(0)		6(2)	6(0)		3(2)	8(5)		47(20)	54(9)	
J, MS (in mo.)	N/A	7.6	N/A	14.2	8.4	0.32	33.4	6.5	0.117	27.9	9.5	0.04
N=58(19); n(cens.)		2(0)		1(0)	1(0)		2(1)	3(1)		27(13)	22(4)	
E + J, MS (in mo.)	10.6	7.2	0.455	14.2	11.3	0.39	NMR	14.0	0.28	25.9	11.6	<0.0001
N=185(57); n(cens.)	2(0)	3(0)		7(2)	7(0)		5(3)	11(6)		74(33)	76(13)	
G, MS (in mo.)	N/A	6.2	N/A	N/A	2.3	N/A	24.1	4.2	0.92	29.5	11.8	0.0005
N=114(38); n(cens.)		4(1)			3(0)		1(0)	3(0)		32(19)	71(18)	
E + J + G, MS (in mo.)	10.7	7.2	0.305	14.2	8.6	0.17	24.1	11.2	0.27	25.9	11.8	<0.0001
N=299(95); n(cens.)	2(0)	7(1)		7(2)	10(0)		6(3)	14(6)		106(52)	147(31)	

Note: Although numbers per bin are relatively small, we tallied survival times by location, genotype and stage for comparison between locally advanced and metastatic tumors. Detailed graphs, including 95% confidence intervals and comparisons of *MET*, *EGFR*, and *HER2* vs. non-amplified group (TN) by location are provided in Supplemental Figure 1, available online. *P*-values, log-rank test.

Abbreviations: cens., censored; E, esophagus; G, gastric; J, junctional; mo., months; MS, median survival, N, total number by site; n, total number in category; N/A, not applicable/not available; NMR, no median reached

Supplemental Figure 1. Overall Survival by Location and Genotype



Kaplan-Meier graphs for locally advanced and metastatic tumors (including 95% confidence intervals) show comparisons of median survival (MS) vs. the triple-negative group (TN; no *MET*/*EGFR*/*HER2* amplification) for each genetic subset and anatomic location. Median survival for each trace is provided below the graphs and corresponding *P*-values are derived from log-rank test and printed in bold, when significant. *P*-values in the combined graphs in the right column (D, H, L, P, and T) are derived from comparison of the genetic subset (as indicated by color) versus the combined median survival of the remaining 3 subgroups (e.g. *MET* vs. *EGFR*/*HER2*/TN). The resulting *P*-values are somewhat lower but illustrate that median survival in MET-amplified subsets is significantly shorter even when other amplified subsets (i.e. *EGFR* and *HER2*) are included. NMR, no median reached.