

## Supplementary Online Content

Shah MA, Bang Y-J, Lordick F, et al. Fluorouracil, leucovorin, and oxaliplatin with or without onartuzumab in HER2-negative, MET-positive gastroesophageal adenocarcinoma: the METGastric randomized clinical trial. *JAMA Oncol*. Published online October 5, 2016. doi:10.1001/jamaoncol.2016.5580

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Baseline Characteristics of the Intent-to-Treat Population**

Characteristics	Placebo + mFOLFOX6 (n = 283)	Onartuzumab + mFOLFOX6 (n = 279)
Age, median (range), y	58.0 (23-84)	60.0 (24-82)
Sex, No. (%)		
Male	183 (64.7)	188 (67.4)
Female	100 (35.3)	91 (32.6)
Race, No. (%)		
White	180 (63.6)	172 (61.6)
Black or African American	2 (0.7)	3 (1.1)
Asian	89 (31.4)	94 (33.7)
Other	12 (4.3)	10 (3.7)
ECOG PS, No. (%)		
0	118 (41.7)	112 (40.1)
1 <sup>a</sup>	158 (55.8)	162 (58.1)
Primary tumor site, No. (%)		
Stomach	218 (77.0)	214 (76.7)
Gastroesophageal junction	65 (23.0)	65 (23.3)
Gastric cancer histologic subtype, No. (%)	(n = 283)	(n = 277)
Intestinal	133 (47.0)	136 (49.1)
Diffuse	98 (34.6)	83 (30.0)
Mixed	42 (14.8)	39 (14.1)
Not evaluable	10 (3.5)	19 (6.9)
Prior gastrectomy		
Yes	101 (35.7)	98 (35.1)
No	182 (64.3)	181 (64.9)
MET score, No. (%)		
1+	173 (61.1)	171 (61.3)
2+	94 (33.2)	85 (30.5)
3+	15 (5.3)	20 (7.2)
Not done	1 (0.4)	3 (1.1)
Region, No. (%)		
Asia-Pacific	88 (31.1)	88 (31.5)
Other	195 (68.9)	191 (68.5)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; MET, mesenchymal-epithelial transition; mFOLFOX6, fluorouracil, leucovorin, and oxaliplatin.

<sup>a</sup>Includes patients who were considered ECOG PS 2 after enrollment.

**eTable 2. MET IHC Scoring Qualification of Central Laboratory Pathologists**

<b>Agreement Rate</b>	<b>n (%)</b>
Overall percent agreement	247/250 (98.8)
Average positive agreement	210/210 (100)
Average negative agreement	37/40 (92.5)

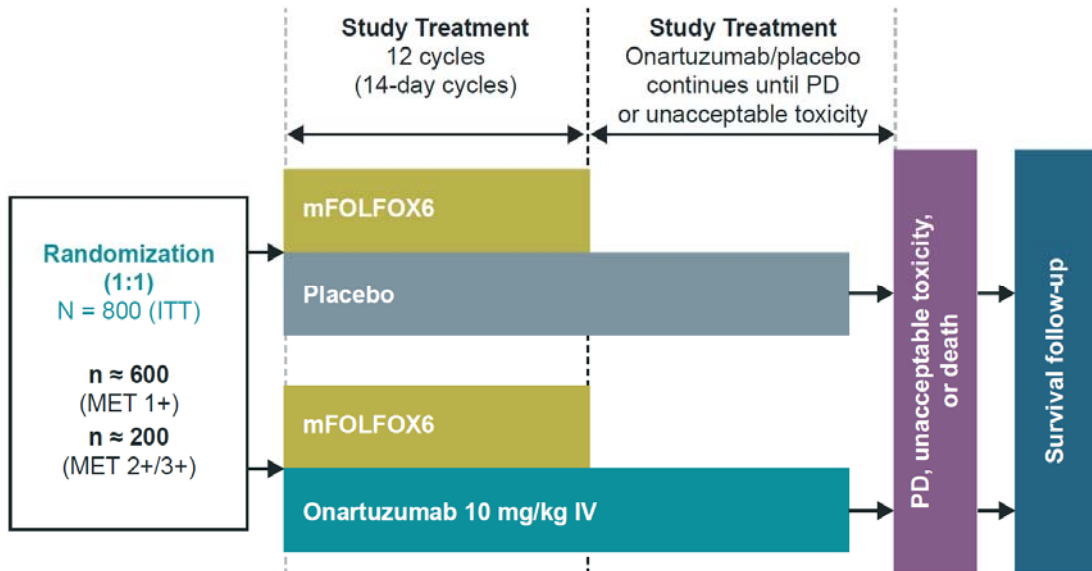
**eTable 3. All Grade<sup>a</sup> and Grade ≥3 AEs**

AE, n (%)	Placebo + mFOLFOX6 (n = 280)		Onartuzumab + mFOLFOX6 (n = 279)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Nausea	141 (50.4)	13 (4.6)	133 (47.7)	7 (2.5)
Neutropenia	112 (40.0)	82 (29.3)	126 (45.2)	98 (35.1)
Fatigue	87 (31.1)	11 (3.9)	77 (27.6)	13 (4.7)
Diarrhea	78 (27.9)	5 (1.8)	85 (30.5)	8 (2.9)
Vomiting	79 (28.2)	12 (4.3)	72 (25.8)	8 (2.9)
Decreased appetite	78 (27.9)	8 (2.9)	75 (26.9)	6 (2.2)
Peripheral edema	22 (7.9)	1 (0.4)	110 (39.4)	13 (4.7)
Constipation	62 (22.1)	1 (0.4)	46 (16.5)	1 (0.4)
Asthenia	54 (19.3)	10 (3.6)	55 (19.7)	13 (4.7)
Peripheral neuropathy	51 (18.2)	5 (1.8)	52 (18.6)	7 (2.5)
Anemia	48 (17.1)	15 (5.4)	48 (17.2)	14 (5.0)
Paresthesia	50 (17.9)	1 (0.4)	40 (14.3)	6 (2.2)
Abdominal pain	40 (14.3)	7 (2.5)	38 (13.6)	3 (1.1)
Thrombocytopenia	29 (10.4)	3 (1.1)	47 (16.8)	12 (4.3)
Alopecia	40 (14.3)	-	33 (11.8)	-
Stomatitis	37 (13.2)	0 (0.0)	35 (12.5)	2 (0.7)
Dysgeusia	34 (12.1)	-	34 (12.2)	-
Hypoalbuminemia	10 (3.6)	1 (0.4)	56 (20.1)	16 (5.7)
Pyrexia	35 (12.5)	1 (0.4)	29 (10.4)	0 (0.0)
Peripheral sensory neuropathy	29 (10.4)	4 (1.4)	18 (6.5)	1 (0.4)
Insomnia	29 (10.4)	-	13 (4.7)	-

<sup>a</sup>Includes all grade AEs occurring at an incidence of >10% in either treatment arm. Multiple occurrences of the same AE in one individual are counted only once. Note, one patient randomized to the placebo arm received onartuzumab during the first treatment cycle; data for this patient were included in the onartuzumab arm for analysis of safety.

Abbreviations: AE, adverse event; mFOLFOX6, 5-fluorouracil, leucovorin, and oxaliplatin.

**eFigure 1. Study design**

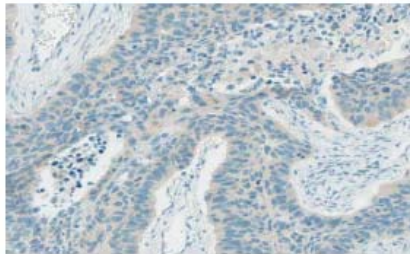


Abbreviations: HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ITT, intent-to-treat; MET, mesenchymal-epithelial transition; mFOLFOX6, 5-fluorouracil, leucovorin, and oxaliplatin; PD, disease progression.

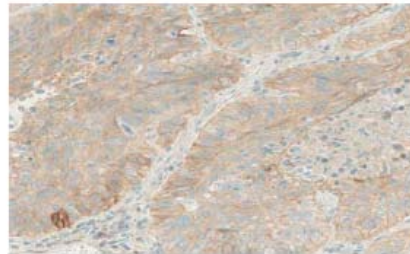
**eFigure 2. Met IHC scoring criteria and representative staining**

Clinical Diagnosis	Clinical Score	Staining Criteria
Negative	0	No or equivocal staining in tumor cells or <50% tumor cells with membrane and/or cytoplasmic staining
Negative	1+	≥50% tumor cells with WEAK or higher membrane and/or cytoplasmic staining but <50% tumor cells with moderate or higher staining intensity
Positive	2+	≥50% tumor cells with MODERATE or higher membrane and/or cytoplasmic staining but <50% tumor cells with strong staining intensity
Positive	3+	≥50% tumor cells with STRONG or higher membrane and/or cytoplasmic staining intensity

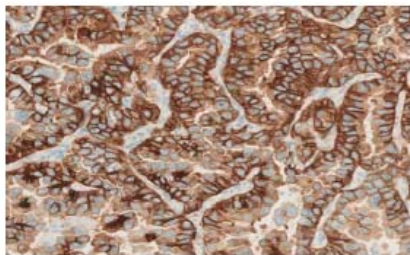
**Clinical Score = 0**



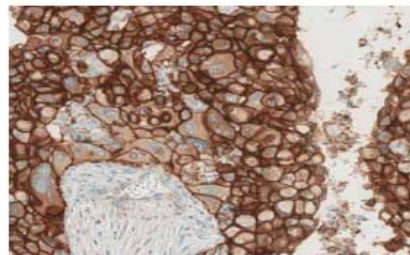
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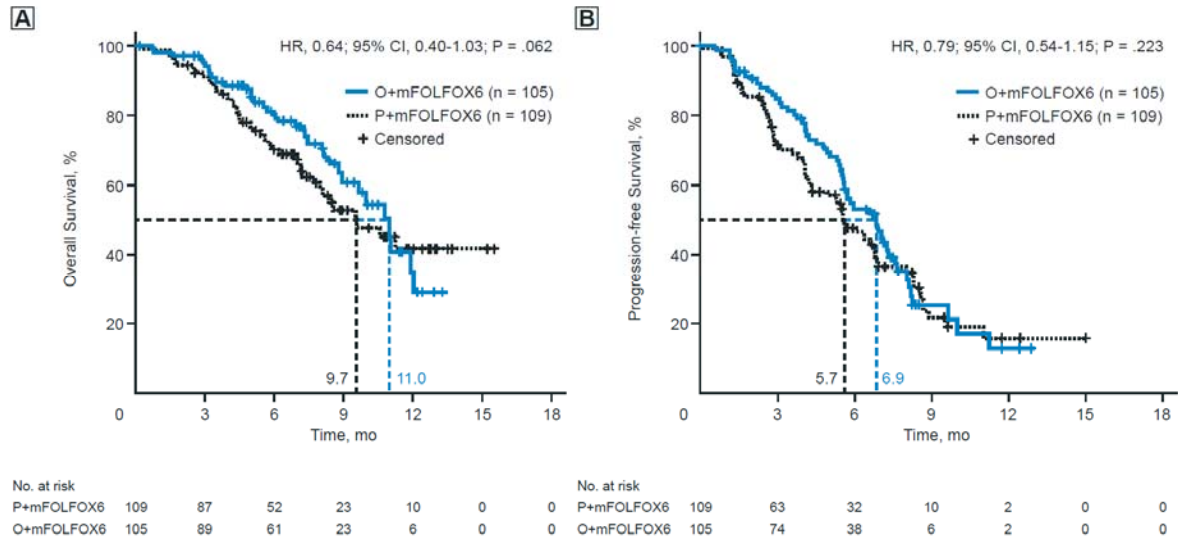
**Clinical Score = 2**



**Clinical Score = 3**



**eFigure 3. OS (A) and PFS (B) in the MET 2+/3+ subpopulation**



**eFigure 4. Overall Survival by MET status, region, and prior gastrectomy**

