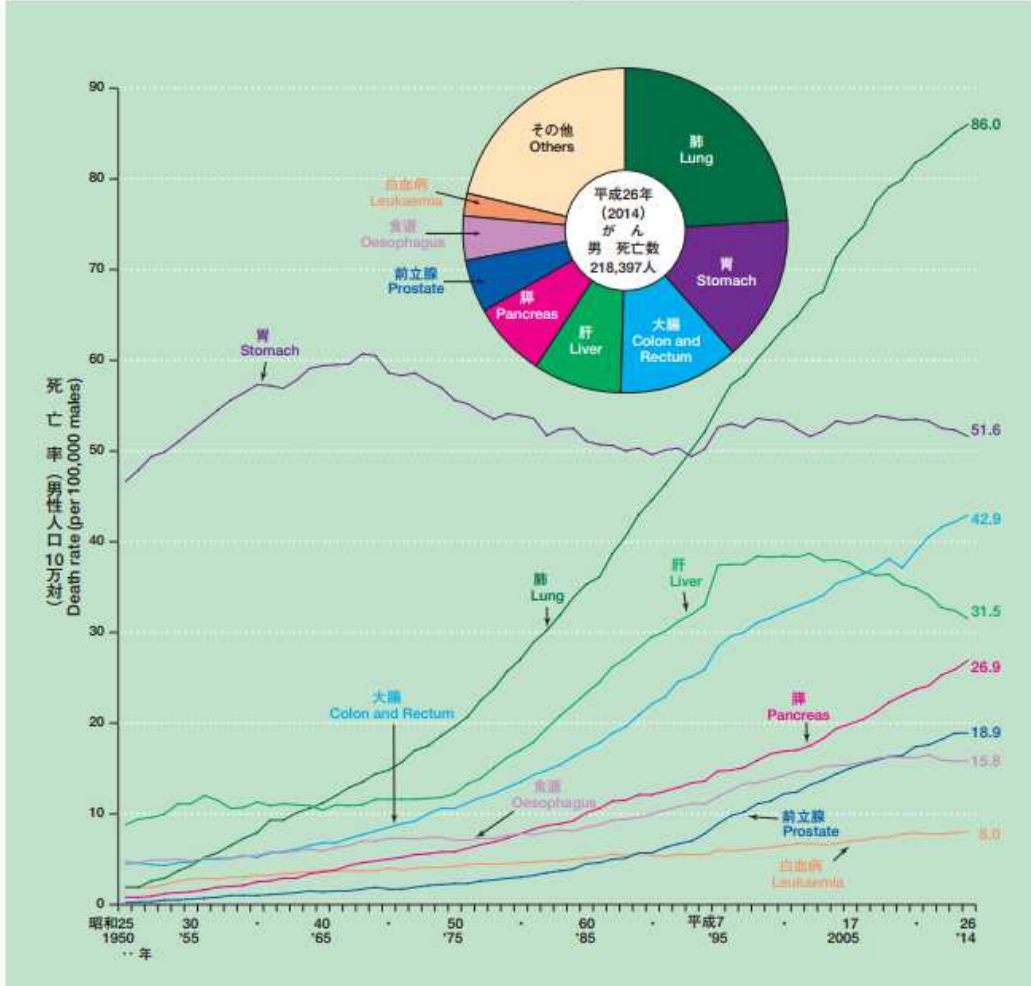


# **第 95回 Medical & Surgical Grand Rounds**

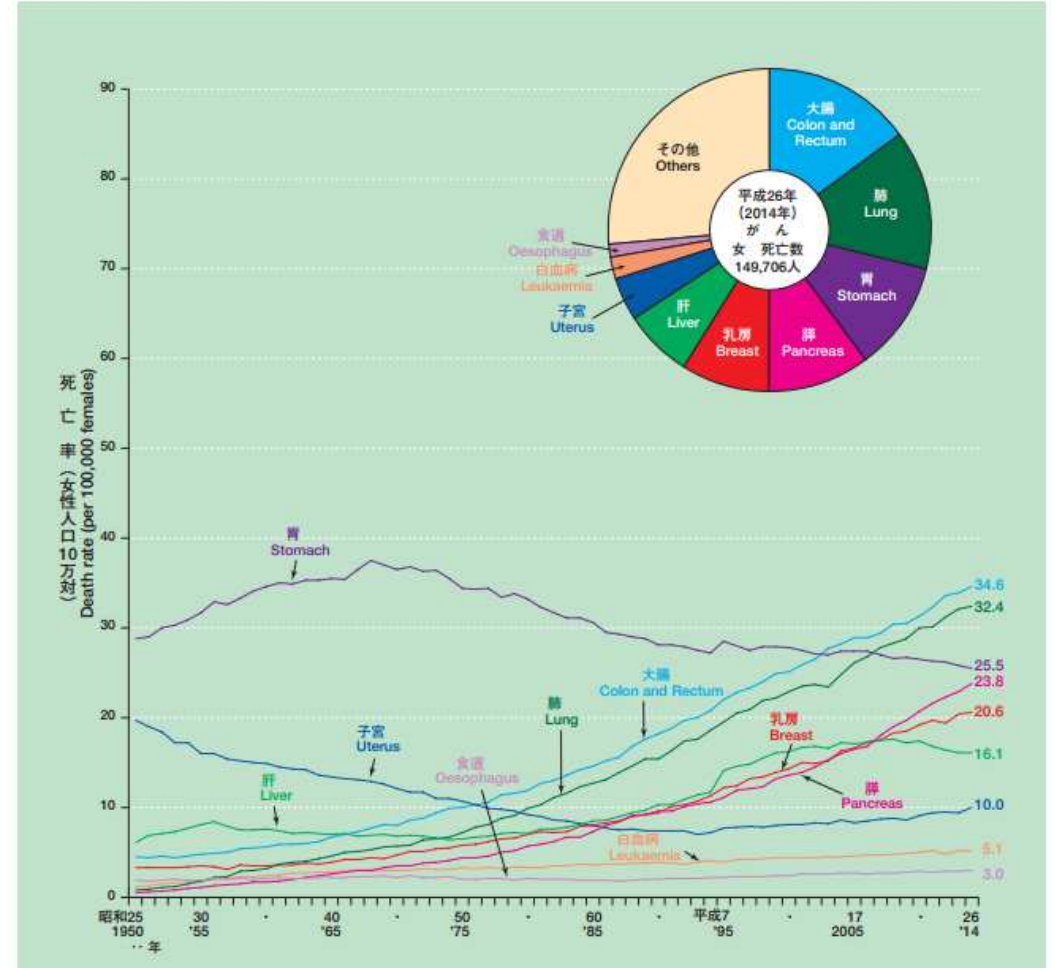
## **RTK coamplification**

# 厚生労働省 人口動態統計

部位別にみたがんの死亡率の年次推移，男—昭和25～平成26年—  
Trends in death rates for cancers by site, Male, 1950-2014



部位別にみたがんの死亡率の年次推移，女—昭和25～平成26年—  
Trends in death rates for cancers by site, Female, 1950-2014



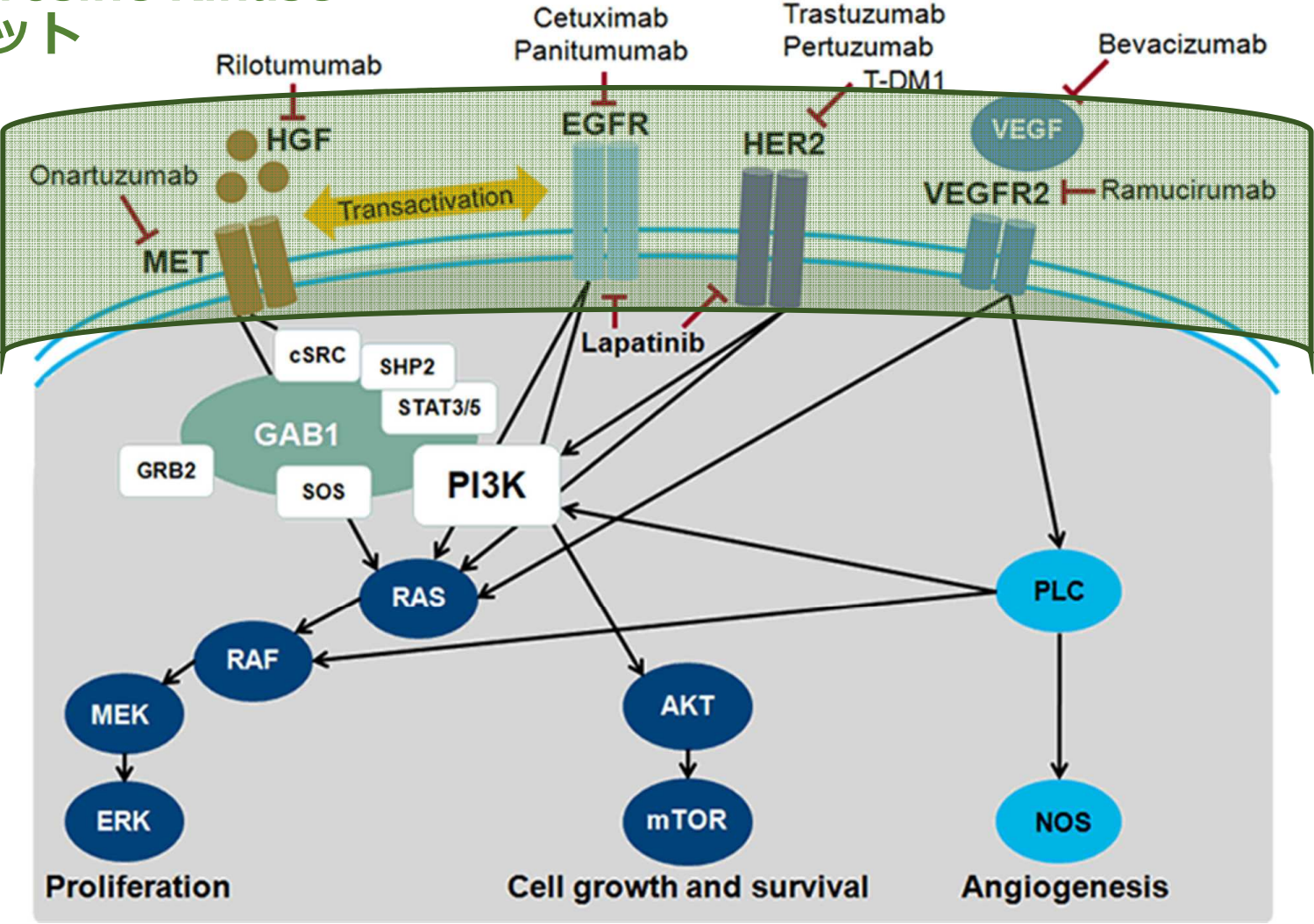
## 日本における切除不能・再発胃癌の化学療法

試験名	レジメン	MST(月)
SPIRIT	S-1+CDDP	<b>13.0</b>
G-SOX	S-1+Oxaliplatin	<b>14.1</b>
ToGA	Cape+CDDP+Trastuzumab	<b>13.8</b>
(2 <sup>nd</sup> -line以降)		
RAINBOW	PTX+Ramucirumab	9.6



どこがターゲットになるか

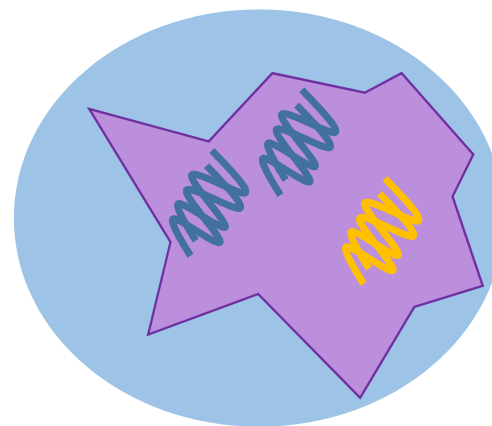
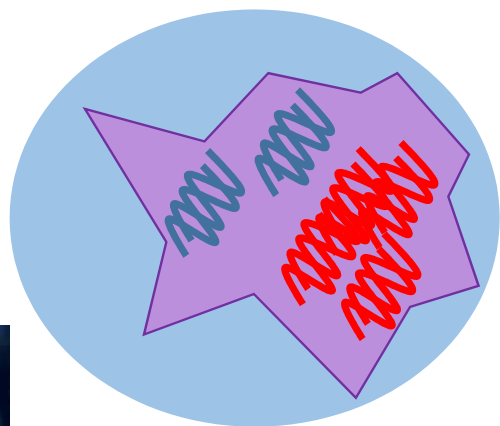
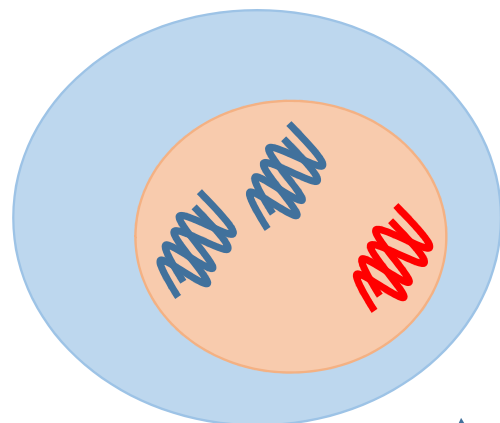
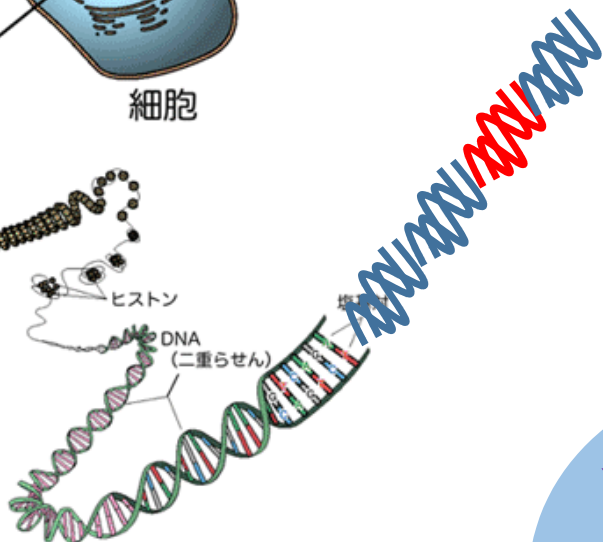
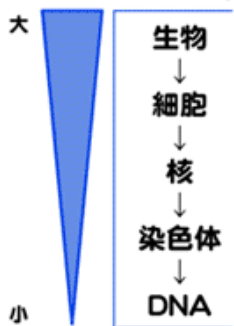
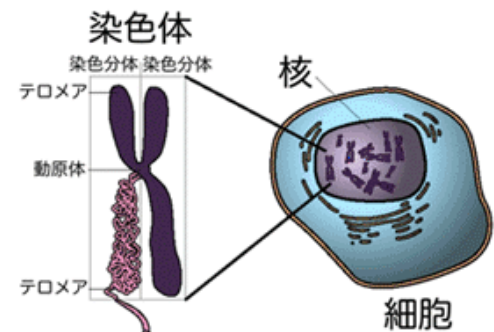
# Receptor Tyrosine Kinase というターゲット



# Comprehensive molecular characterization of gastric adenocarcinoma

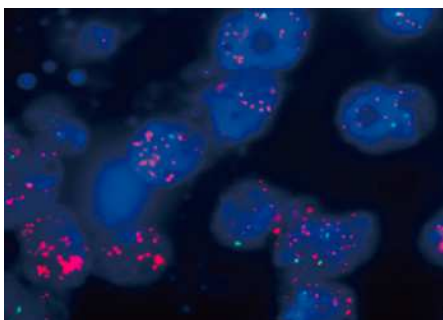
The Cancer Genome Atlas Research Network\*



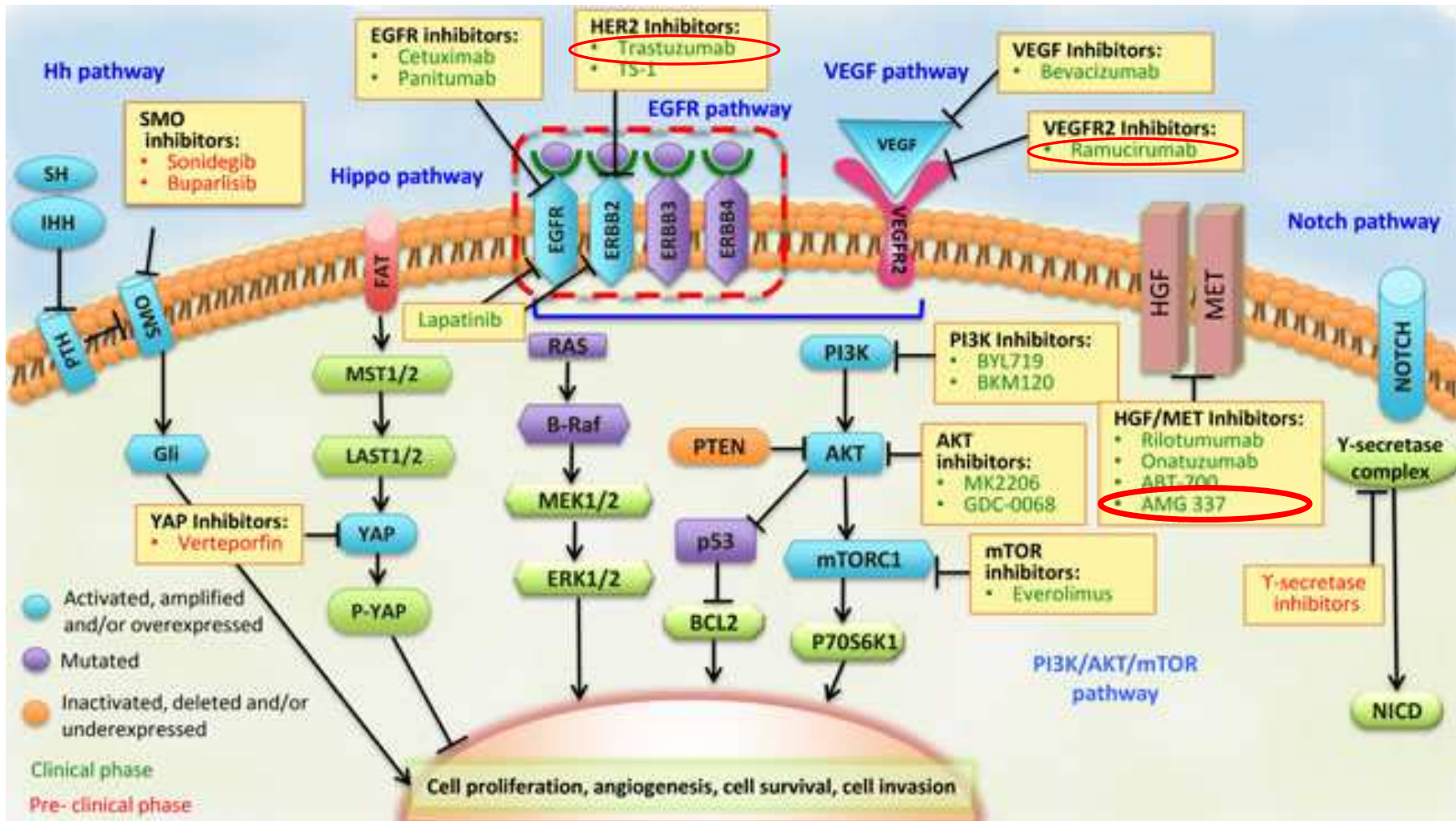


Amplification 増幅

mutation 変異



# 胃癌で標的となり得る遺伝子異常

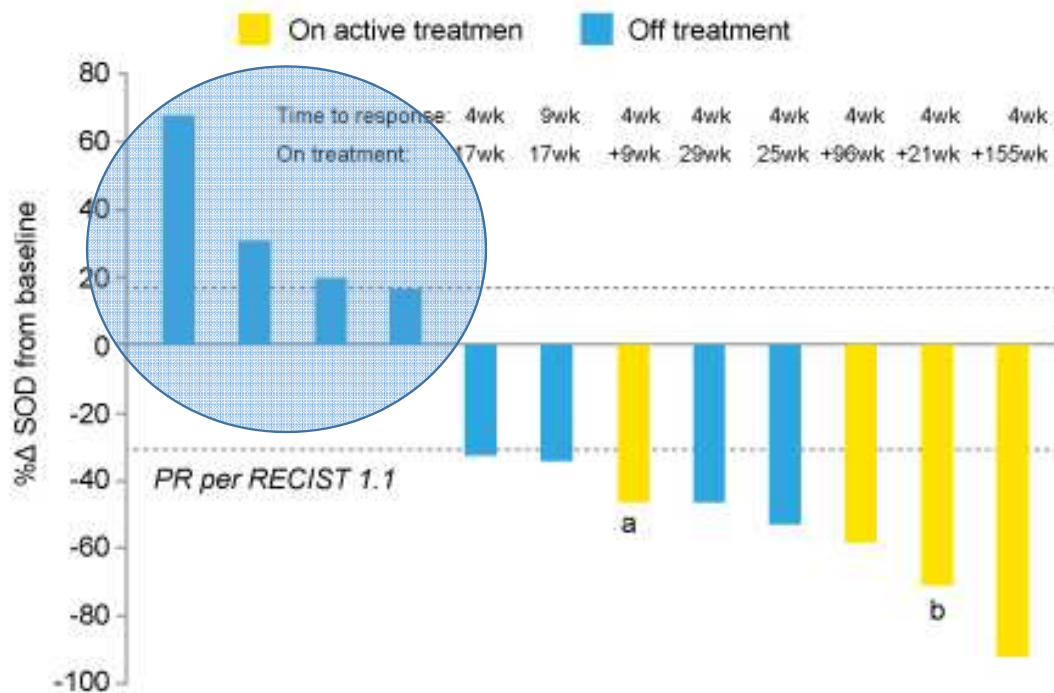






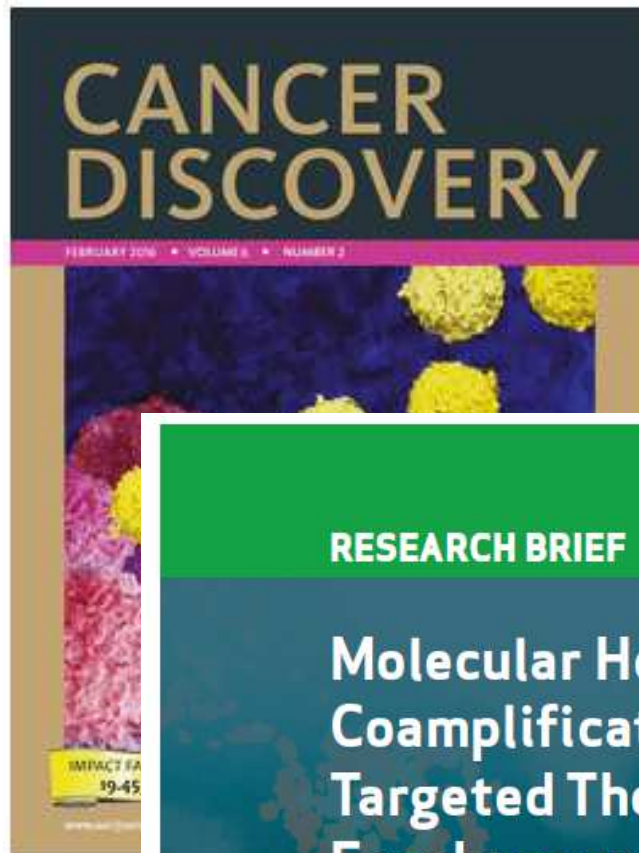
Abstract #1

経口METキナーゼ阻害剤AMG337の臨床活性：MET増幅胃食道接合部癌・胃癌・食道癌成人患者における検討



13 patients with MET-amplified GEJ/gastric/esophageal cancer treated to date; ORR=8/13 (62%)

<sup>a</sup>Local read as of Dec 8, 2014. <sup>b</sup>Local read as of Sept 10, 2014. Central read as of Sept 18, 2014 for all other patients. One patient not shown with non-target lesions had clinical progression.



## RESEARCH BRIEF

# Molecular Heterogeneity and Receptor Coamplification Drive Resistance to Targeted Therapy in *MET*-Amplified Esophagogastric Cancer

Eunice L. Kwak<sup>1,2</sup>, Leanne G. Ahronian<sup>1,2</sup>, Giulia Siravegna<sup>3,4</sup>, Benedetta Mussolin<sup>3,4</sup>, Jason T. Godfrey<sup>1,2</sup>, Jeffrey W. Clark<sup>1,2</sup>, Lawrence S. Blaszowsky<sup>1,2</sup>, David P. Ryan<sup>1,2</sup>, Jochen K. Lennerz<sup>5</sup>, A. John Iafrate<sup>5</sup>, Alberto Bardelli<sup>3,4</sup>, Theodore S. Hong<sup>1,6</sup>, and Ryan B. Corcoran<sup>1,2</sup>

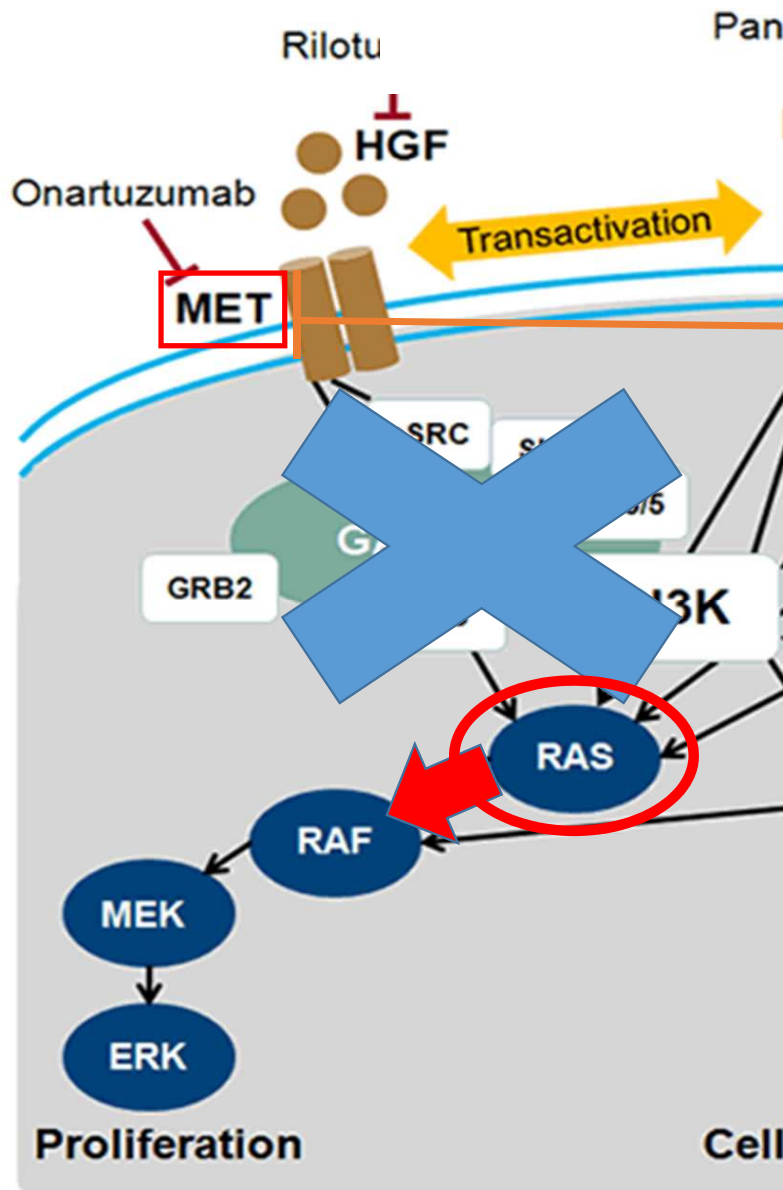
Type#1

Clinical Acquired Resistance  
to MET Kinase Inhibition

# Patient#1: Adenocarcinoma of the distal esophagus



Gene	Pretreatment	Postprogression
<i>MET</i>	Amplified	Amplified
<i>KRAS</i>	WT	G12D



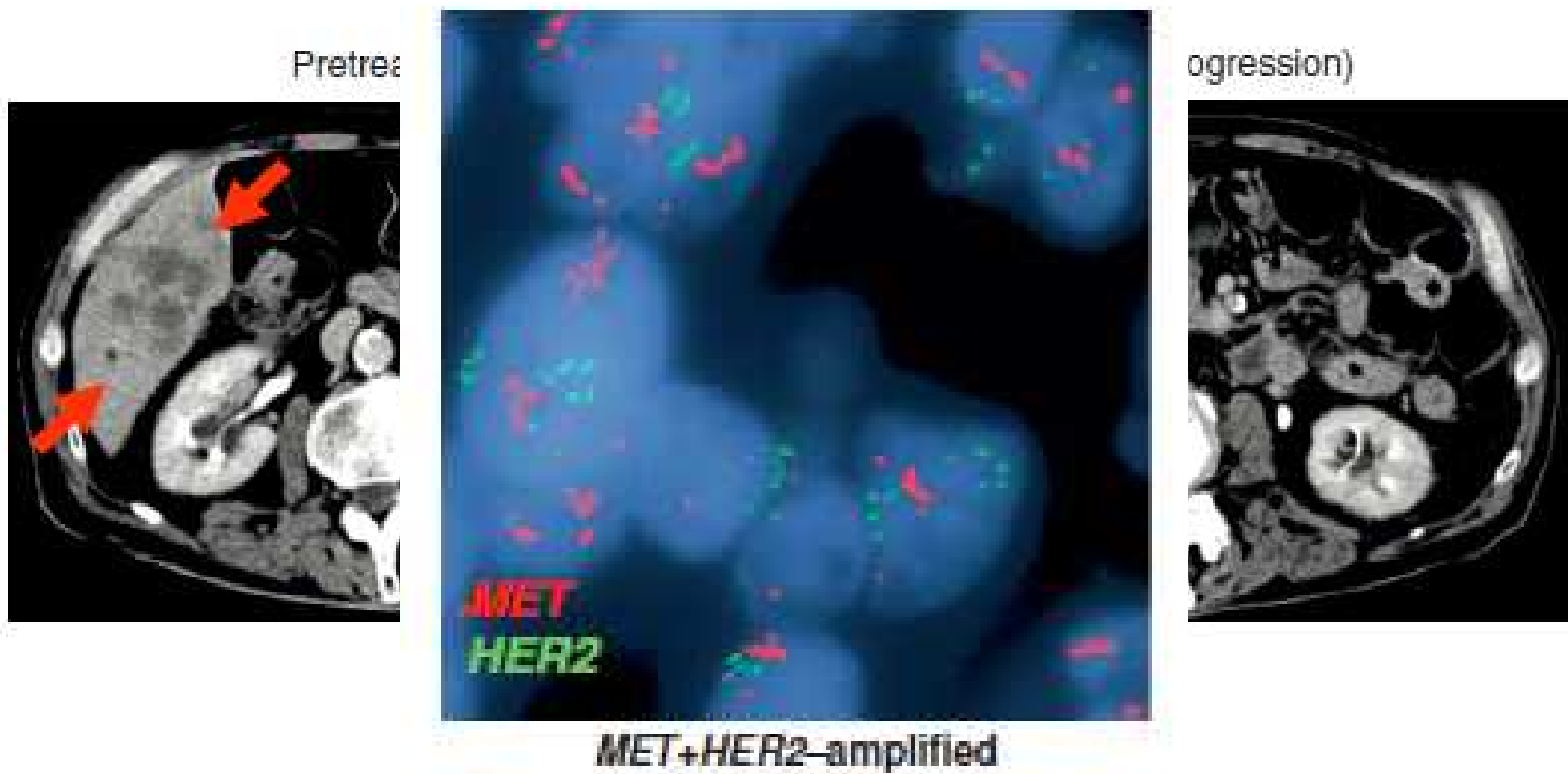
# Crizotinib

MET inhibitor/ALK inhibitor

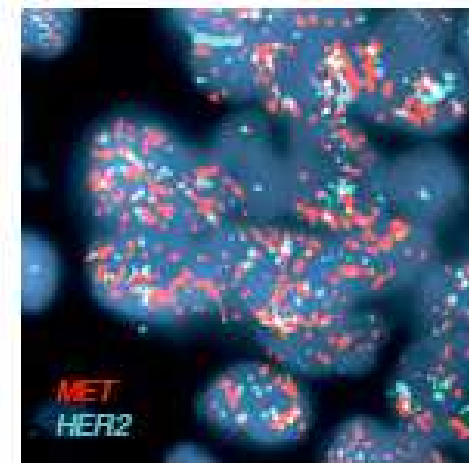
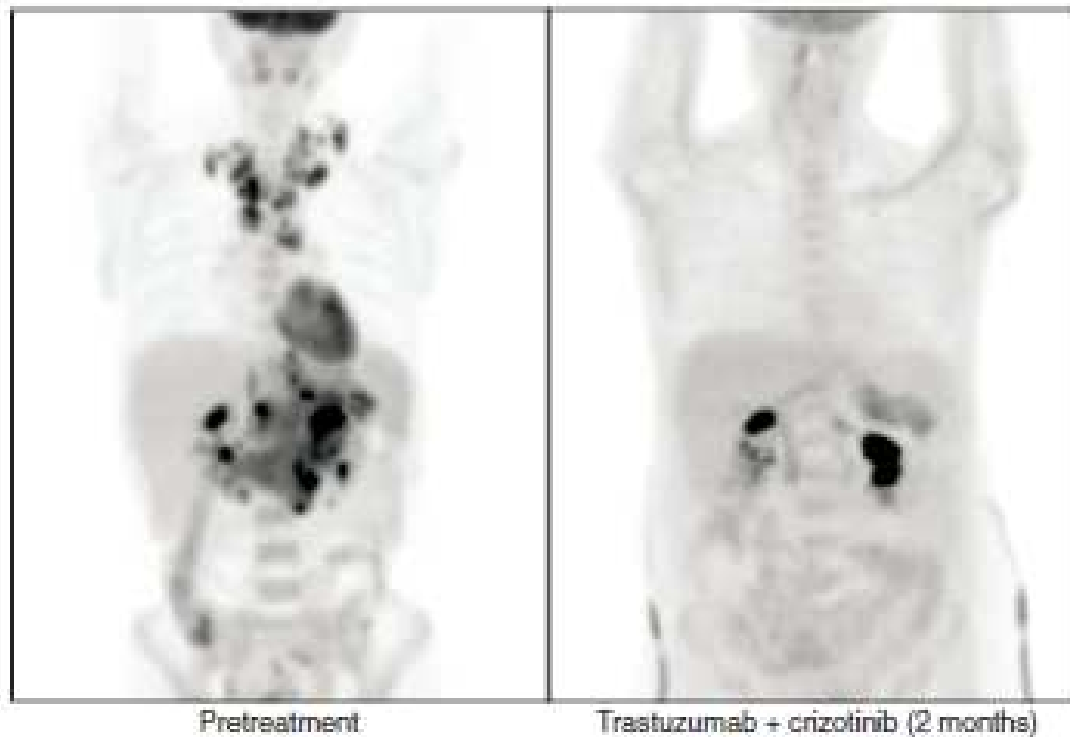
Type#2

RTK Coamplification Drives  
de novo Resistance

# Patient#2: Metastatic gastric adenocarcinoma



Patient#3 :  
Gastric adenocarcinoma with  
amplification of HER2

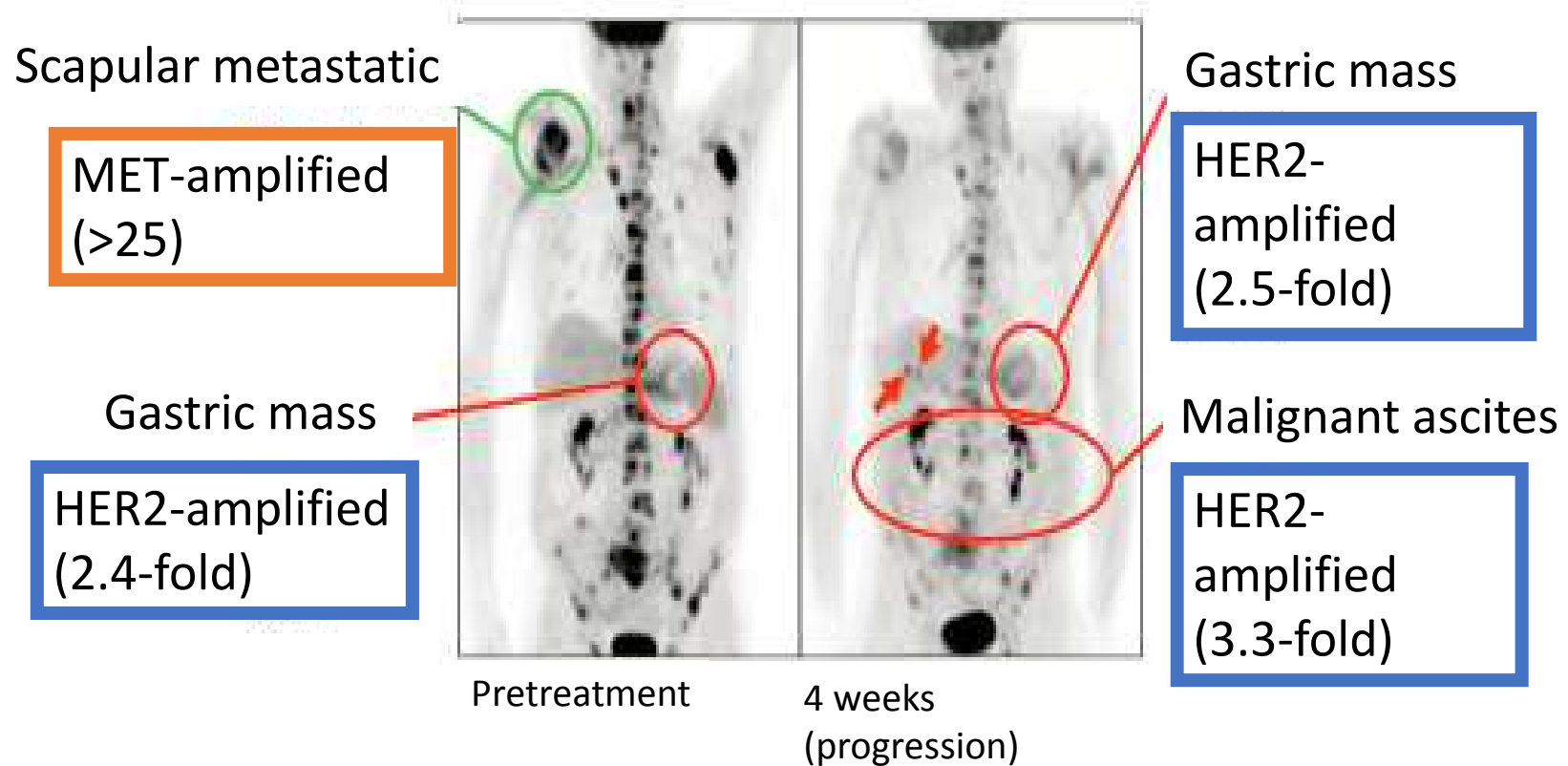


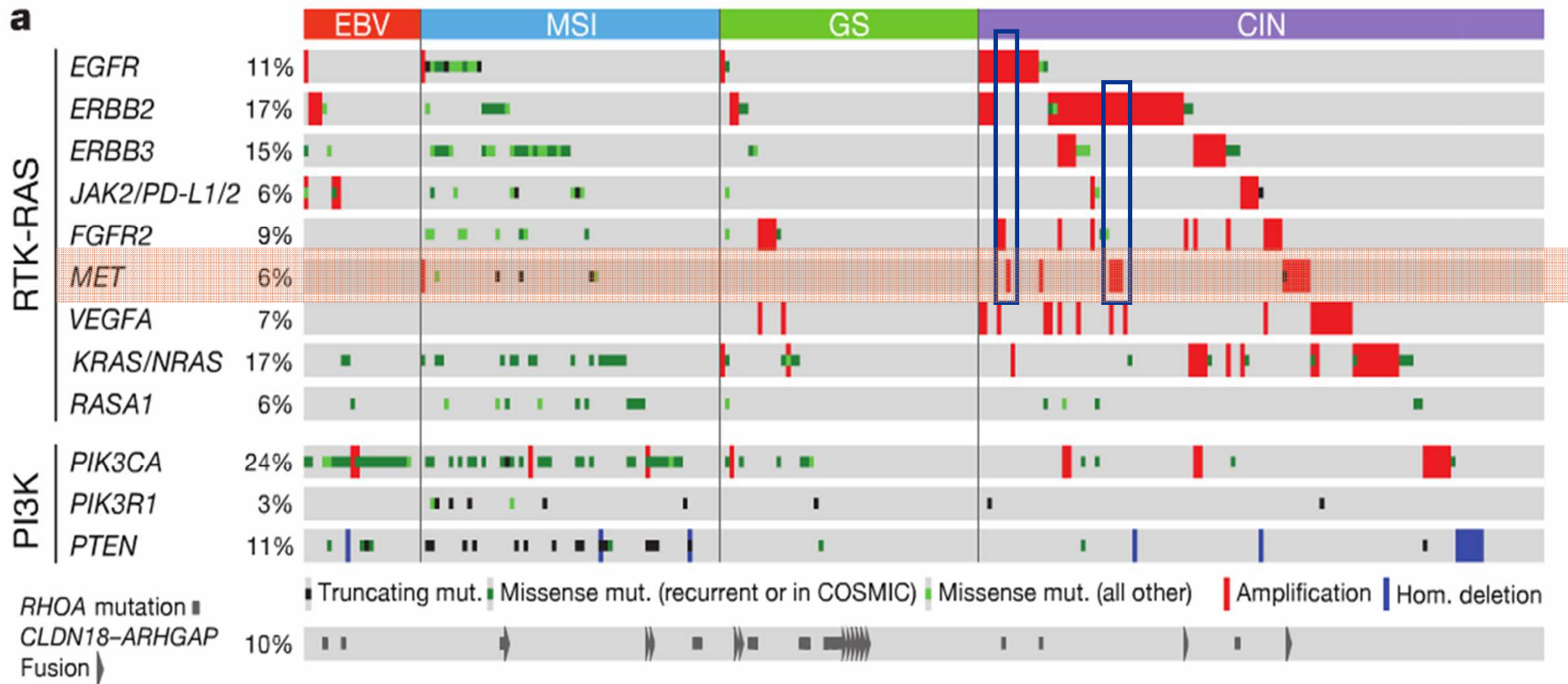


# Type#3

Heterogeneity as a Driver of Resistance  
and  
Mixed Response in EGC

# Patient#4: Gastric adenocarcinoma with Scapular metastatic





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# 当院のStageIV胃癌の治療状況

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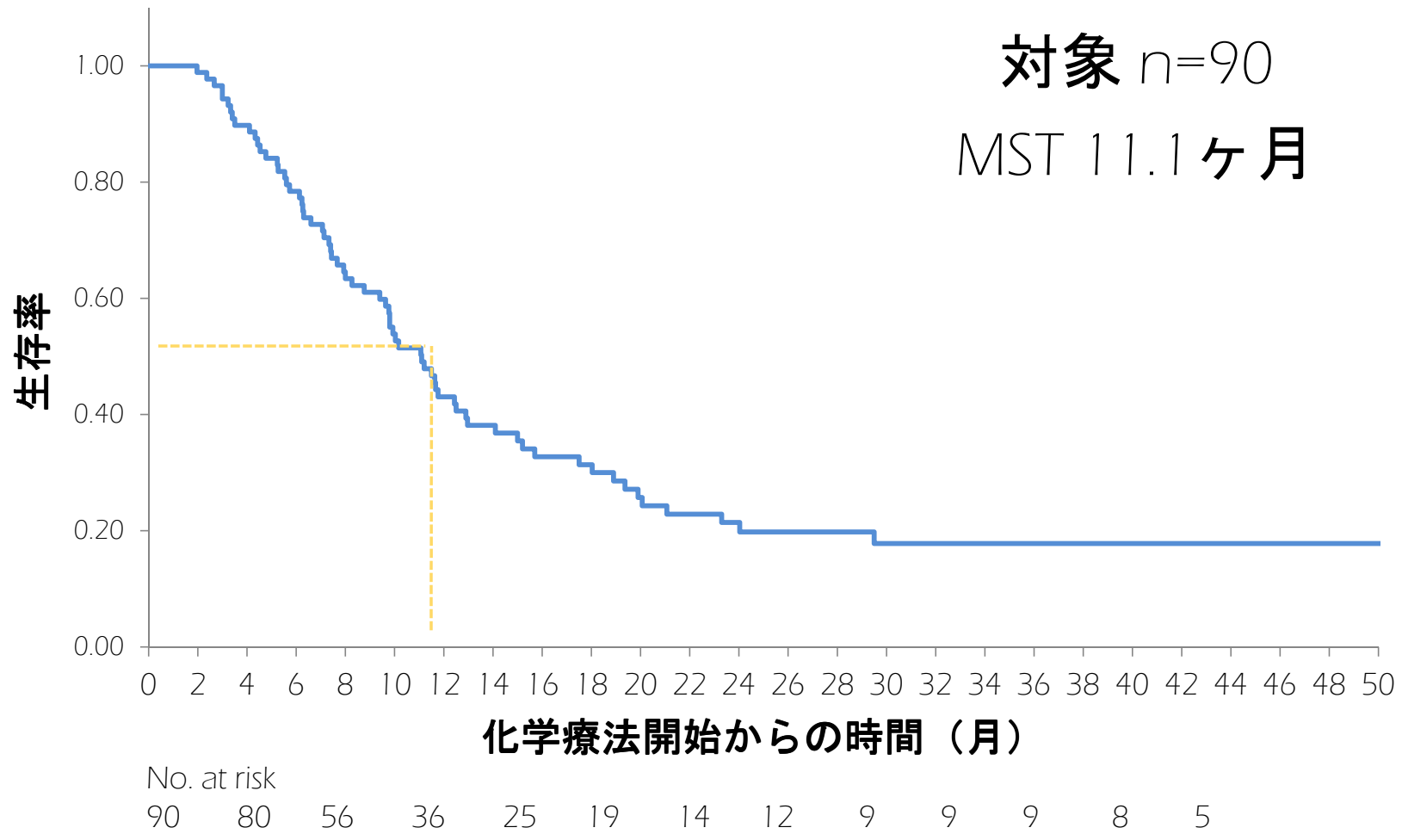
2010年1月～2014年12月  
当院で診断されたStageIV胃癌  
173人

全身化学療法を行った90人  
(重複進行癌2人を除く)

## 対象患者 n=90

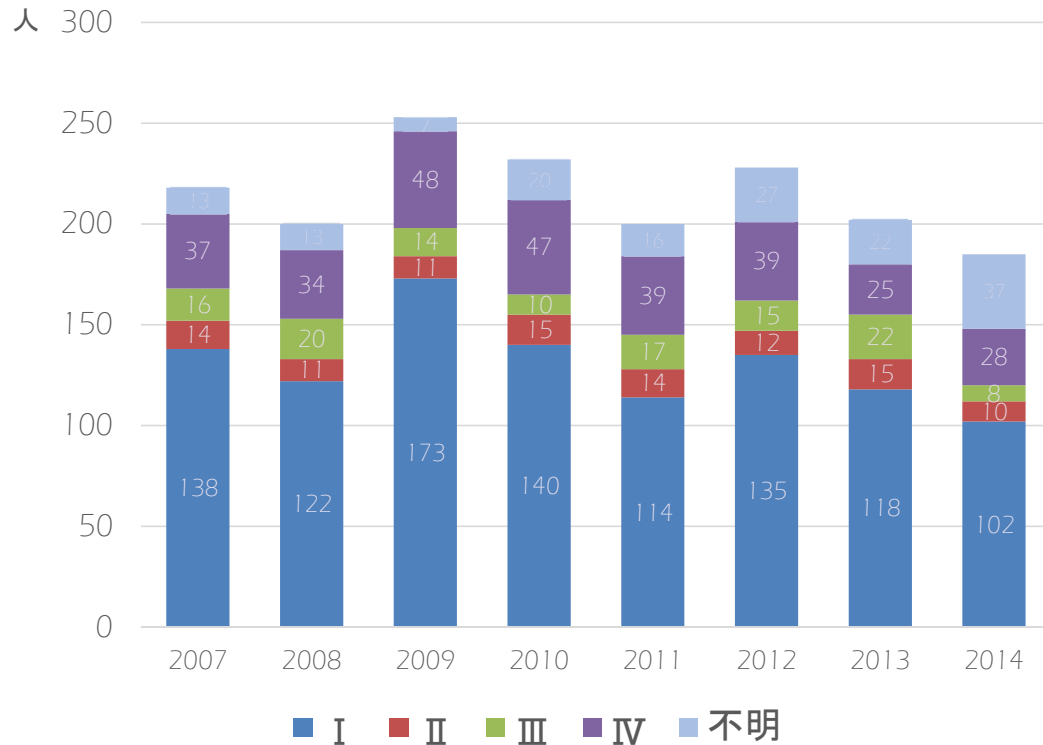
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年齢(中央値)	67歳 (31-90)
男女比	1.8 : 1
TNM分類 M因子 (重複あり)	
遠隔転移 ; 肝/肺/骨	26% / 4% / 2%
M1リンパ節転移	27%
腹膜播種	33%
腹水細胞診のみ	12%
組織型(生検診含む)	
低分化・印環細胞癌	69%
分化型	28%



# 進行癌は減ってるか 2007年～2014年の変遷

胃癌 患者数



Stage割合の変遷

