AT THE FOREFRONT
UChicago Medicine

Optimal Management of HER2-Positive and FGFR2-Positive Gastroesophageal Cancers

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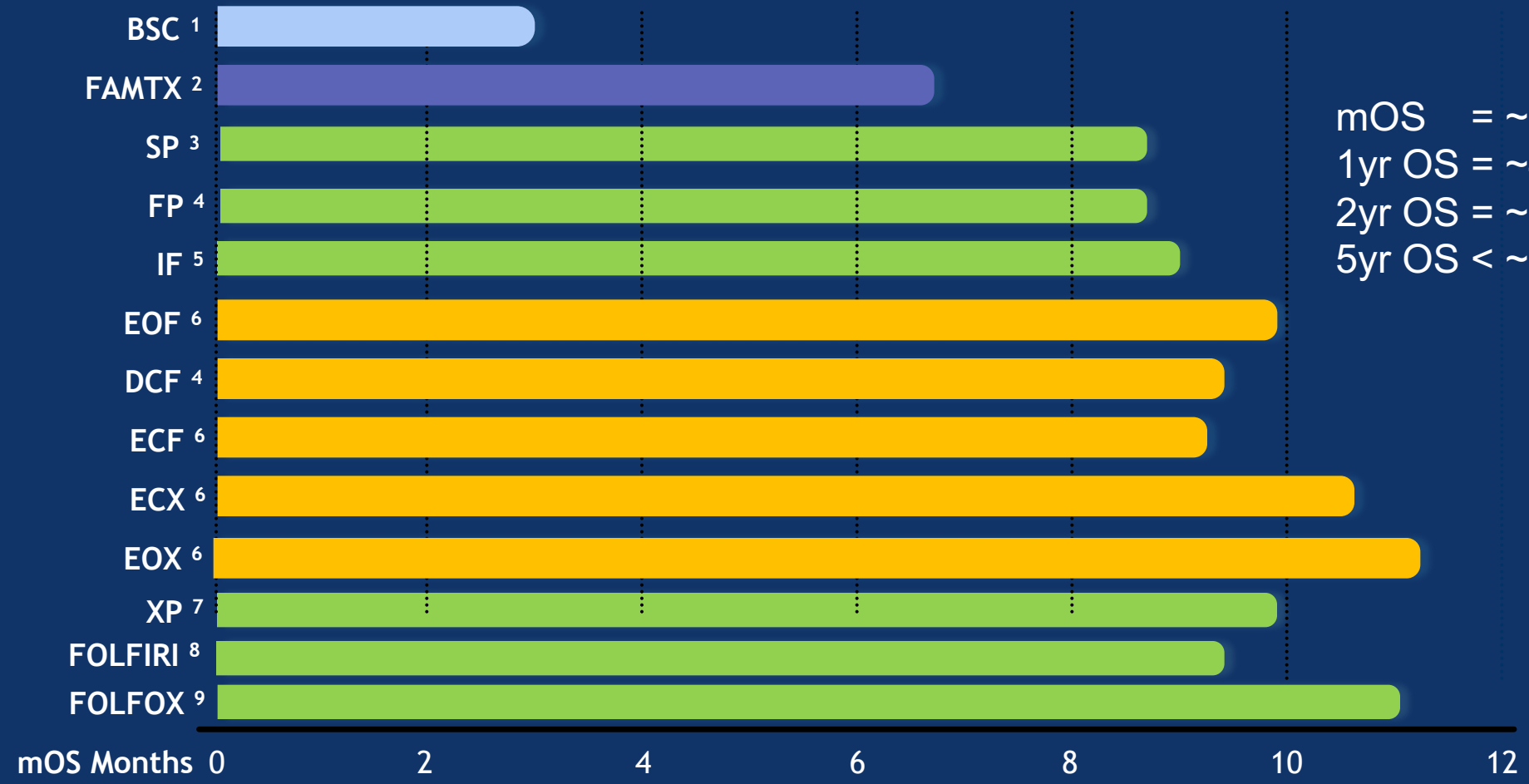
First Line Management of Advanced Gastroesophageal Adenocarcinoma



mOS = ~10-11m
1yr OS = ~40%
2yr OS = ~15-20%
5yr OS < ~2%

BSC = best supportive care;
MTX = methotrexate; S = S-1; A = doxorubicin
F = 5-FU; C/P = cisplatin; I = irinotecan;
E = epirubicin; O = oxaliplatin; D = docetaxel

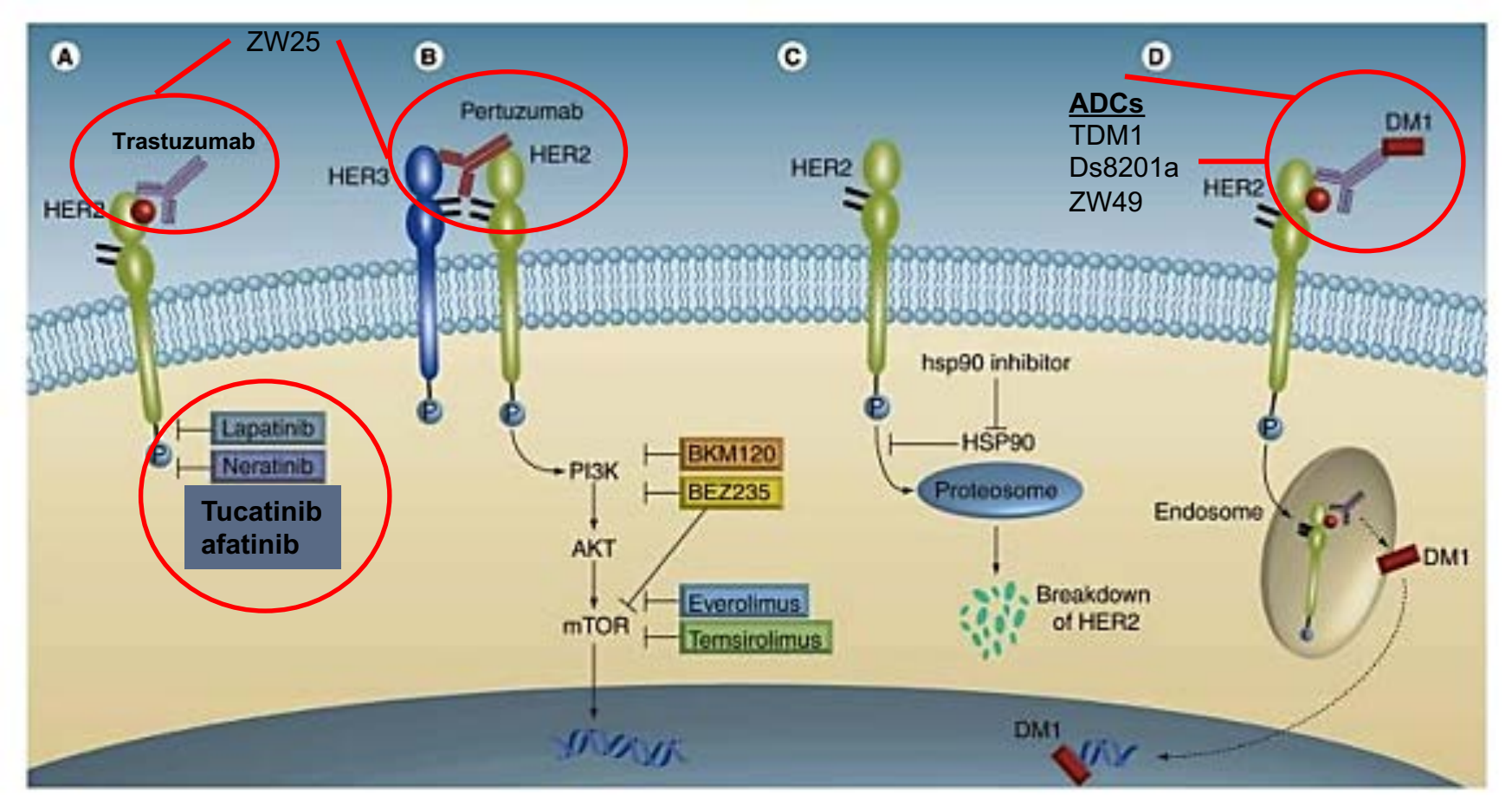
1. Murad, et al. Cancer 1993
2. Vanhoefer, et al. JCO 2000
3. Ajani, et al. ASCO 2009
4. Van Cutsem, et al. JCO 2006
5. Dank, et al. Ann Oncol 2008
6. Cunningham, et al. NEJM 2008
7. Kang, et al. Ann Oncol 2009
8. Guimbaud, et al. JCO 2014
9. Shah, et al. JAMA ONC 2016

Courtesy of Daniel Catenacci, MD

Anti-HER2 therapies

HER2 amp
~10-15% GEA

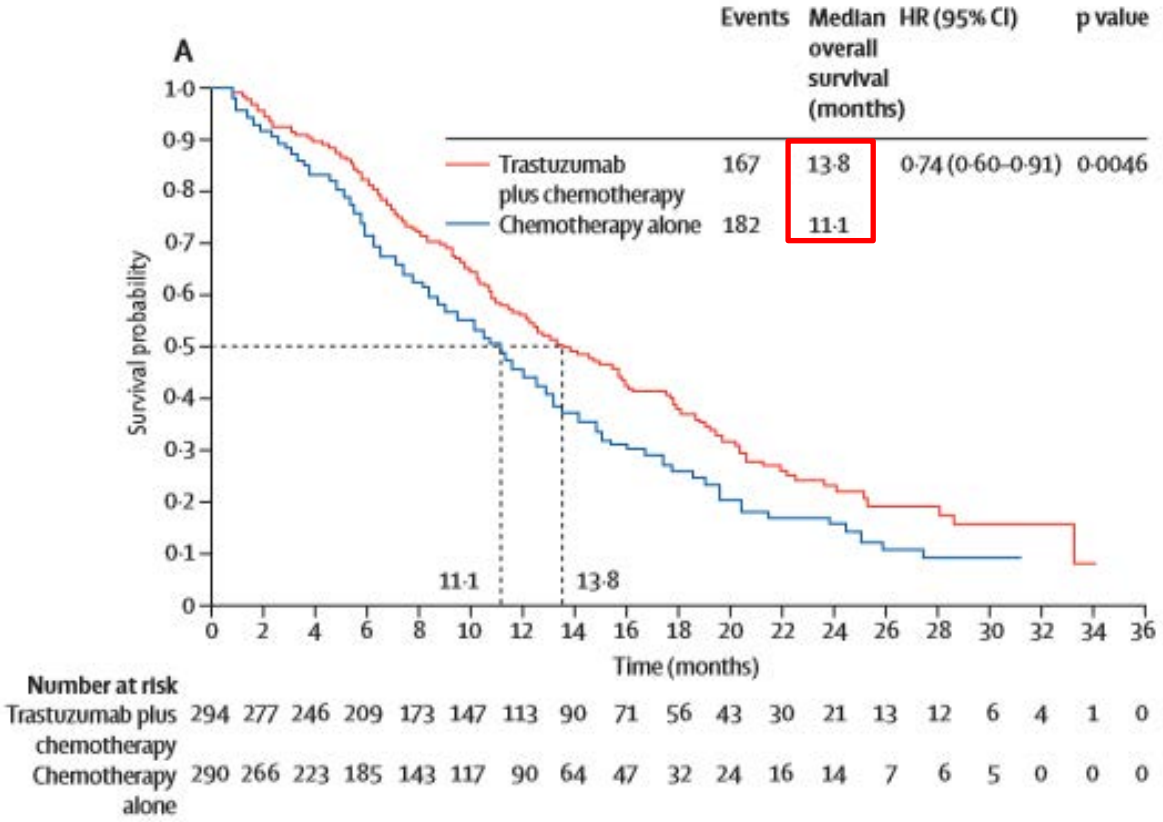
~10% Gastric
~15-20% EGJ

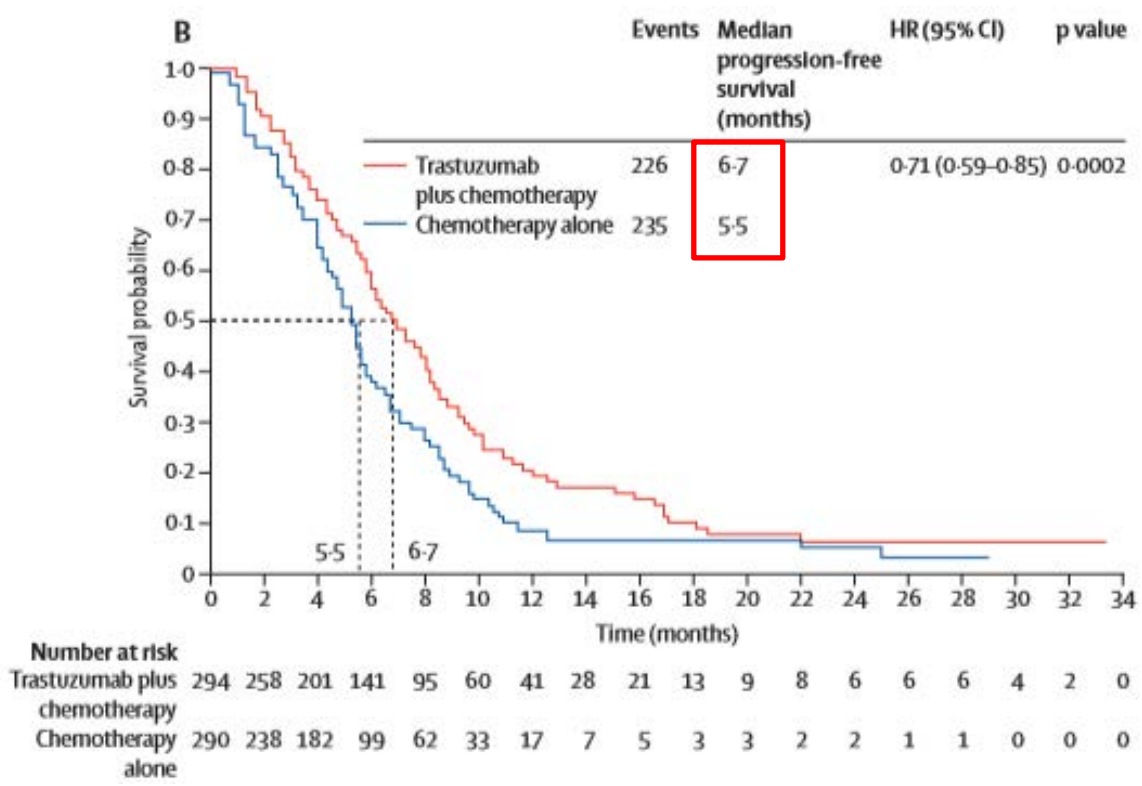


Gajria, Chandarlapaty. HER2-amplified Breast Cancer: mechanisms of trastuzumab resistance and novel targeted therapies. *Expert Rev Anticancer Ther* 2011.

Courtesy of Daniel Catenacci, MD

The ToGA phase III study for HER2-positive advanced gastric or gastro-esophageal junction cancer

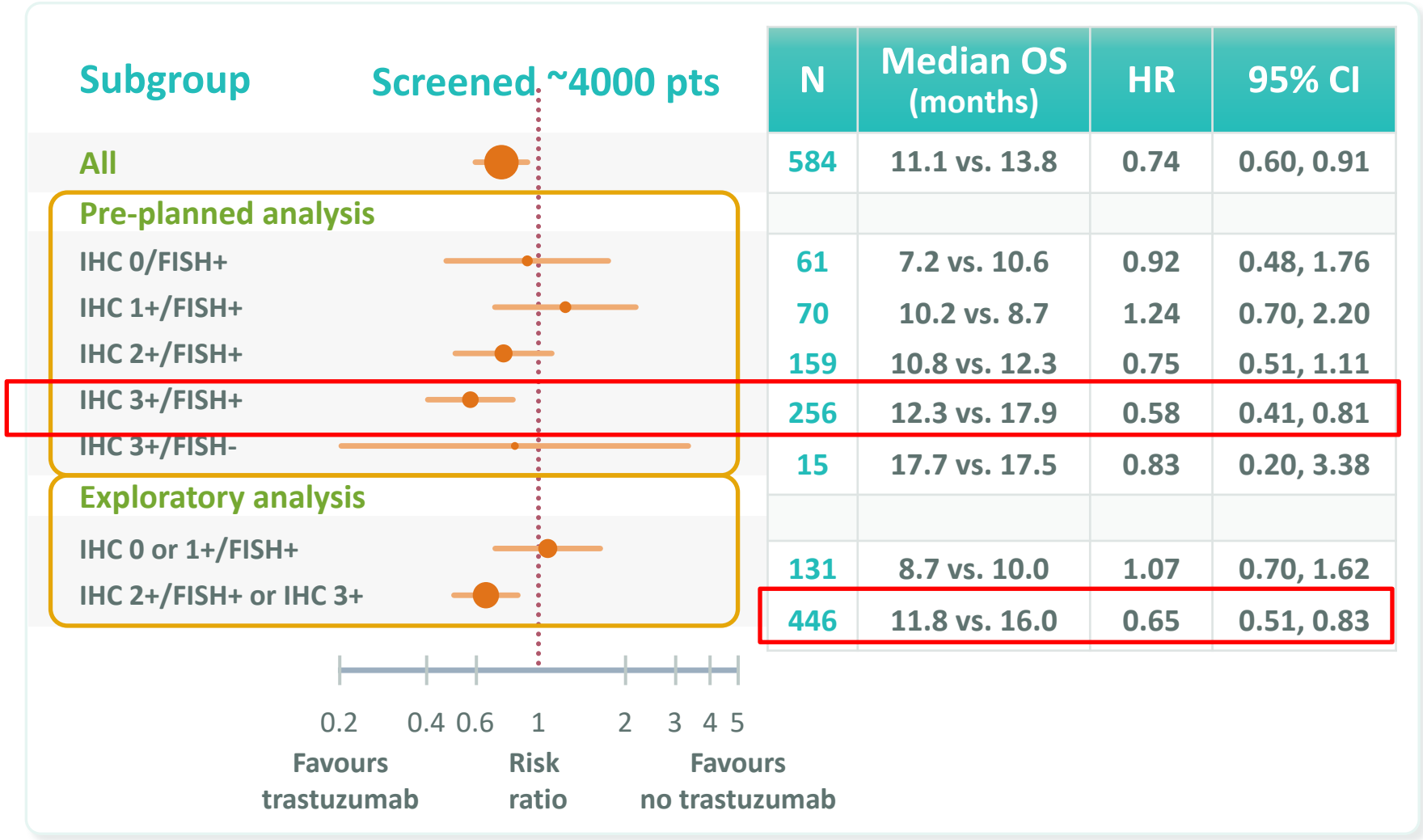




Bang et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010

Courtesy of Daniel Catenacci, MD

ToGA: Subgroup analysis by HER2 status



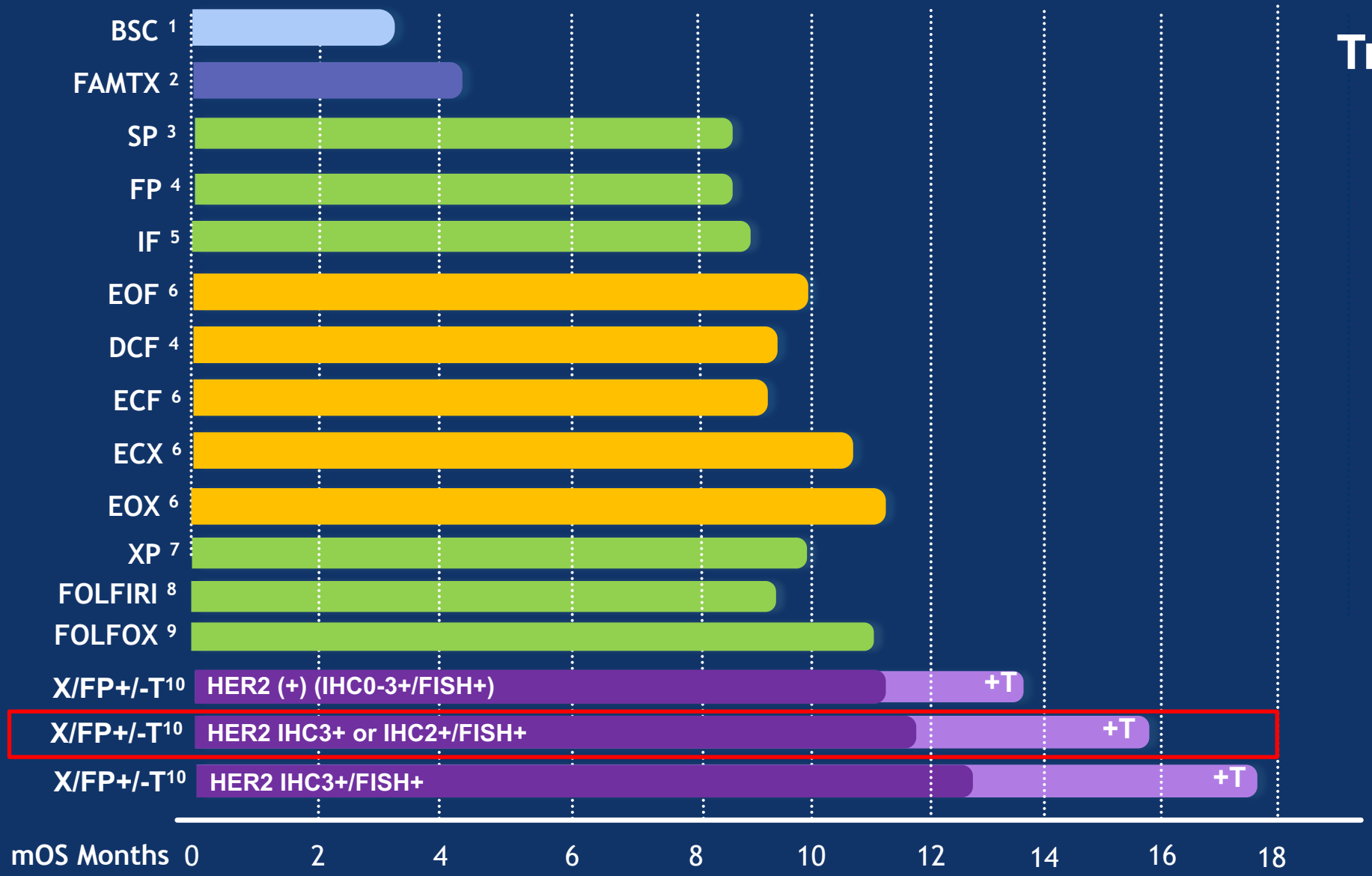
Subgroup	N	Median OS (months)	HR	95% CI
All	584	11.1 vs. 13.8	0.74	0.60, 0.91
Pre-planned analysis				
IHC 0/FISH+	61	7.2 vs. 10.6	0.92	0.48, 1.76
IHC 1+/FISH+	70	10.2 vs. 8.7	1.24	0.70, 2.20
IHC 2+/FISH+	159	10.8 vs. 12.3	0.75	0.51, 1.11
IHC 3+/FISH+	256	12.3 vs. 17.9	0.58	0.41, 0.81
IHC 3+/FISH-	15	17.7 vs. 17.5	0.83	0.20, 3.38
Exploratory analysis				
IHC 0 or 1+/FISH+	131	8.7 vs. 10.0	1.07	0.70, 1.62
IHC 2+/FISH+ or IHC 3+	446	11.8 vs. 16.0	0.65	0.51, 0.83

Interaction of treatment effect with HER2 results in exploratory analysis, *p=0.0368*

Bang et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010

Courtesy of Daniel Catenacci, MD

Treatment Options



All-comers
mOS = ~10-11m
1yr OS = ~40%
2yr OS = ~15-20%
5yr OS < ~2%

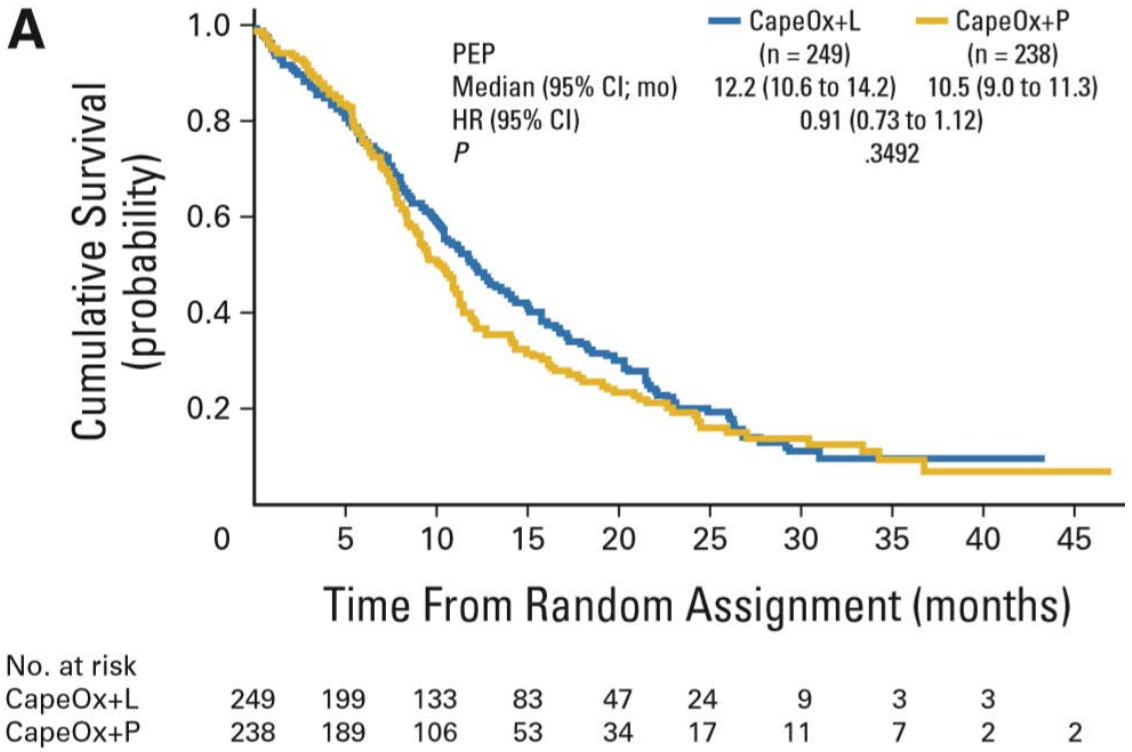
HER2+
mOS = ~14-16m
1yr OS = ~55-65%
2yr OS = ~25-30%
5yr OS < ~10-15%

1. Murad, et al. Cancer 1993 2. Vanhoefer, et al. JCO 2000 3. Ajani, et al. ASCO 2009 4. Van Cutsem, et al. JCO 2006
5. Dank, et al. Ann Oncol 2008 6. Cunningham, et al. NEJM 2008 7. Kang, et al. Ann Oncol 2009 8. Guimbaud, et al. JCO 2014
9. Shah et al. JAMA Oncol 2016. **10. Bang et al. Lancet 2010.**

Courtesy of Daniel Catenacci, MD

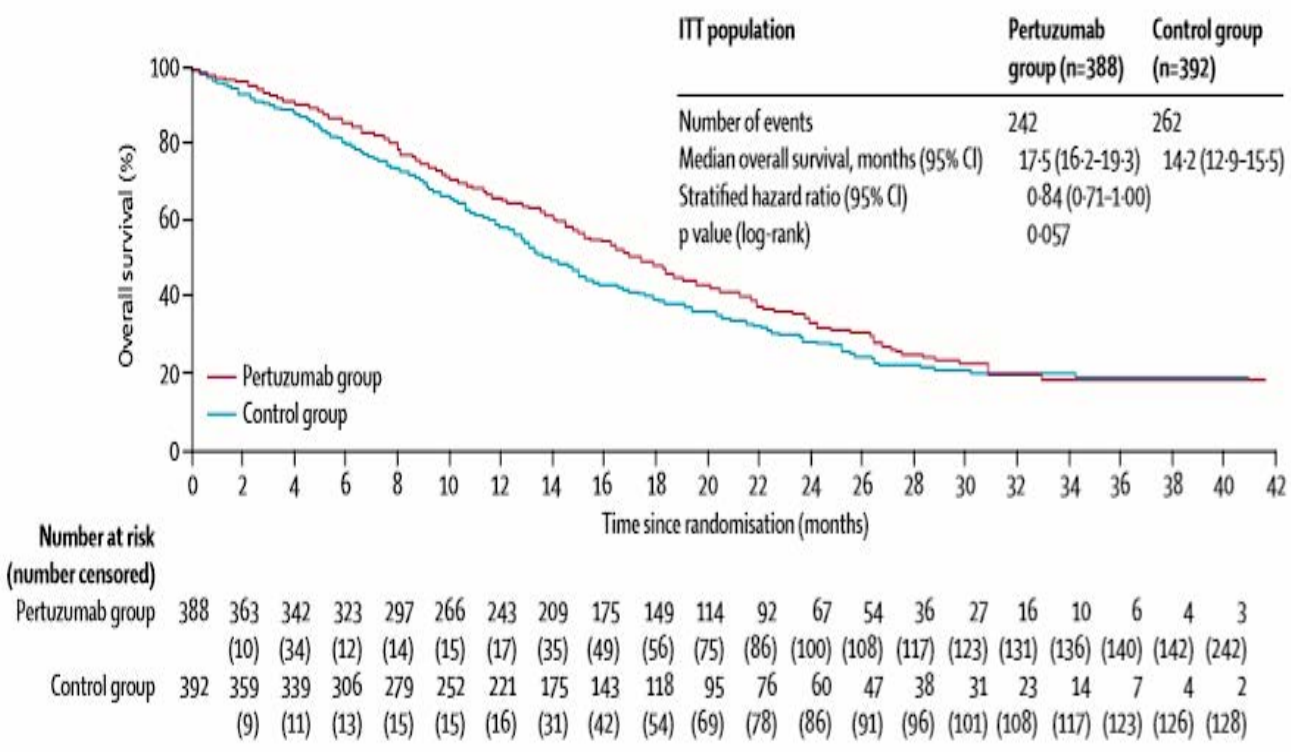
Other First Line Studies for HER2-Positive Advanced Disease

LOGiC



Hecht et al**. Lapatinib** in Combination With Capecitabine Plus Oxaliplatin in Human Epidermal Growth Factor Receptor 2–Positive Advanced or Metastatic Gastric, Esophageal, or Gastroesophageal Adenocarcinoma: TRIO-013/LOGiC— A Randomized Phase III Trial. *JCO* 2015

JACOB

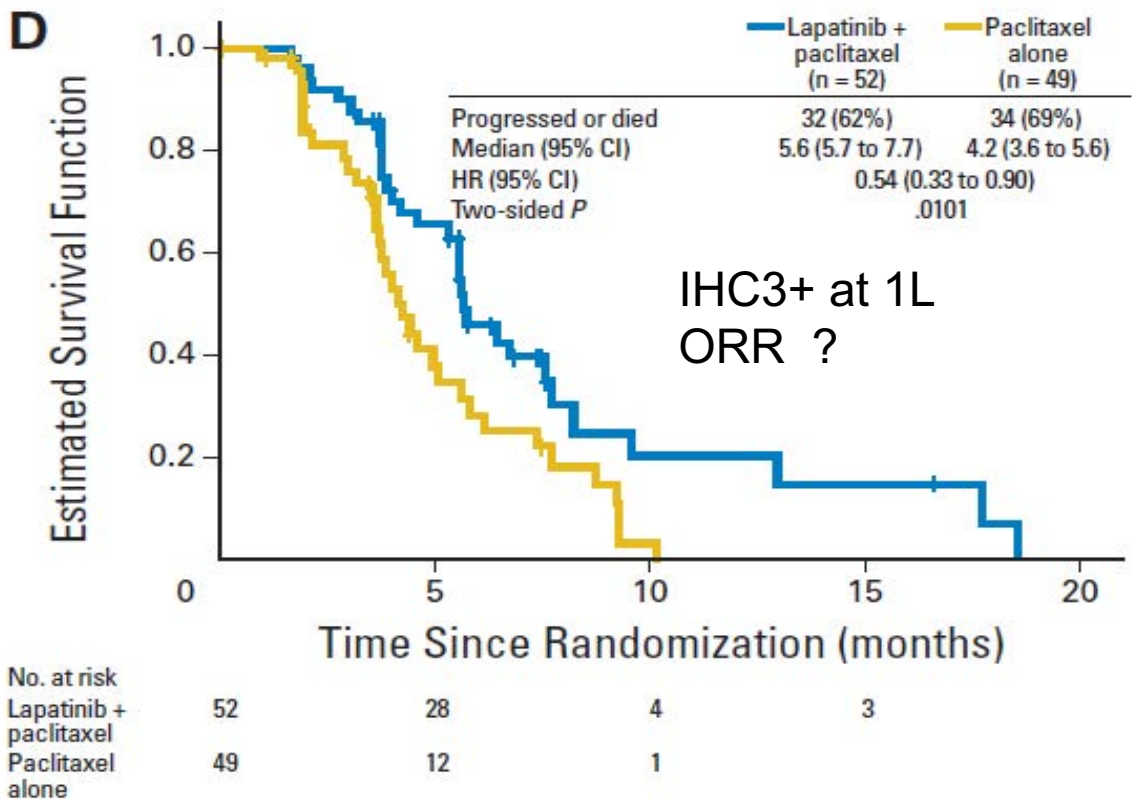


Tabernero et al. **Pertuzumab** plus trastuzumab and chemotherapy for HER2-positive metastatic gastric or gastro-oesophageal junction cancer (JACOB): final analysis of a double-blind, randomised, placebo-controlled phase 3 study. *Lancet Oncol* 2018

Courtesy of Daniel Catenacci, MD

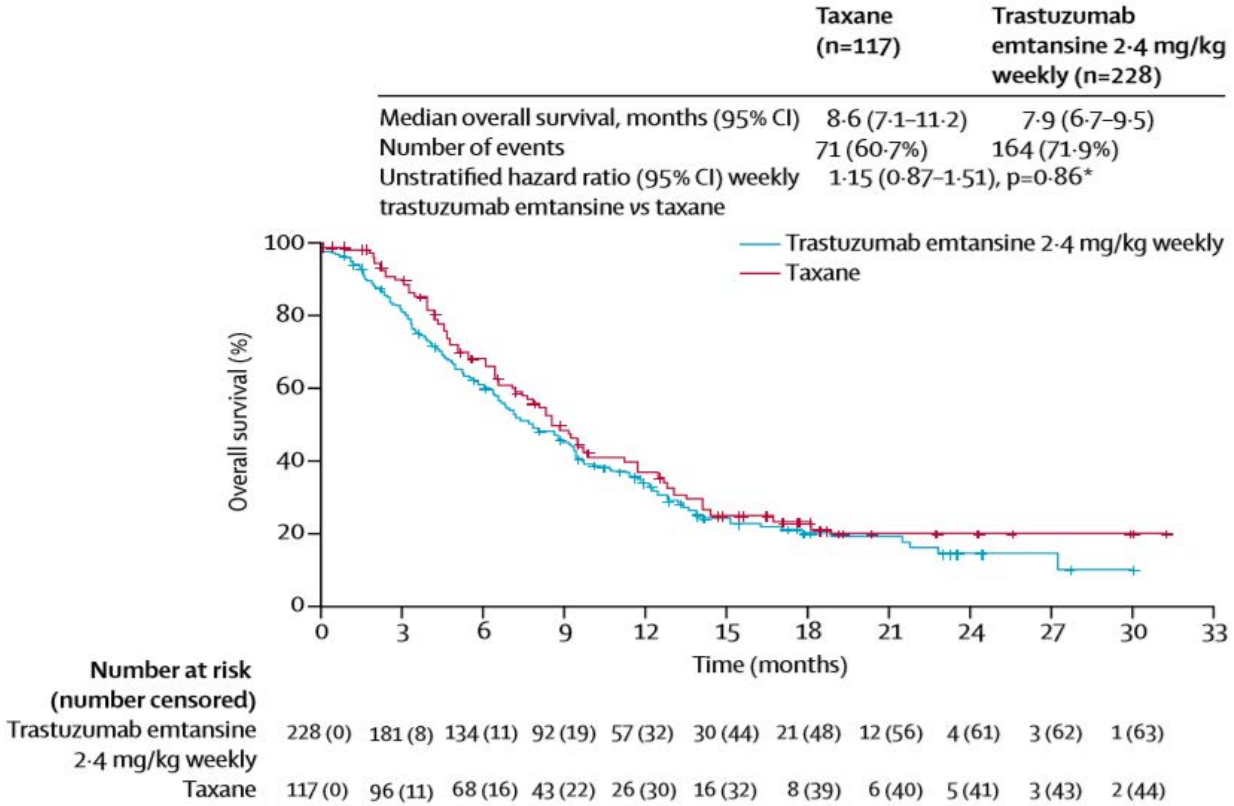
Other Second Line Studies for HER2-Positive Advanced Disease

TyTAN



Satoh et al. **Lapatinib** Plus Paclitaxel Versus Paclitaxel Alone in the Second-Line Treatment of HER2-Amplified Advanced Gastric Cancer in Asian Populations: TyTAN— A Randomized, Phase III Study. *JCO* 2014

GATSBY



Thuss-Patience et al. **Trastuzumab emtansine** versus taxane use for previously treated HER2-positive locally advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma (GATSBY): an international randomised, open-label, adaptive, phase 2/3 study. Lancet Oncol 2018

Courtesy of Daniel Catenacci, MD

Second Line – Margetuximab/Pembrolizumab (Phase Ib/II CP-MGAH222-05 Trial)

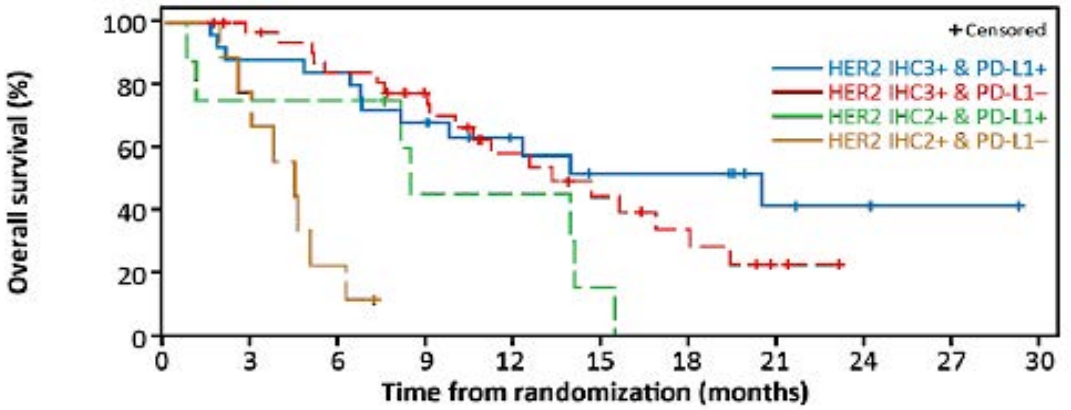
	Number of patients	Patients with an objective response* (%; 95% CI)	Disease control rate† (%; 95% CI)
Response-evaluable population‡	92	17 (18%; 11–28)§	49 (53%; 43–64)
HER2 IHC3-positive **tissue prior to 1L**	71	100% 17 (24%; 15–36)	44 (62%; 50–73)
HER2 IHC2-positive	21	0	5 (24%; 8–47)
PD-L1-positive **tissue prior to 1L**	33	79% 11 (33%; 18–52)	22 (67%; 48–82)
PD-L1-negative	43	3 (7%; 1–19)	19 (44%; 29–60)
HER2 IHC3-positive and PD-L1-positive	25	11 (44%; 24–65)	18 (72%; 51–88)
HER2 IHC3-positive and PD-L1-negative	34	3 (9%; 2–24)	19 (56%; 38–73)
HER2 IHC2-positive and PD-L1-positive	8	0	4 (50%; 16–84)
HER2 IHC2-positive and PD-L1-negative	9	0	0
HER2^{amp}-positive **ctDNA prior to 2L**	48	88% 15 (31%; 19–46)	31 (65%; 49–78)
HER2^{amp}-negative	35	2 (6%; 1–19)	14 (40%; 24–58)
HER2^{amp}-positive and PD-L1-positive	18	9 (50%; 26–74)	14 (78%; 52–94)
HER2^{amp}-positive and PD-L1-positive and HER2 IHC3-positive	15	9 (60%; 32–84)	12 (80%; 52–96)
HER2^{amp}-positive and PD-L1-negative	19	3 (16%; 3–40)	12 (63%; 38–84)
HER2^{amp}-positive and HER2 IHC2-positive	9	0	2 (2%; 3–60)
HER2^{amp}-positive and PD-L1-negative and HER2 IHC2-positive	4	0	0

This table includes only confirmed responses; there were three additional unconfirmed responses. ctDNA=circulating tumour DNA. *HER2^{amp}*=*HER2* amplification by ctDNA. IHC=immunohistochemistry. *Confirmed complete response and confirmed partial response. †Confirmed complete response, confirmed partial response, and stable disease. ‡Patients who received at least one dose of margetuximab 15 mg/kg intravenously every 3 weeks and had baseline measurable disease. §One confirmed complete response was observed in the double-positive (HER2 IHC3-positive and PD-L1-positive) subgroup.

Table 4: **Objective response and disease control rates overall and by biomarker expression (n=92)**

F. HER2 & PD-L1 IHC OS (n=76)[a]

	HER2 IHC3+ & PD-L1+ (n=25)	HER2 IHC3+ & PD-L1− (n=34)	HER2 IHC2+ & PD-L1+ (n=8)	HER2 IHC2+ & PD-L1− (n=9)
# of events	12	19	7	8
Median OS (95% CI)	**20·47** months (8·08–NA)	**13·27** months (9·95–18·00)	**8·41** months (0·72–14·03)	**4·44** months (1·87–6·21)
Double positive vs others: HR by Cox model, **0·54**; 95% CI, 0·28–1·04; Log-rank **p=0·0628**				
12-month OS rate (95% CI)	63·14% (40·91–78·94)	58·06% (37·64–73·89)	45·00% (10·76–75·13)	0



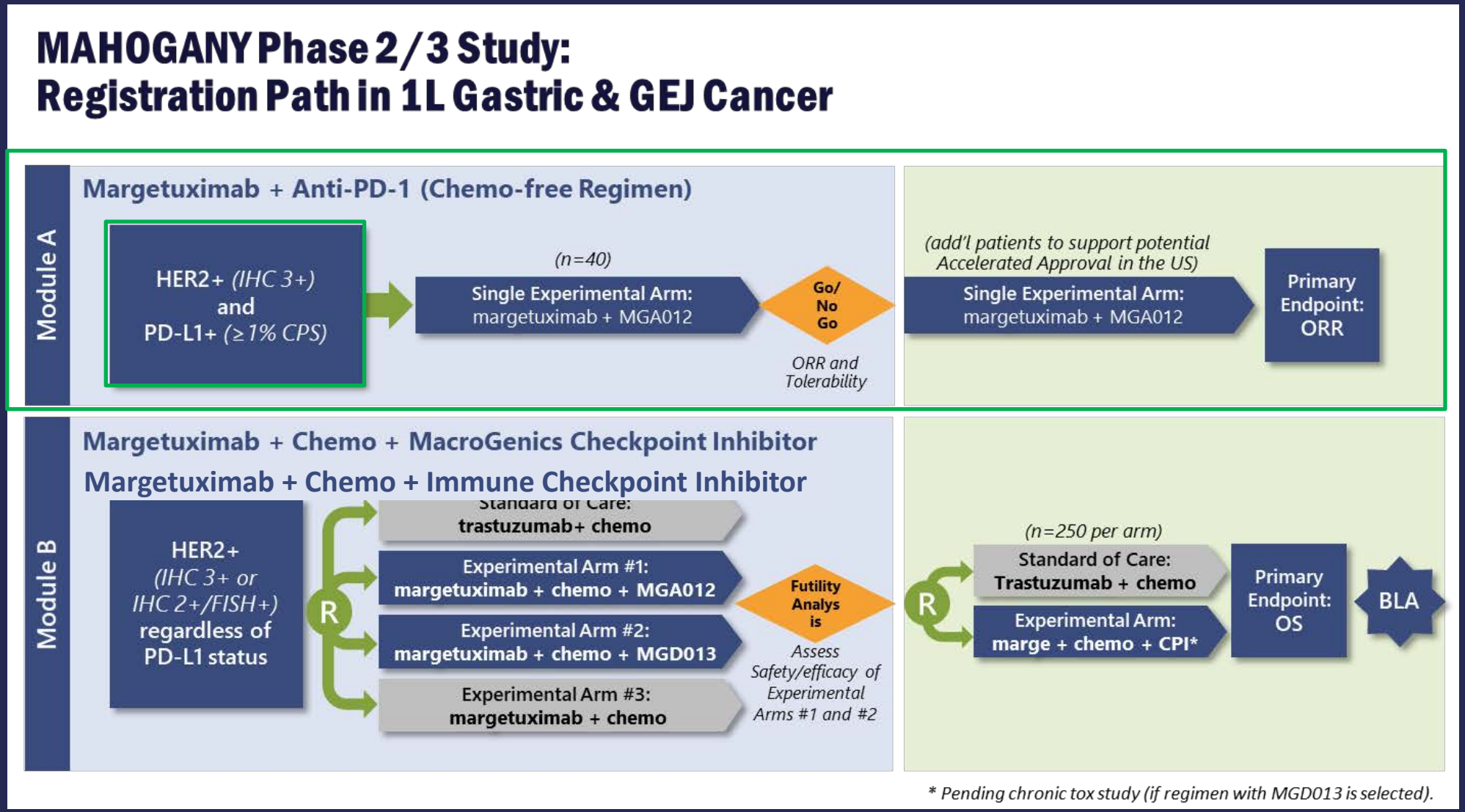
At risk (censored)

HER2 IHC3+ & PD-L1+	25(0)	22(0)	21(0)	16(1)	11(5)	8(6)	8(6)	4(9)	3(10)	1(12)	0(13)
HER2 IHC3+ & PD-L1−	34(0)	31(2)	26(3)	21(6)	13(9)	9(10)	6(11)	2(13)	0(15)	0(15)	0(15)
HER2 IHC2+ & PD-L1+	8(0)	6(0)	6(0)	3(1)	3(1)	1(1)	0(1)	0(1)	0(1)	0(1)	0(1)
HER2 IHC2+ & PD-L1−	9(0)	6(0)	2(0)	0(1)	0(1)	0(1)	0(1)	0(1)	0(1)	0(1)	0(1)

Courtesy of Daniel Catenacci, MD

Catenacci et al. Margetuximab plus pembrolizumab for previously treated, HER2-positive GEA (CP-MGAH22–05): a single-arm, phase 1b–2 trial. *Lancet Oncology* 2020

First Line – Margetuximab Plus Immune Checkpoint Inhibitor

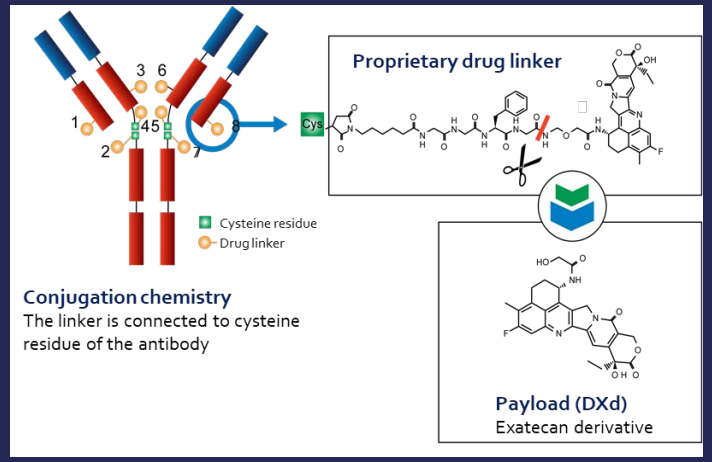


MGA012 is an investigational anti-PD-1 monoclonal antibody

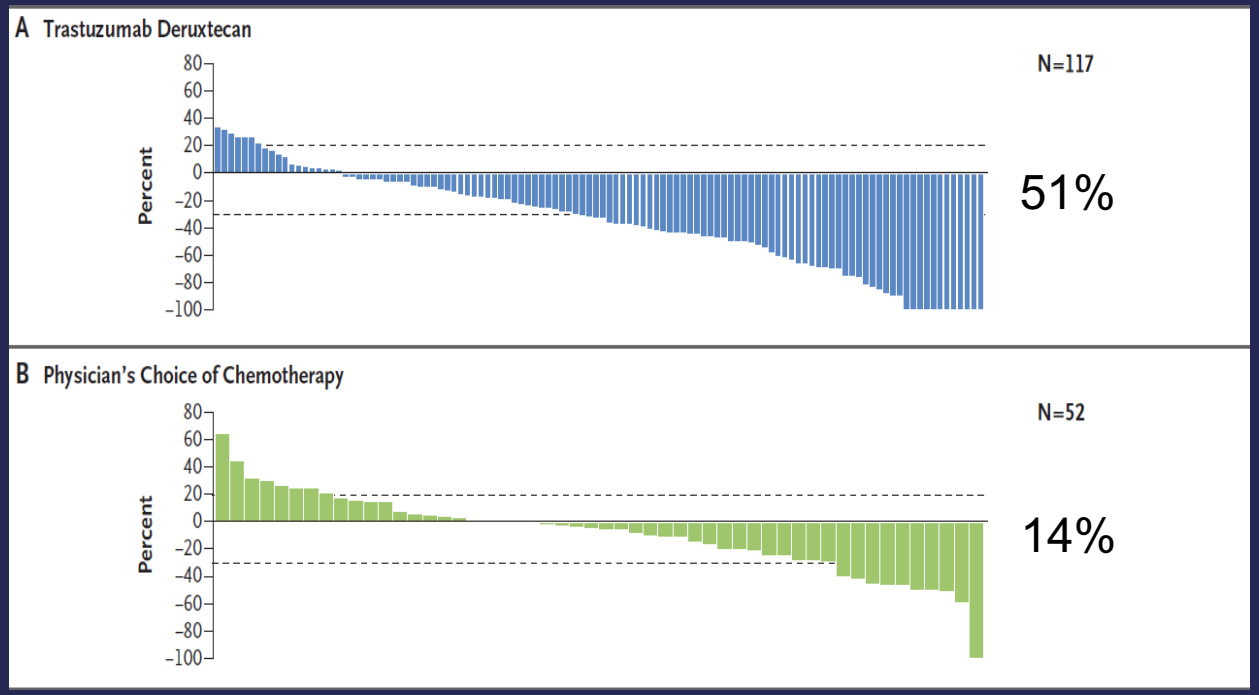
MGD013 is an investigational agent targeting both PD-1 and LAG-3

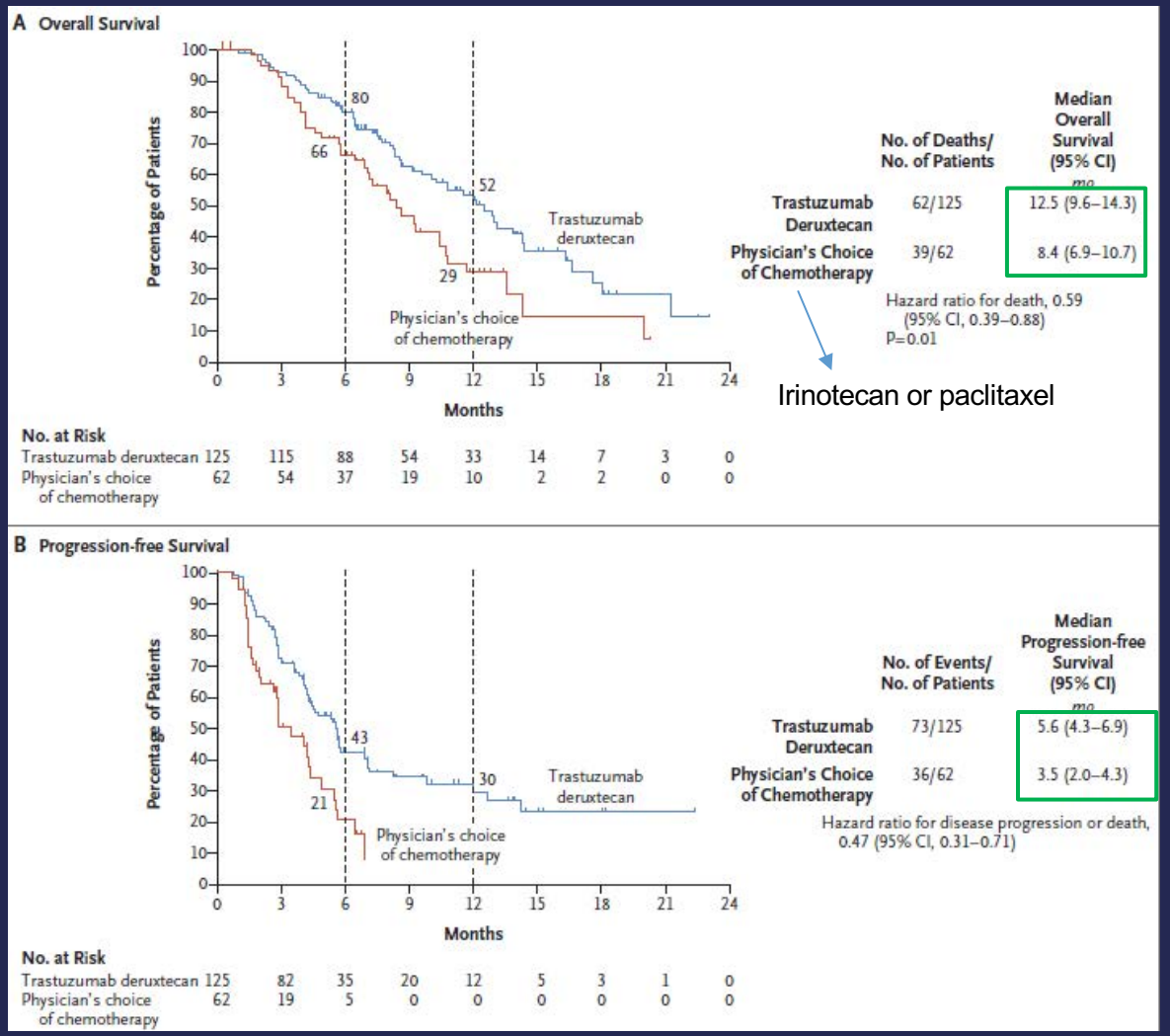
Courtesy of Daniel Catenacci, MD

DESTINY-Gastric01 Trial: Third Line – Trastuzumab Deruxtecan



N= 125 pts
R 2:1
100% Asian





Shitara *et al*. Trastuzumab Deruxtecan in Previously Treated HER2-Positive Gastric Cancer. *NEJM* 2020

Courtesy of Daniel Catenacci, MD

DESTINY-Gastric01: TRAE in ≥20% of Pts

A total of 12 pts had trastuzumab deruxtecan-related interstitial lung disease or pneumonitis (Grade 1 or 2 in 9 patients and Grade 3 or 4 in 3)

Pneumonitis:

12 patients **(9.6%)**

G1/2: 9 (7.2%)
- G1: 3 (2.4%)
- G2: 6 (4.8%)

G3/4: 3 (2.4%)
- G3: 2 (1.6%)
- G4: 1 (0.8%)

	T-DXd (n = 125)			PC Overall (n = 62)		
	Grade			Grade		
Preferred Term, %	Any	3	4	Any	3	4
Any	100.0	60.8	8.4	98.4	41.9	11.3
Nausea	63.2	4.8	0	46.8	1.6	0
Neutrophil count decreased[a]	63.2	38.4	12.8	35.5	16.1	8.1
Decreased appetite	60.0	16.8	0	45.2	12.9	0
Anemia[b]	57.6	37.6	0	30.6	21.0	1.6
Platelet count decreased[c]	39.2	9.6	1.6	6.5	1.6	1.6
White blood cell count decreased[d]	37.6	20.8	0	35.5	8.1	3.2
Malaise	34.4	0.8	0	16.1	0	0
Diarrhea	32.0	2.4	0	32.3	1.6	0
Vomiting	26.4	0	0	8.1	0	0
Constipation	24.0	0	0	22.6	0	0
Pyrexia	24.0	0	0	16.1	0	0
Alopecia	22.4	0	0	14.5	0	0
Fatigue	21.6	7.2	0	24.2	3.2	0
Lymphocyte count decreased[e]	21.6	6.4	4.8	3.2	0	1.6

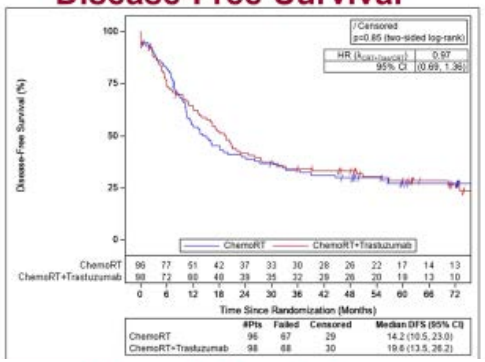
Shitara K, et al. ASCO 2020. Abs 4513.

Courtesy of Daniel Catenacci, MD

Perioperative anti-HER2 studies

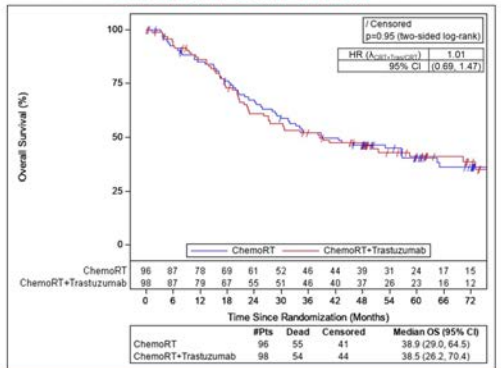
RTOG-1010 Trial
N=194

Disease-Free Survival



NRG ONCOLOGY™

Overall Survival



NRG ONCOLOGY™

Surgery and Pathologic Complete Response (pCR)

	ChemoRT + Trastuzumab (n=98)	ChemoRT (n=96)	Chi-squared p-value
Surgery			
Yes	**82 (84%)**	**78 (81%)**	
No (progression, mets, death)	5 (5%)	8 (8%)	
No (other)	11 (11%)	10 (10%)	
pCR			0.71
Yes	22 (27%)	23 (29%)	
No	60 (73%)	55 (71%)	

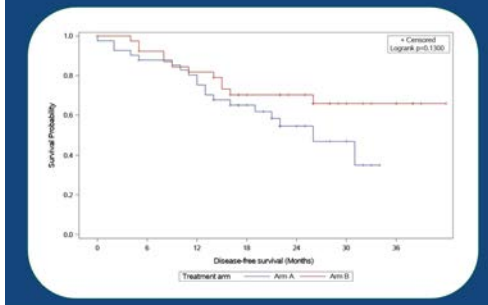
NRG ONCOLOGY™

NRG/RTOG 1010

Safran et al. RTOG1010 Phase III. ASCO 2020

PETRARCA Trial
N=81

Disease-free Survival (DFS)

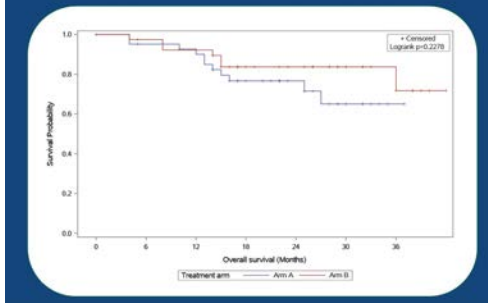


	FLOT	FLOT / T + P
mDFS *	26 months [13 - n.r.]	not reached

HR (95% CI) for Arm B vs. Arm A: 0.576 (0.278 - 1.139), p = 0.14

*Median Follow-up 22 months

Overall Survival (OS)



	FLOT	FLOT / T + P
mOS*	not reached	not reached

HR (95% CI) for Arm B vs. Arm A: 0.558 (0.212 - 1.470), p = 0.24

*Median Follow-up 22 months

Histopathology & primary endpoint (pCR)

ypT-stage	FLOT N = 41	FLOT + Tras / Per N = 40	P-value
≤T1	11 (27%)	17 (43%)	
T2	9 (22%)	8 (20%)	
T3	17 (41%)	14 (35%)	
T4	3 (7%)	0 (0%)	
N0	16 (39%)	27 (68%)	
pCR	5 (12%)	14 (35%)	p = 0.02

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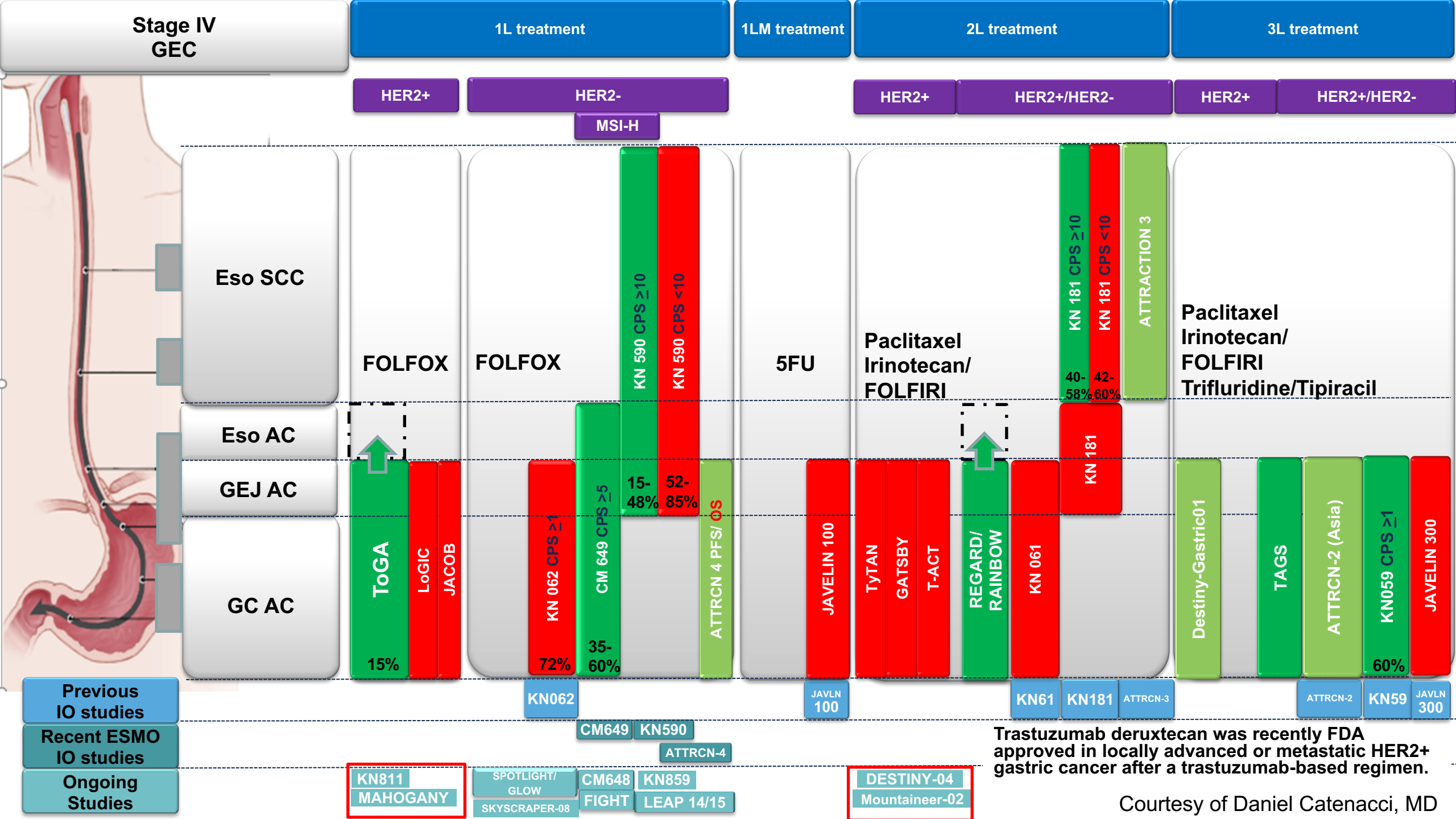
Hofheinz et al. PETRARCA Phase II. ASCO 2020

Courtesy of Daniel Catenacci, MD



Trastuzumab deruxtecan was recently FDA approved in locally advanced or metastatic HER2+ gastric cancer after a trastuzumab-based regimen.

Courtesy of Daniel Catenacci, MD

FIGHT The FIGHT Clinical Trial

A double-blind randomized study of bemarituzumab (bema) plus mFOLFOX6 versus placebo plus mFOLFOX6 as first-line treatment for advanced gastric/gastroesophageal junction cancer (FIGHT)

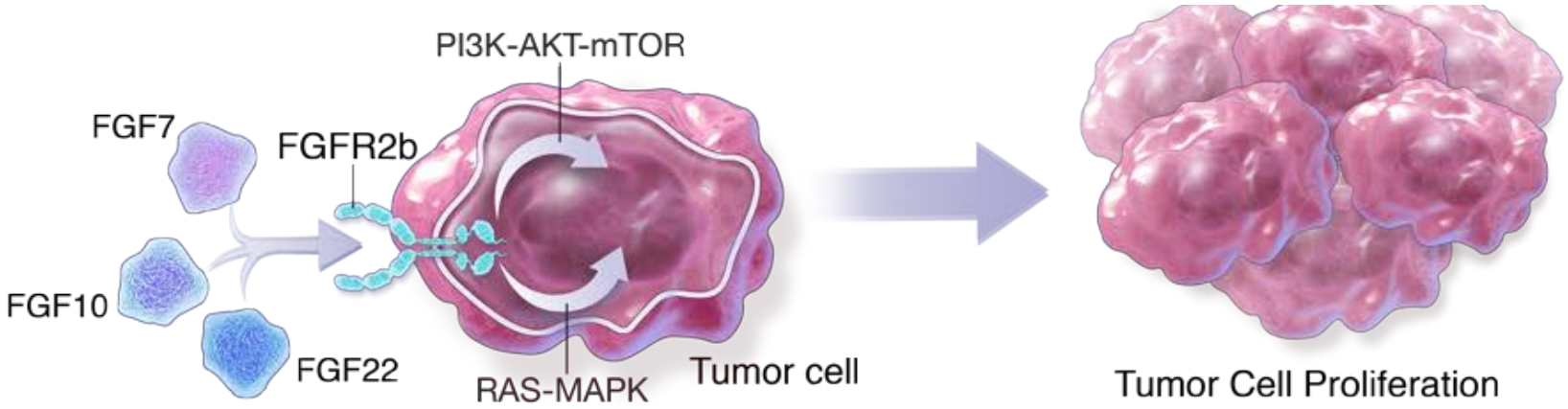
Authors: Zev Wainberg,[1] Peter Enzinger,[2] Yoon-Koo Kang[3], Kensai Yamaguchi,[4] Shukui Qin,[5] Keun-Wook Lee,[6] Sang Cheul Oh,[7] Jin Li,[8] Haci Mehmet Turk,[9] Alexandra Teixeira,[10] Giovanni Gerardo Cardellino,[11] Rachel Guardeno Sanchez,[12] Siddhartha Mitra,[13] Yingsi Yang,[13] Helen Collins,[13] Daniel V Catenacci[14]

[1]University of California, Los Angeles, USA, [2]Dana Farber Cancer Institute, Boston, USA, [3]Asan Medical Center, Seoul, South Korea, [4]The Cancer Institute Hospital of JFCR, Koto-Ku , Tokyo, Japan, [5]81 Hospital Nanjing University of Chinese Medicine, Nanjing, China, [6]Seoul National University Bundang Hospital, Seongnam-si, Gyeonggi-do, S.Korea, [7]Korea University Guro Hospital, Seoul, S.Korea, [8]Shanghai East Hospital, Shanghai, China, [9]Bezmialem Vakif Universitesi Tip Fakultesi Hastanesi, Fatih, Turkey, [10]Hospital Senhora Da Oliveira, Guimaraes, Portugal, [11]Dipartimento di Oncologia, Azienda Ospedaliero Universitaria, Udine, Italy, [12]Institut Catala d Oncologia Girona, Spain, [13]FivePrime Therapeutics, South San Francisco, USA, [14]University of Chicago, Chicago, USA

Courtesy of Daniel Catenacci, MD

Fibroblast Growth Factor Receptor 2b (FGFR2b) in Cancer

- FGFR2b is a member of the FGFR family (FGFR1-4) and is a splice isoform of FGFR2
- FGFR2b overexpression: 3-61% of gastric cancer depending on tumor stage and assay[1]

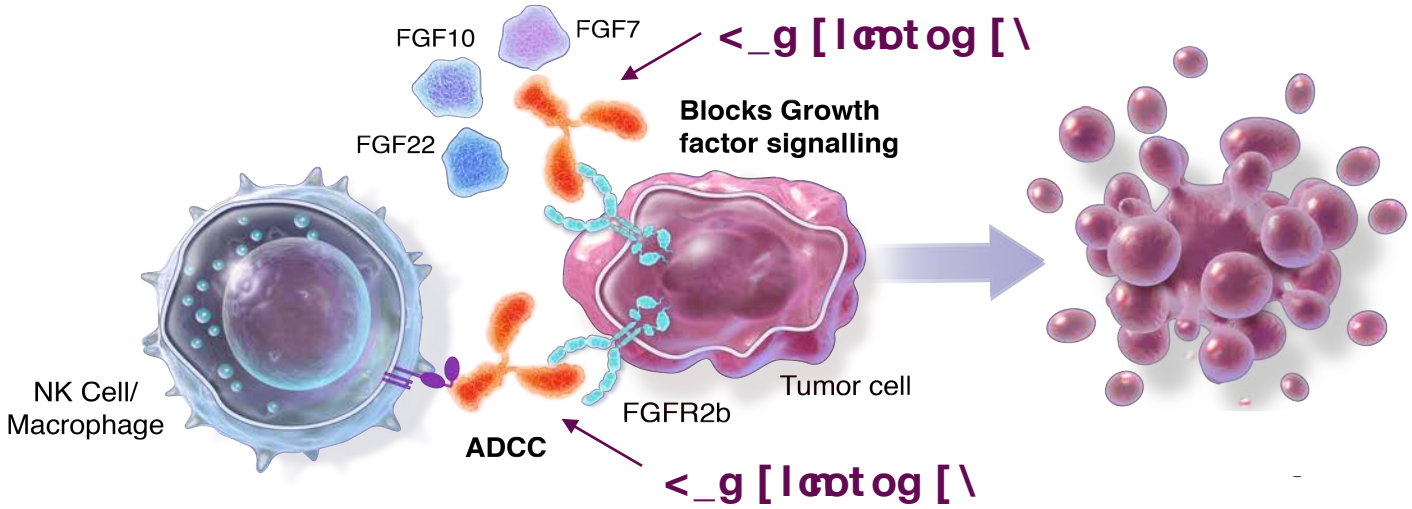


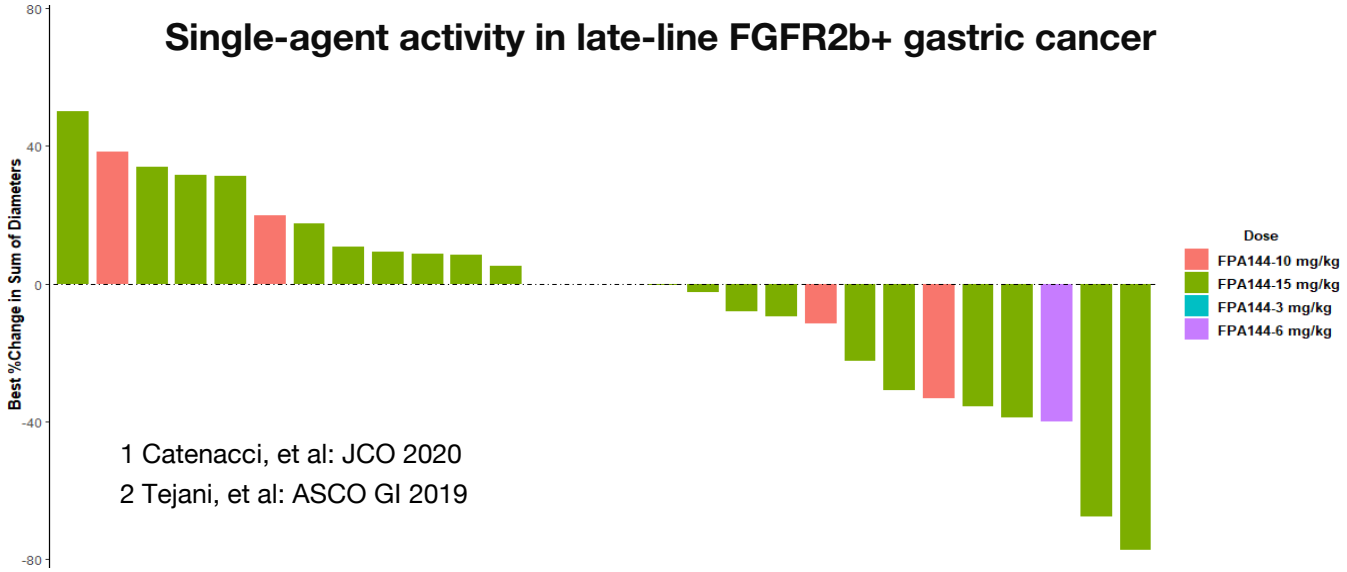
- FGFR tyrosine kinase inhibitors[2] have shown clinical benefit in cancers with FGFR mutations, fusions or translocations

[1]Han et al, Pathobiology 2015, Ahn et al, Modern Pathology 2016, Nagatsuma et al, Gastric Cancer 2015, Tokunga et al, Oncotarget 2016
[2]Abou-Alfa GK et al, Lancet Onc 2020; Loriot Y et al, NEJM 2019

Courtesy of Daniel Catenacci, MD

Bemarituzumab is an IgG1 antibody specific for the FGFR2b Receptor





1 Catenacci, et al: JCO 2020
2 Tejani, et al: ASCO GI 2019

- Confirmed ORR = 18% (n=28)[1]
- No dose-limiting toxicities
- Corneal adverse events in 3/28 patients
- Recommended Phase 2 dose: 15mg/kg Q2W with a single 7.5mg/kg dose on Cycle 1 Day 8[2]

Courtesy of Daniel Catenacci, MD

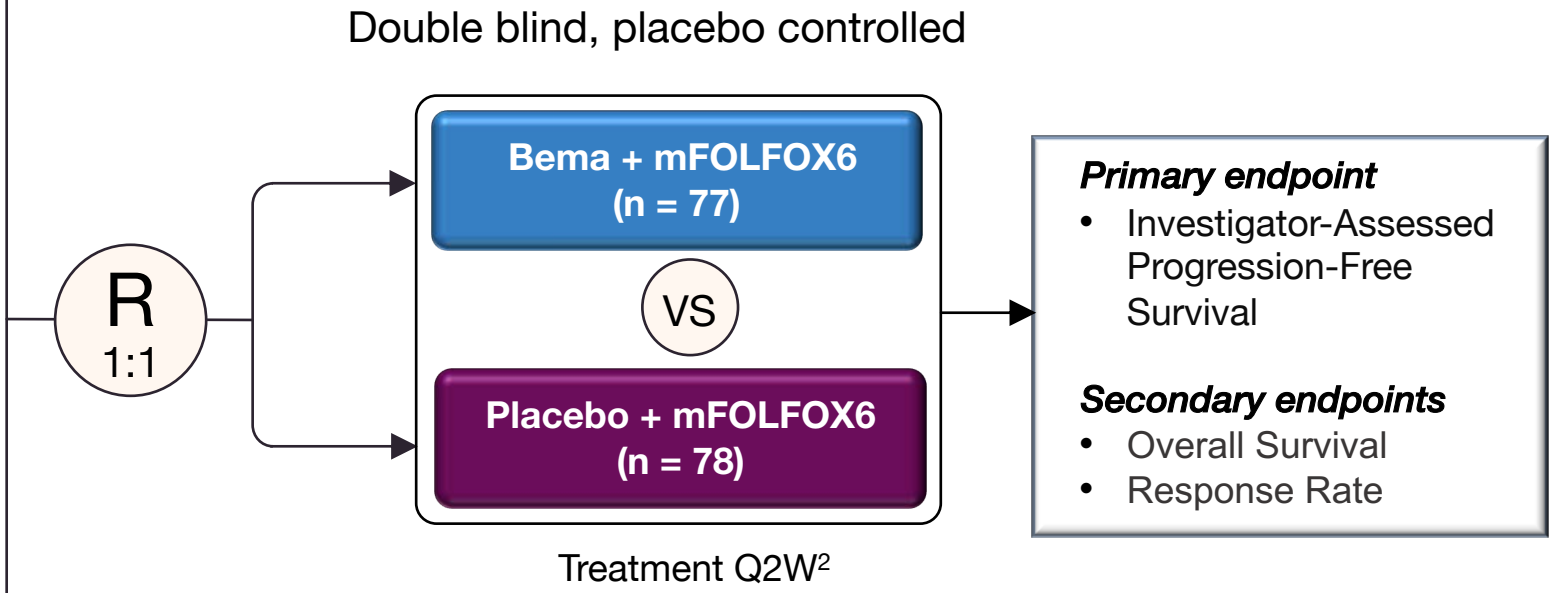
FIGHT Trial Design

Key Eligibility Criteria

- No prior therapy for unresectable locally advanced or metastatic gastric/GEJ adenocarcinoma
- RECIST v1.1 evaluable disease
- FGFR2b overexpression by IHC and/or *FGFR2* gene amplification by ctDNA[1]
- ECOG 0/1
- HER2 not positive
- May receive 1 dose of mFOLFOX6

Stratification Factors

- Geographic region
- Single dose of mFOLFOX6 during screening
- Prior adjuvant or neo-adjuvant chemotherapy



Statistical Plan

Trial initially designed as registrational Phase 3 (n=548) with 2-sided α 0.05
Amended after enrolling n = 155 to a proof-of-concept Phase 2 with pre-specified statistical assumptions of:

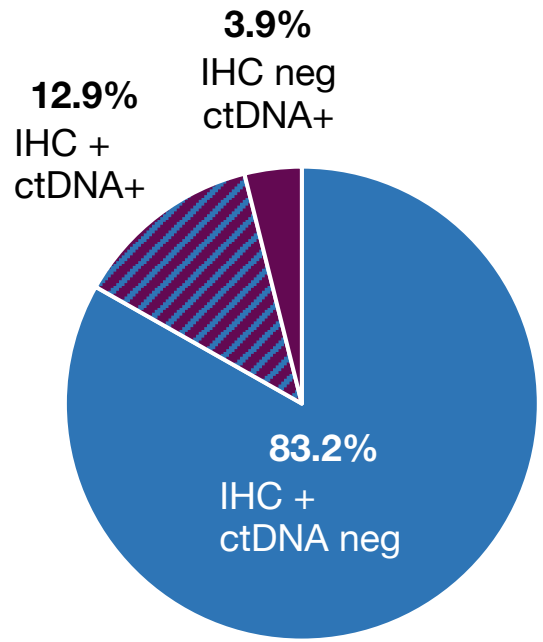
- Hierarchical sequential testing: PFS, then OS/ORR
- ≥84 events to demonstrate benefit at a HR≤0.76 for PFS at 2-sided α of 0.2

1 Central testing: Immunohistochemical stain (Ventana): cut-off any 2+/3+; circulating tumor DNA (PGDx): cut-off 1.5X
2 15mg/kg Q2W with a single 7.5mg/kg dose on Cycle 1 Day 8[2]

Courtesy of Daniel Catenacci, MD

Demographics and Baseline Characteristics

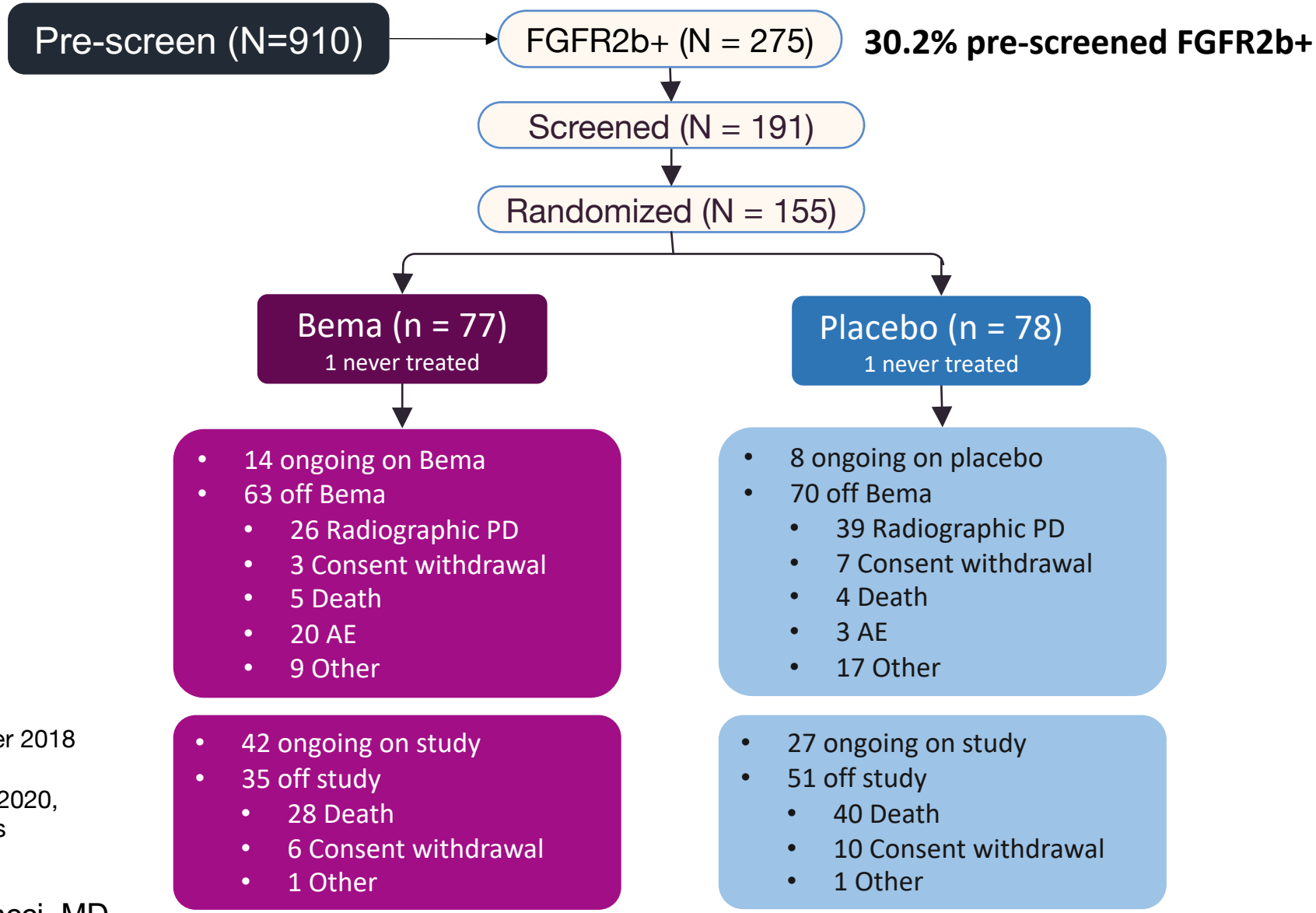
Demographics/Characteristics n (%)	Bema + mFOLFOX6 (N = 77)	Placebo + mFOLFOX6 (N = 78)
Age, median (range), years	60.0 (23, 80)	59.5 (33, 84)
Gender, male (%)	52 (67.5%)	59 (75.6%)
Race, Asian (%)	45 (58.4%)	44 (56.4%)
Region		
US/EU	32 (41.6%)	34 (43.6%)
China	14 (18.2%)	13 (16.7%)
Rest of Asia	31 (40.3%)	31 (39.7%)
Single Dose of mFOLFOX6 Prior to Randomization	35 (45.5%)	36 (46.2%)
Measurable Disease at Baseline	66 (85.7%)	60 (76.9%)
FGFR2b status		
Overexpression based on IHC	73 (94.8%)	76 (97.4%)
Amplification based on ctDNA	12 (15.6%)	14 (17.9%)
Both Overexpression and Amplification	8 (10.4%)	12 (15.4%)



FGFR2b status of enrolled patients

Courtesy of Daniel Catenacci, MD

Study Disposition

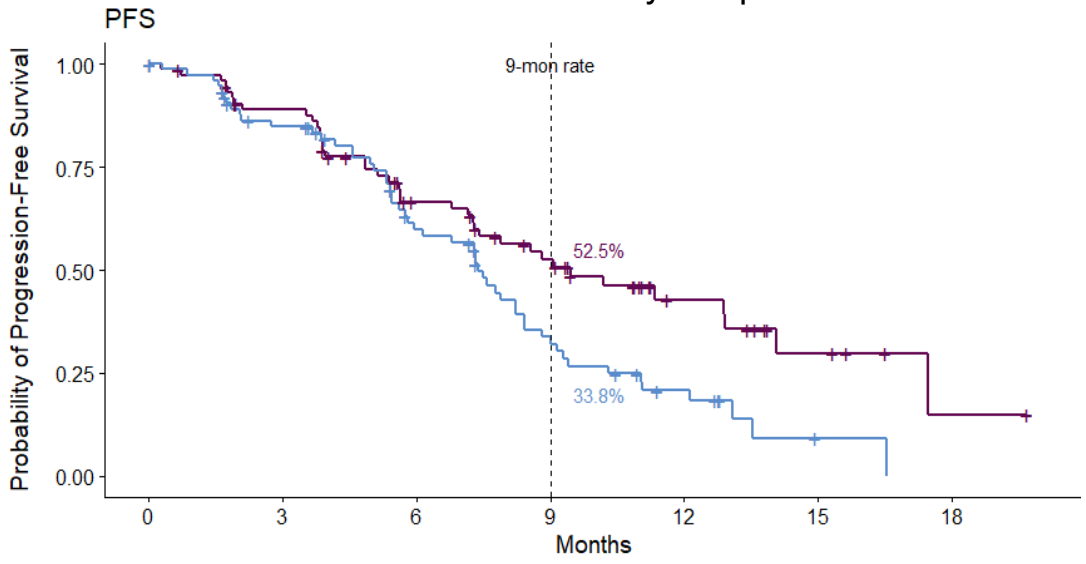


Enrollment period: 28 September 2018 to 12 May 2020
Data cutoff date 23 September 2020, median follow up is 10.9 months (range, 0.03-22)

Courtesy of Daniel Catenacci, MD

Progression-Free Survival and Overall Survival: Intent to Treat

PFS Primary Endpoint

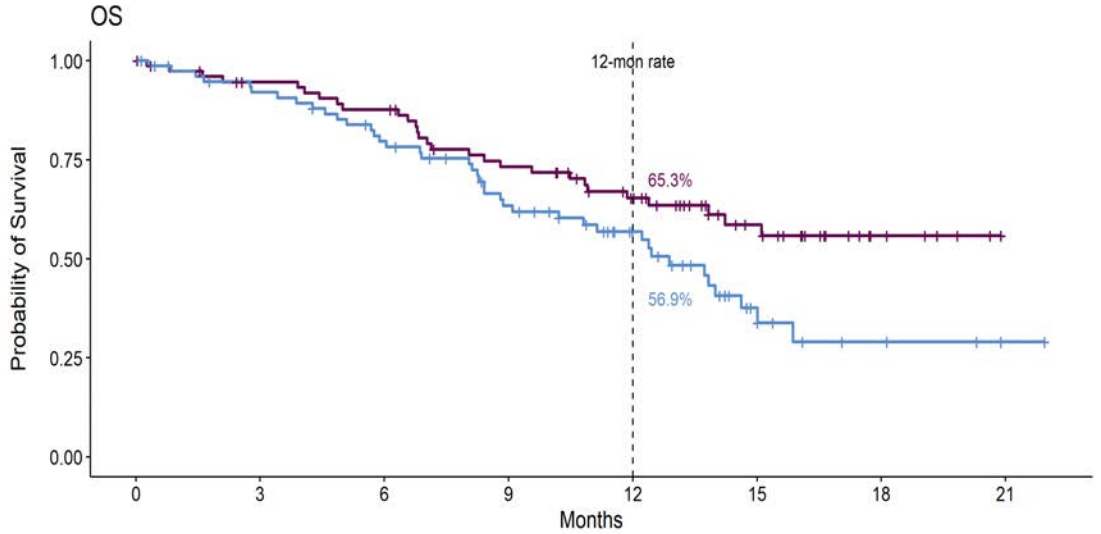


Number at risk

BEMA + mFOLFOX6	77	62	40	28	12	5	1
PLACEBO + mFOLFOX6	78	59	37	19	9	1	0

	Bema N = 77	Placebo N = 78
Median PFS, mo (95% CI)	9.5 (7.3, 12.9)	7.4 (5.8, 8.4)
	P=0.0727	
HR (95% CI)	0.68 (0.44, 1.04)	

OS Key Secondary Endpoint



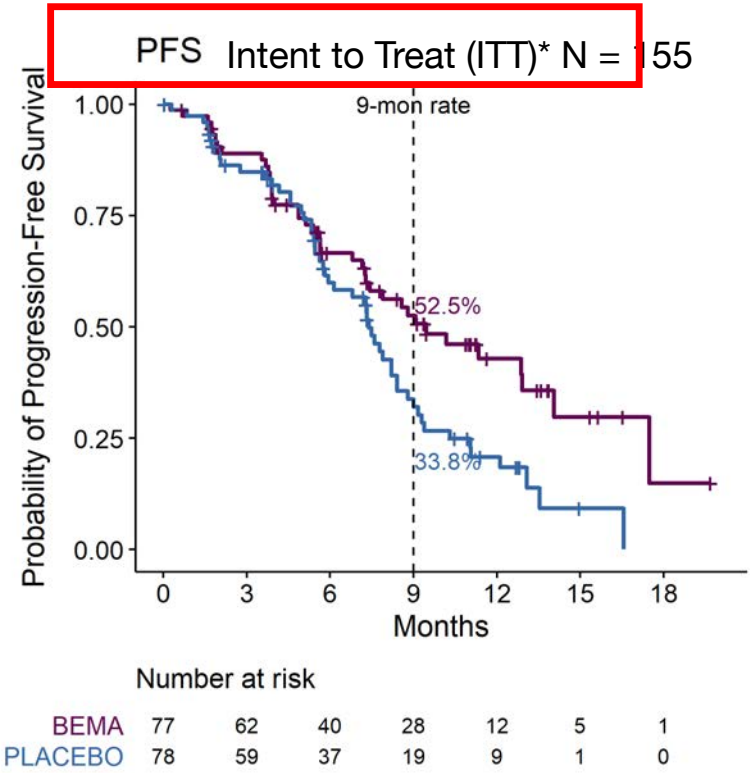
Number at risk

BEMA + mFOLFOX6	77	68	63	50	38	21	6	0
PLACEBO + mFOLFOX6	78	68	57	42	27	10	4	1

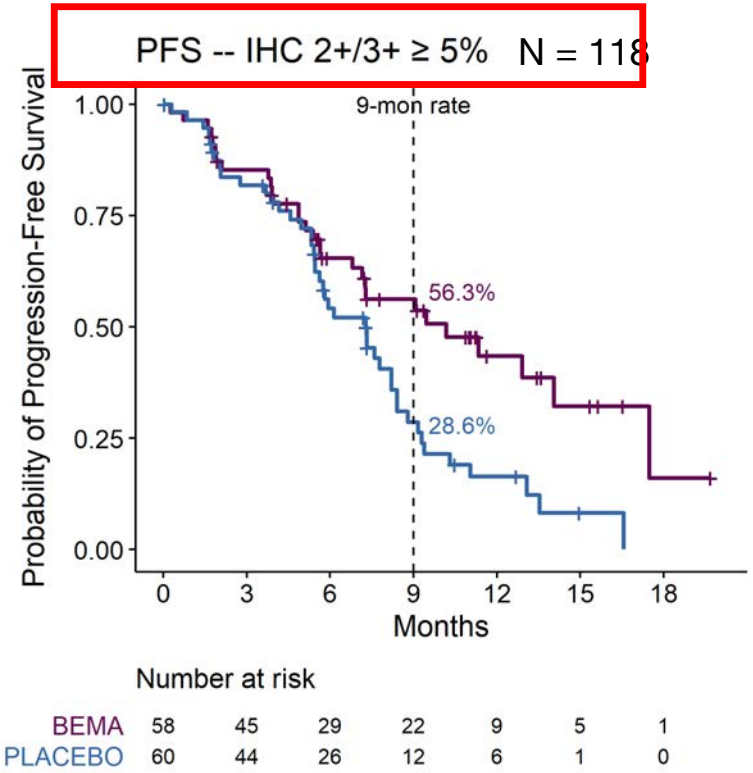
	Bema N = 77	Placebo N = 78
Median OS, mo (95% CI)	NR (13.8, NR)	12.9 (9.1, 15.0)
	P=0.0268	
HR (95% CI)	0.58 (0.35, 0.95)	

Courtesy of Daniel Catenacci, MD

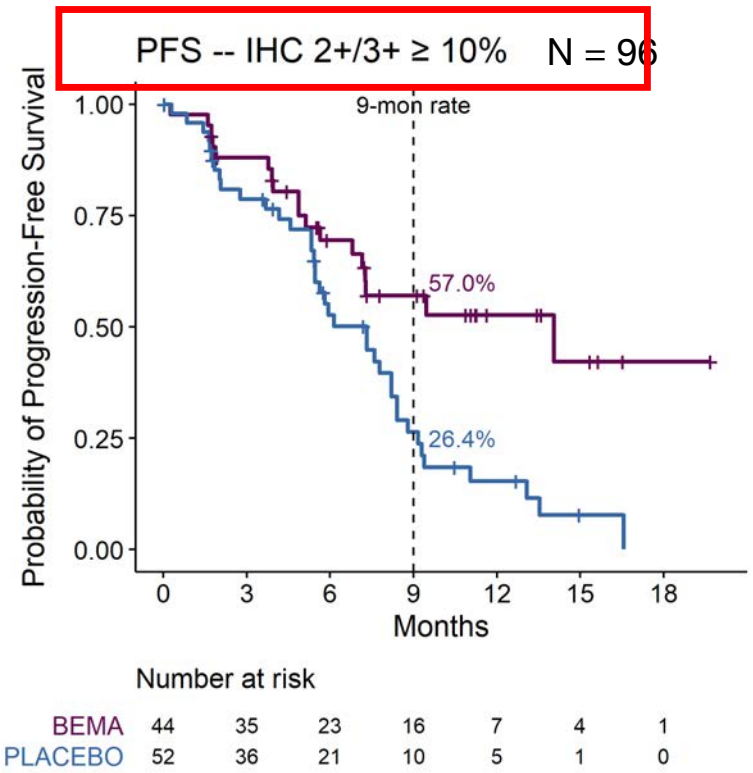
Progression-Free Survival Benefit Increased with Higher Levels of FGFR2b Overexpression



	Bema N = 77	Placebo N = 78
mPFS, mo (95% CI)	9.5 (7.3, 12.9)	7.4 (5.8, 8.4)
	P=0.0727	
HR (95% CI)	0.68 (0.44, 1.04)	



	Bema N = 58	Placebo N = 60
mPFS, mo (95% CI)	10.2 (6.8, 14.1)	7.3 (5.5, 8.2)
HR (95% CI)	0.54 (0.33, 0.87)	

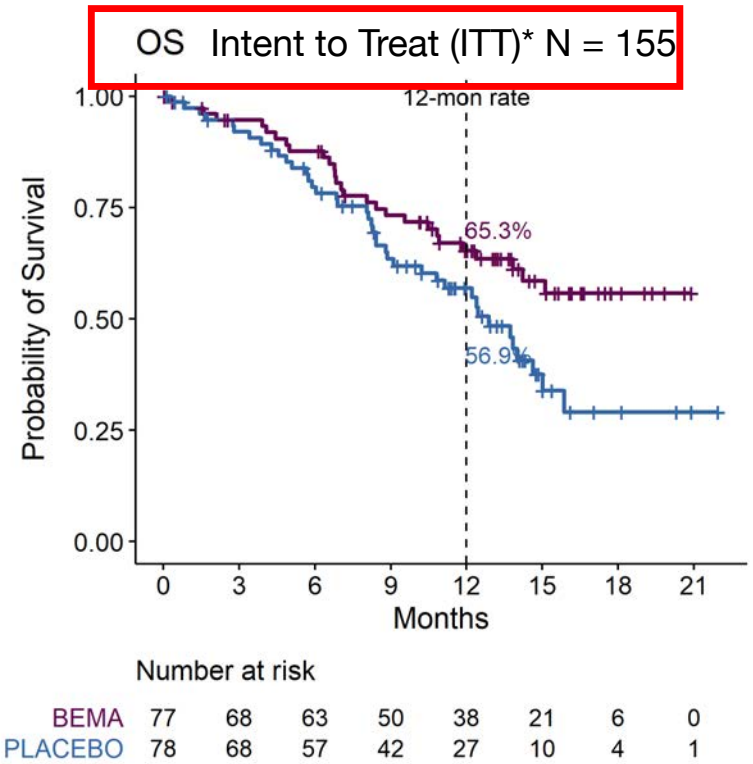


	Bema N = 44	Placebo N = 52
mPFS, mo (95% CI)	14.1 (6.8, NR)	7.3 (5.4, 8.2)
HR (95% CI)	0.44 (0.25, 0.77)	

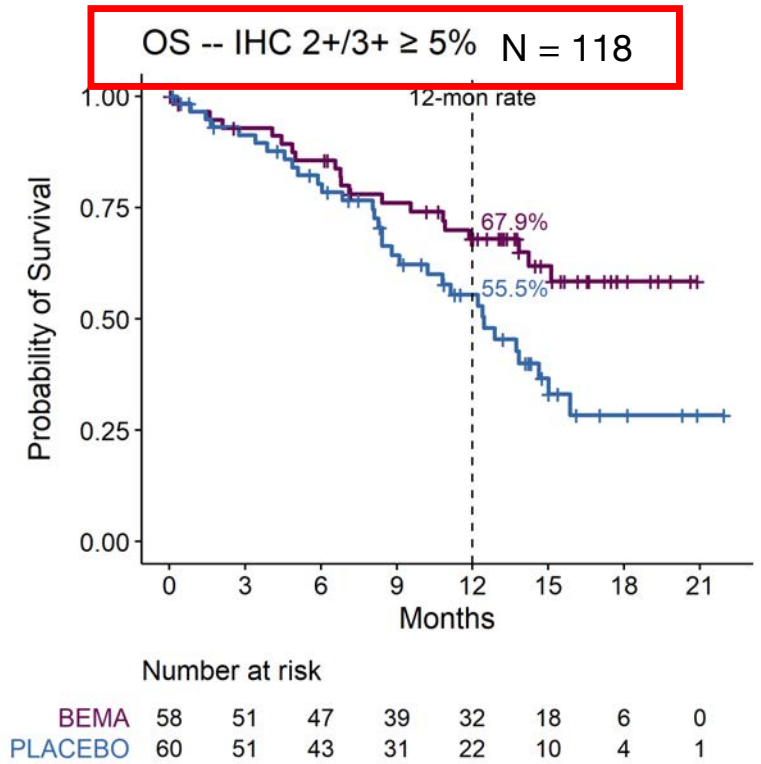
*ITT = 149 with IHC 2+/3+ and 6 pts with IHC <2+ or not available who were enrolled based on ctDNA alone

Courtesy of Daniel Catenacci, MD

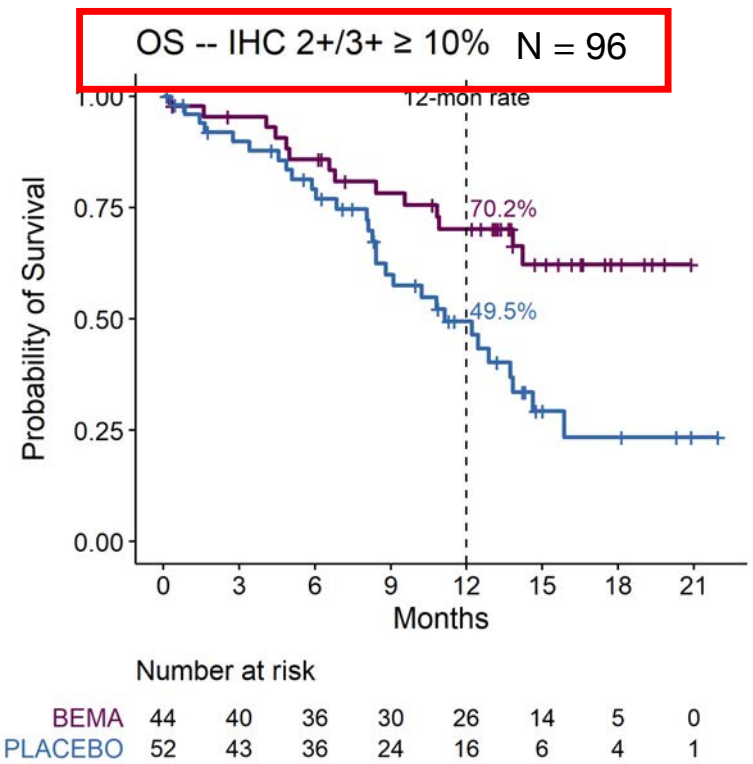
Overall Survival Benefit Increased with Higher Levels of FGFR2b Overexpression



	Bema N = 77	Placebo N = 78
mOS, mo (95% CI)	NR (13.8, NR)	12.9 (9.1, 15.0)
	P=0.0268	
HR (95% CI)	0.58 (0.35, 0.95)	



	Bema N = 58	Placebo N = 60
mOS, mo (95% CI)	NR (13.8, NR)	12.5 (8.8, 15.0)
HR (95% CI)	0.52 (0.30, 0.91)	

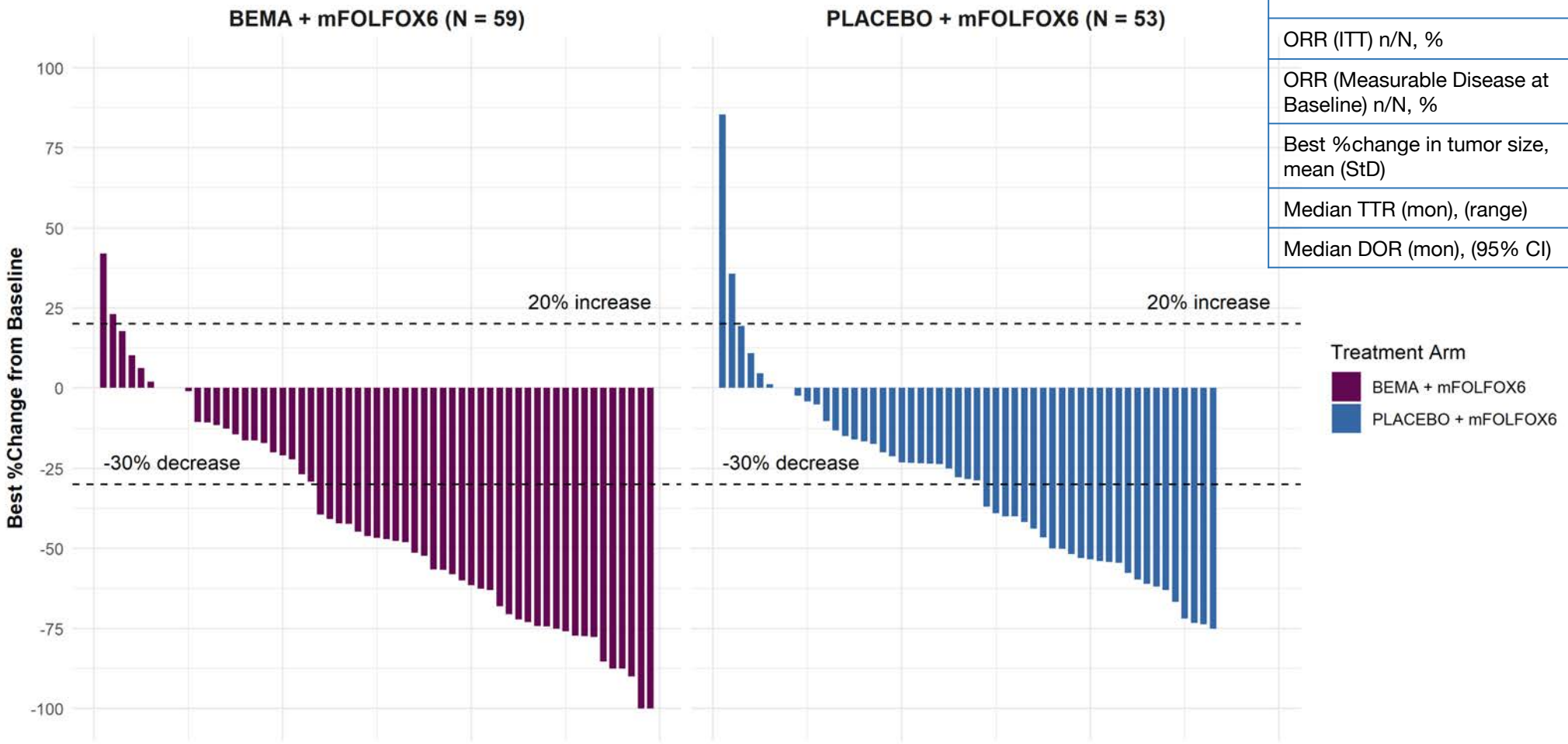


	Bema N = 44	Placebo N = 52
mOS, mo (95% CI)	NR (13.8, NR)	11.1 (8.4, 13.8)
HR (95% CI)	0.41 (0.22, 0.79)	

*ITT = 149 with IHC 2+/3+ and 6 pts with IHC <2+ or not available who were enrolled based on ctDNA alone

Courtesy of Daniel Catenacci, MD

Best % Change in Target Lesions from Baseline



	Bema + mFOLFOX6	Placebo + mFOLFOX6
ORR (ITT) n/N, %	36/77, 47%	26/78, 33%
ORR (Measurable Disease at Baseline) n/N, %	35/66, 53%	24/60, 40%
Best %change in tumor size, mean (StD)	-41.7 (33.76)	-29.9 (30.49)
Median TTR (mon), (range)	1.84 (1.7, 7.6)	1.87 (1.6, 7.3)
Median DOR (mon), (95% CI)	12.2 (5.5,15.6)	7.1 (4.3,11.7)

Only subjects with measurable disease at baseline and at least 1 evaluable scan postbaseline are included in the waterfall plot.
DOR = Duration of response; TTR = Time to response
^: estimated among subjects with measurable disease at baseline

Courtesy of Daniel Catenacci, MD

Summary of Adverse Events

Adverse Events	<_g ['H 7 10#	J f[ ] _\ i 'H 7 11#
All Treatment-Emergent Adverse Events (TEAE)	76 (100.0%)	76 (98.7%)
Grade ≥ 3	63 (82.9%)	57 (74.0%)
Leading to Death (Grade 5)	5 (6.6%)	4 (5.2%)
Serious Adverse Events	24 (31.6%)	28 (36.4%)
Leading to any component of mFOLFOX6 discontinuation	35 (46.1%)	28 (36.4%)
Leading to Bema/placebo discontinuation	26 (34.2%)	4 (5.2%)

Exposure	Bema (N = 76)	Placebo (N = 77)
Duration of Exposure to mFOLFOX6 (weeks), median (range)	29.80 (2.1, 73.0)	26.47 (2.1, 66.7)
Duration of Exposure to bema/placebo (weeks), median (range)	24.00 (2.0, 71.6)	26.00 (2.0, 73.6)

Courtesy of Daniel Catenacci, MD

Summary of Selected Treatment-Emergent Adverse Events

Selected Adverse Events	Any Grade		Grade 3	
	Bema (N = 76)	Placebo (N = 77)	Bema (N = 76)	Placebo (N = 77)
Preferred Term	76 (100.0%)	76 (98.7%)	63 (82.9%)	57 (74.0%)
Nausea	36 (47.4%)	41 (53.2%)	0	3 (3.9%)
Vomiting	22 (28.9%)	24 (31.2%)	2 (2.6%)	2 (2.6%)
Diarrhoea	31 (40.8%)	24 (31.2%)	2 (2.6%)	1 (1.3%)
Stomatitis	24 (31.6%)	10 (13.0%)	7 (9.2%)	1 (1.3%)
Peripheral sensory neuropathy	15 (19.7%)	15 (19.5%)	4 (5.3%)	3 (3.9%)
Neutrophil count decreased	31 (40.8%)	33 (42.9%)	23 (30.3%)	27 (35.1%)
Platelet count decreased	14 (18.4%)	21 (27.3%)	1 (1.3%)	0
Aspartate aminotransferase increased	23 (30.3%)	15 (19.5%)	4 (5.3%)	2 (2.6%)
Alanine aminotransferase increased	22 (28.9%)	11 (14.3%)	2 (2.6%)	1 (1.3%)
Dry eye	20 (26.3%)	5 (6.5%)	2 (2.6%)	0

Courtesy of Daniel Catenacci, MD

Corneal-Related Adverse Events

Trial required corneal evaluation at baseline and every 8 weeks until the end of treatment[1]

	Bema (N = 76)	Placebo (N = 77)
Corneal Adverse Events (SMQ)[2] All Grade[3]	51 (67.1%)	8 (10.4%)
Corneal Adverse Events (SMQ) Grade 3[4]	18 (23.7%)	0
Median time to onset to any grade, weeks (range)	16.1 (0.1, 41.0)	11.6 (6.0, 29.0)
Corneal AE leading to bema/placebo discontinuation[5]	20 (26.3%)	0
AE resolved	12 (60.0%)	0
AE not resolved as of 23 Sept 2020	8 (40.0%)	0
Median time to resolution, weeks (95%CI)	27.0 (18.9, NR)	NA

[1] If any event reported, examinations were to continue every 8W until resolution, even if drug discontinued
[2] SMQ = Standardised MedDRA Query
[3] Most common: dry eye (26.3%), keratitis (15.8%), punctate keratitis (14.5%), vision blurred (15.0%), corneal epithelium defect (10.5%)
[4] No ≥ grade 4 event reported
[5] Most common: dry eye (n=4), keratitis (n=4), corneal disorder (n=2), eye disorder (n=2) limbal stem cell deficiency (n=2), punctate keratitis (n=2)

Courtesy of Daniel Catenacci, MD

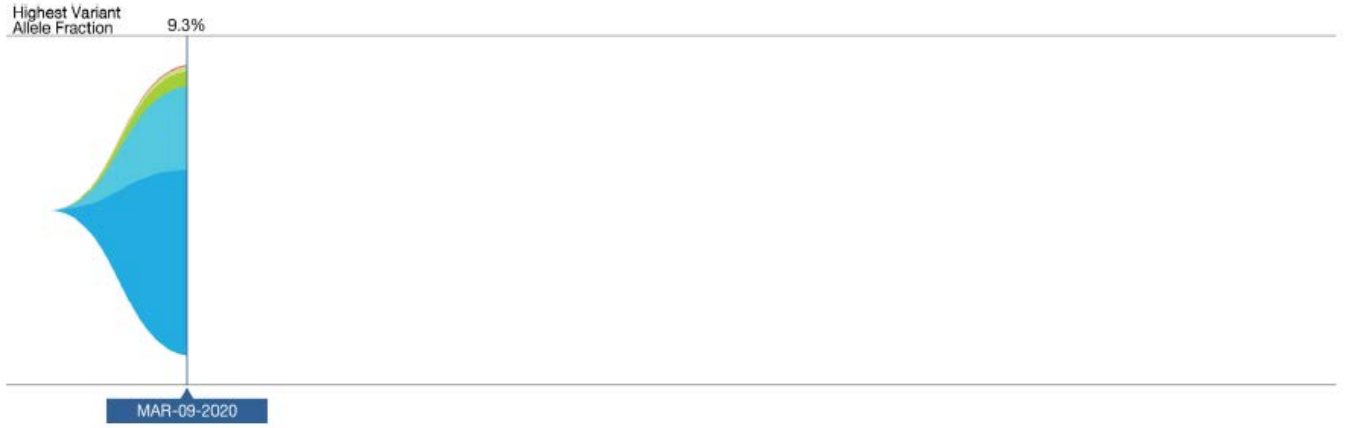
Summary

- The FIGHT trial is the first study to evaluate targeting overexpression of FGFR2b
- ~ 30% of 1L advanced non-HER2+ GC/GEA overexpress FGFR2b+ by a centrally performed IHC test
- Bemarituzumab, added to mFOLFOX6 chemotherapy, led to clinically meaningful and statistically significant improvements in PFS, OS and ORR
- Bemarituzumab was associated with an increase in corneal adverse events and stomatitis, the majority of which were reversible
- The FIGHT trial results support
  - A prospective randomized phase 3 study in gastric/gastroesophageal adenocarcinoma
  - The evaluation of bemarituzumab to treat other FGFR2b+ tumor types

Courtesy of Daniel Catenacci, MD

Case 1

- 35 year F presented with epigastric pain and early satiety, diagnosed with distal esophageal adenocarcinoma
- EGD with nodularity and mass involving ~9cm of the distal esophageal to the GEJ
- Biopsy poorly diff adenocarcinoma
- HER2 IHC3+ in >80% of cells
- CT and PET with diffuse M1 LNs
- FNA of left supraclavicular LN adenocarcinoma
- Treated with FOLFOX-trastuzumab 1L
  - For ~12 months then PD with new left pleural effusion and carcinomatosis
- EGD with biopsy → Persistent HER2 IHC3+
- DESTINY-Gastric02 trial: 2L trastuzumab-deruxtecan x 4 cycles (~2 months) rapid PD and respiratory failure attributed to progressed pleural effusion
- Hospice



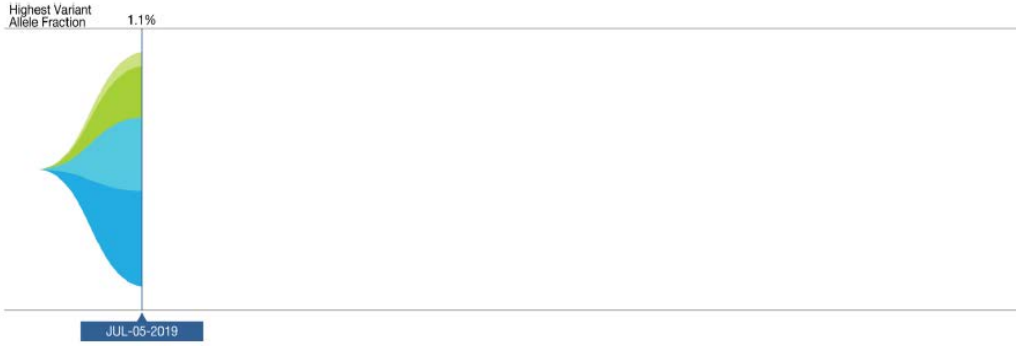
Alteration	% cfDNA or Amp	
TP53 R248W	9.3%	
PIK3CA E545K	3.4%	
APC N818I	0.4%	Variant of Uncertain Significance §
ALK H1063H	0.1%	Synonymous Alteration §
KRAS Q61H	0.02%	
KRAS Amplification Amplifications not graphed above	High (+++) Plasma Copy Number: 8.1	
CCNE1 Amplification Amplifications not graphed above	High (+++) Plasma Copy Number: 7.0	
MYC Amplification Amplifications not graphed above	Medium (++) Plasma Copy Number: 3.3	

ctDNA analysis after progression on 1L, prior to 2L

Courtesy of Daniel Catenacci, MD

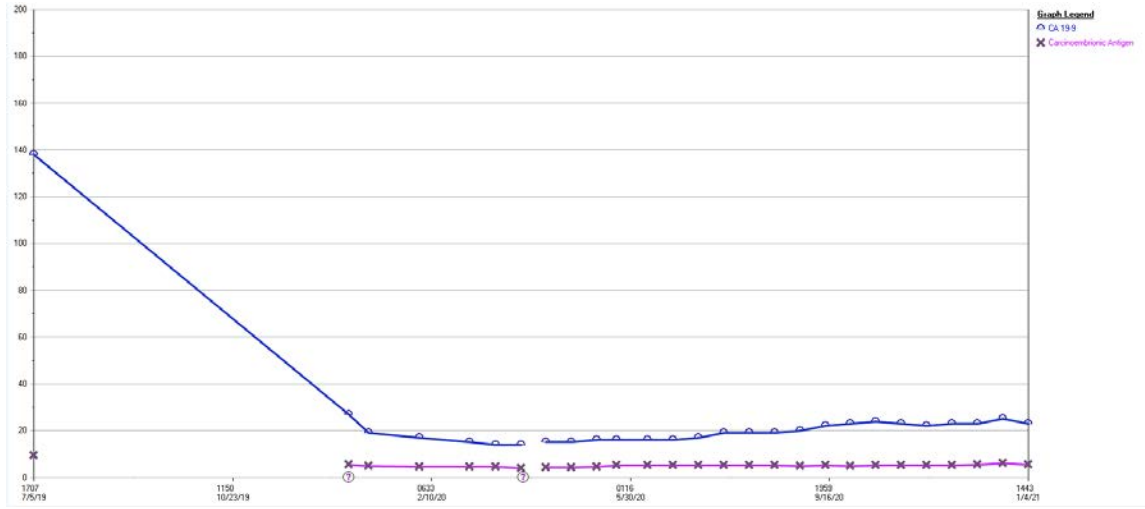
Case 2

- 76 year M with history NHL s/p CHOP 1999, diagnosed with dysphagia and found to have a GEJ adenocarcinoma 7/2019
- Staging cT3N3M1 (supraclav/retroperitoneum LNs)
- Primary tumor and supraclav LN bx with adenocarcinoma, both:
- PD-L1 CPS 2**,** HER2 neg, MSS, TMB 5.8 mt/Mb, FGFR2 amplified
- ctDNA FGFR2 amplification
- Treated with FOLFOX + bemarituzumab/placebo 8/20/19
- Near CR (minimal residual lymph nodes all <1.5cm).
  - mild left eye punctate epithelial erosions,
  - mild drusen both eyes,
  - mild cataracts both eyes,
  - not clinically significant
- Continues on therapy
  - 5FU bolus and LV dropped after C4 (nausea)
  - Oxaliplatin dropped to 65mg/m^2 at C6, and off after C8 due to neuropathy
  - On first line maintenance (1LM) since with 5FU-bema/placebo, now at C37 to present



Alteration	% cfDNA or Amp	
TP53 R248Q	1.1%	
EGFR A955T	0.8%	Variant of Uncertain Significance §
MET P1008L	0.5%	Variant of Uncertain Significance §
ARID1A A1626T	0.1%	Variant of Uncertain Significance §
FGFR2 Amplification Amplifications not graphed above	High (+++) Plasma Copy Number: 12.3	

ctDNA analysis at diagnosis



Courtesy of Daniel Catenacci, MD

Thank You