Esophageal and Gastric Cancer 2020 Updates

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I **do not** have any commercial or financial relationship to any topics or products discussed.

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Overview

Locoregional

- RTOG 1010
- Checkmate 577

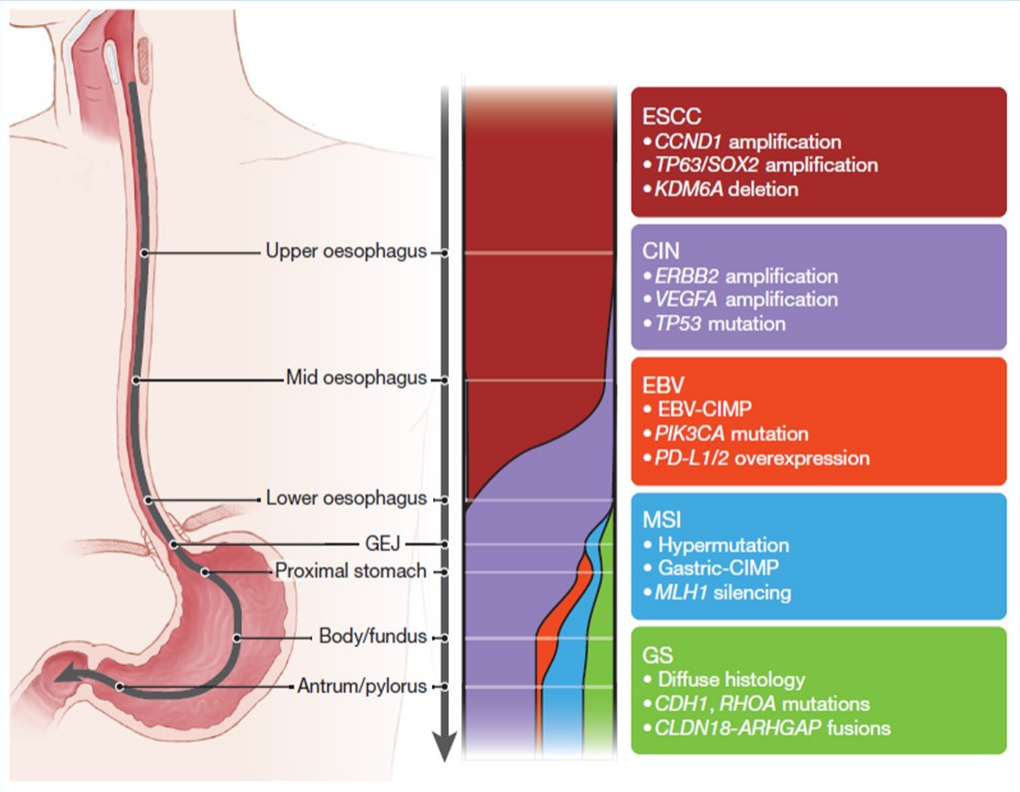
Metastatic Newly Diagnosed

- Checkmate 649
- Attraction 4
- Keynote 590

Metastatic Recurrent

- Destiny Gastric 01

Esophago-Gastric Cancer Subclasses



ESCC - Similarities with Head-Neck Cancer

CIN – Immunogenic ???
HER2 / VEGF amplications

EBV - Immunogenic
Immune infiltrates, PD-L1 high

MSI - Immunogenic
High mutational burden

Genomic stable (silent)
Lower mutational burden

The Cancer Genome Atlas Research Network. *Nature.* 2017;541:169-175

Locoregional Disease

RTOG 1010

RTOG 1010: Background

- ToGA trial demonstrated that addition of HER2-targeting trastuzumab to chemotherapy improved survival in patients with HER2-positive advanced gastroesophageal cancer[1]
- Median follow up of 18.6 months overall survival benefit 13.8 versus 11.1 months
- A pilot study showed that addition of trastuzumab to trimodality therapy might be beneficial in patients with locally advanced HER2-expressing esophageal adenocarcinoma[2]
- Current study reports 5-yr results from phase III study of neoadjuvant/adjuvant trastuzumab in combination with trimodality therapy (chemoradiotherapy + surgery) in patients with resectable, HER2-overexpressing esophageal adenocarcinoma[3]

Slide credit: clinicaloptions.com

1. Bang. Lancet. 2010;376:687. 2. Safran. Int J Rad Onc Biol Phys. 2007;67:405. 3. Safran. ASCO 2020. Abstr 4500.

RTOG 1010: Study Design

- Randomized, open-label phase III trial

Stratified by presence of adenopathy
(no vs yes—celiac absent vs yes—celiac present ≤ 2 cm)

Patients with newly diagnosed stage T1N1-2, T2-3N0-2 esophageal adenocarcinoma involving mid (≤ 25 cm), distal, or esophagogastric junction and up to 5 cm of stomach; HER2 positive (IHC3+ or FISH+); candidate for potential curative resection; PS 0-2; LVEF ≥ LLN
(N = 203)

- Primary endpoint: DFS
- Secondary endpoints: pCR, OS, safety,
  biomarkers for response and survival, QoL

Trastuzumab* + Trimodality Therapy†
(n = 102)

Trimodality Therapy†
(n = 101)

*Trastuzumab dosed at 4 mg/kg in Wk 1, 2 mg/kg/wk x 5 during chemoradiotherapy, 6 mg/kg for 1 dose prior to surgery; and 6 mg/kg Q3W for 13 treatments after surgery.

†Trimodality therapy consisted of paclitaxel 50 mg/m^2 plus carboplatin AUC 2 QW x 6 wks + concurrent radiation (50.4 Gy) over 5.5 wks, followed by surgery 5-8 wks after completion of radiation.

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RTOG 1010: Baseline Characteristics

Characteristic	Trastuzumab + Trimodality Therapy (n = 98)	Trimodality Therapy (n = 96)
Median age, yrs (range)	63 (40-80)	65.5 (24-83)
Male, n (%)	85 (87)	79 (82)
Zubrod performance status, n (%)		
▪ 0	62 (63)	62 (65)
▪ 1	34 (35)	31 (32)
▪ 2	2 (2)	3 (3)
T stage (clinical), n (%)		
▪ T1	1 (1)	4 (4)
▪ T2	18 (18)	17 (18)
▪ T3	79 (81)	75 (78)
Presence of adenopathy, n (%)		
▪ No	38 (39)	38 (40)
▪ Yes—celiac absent	48 (49)	48 (50)
▪ Yes—celiac present ≤ 2 cm	12 (12)	10 (10)

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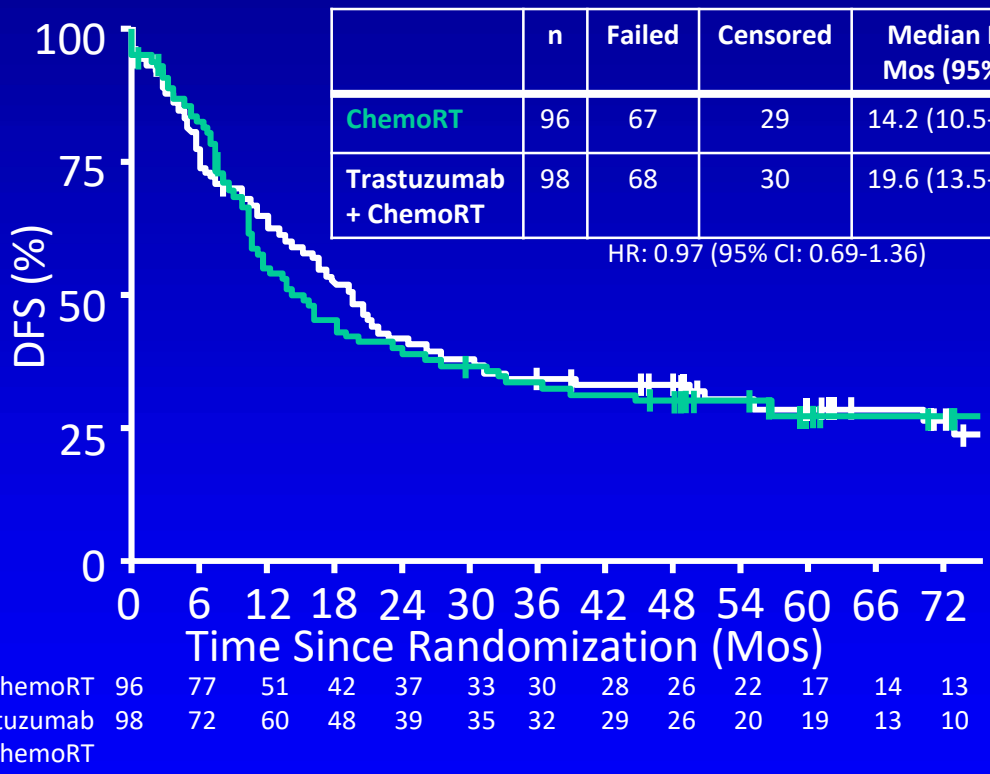
RTOG 1010: DFS (Primary Endpoint) and OS



	n	Failed	Censored	Median PFS, Mos (95% CI)
ChemoRT	96	67	29	14.2 (10.5-23.0)
Trastuzumab + ChemoRT	98	68	30	19.6 (13.5-26.2)

HR: 0.97 (95% CI: 0.69-1.36)

- Median OS, trastuzumab + chemoRT vs chemoRT: 38.5 vs 38.9 mos; HR 1.01 (95% CI: 0.69-1.47)

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RTOG 1010: DFS Multivariate Analysis

Variable	Comparison	HR	95% CI	*P* Value
Treatment	Trastuzumab + chemoRT vs chemoRT	1.07	0.76-1.51	.70
Age	≥ 65 yrs vs < 65 yrs	1.90	1.34-2.70	.0003
T stage	T3 vs T1/T2	1.92	1.21-3.06	.0058
Adenopathy	Yes—celiac absent vs no	1.06	0.73-1.53	.76
	Yes—celiac present ≤ 2 cm vs no	1.09	0.61-1.93	.78

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RTOG 1010: Select Treatment-Related Adverse Events

Selected TRAEs, %	Trastuzumab + Trimodality Therapy (n = 95)		Trimodality Therapy (n = 96)	
	All Grades	Grades ≥ 3	All Grades	Grades ≥ 3
Cardiac disorders	NR	5	NR	3
▪ Atrial fibrillation	2	2	1	1
▪ Atrial flutter	1	1	1	0
▪ Cardiac arrest	0	0	1	1
▪ LV function	1	1	0	0
Infections	NR	12	NR	7
Metabolism and nutrition disorders	NR	13	NR	20

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RTOG 1010: Conclusions

- Adding neoadjuvant/adjuvant trastuzumab to neoadjuvant chemoradiotherapy + surgery in patients with resectable HER2-positive esophageal adenocarcinoma did not improve outcomes compared with trimodality therapy alone
  - No improvement in DFS (HR: 0.97; 95% CI: 0.69-1.36) or OS (HR: 1.01; 95% CI: 0.69-1.47)
  - No increase in pCR (27% vs 29%)
- Adding trastuzumab to trimodality therapy did not increase cardiac toxicity or other Aes
- Analyses underway to explore factors associated with outcomes, including degree of HER2 expression, presence of resistance mutations, and genomic analyses
- Investigators suggest that other, more potent HER2-targeted therapies should be explored for resectable esophageal adenocarcinoma (eg, T-DXd)

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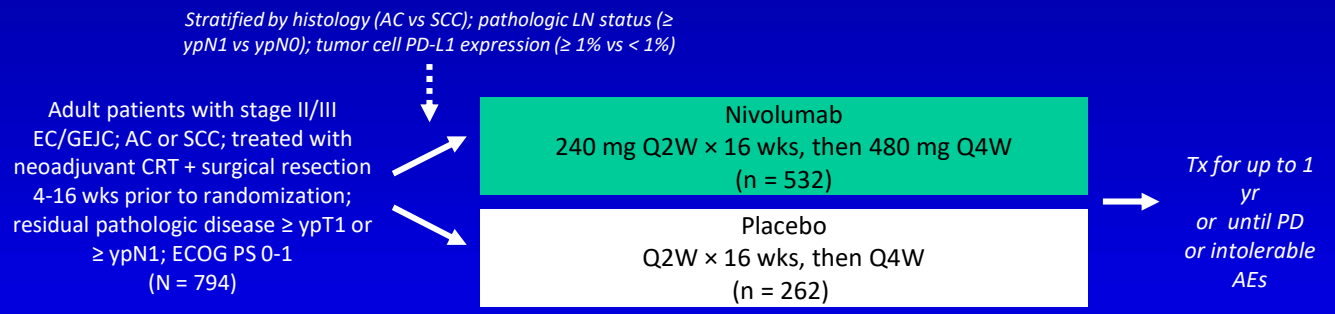
Checkmate 577

CheckMate 577: Adjuvant Nivolumab vs Observation Following Neoadjuvant CRT and Resection in EC/GEJC

- Global, randomized, double-blind, phase III, placebo-controlled



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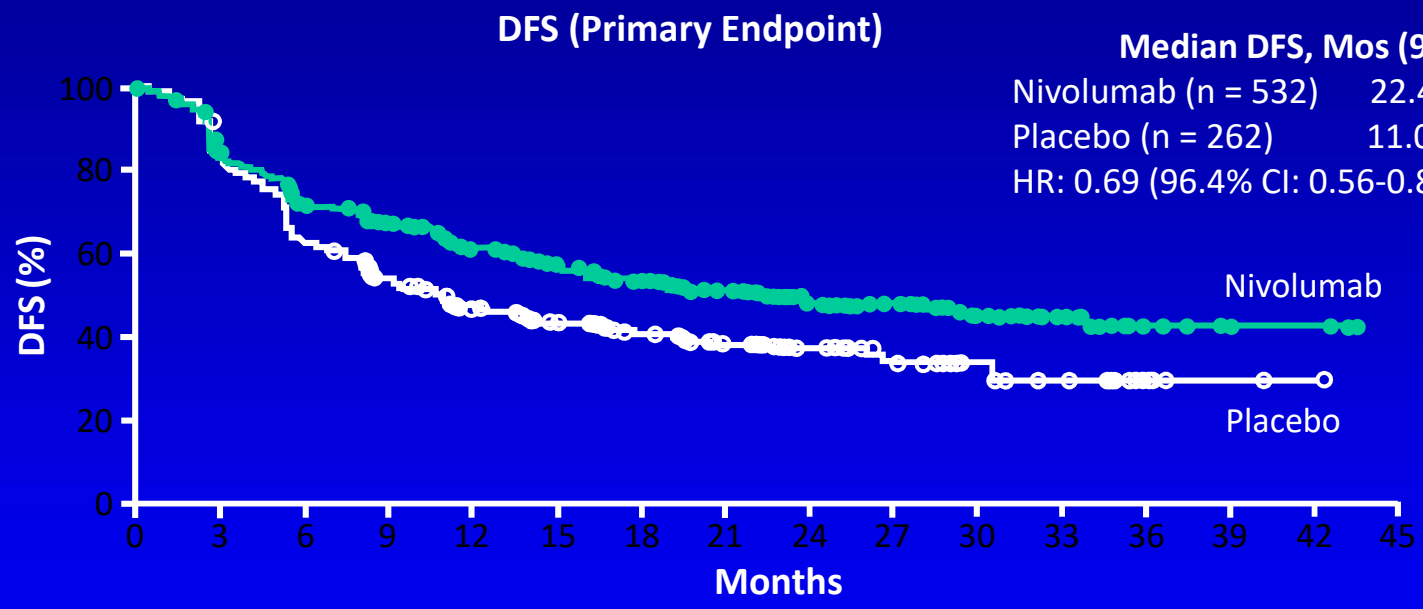
- Median follow-up: 24.4 mos (range, 6.2-44.9)
- Primary endpoint: DFS assessed by investigator
- Secondary endpoints: OS, OS rate at 1, 2, and 3 yrs

Kelly. ESMO 2020. Abstr LBA9_PR. NCT02743494.

CheckMate 577: DFS



- 6-mo DFS rate was 72% in nivolumab group vs 63% in placebo group
- DFS favored nivolumab vs placebo across prespecified subgroups

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CheckMate 577: Safety

Event, n (%)	Nivolumab (n = 532)		Placebo (n = 260)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Any AEs*	510 (96)	183 (34)	243 (93)	84 (32)
▪ Serious AEs	158 (30)	107 (20)	78 (30)	53 (20)
▪ AEs leading to d/c	68 (13)	38 (7)	20 (8)	16 (6)
Any TRAEs*	376 (71)	71 (13)	119 (46)	15 (6)
▪ Serious TRAEs	40 (8)	29 (5)	7 (3)	3 (1)
▪ TRAEs leading to d/c	48 (9)	26 (5)	8 (3)	7 (3)
TRAEs in ≥ 10% of treated patients in either arm*				
▪ Fatigue	90 (17)	6 (1)	29 (11)	1 (< 1)
▪ Diarrhea	88 (17)	2 (< 1)	39 (15)	2 (< 1)
▪ Pruritis	53 (10)	2 (< 1)	9 (3)	0
▪ Rash	52 (10)	4 (< 1)	10 (40)	1 (< 1)

*AEs recorded between 1st dose and D30 after last dose of drug.

- One grade 5 TRAE (cardiac arrest) with nivolumab, reported as not treatment-related after database lock

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Kelly. ESMO 2020. Abstr LBA9_PR.

CheckMate 577: Conclusions

- Nivolumab adjuvant therapy provided a statistically significant and clinically meaningful DFS improvement vs placebo in patients with resected esophageal and gastroesophageal junction cancers following neoadjuvant CRT
  - 31% reduction in the risk of recurrence or death
  - Median DFS doubled nivo (22.4 mos) vs placebo arm (11.0 mos)
  - DFS benefit across multiple prespecified subgroups
  - Immunotherapy well tolerated, with an acceptable safety profile
- Incidence of serious TRAEs and TRAEs leading to discontinuation ≤ 9% with nivolumab vs 3% with placebo
- Adjuvant nivolumab could become a new standard of care in patients with resected esophageal and gastroesophageal junction cancers

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Kelly. ESMO 2020. Abstr LBA9_PR.

CheckMate 577: Expert Insight

- This is the first trial to show a benefit for adjuvant immunotherapy in resected esophageal and gastroesophageal junction with both adenocarcinoma and SCC histology
  - DFS benefit was seen in all patients irrespective of PD-L1 expression
  - Tumor PD-L1 testing was not a good predictor of outcomes
- A large percentage of the patient population (71%) had adenocarcinoma histology, which is the most common histology in the United States and Europe
- Given the robust DFS, these data are clinically meaningful and potentially practice changing, and will likely be incorporated into clinical practice once approved

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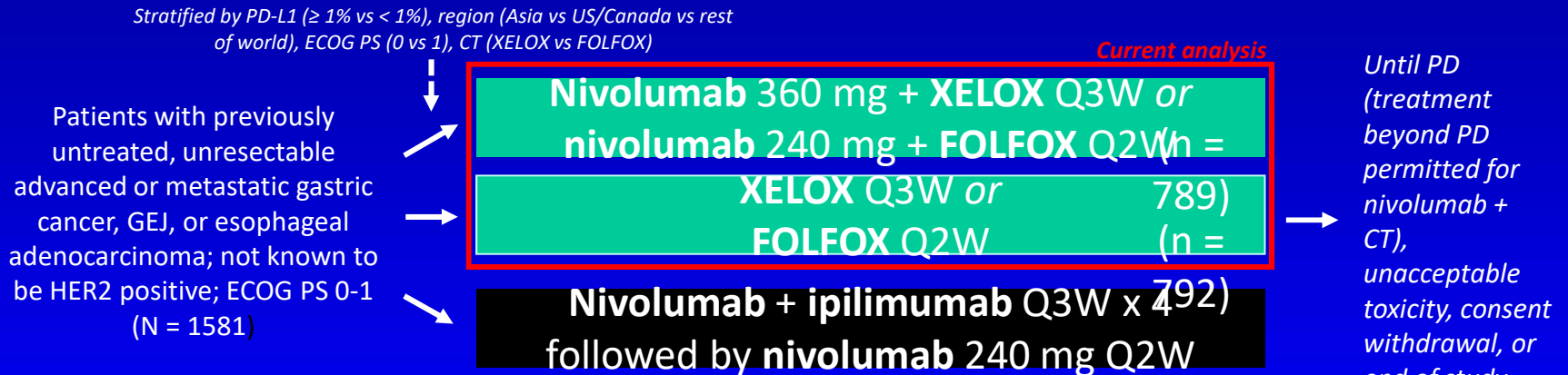
Advanced Disease

Phase III CheckMate 649: First-line Nivolumab + CT vs CT in Advanced Gastroesophageal Cancers

- Final PFS and prespecified interim OS analyses of international, randomized, open-label phase III trial (data cutoff: May 27, 2020; minimum follow-up: 12.1 mos)



- Coprimary endpoints: OS and PFS in patients with PD-L1 CPS ≥ 5
  - If coprimary endpoints statistically significant (α = .03 and .02, respectively), followed by hierarchical testing of OS in patients with PD-L1 CPS ≥ 1 (α = .007), then in all randomized patients (α = .007)
- Secondary endpoints: OS and PFS in all randomized patients and with PD-L1 CPS ≥ 10 and ≥ 1, ORR

Moehler. ESMO 2020. Abstr LBA6_PR. NCT02872116.

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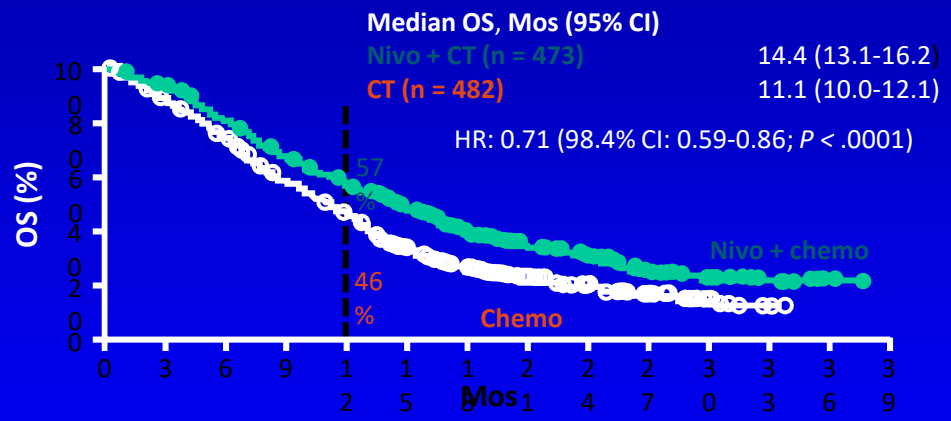
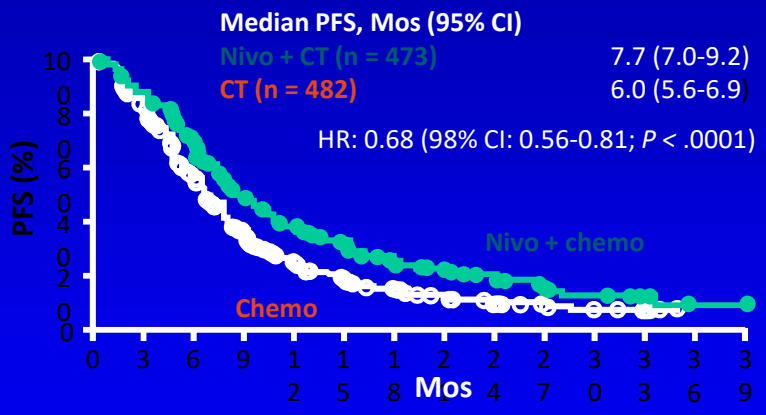
CheckMate 649: OS and PFS in Patients With PD-L1 CPS ≥ 5 (Coprimary Endpoints)

Median OS in Patients With PD-L1 CPS ≥ 5



Median PFS in Patients With PD-L1 CPS ≥ 5



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CheckMate 649: Response in Patients With PD-L1 CPS ≥ 5

Outcome	Nivo + CT (n = 378)	CT (n = 391)
ORR, %	60	45
Best overall response, %		
▪ CR	12	7
▪ PR	48	38
▪ SD	28	34
▪ PD	7	11
▪ NE	6	10
Median TTR, mos (range)	1.5 (0.8-10.2)	1.5 (1.0-7.1)
Median DoR, mos	9.5	7.0

- ORR significantly higher with nivolumab + CT vs CT (descriptive *P* < .0001)

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CheckMate 649: Safety

TRAEs, n (%)	Nivo + CT (n = 782)		CT (n = 767)	
	Any Gr	Gr 3/4	Any Gr	Gr 3/4
Any	738 (94)	462 (59)	679 (89)	341 (44)
Serious	172 (22)	131 (17)	93 (12)	77 (10)
Leading to d/c	384 (36)	132 (17)	181 (24)	67 (9)
Death	12 (2)*		4 (< 1)†	

*1 death each due to febrile neutropenia, gastrointestinal bleeding, gastrointestinal toxicity, infection, interstitial lung disease, intestinal mucositis, neutropenic fever, pneumonia, pneumonitis, pulmonitis, capecitabine-related septic shock, and stroke. †1 death each due to diarrhea-associated toxicity, asthenia and severe hyperoxia, pulmonary thromboembolism, and interstitial pneumonia.

Select TRAEs With Potential Immunologic Etiology, n (%)	Nivo + CT (n = 782)		CT (n = 767)	
	Any Gr	Gr 3/4	Any Gr	Gr 3/4
Endocrine	107 (14)	5 (< 1)	3 (< 1)	0
Gastrointestinal	262 (34)	43 (5)	207 (27)	25 (3)
Hepatic	203 (26)	29 (4)	134 (17)	16 (2)
Pulmonary	40 (5)	14 (2)	4 (< 1)	1 (< 1)
Renal	26 (3)	6 (< 1)	8 (1)	1 (< 1)
Skin	214 (27)	26 (3)	105 (14)	6 (< 1)

- Safety profile consistent between all treated patients vs those with PD-L1 CPS ≥ 5

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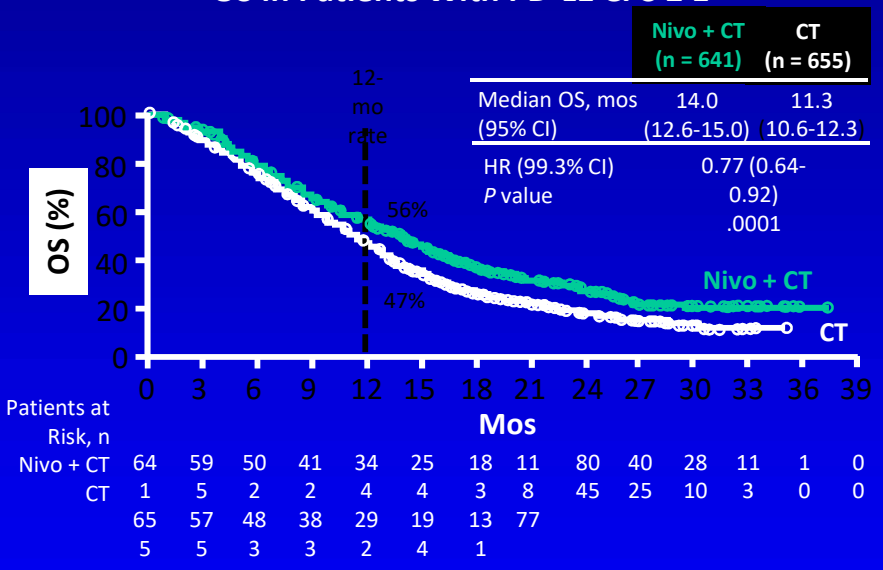
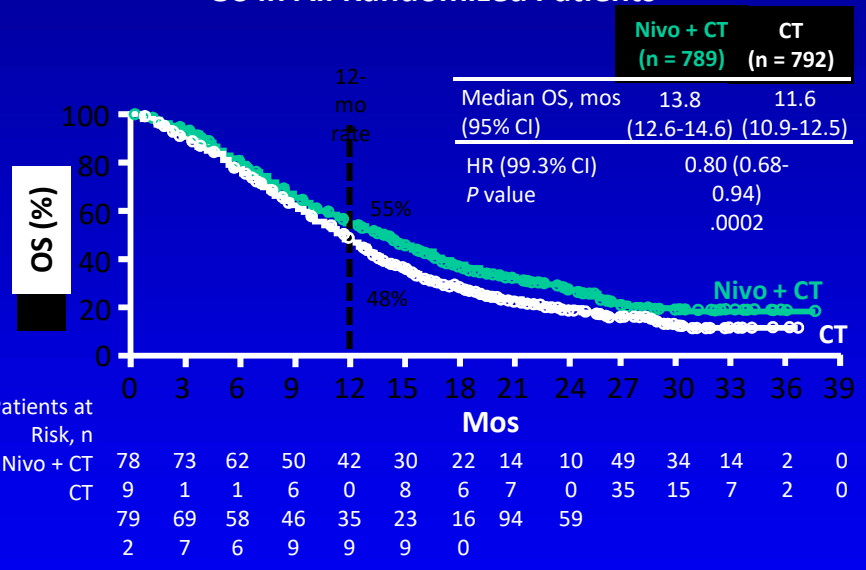
Moehler. ESMO 2020. Abstr LBA6_PR

CheckMate 649: OS and PFS in Patients With CPS ≥ 1 and All Randomized Patients

OS in Patients With PD-L1 CPS ≥ 1



OS in All Randomized Patients



- Prolonged PFS with nivolumab + CT vs CT in patients with PD-L1 CPS ≥ 1 (HR: 0.74; 95% CI: 0.65-0.85) and in all randomized patients (HR: 0.77; 95% CI: 0.68-0.87)

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CheckMate 649: Conclusions

- Phase III CheckMate 649 patients with advanced GE cancers, nivolumab + CT significantly prolonged OS and PFS in patients with PD-L1 CPS ≥ 5 (coprimary endpoints)
  - Median OS, 14.4 vs 11.1 mos (HR: 0.71; *P* < .0001); median PFS, 7.7 vs 6.0 mos (HR: 0.68; *P* < .0001)
  - Significant OS benefit also observed in all randomized patients and those with PD-L1 CPS ≥ 1
- No new safety signals observed with nivolumab + CT
- Investigators concluded that First-line treatment with nivolumab + CT may be new potential standard of care for patients with advanced gastroesophageal cancers

Moehler. ESMO 2020. Abstr LBA6_PR

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Attraction-4

ATTRACTION-4: First-line Nivolumab + Chemotherapy vs Chemotherapy Alone for Advanced Gastric/GEJ Cancer

- Randomized phase II/III trial of **nivolumab + CT*** vs **placebo + CT*** for **previously untreated** unresectable, advanced, or recurrent HER2- **gastric/GEJ cancer** (phase III part, N = 724)
- Enrolled patients in Japan, Korea, and Taiwan
- Coprimary endpoints of PFS and OS

Outcome	Nivo + CT (n = 362)	CT (n = 362)
Median PFS, mos	10.45	8.34
	HR: 0.68 (98.51% CI: 0.51-0.90; *P* = .0007)	
Median OS, mos	17.45	17.15
	HR: 0.90 (95% CI: 0.75-1.08; *P* = .257)	
ORR, %	57.5	47.8
Median DoR, mos	12.91	8.67

- Coprimary endpoint of PFS was met, but OS was not
- Responses were higher and more durable with addition of nivolumab to CT

*SOX or CapOX.

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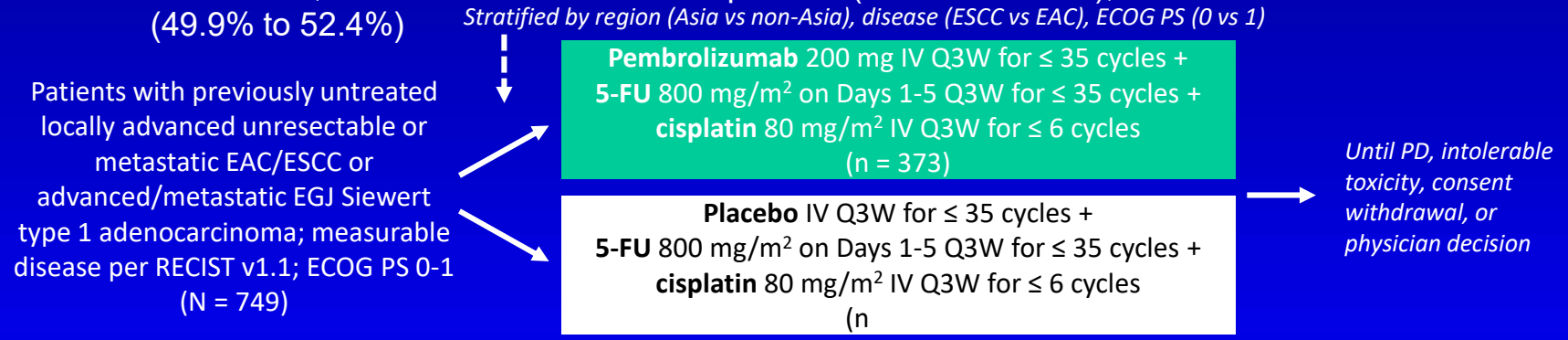
Boku. ESMO 2020. Abstr LBA7.

Keynote 590

KEYNOTE-590: First-line Pembrolizumab + CT vs Placebo + CT in Patients With Advanced Esophageal Cancer

- Interim analysis of international, randomized, double-blind phase III trial (data cutoff: July 2, 2020)
  - At baseline, metastatic disease in most patients (90.2% to 92.2%), PD-L1 CPS ≥ 10 in half (49.9% to 52.4%)



- Coprimary endpoints: OS, investigator-assessed PFS per RECIST v1.1
  - Prespecified hypothesis testing in parallel that pembrolizumab + CT would show superior PFS in ESCC (α = .002), superior OS in ESCC with PDL-1 CPS ≥ 10 (α = .012), and superior OS in ESCC (α = .011)
- Secondary endpoints: investigator-assessed ORR per RECIST v1.1

Kato. ESMO 2020. Abstr LBA8_PR. NCT03189719.

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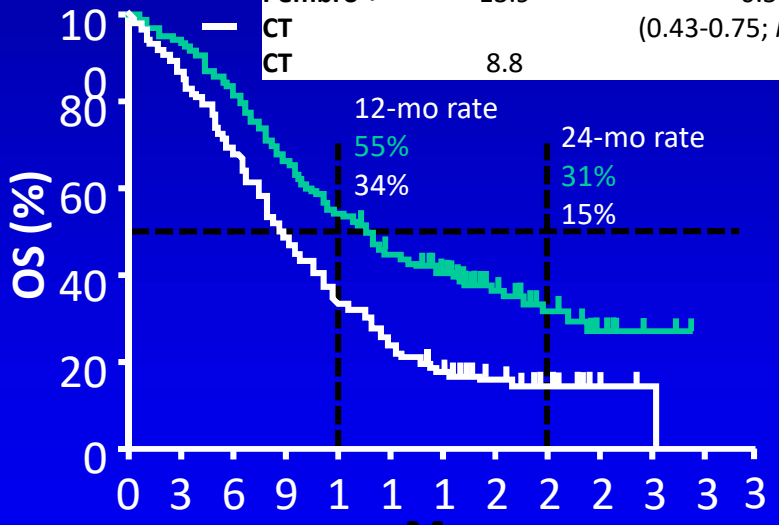
KEYNOTE-590: OS in Patients With ESCC

OS in Patients With ESCC and PD-L1 CPS ≥ 10

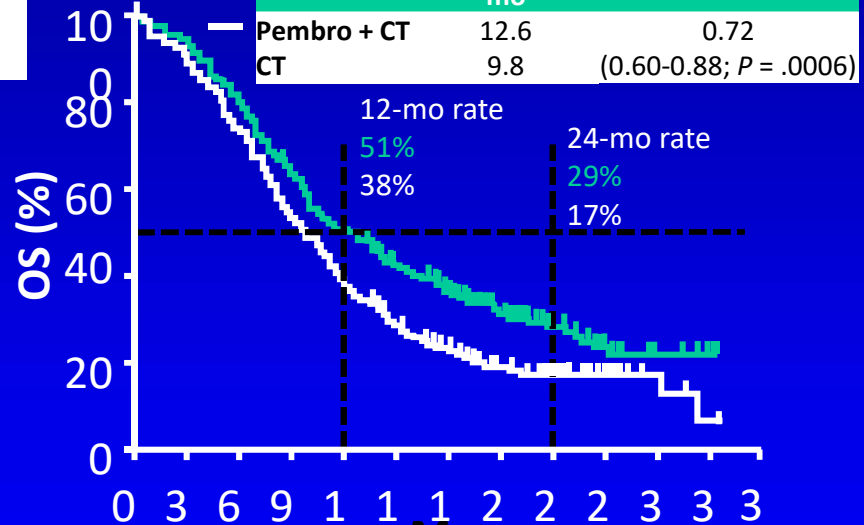
	Median OS, mo	HR (95% CI)
Pembro + CT	13.9	0.57 (0.43-0.75; *P* < .0001)
CT	8.8	



Patients at Risk, n													
Pembro + CT	143	134	119	96	78	61	51	29	16	7	3	0	0
CT	143	124	99	70	48	34	24	15	10	4	1	0	0

OS in All Patients With ESCC

	Median OS, mo	HR (95% CI)
Pembro + CT	12.6	0.72 (0.60-0.88; *P* = .0006)
CT	9.8	



Patients at Risk, n													
Pembro + CT	274	258	221	175	135	111	89	60	27	14	6	2	0
CT	274	248	201	145	109	75	57	34	23	13	4	1	0

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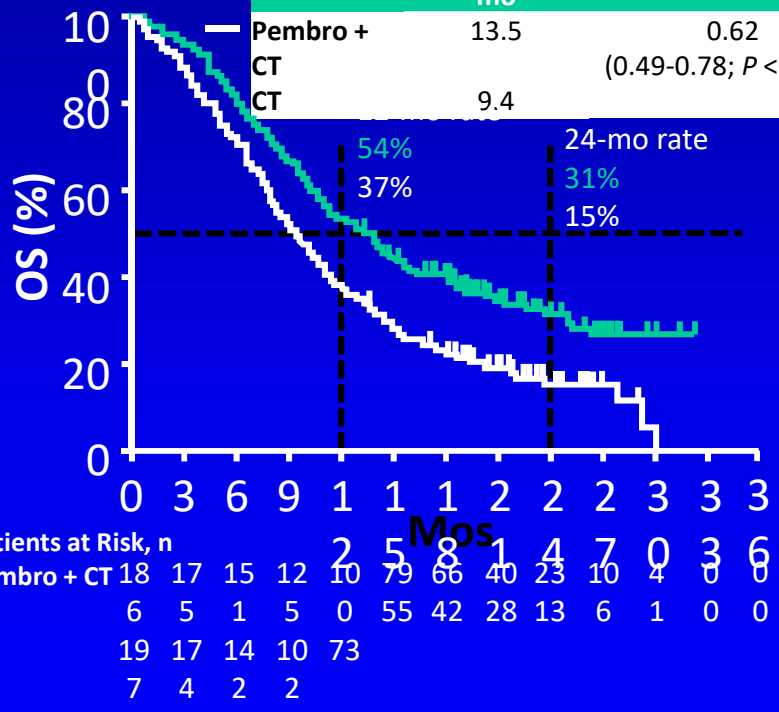
KEYNOTE-590: OS in PD-L1 CPS ≥ 10 and in All Patients

OS in Patients With PD-L1 CPS ≥ 10

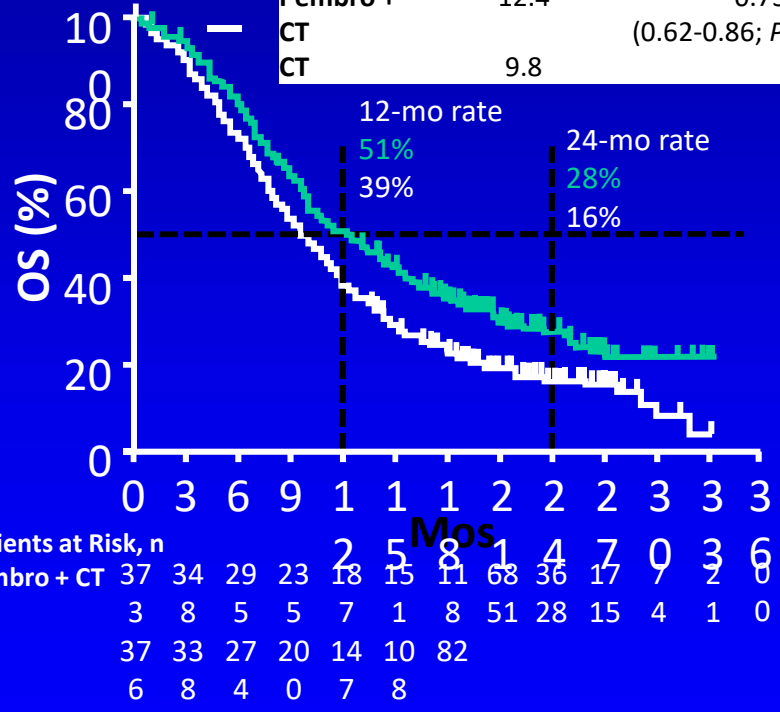
	Median OS, mo	HR (95% CI)
Pembro + CT	13.5	0.62 (0.49-0.78; *P* < .0001)
CT	9.4	



Patients at Risk, n													
Pembro + CT	18	17	15	12	10	79	66	40	23	10	4	0	0
CT	6	5	1	5	0	55	42	28	13	6	1	0	0
	19	17	14	10	73								
	7	4	2	2									

OS in Total Study Population

	Median OS, mo	HR (95% CI)
Pembro + CT	12.4	0.73 (0.62-0.86; *P* < .0001)
CT	9.8	



Patients at Risk, n													
Pembro + CT	37	34	29	23	18	15	11	68	36	17	7	2	0
CT	3	8	5	5	7	1	8	51	28	15	4	1	0
	37	33	27	20	14	10	82						
	6	8	4	0	7	8							

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KEYNOTE-590: Other Efficacy Outcomes

Outcome	All Patients		Patients With PD-L1 CPS ≥ 10		ESCC	
	Pembro + CT (n = 373)	CT (n = 376)	Pembro + CT (n = 186)	CT (n = 197)	Pembro + CT (n = 274)	CT (n = 274)
mPFS, mos	6.3	5.8	7.5	5.5	6.3	5.8
▪ HR (95% CI)	0.65 (0.55-0.76; *P* < .0001)		0.51 (0.41-0.65; *P* < .0001)		0.65 (0.54-0.78; *P* < .0001)	
ORR, %	45.0	29.3	--	--	--	--
▪ Difference	15.8 (*P* < .0001)		--		--	
mDoR, mos	8.3	6.0	--	--	--	--

- OS and PFS favored pembrolizumab + CT vs CT in most patient subgroups

Kato. ESMO 2020. Abstr LBA8_PR

KEYNOTE-590: Safety

AE, %	Pembrolizumab + CT (n = 370)	CT (n = 370)
Any	100	99.5
Treatment-related AE	98.4	97.3
▪ Grade ≥ 3	71.9	67.6
▪ Led to discontinuation	19.5	11.6
▪ Led to death	2.4	1.4
Immune-mediated AEs and infusion reactions	25.7	11.6
▪ Grade ≥ 3	7.0	2.2

- Common treatment-related AEs included nausea, decreased appetite, anemia, fatigue, vomiting, diarrhea, neutropenia, decreased neutrophil count

Kato. ESMO 2020. Abstr LBA8_PR

KEYNOTE-590: Conclusions

- Randomized phase III trial, First-line pembrolizumab + CT significantly improved OS, PFS, and ORR vs CT alone in patients with advanced esophageal cancer
  - Significantly prolonged OS in all patients and subgroups, including PD-L1 CPS ≥ 10, ESCC, and ESCC with PD-L1 CPS ≥ 10 (all $P \leq .0006$)
  - Significantly prolonged PFS in all patients and subgroups, including PD-L1 CPS ≥ 10, ESCC (all $P < .0001$)
  - Significantly higher ORR in all patients (45.0% vs 29.3%; $P < .0001$)
- No new safety signals observed
- Investigators concluded that First-line pembrolizumab + CT represents new standard of care for patients with locally advanced/metastatic esophageal cancer

Kato. ESMO 2020. Abstr LBA8_PR

HER2

Destiny-Gastric01

- FDA granted priority review designation and breakthrough designation to ADC Trastuzumab deruxtecan for use in HER2 + GEJ and gastric adenocarcinoma

- Open label Phase 2 that showed higher objective response rate (ORR) compared with chemotherapy

Original Article

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Gastric Cancer

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DESTINY-Gastric01:
Trastuzumab Deruxtecan for HER2+ Advanced Gastric or GEJ Adenocarcinoma

- Multicenter, open-label, randomized phase II study

Stratified by region (Japan vs Korea), ECOG PS (0 vs 1), HER2 status (IHC 3+ vs IHC 2+/ISH+)

Adult patients with HER2+* locally advanced or metastatic gastric or GEJ cancer that progressed on ≥ 2 prior regimens† (N = 188)

Randomized 2:1

T-DXd 6.4 mg/kg, 3-week cycles (n = 126)

Physician's choice:
Irinotecan 150 mg/m^2 every 2 weeks or
Paclitaxel 80 mg/m^2 Days 1, 8, 15 every 4 weeks
(n = 62)

Until PD, unacceptable AEs, or pt withdrawal

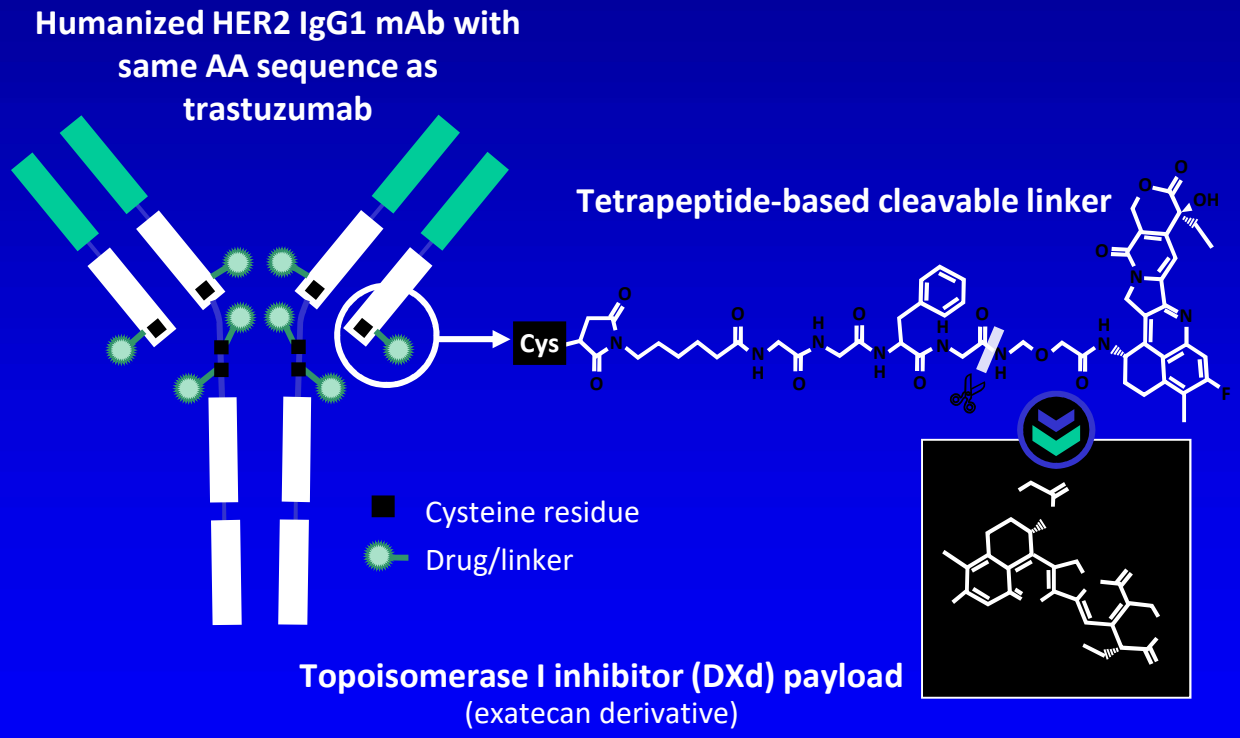
*HER2+ based on IHC 3+ or IHC 2+/ISH+ according to ASCO/CAP guidelines.
†Prior regimens included fluoropyrimidine, a platinum agent, and trastuzumab or approved biosimilar.

- Primary endpoint: ORR by ICR (RECIST v1.1)
- Secondary endpoints: OS (key), DoR, PFS, DCR, confirmed ORR, safety

Shitara. ASCO 2020. Abstr 4513. Shitara. NEJM. 2020;[Epub].

Slide credit: clinicaloptions.com

HER2-Targeted ADC: Trastuzumab Deruxtecan (DS-8201)

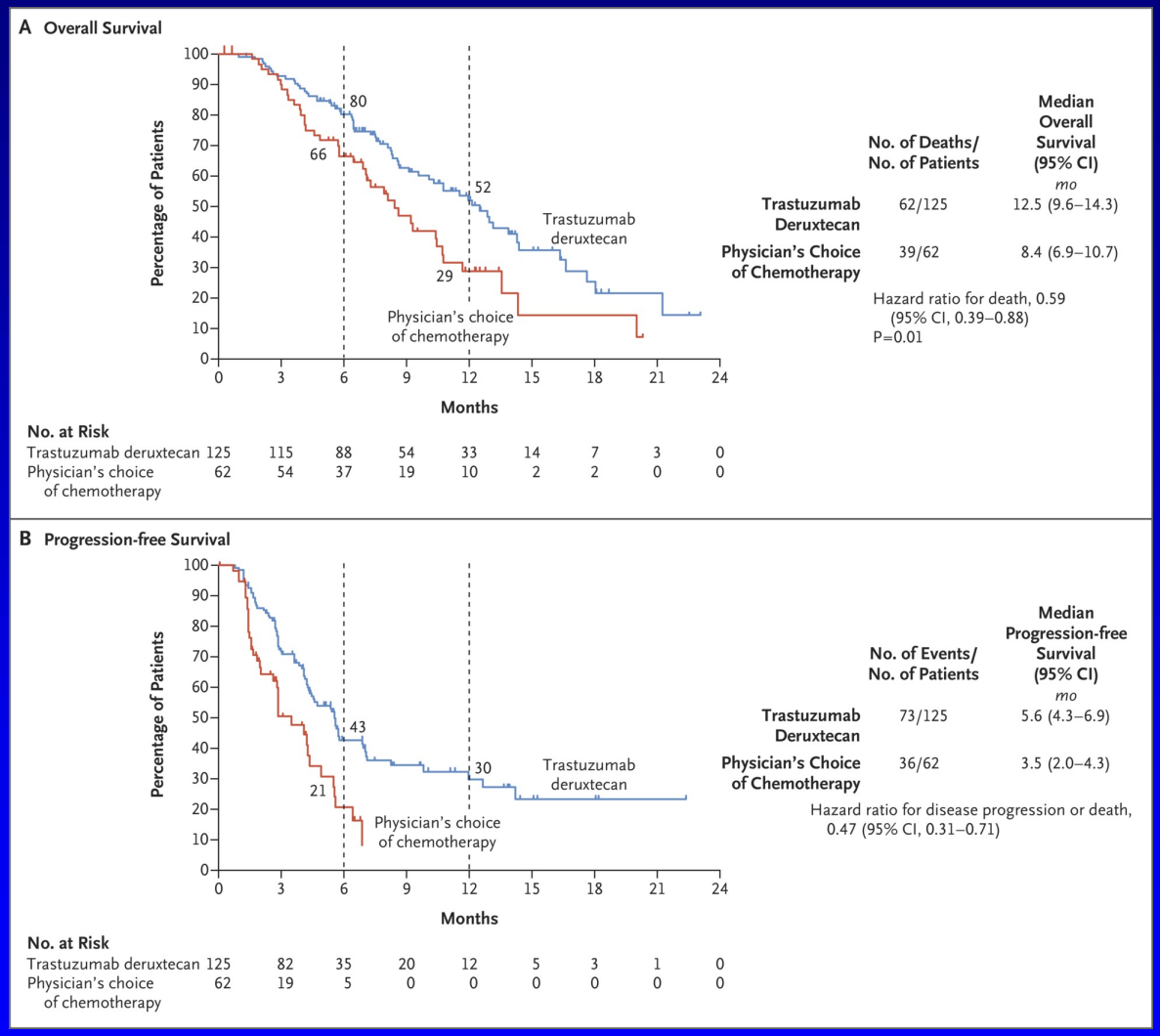


- High drug:antibody ratio: ~ 8
- Stable linker-payload
- Tumor-selectable cleavable linker
- High potency, membrane-permeable payload with short systemic half-life
- Bystander killing effect

Nakada. Chem Pharm Bull (Tokyo). 2019;67:173. Trail. Pharmacol Ther. 2018;181:126. Ogitani. Cancer Sci. 2016;107:1039.

Slide credit: clinicaloptions.com

Overall Survival and Progression-free Survival.



Shitara K et al. N Engl J Med 2020;382:2419-2430

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Summary of Efficacy.

Table 2. Summary of Efficacy.*

Variable	Trastuzumab Deruxtecan (N=119)	Physician's Choice of Chemotherapy (N=56)
Objective response†		
No. of patients	61	8
Percent of patients (95% CI)	51 (42–61)	14 (6–26)
Best response — no. (%)		
Complete response	11 (9)	0
Partial response	50 (42)	8 (14)
Stable disease	42 (35)	27 (48)
Progressive disease	14 (12)	17 (30)
Could not be evaluated	2 (2)	4 (7)
Confirmed objective response‡		
No. of patients	51	7
Percent of patients (95% CI)	43 (34–52)	12 (5–24)
Confirmed best response — no. (%)		
Complete response	10 (8)	0
Partial response	41 (34)	7 (12)
Stable disease	51 (43)	28 (50)
Progressive disease	14 (12)	17 (30)
Could not be evaluated	3 (3)	4 (7)
Confirmed disease control§		
No. of patients	102	35
Percent of patients (95% CI)	86 (78–91)	62 (49–75)

* The analyses included all the patients who underwent randomization, received at least one dose of trial drug, and had measurable tumors as assessed on independent central review at baseline. In the physician's choice group, 51 patients received irinotecan and 5 received paclitaxel. Percentages may not total 100 because of rounding. CI denotes confidence interval.

† An objective response was defined as a complete or partial response. The comparison was evaluated by Cochran–Mantel–Haenszel tests stratified according to region ($P<0.001$). Fisher's exact test between treatment groups was performed as a sensitivity analysis (unstratified $P<0.001$).

‡ A confirmed objective response was defined as a complete or partial response that was confirmed on a follow-up scan performed at least 4 weeks after the initial complete or partial response was noted.

§ Confirmed disease control was defined as a confirmed objective response or stable disease.

Shitara K et al. N Engl J Med 2020;382:2419-2430

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DESTINY-Gastric01: Safety

AE*, %	T-DXd (n = 125)			PC (n = 62)		
	Any	Gr 3	Gr 4	Any	Gr 3	Gr 4
Nausea	63	5	0	47	2	0
Decreased ANC	63	38	13	35	16	8
Decreased appetite	60	17	0	45	13	0
Anemia	58	38	0	31	21	2
Decreased platelet count	39	10	2	6	2	2
Decreased WBC	38	21	0	35	8	3
Malaise	34	1	0	16	0	0
Diarrhea	32	2	0	32	2	0
Vomiting	26	0	0	8	0	0
Constipation	24	0	0	23	0	0
Pyrexia	24	0	0	16	0	0
Alopecia	22	0	0	15	0	0
Fatigue	22	7	0	24	3	0
Decreased lymphocyte count	22	6	5	3	0	2

TEAE, %	T-DXd (n = 125)	PC (n = 62)
Associated with discontinuation	15.2	6.5
Associated with dose reduction	32.0	33.9
Associated with dose interruption	62.4	37.1
ILD/pneumonitis	9.6	0

*Occurring in ≥ 20% of pts receiving T-DXd. †ILD cases: grade 1 (n = 3), grade 2 (n = 6), grade 3 (n = 2), grade 4 (n = 1); median time to first onset: 84.5 days (range: 36-638).

Slide credit: clinicaloptions.com

Summary

- Currently no role for anti-HER2 therapy in locoregional disease
- Nivolumab prolonged survival following chemoradiation and surgery in locoregional GE disease
- First line combination chemo and immunotherapy in GE cancers shows overall survival benefit
- Degree of benefit might be highest in CPS high patients