OVERVIEW OF GASTRIC & ESOPHAGEAL CANCERS

Winter Cancer Symposium
March 2022

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Real Life stories !!

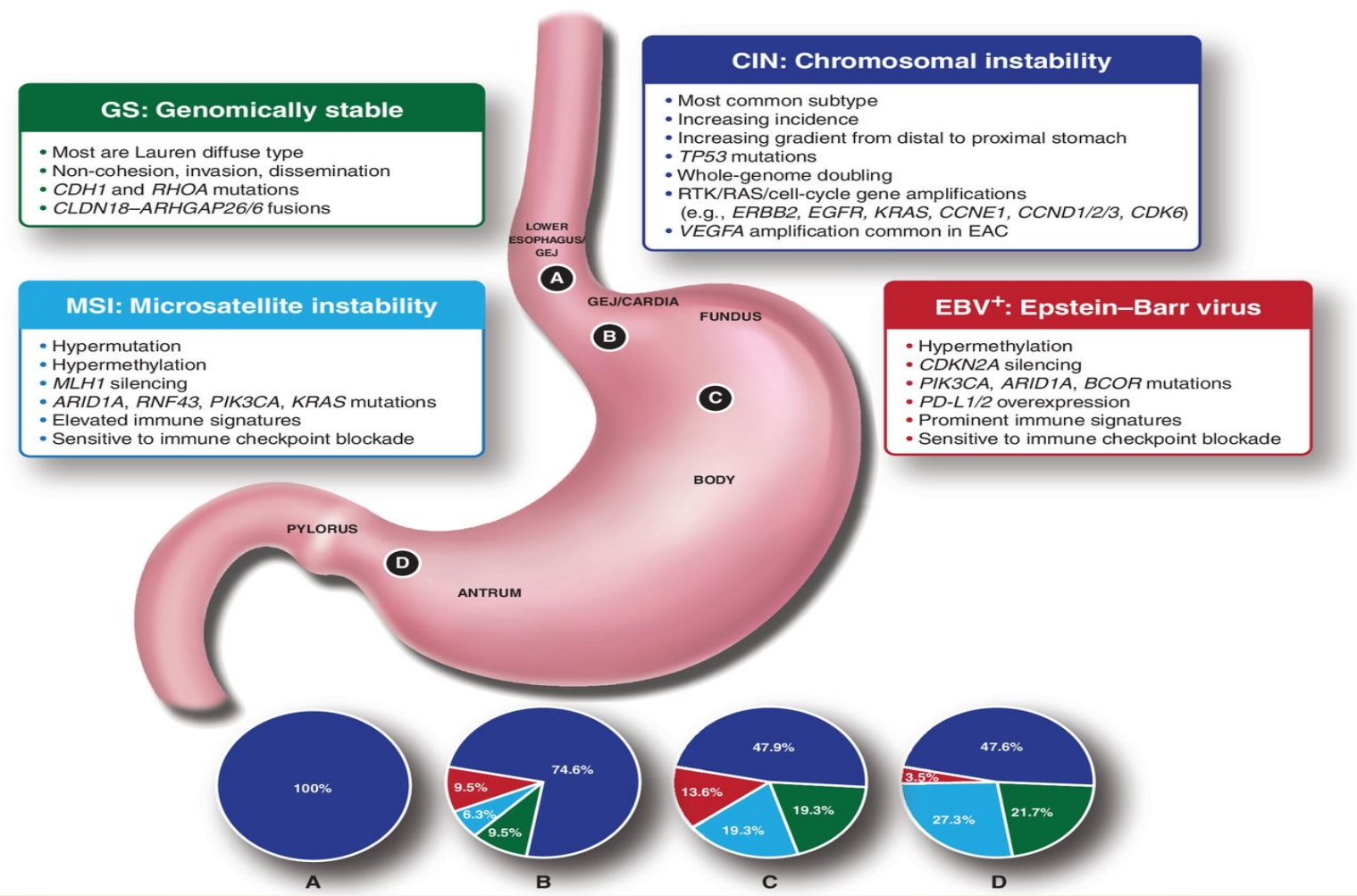
- **Case 1: John**
- **62 y/o AA male with HTN, HLD, previously smoker with dysphagia, 10 lb weight loss**
- **EGD/EUS : T4N1 Esophageal Ca: SCC**
- **Staging Scans: No mets**
- **ECOG : 0-1**

- **Case 2 : Beth**
- **58 y/o WF with Mild obesity, HTN, GERD**
- **Presented dysphagia, wght Loss 10-12lbs**
- **EGD/EUS: T3N2 Esoph Ca, Adeno. Heur2 (-), PDL1 CPS 2**
- **Staging Scans/PET scan: No distant Mets**
- **Increase uptake GE Junction**

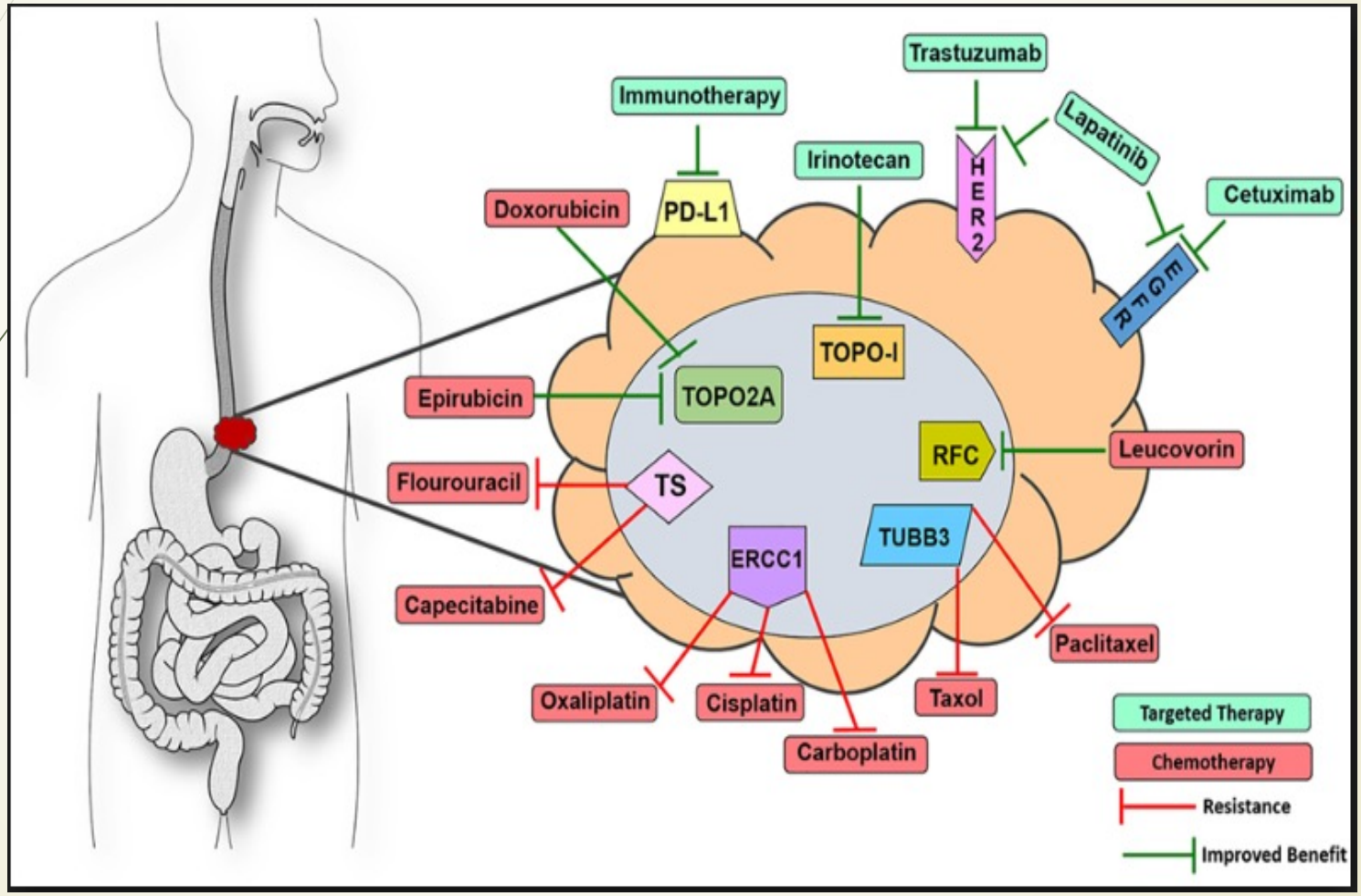
OVERVIEW OF GASTRIC & ESOPHAGEAL CANCERS

- Review of the Genomics of Esophageal and Gastric cancer
- Mutidisciplanary approach Localized & Locally advanced Esoph and Gastric cancer
- Case Presentation
- Management of advanced Esoph. And Gastric cancers beyond cytotoxic agents

Genomic Profiling for Esoph. & Gastric Cancers



Pharmacogenomic for systemic Therapy



National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Esophageal and Esophagogastric Junction Cancers

NCCN Guidelines Index
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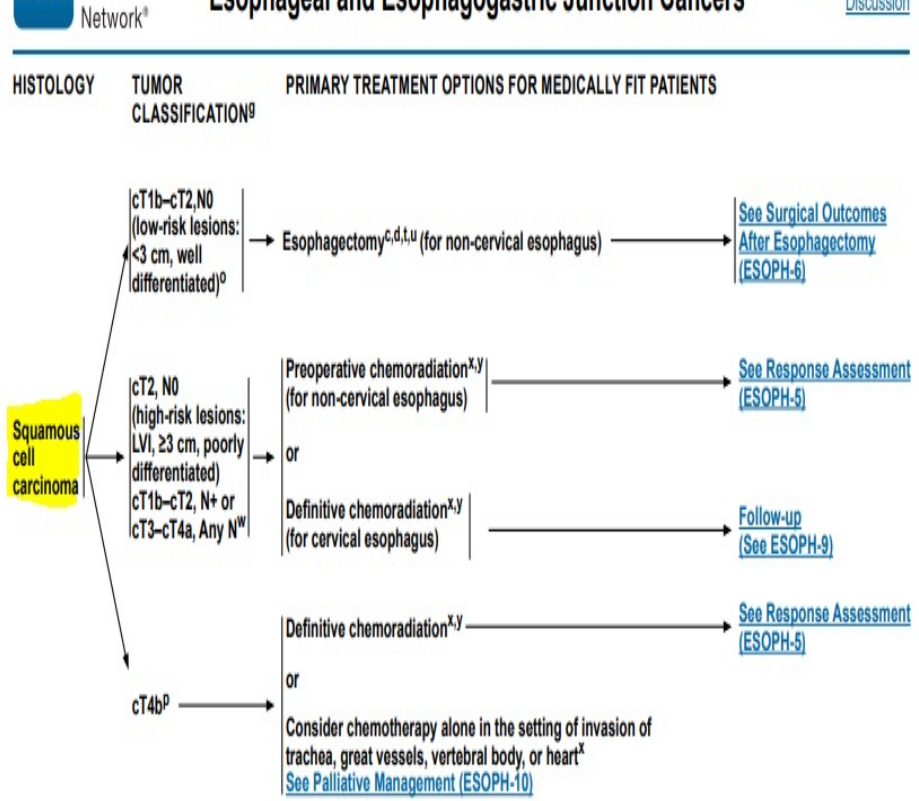

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Esophageal and Esophagogastric Junction Cancers

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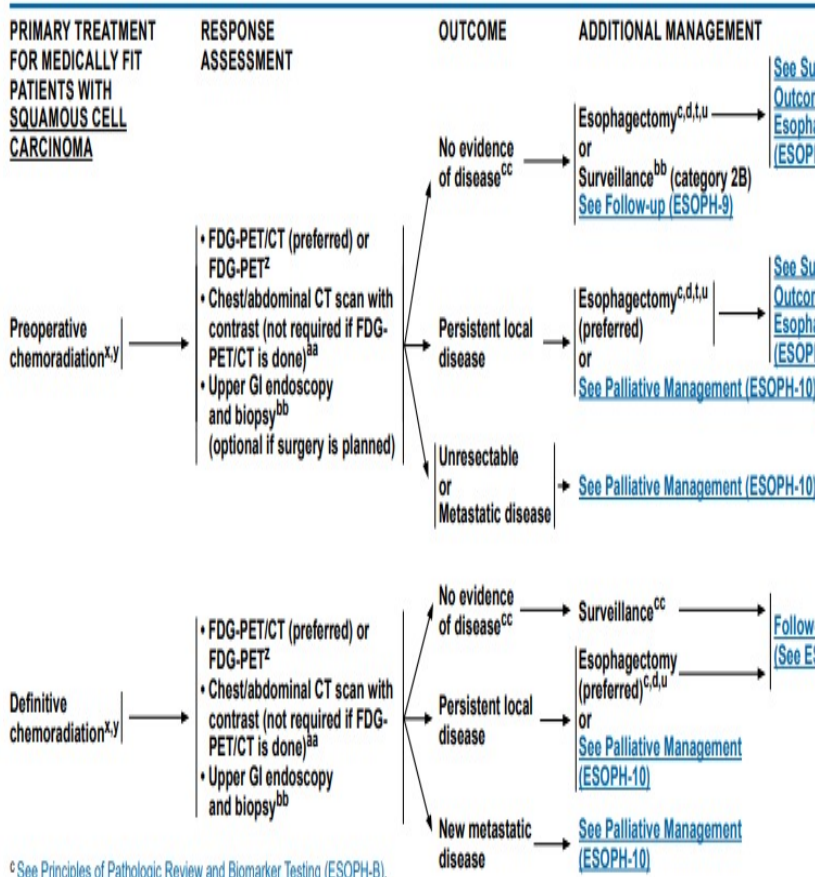

[c] See Principles of Pathologic Review and Biomarker Testing (ESOPH-B).
[d] See Principles of Surgery (ESOPH-C).
[t] Transhiatal or transthoracic, or minimally invasive; gastric reconstruction preferred.

Options to Navigate for Esophag. Adeno & GE cancer

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Esophageal and Esophagogastric Junction Cancers

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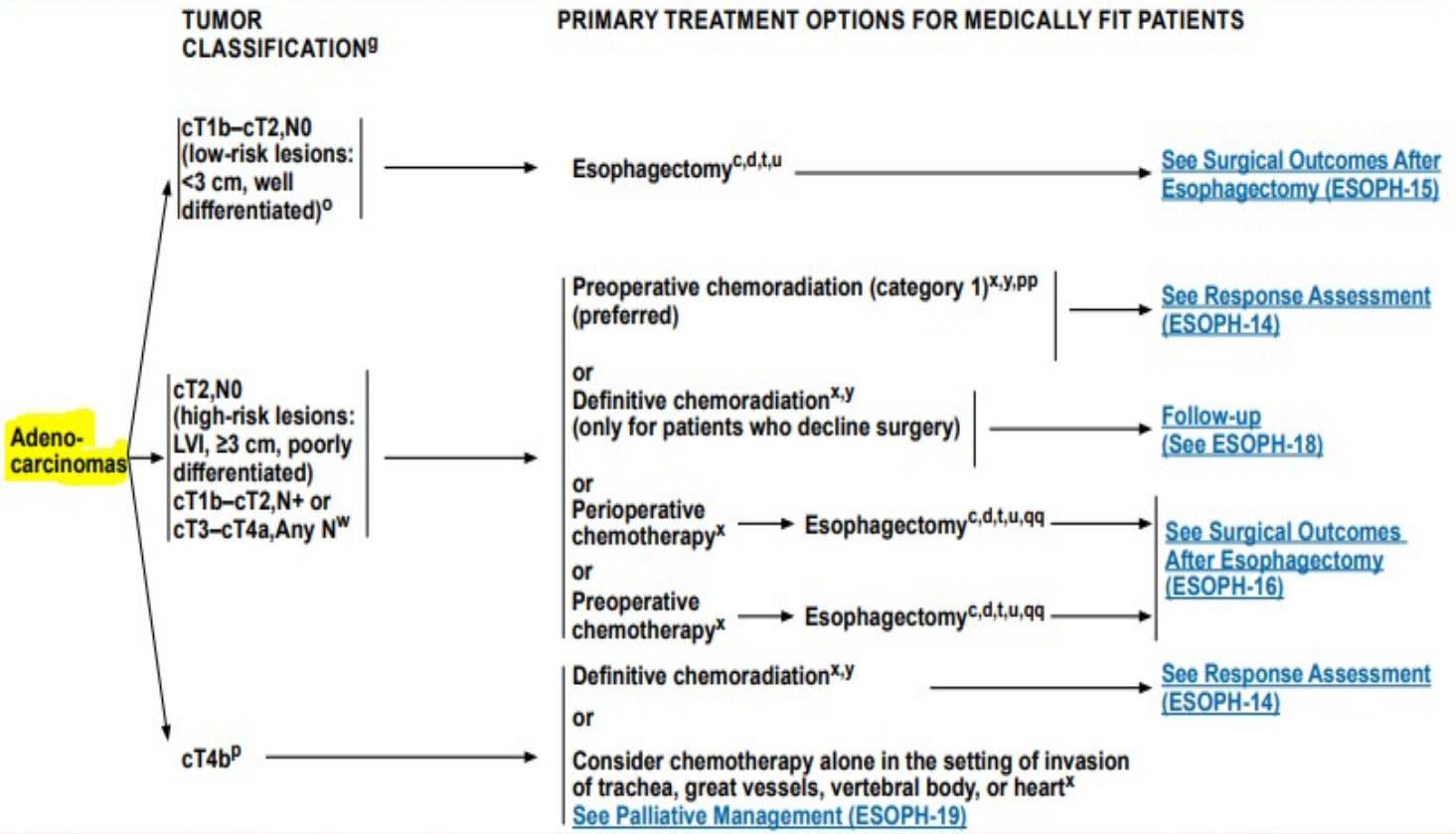
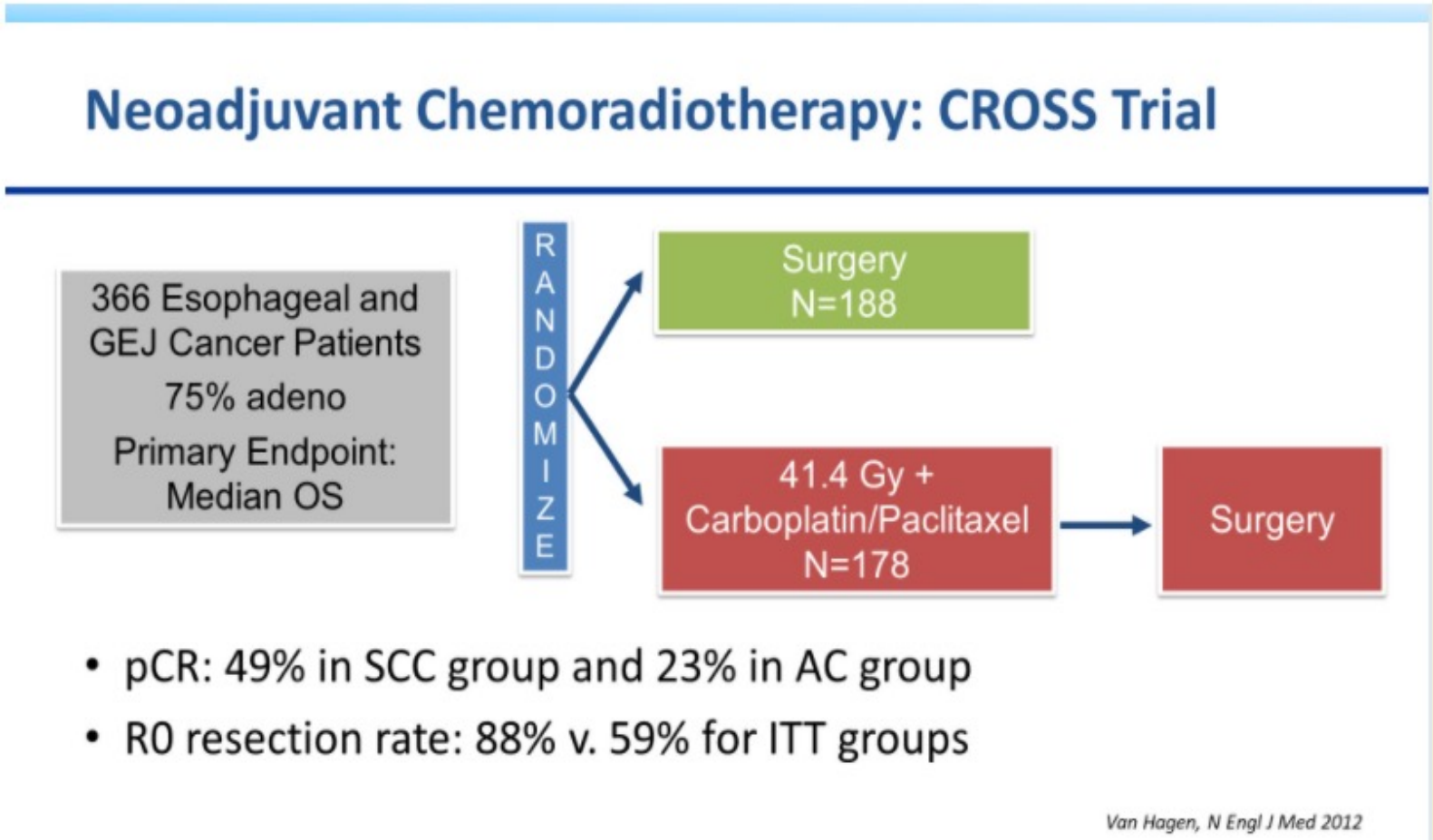
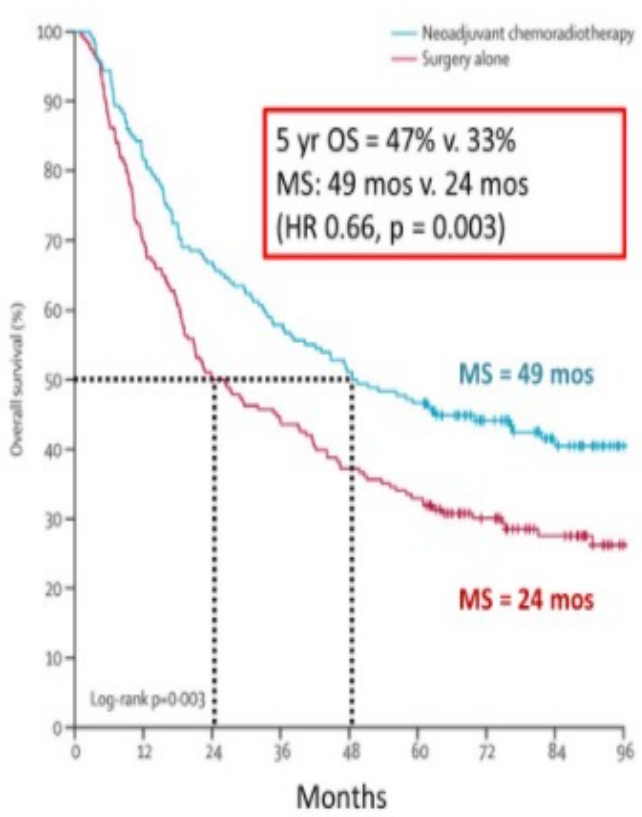
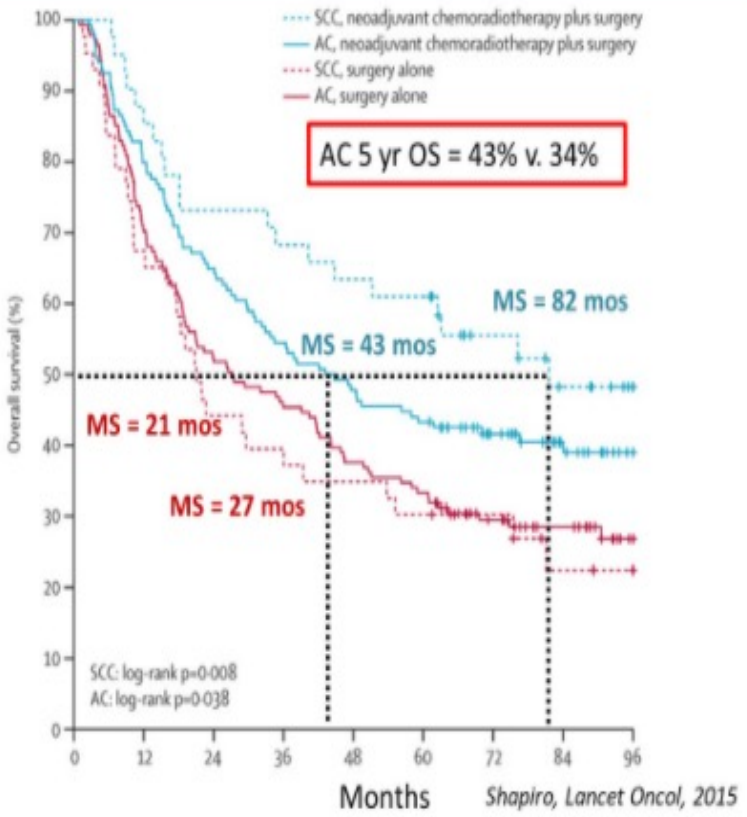


Pivotal Trial Chemotherapy-Radiation for Esophag Cancer : CROSS Trial



Neoadjuvant Chemoradiotherapy: CROSS Trial





Shapiro, Lancet Oncol, 2015

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Ten-Year Outcome of Neoadjuvant Chemoradiotherapy Plus Surgery for Esophageal Cancer: The Randomized Controlled CROSS Trial

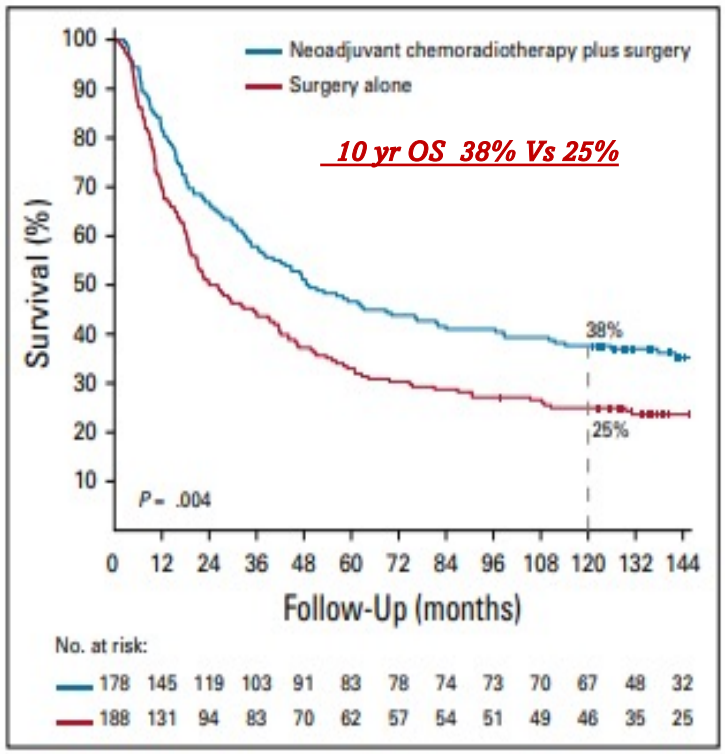


FIG 2. Kaplan-Meier estimates of overall survival.

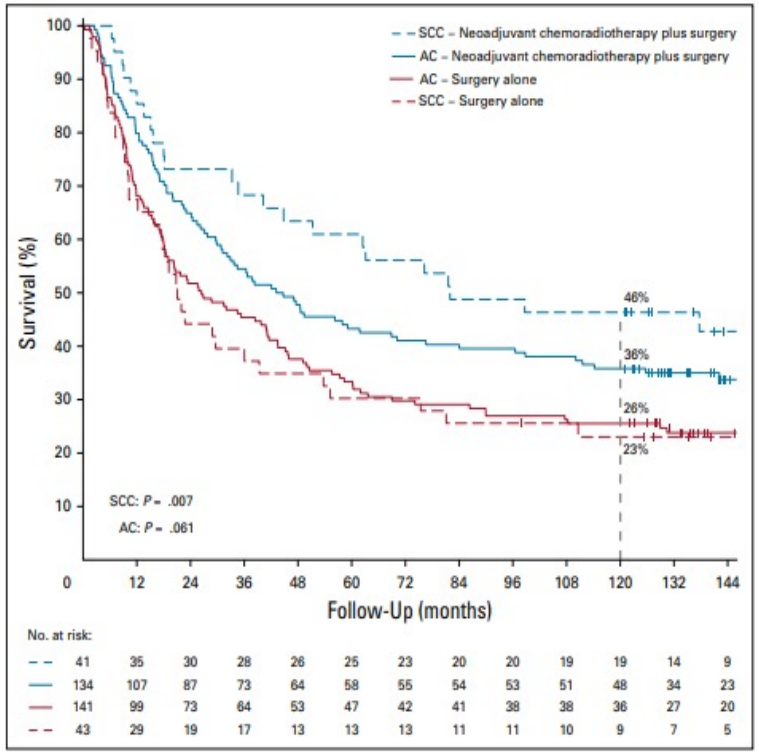
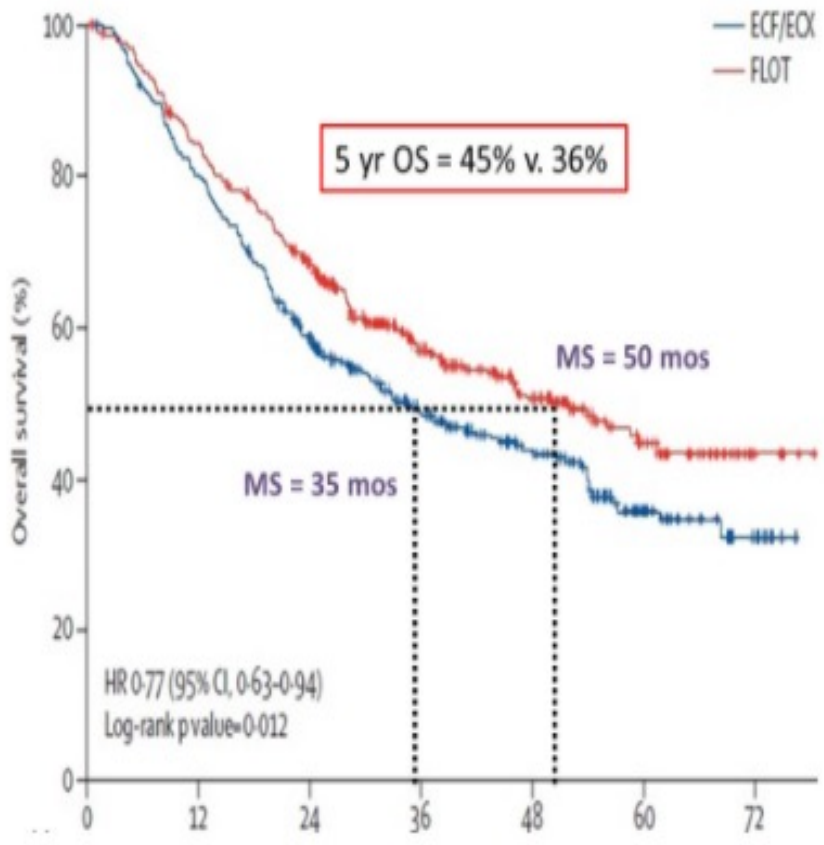


FIG 3. Kaplan-Meier estimates of overall survival stratified by tumor histology. AC, adenocarcinoma; SCC, squamous cell carcinoma.

Perioperative Chemotherpay FLOT4

(The Lancet 2019)

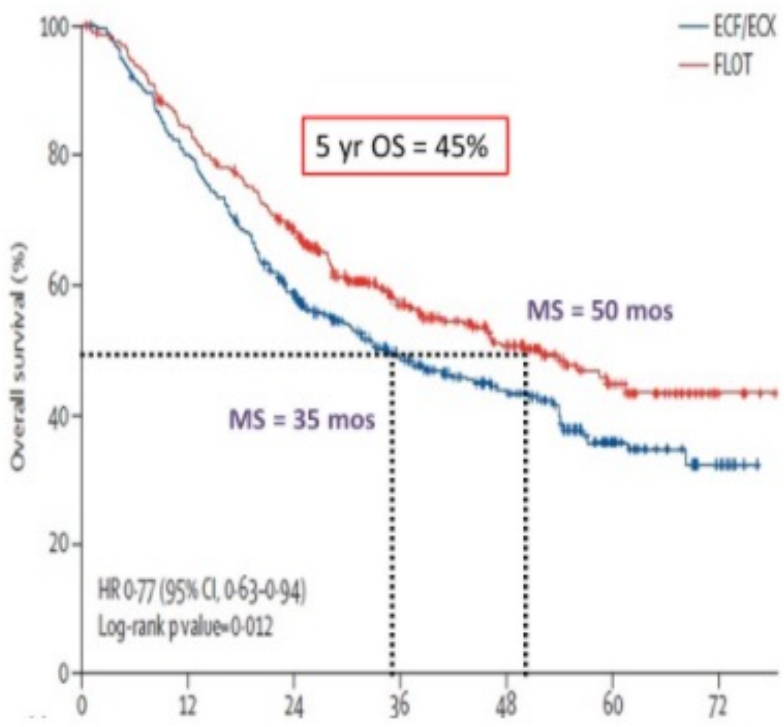


- Modern trial
- 716 pts with GEJ and gastric cancers randomized
- Perioperative FLOT4 v. ECF/ECX
- R0 resection: 85% v. 78%

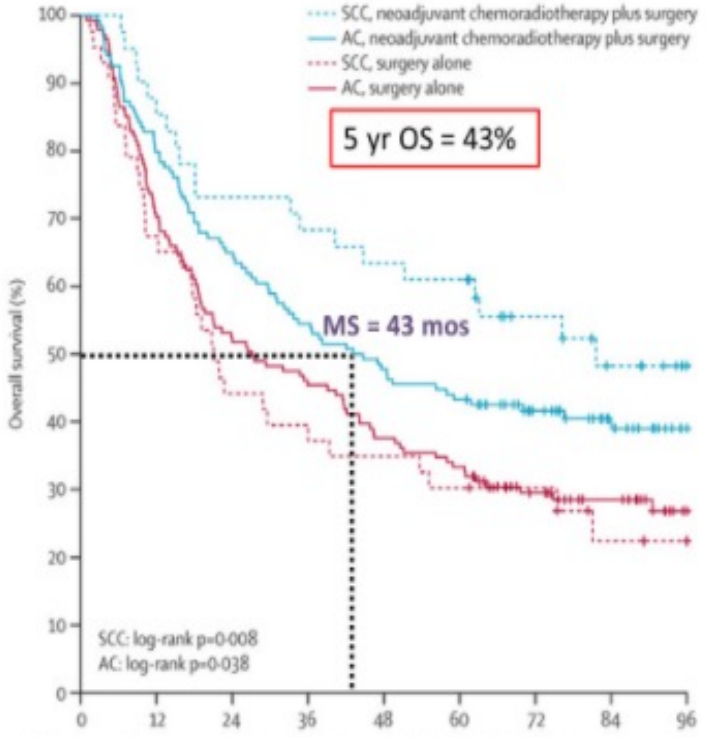
Al-Batran S, Lancet, 2019

Preiop ChemoRx Trial Vs Chemo-RT

FLOT



CROSS



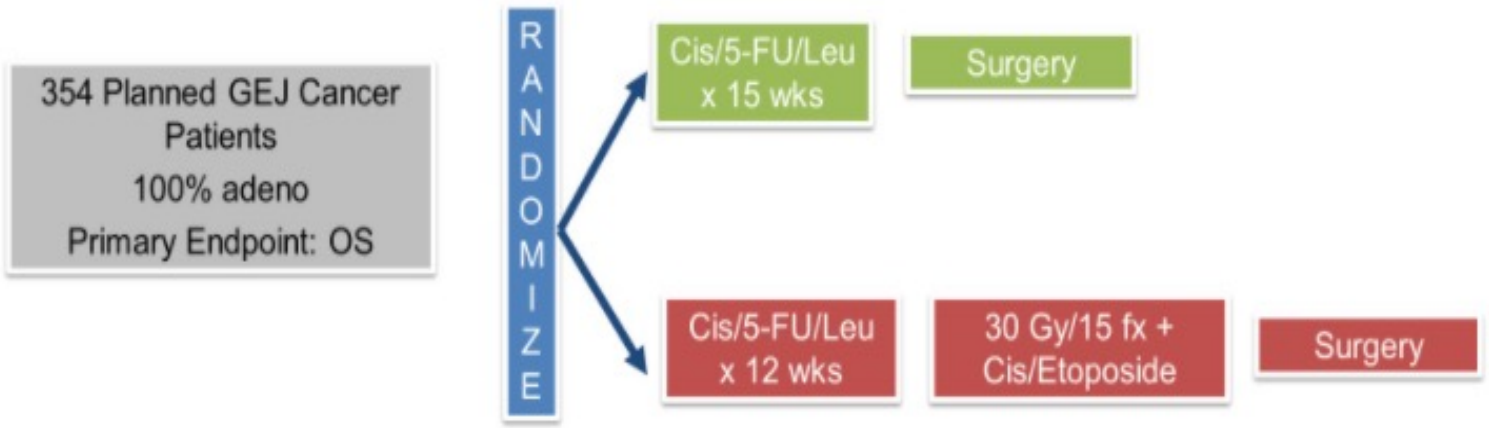
Al-Batran S, Lancet, 2019; Van Hagen NEJM, 2012; Shapiro, Lancet Oncol, 2015

Preiop ChemoRx Trial Vs Chemo-RT

Location	CROSSS Trial	FLOT4 Trial
Esophagus	74%	0%
GE Junction	22%	56%
Gastric	0%	44%
Histology		
SCC	25%	0%
AdenoCa	75%	all
5 Yr OS	43%	45%

POET TRIAL: Neoadj. ChemoRx Vs ChemoRadiation

- Locally advanced GE junction cancers



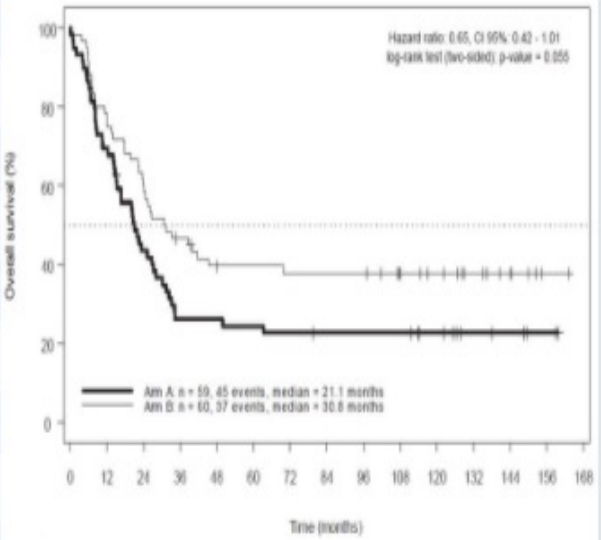
Stahl, M. et al. J Clin Oncol; 2009

POET TRIAL: Neoadj. ChemoRx Vs ChemoRadiation

- Closed early due to poor accrual, only 126 of 354 patients

	Chemo	ChemoRT	p value
pCR rate	1.9%*	14.3%*	.03
N0 rate	37.7%	64.4%	<.05
R1 resection	15.4%	4.1%	<.05
3 year OS	28%	47%	.07
5 year OS	24.4%	39.5%	
Median OS	21.1 mos	30.8 mos	
OS HR		0.65	.055
PFS HR		0.64	.03
LRR	38%	21%	
Local PFS HR		0.37	.01

*Improved survival in pCR patients: MS not reached, 5 yr OS = 88%



Stahl M, J Clin Oncol, 2009; Stahl M, E J Cancer, 2017

NEOAegis TRIAL
Neoadj. ChemoRx Vs Chemo-RT

Neoadjuvant trial in Adenocarcinoma of the Esophagus and EG Junction International Study

377 Esophageal and GEJ Cancer Patients
100% adeno
Primary Endpoint: OS
Non-inferiority

RANDOMIZE

EC(O)F(X) or FLOT → Surgery → EC(O)F(X) or FLOT

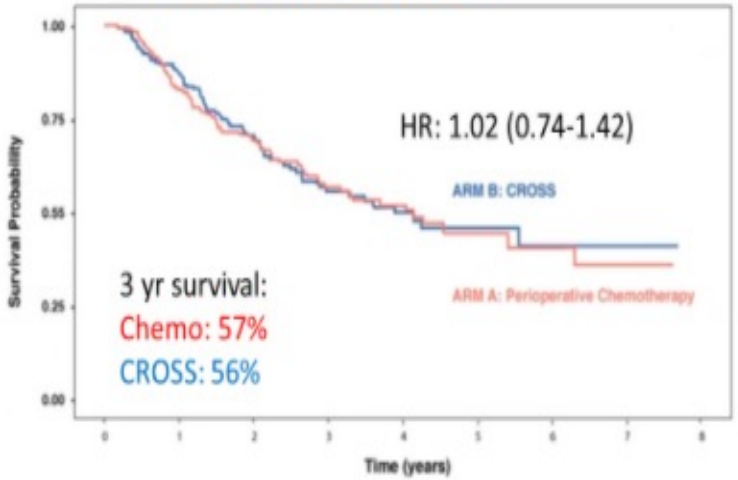
41.4 Gy + Carboplatin/Paclitaxel → Surgery

	Peri-op Chemo	CROSS	p-value
pCR	5%	16%	0.001
R0	82%	95%	<0.001
LN negative	44.5%	60%	0.004

Reynolds JV, Proc ASCO, 2021

NEOAegis TRIAL
Neoadj. ChemoRx Vs Chemo-RT

Overall Survival



Conclusion

- No evidence that peri-operative chemotherapy is unacceptably inferior to multimodal therapy, notwithstanding greater proxy markers of local tumor response in the CROSS arm
- No significant difference in severity of complications or post-op mortality, no negative effects of pre-op chemoradiation
- Data support equipoise

Reynolds JV, Proc ASCO, 2021

How Can We optimize our Treatment Options after Surgery for Esoph. & GE Junction Cancers?

- Studies of adjuvant chemotherapy have not shown any survival benefit
- Most patients unable to tolerate chemo after esophagectomy
- Need to deliver adequate systemic therapy upfront and tailor it to the tumor biology

VIRTUAL 2020 ESMO congress

Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiation therapy: first results of the CheckMate 577 study

Ronan J. Kelly,[1] Jaffer A. Ajani,[2] Jaroslaw Kuzdzal,[3] Thomas Zander,[4] Eric Van Cutsem,[5] Guillaume Piessen,[6] Guillermo Mendez,[7] Josephine Feliciano,[8] Satoru Motoyama,[9] Astrid Lièvre,[10] Hope Uronis,[11] Elena Elimova,[12] Cecile Grootscholten,[13] Karen Geboes,[14] Jenny Zhang,[15] Lili Zhu,[15] Ming Lei,[15] Kaoru Kondo,[15] James M. Cleary,[16] Markus Moehler[17]

[1]The Charles A. Sammons Cancer Center at Baylor University Medical Center, Dallas, TX, USA; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Jagiellonian University, John Paul II Hospital, Cracow, Poland; [4]University Hospital of Cologne, Cologne, Germany; [5]University Hospitals Gasthuisberg, Leuven and KULeuven, Leuven, Belgium; [6]University of Lille, Claude Huriez University Hospital, Lille, France; [7]Fundacion Favaloro, Buenos Aires, Argentina; [8]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD, USA; [9]Akita University Hospital, Akita, Japan; [10]CHU Pontchaillou, Rennes 1 University, Rennes, France; [11]Duke Cancer Institute, Durham, NC, USA; [12]Princess Margaret Cancer Centre, Toronto, ON, Canada; [13]Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [14]UZ Gent, Gent, Belgium; [15]Bristol Myers Squibb, Princeton, NJ, USA; [16]Dana Farber Cancer Institute, Boston, MA, USA; [17]Johannes-Gutenberg University Clinic, Mainz, Germany

Presentation number LBA9

CheckMate 577 study design

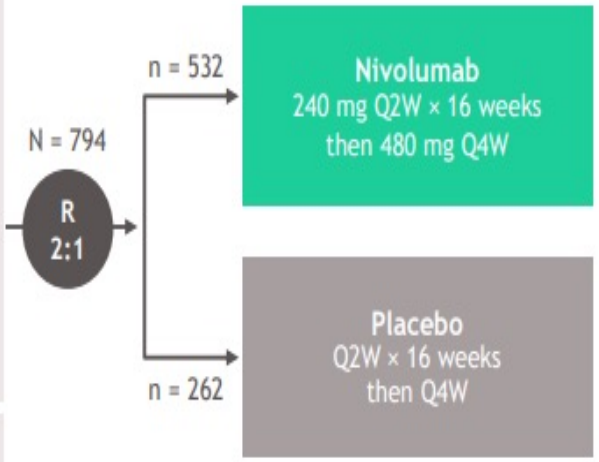
- CheckMate 577 is a global, phase 3, randomized, double-blind, placebo-controlled trial[a]

Key eligibility criteria

- Stage II/III EC/GEJC
- Adenocarcinoma or squamous cell carcinoma
- Neoadjuvant CRT + surgical resection (R0,[b] performed within 4-16 weeks prior to randomization)
- Residual pathologic disease
  - ≥ ypT1 or ≥ ypN1
- ECOG PS 0-1

Stratification factors

- Histology (squamous vs adenocarcinoma)
- Pathologic lymph node status (≥ ypN1 vs ypN0)
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[c])



Primary endpoint:

- DFS[e]

Secondary endpoints:

- OS[f]
- OS rate at 1, 2, and 3 years

Total treatment duration of up to 1 year[d]

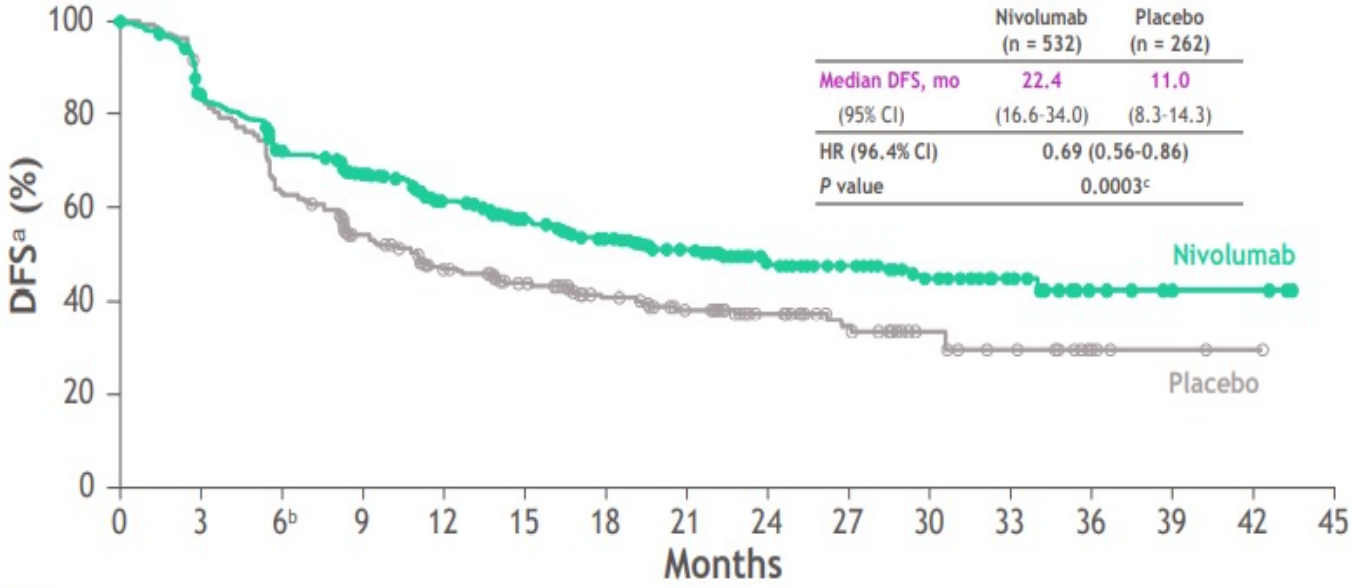
- Median follow-up was 24.4 months (range, 6.2-44.9)[g]
- Geographical regions: Europe (38%), US and Canada (32%), Asia (13%), rest of the world (16%)

[a]ClinicalTrials.gov number, NCT02743494; [b]Patients must have been surgically rendered free of disease with negative margins on resected specimens defined as no vital tumor present within 1 mm of the proximal, distal, or circumferential resection margins; [c]< 1% includes indeterminate/nonevaluable tumor cell PD-L1 expression; [d]Until disease recurrence, unacceptable toxicity, or withdrawal of consent; [e]Assessed by investigator, the study required at least 440 DFS events to achieve 91% power to detect an average HR of 0.72 at a 2-sided α of 0.05, accounting for a pre-specified interim analysis; [f]The study will continue as planned to allow for future analysis of OS; [g]Time from randomization date to clinical data cutoff (May 12, 2020).

Checkmate 577 DFS

CheckMate 577

Disease-free survival



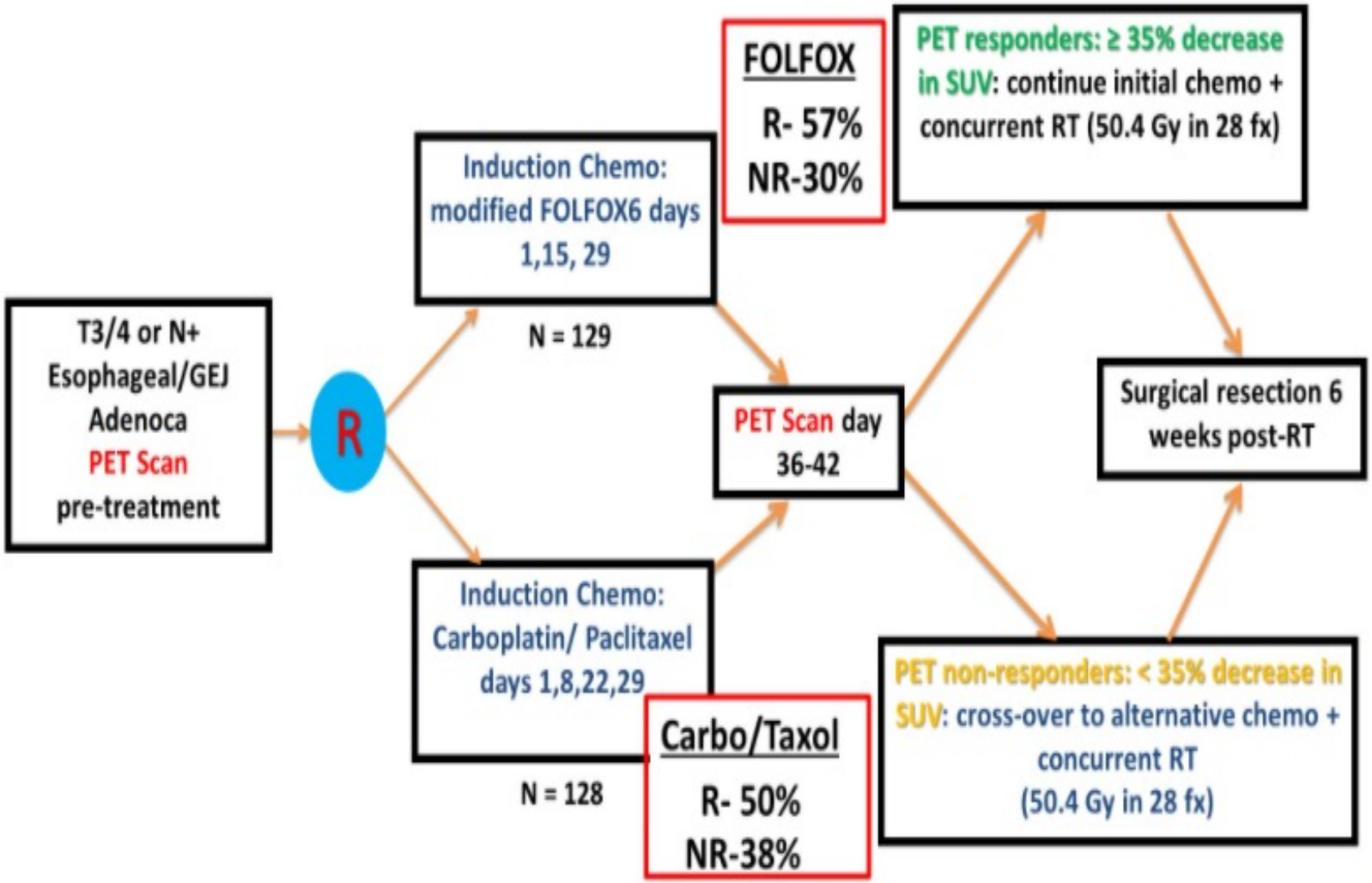
	Nivolumab (n = 532)	Placebo (n = 262)
Median DFS, mo	22.4	11.0
(95% CI)	(16.6-34.0)	(8.3-14.3)
HR (96.4% CI)	0.69 (0.56-0.86)	
P value	0.0003[c]	

No. at risk																
Nivolumab	532	430	364	306	249	212	181	147	92	68	41	22	8	4	3	0
Placebo	262	214	163	126	96	80	65	53	38	28	17	12	5	2	1	0

- Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo

[a]Per investigator assessment; [b]6-month DFS rates were 72% (95% CI, 68-76) in the nivolumab arm and 63% (95% CI, 57-69) in the placebo arm; [c]The boundary for statistical significance at the pre-specified interim analysis required the *P* value to be less than 0.036.

CALGB 80803: PET-Directed Therapy



Gastric & Gastroesophageal Cancers

CALGB 80803 (Alliance)—Survival Analysis

- PET directed combined modality treatment for esophageal cancer
  - FOLFOX → PET → FOLFOX/RT (R), Carbo/Taxol/RT (NR)
  - Carbo/Taxol → PET → Carbo/Taxol/RT (R), FOLFOX/RT (NR)
- Positive improvement in pCR rate in non-responders (1˚ endpoint)

Suggestion that switch therapy may improve outcomes in an appropriately selected population

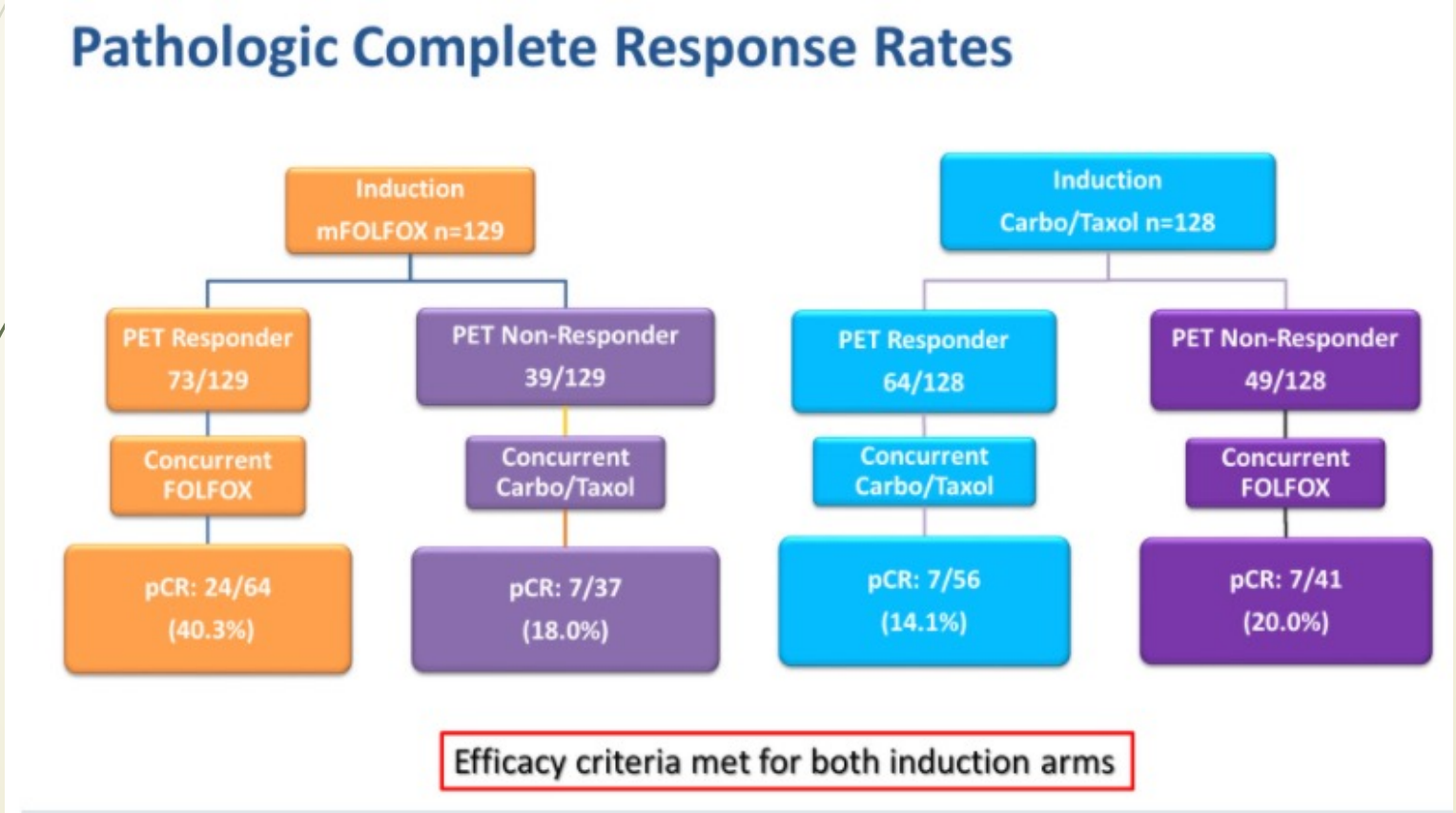
Regimen	Median Overall Survival	4-year Survival Rate
CARBO/PACLITAXEL→FOLFOX	27.6 months	41.9%
FOLFOX→ CARBO/PACLITAXEL	30.9 months	37.6%
CARBO/PACLITAXEL→ CP	39.6 months	44.7%
FOLFOX→ FOLFOX	50.3 months	52.7%

Suggestion that induction chemotherapy may contribute in an appropriately selected population

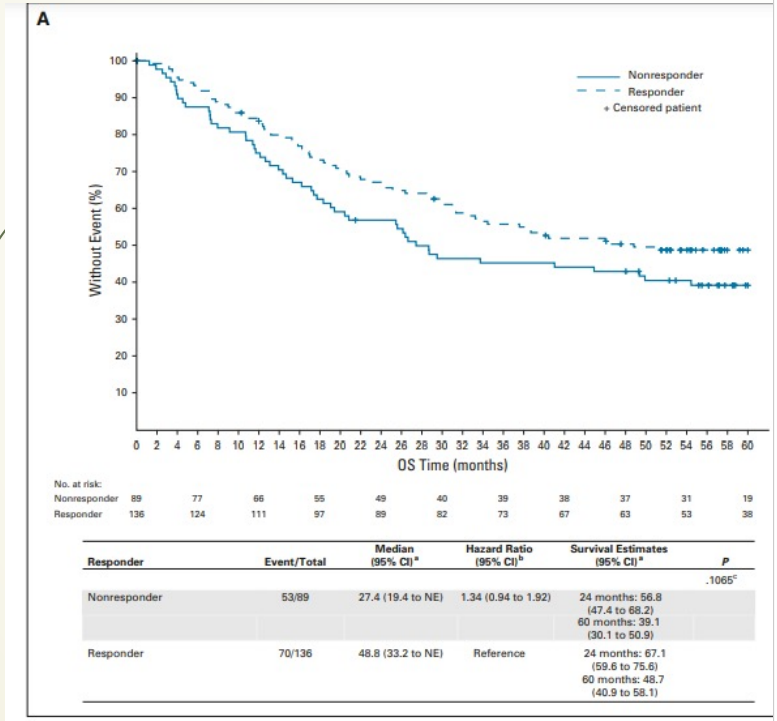
Goodman KA et al, ASCO 2018

ALLIANCE Trial

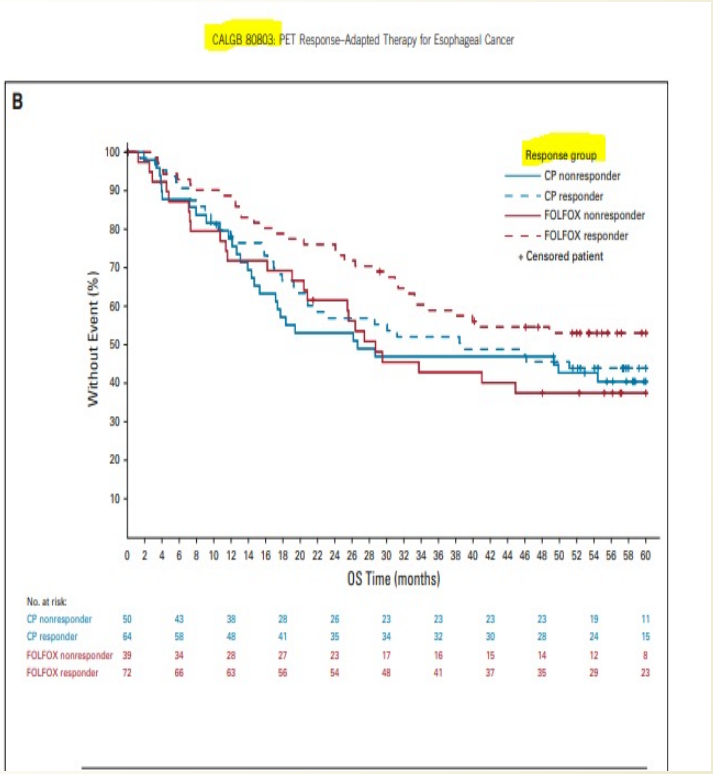
PET Directed Combined Modality



ALLIANCE Trial
PET Directed Combined Modality
(Goodman et al JCO 2021)



Responder	Event/Total	Median (95% CI)[a]	Hazard Ratio (95% CI)[b]	Survival Estimates (95% CI)[a]	P
					.1065[c]
Nonresponder	53/89	27.4 (19.4 to NE)	1.34 (0.94 to 1.92)	24 months: 56.8 (47.4 to 68.2) 60 months: 39.1 (30.1 to 50.9)	
Responder	70/136	48.8 (33.2 to NE)	Reference	24 months: 67.1 (59.6 to 75.6) 60 months: 48.7 (40.9 to 58.1)	



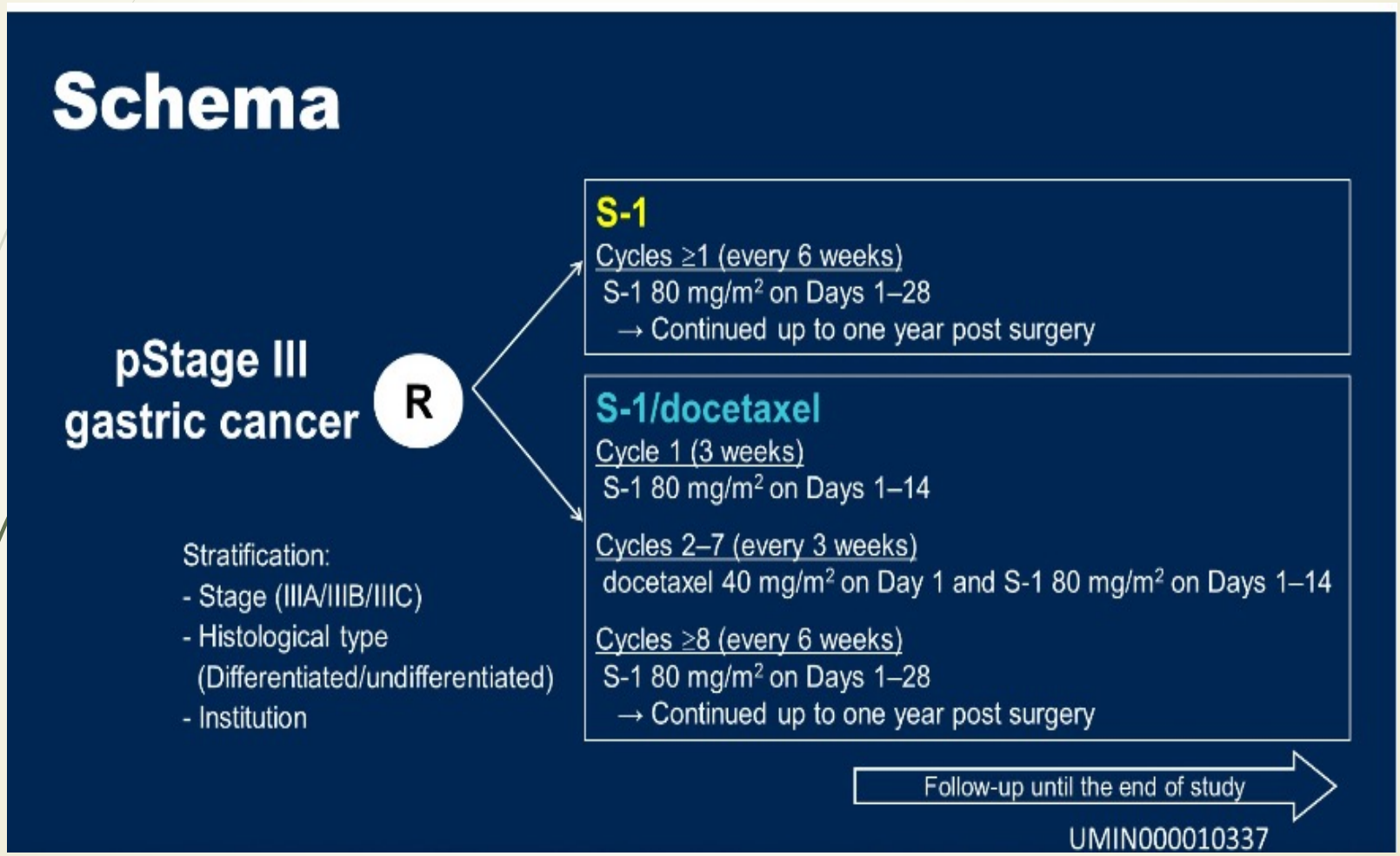
ALLIANCE Trial
PET Directed Combined Modality

	Events/ Total	Median OS (mos)	2-year OS (%)	5-year OS (%)	P-value*
CP → FF Non-Responder	29/50	26.6	53.1	40.4	0.20
CP → CP Responder	37/64	38.7	56.9	43.9	
FF → CP Non-Responder	24/39	28.7	61.5	37.5	
FF → FF Responder	33/72	NE	76.1	53.0	

GASTRIC CANCER

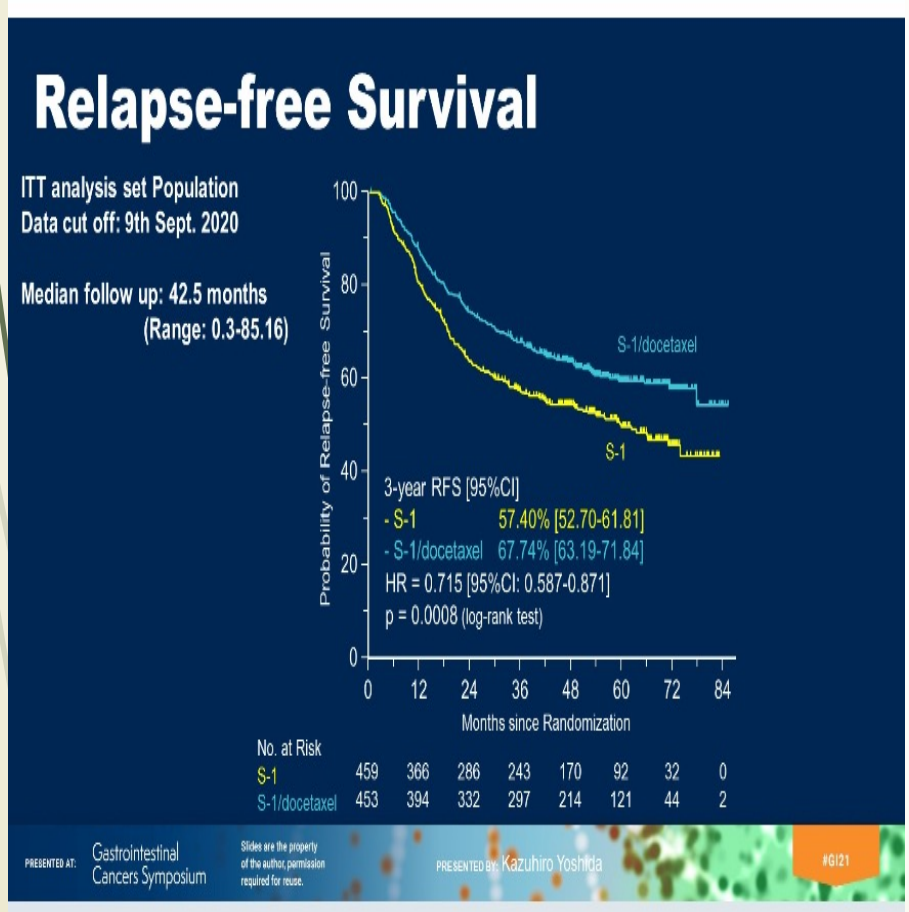
(JACCRO-GC 07 Adjuvant Therapy)

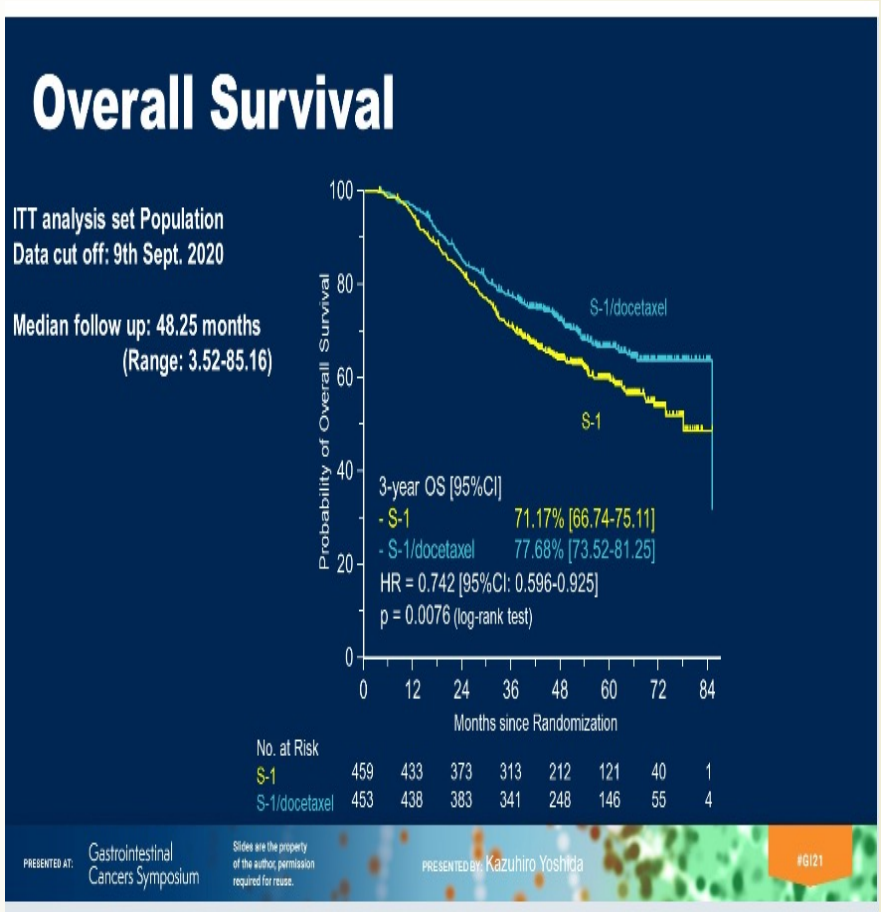
GASTRIC CANCER
(JACCRO-GC 07 Adjuvant Therapy)

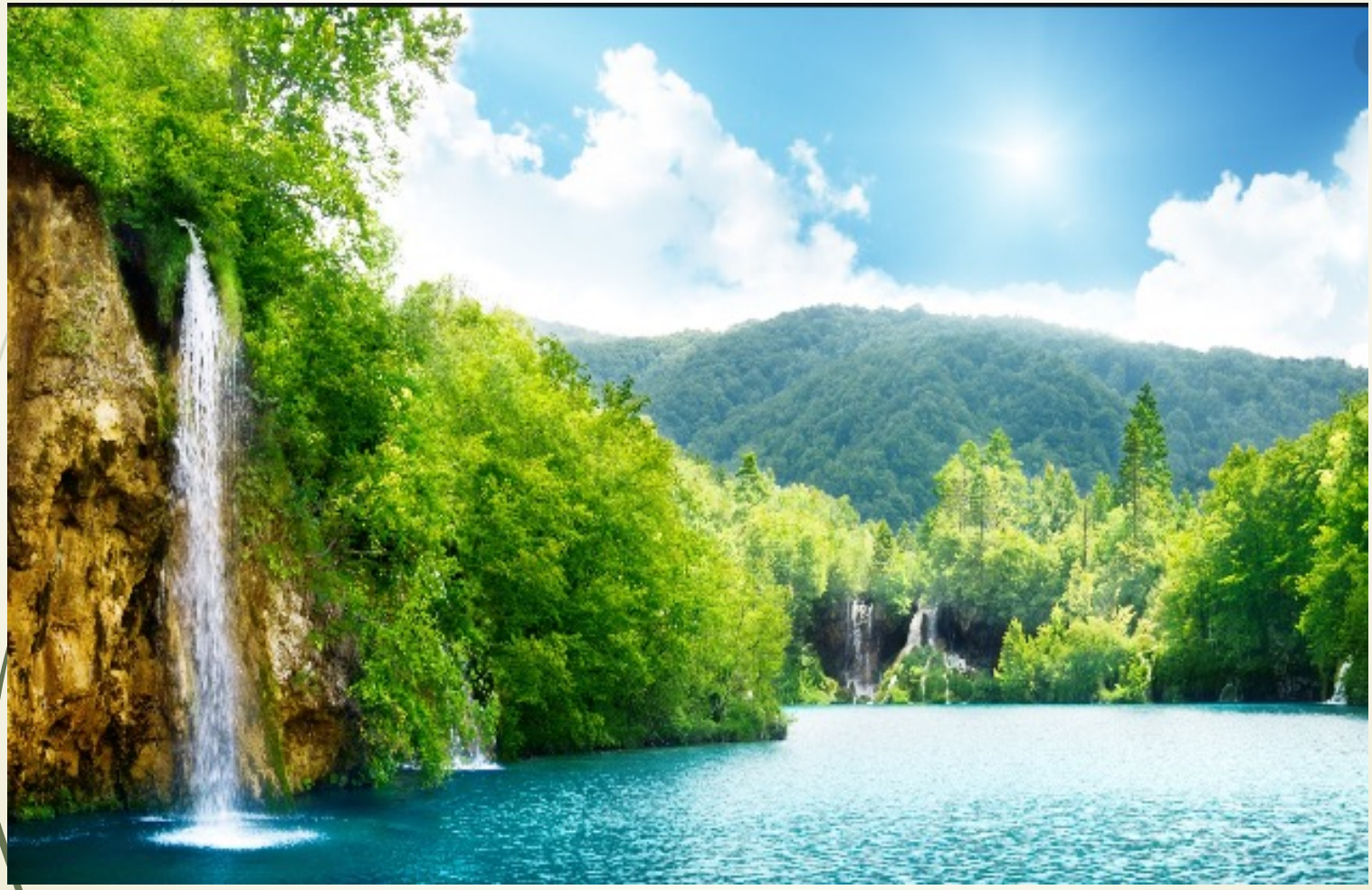


GASTRIC CANCER

JACCRO-GC 07







Real Life stories: Advanced GE/Gastric cancers

- **Case 1 : Sue**
- **46 y/o Female Presented with abdominal pain, recurrent emesis**
- **EGD: GE adenoCa.**
- **CT scan in Uruguay : No distant Mets**
- **Ex-lap → carcinomatosis**
- **In the US: PET scan periaortic LND, Omental Involvmnt**
- **Heur 2 + by FISH**
- **PDL1 (-) CPS 0**

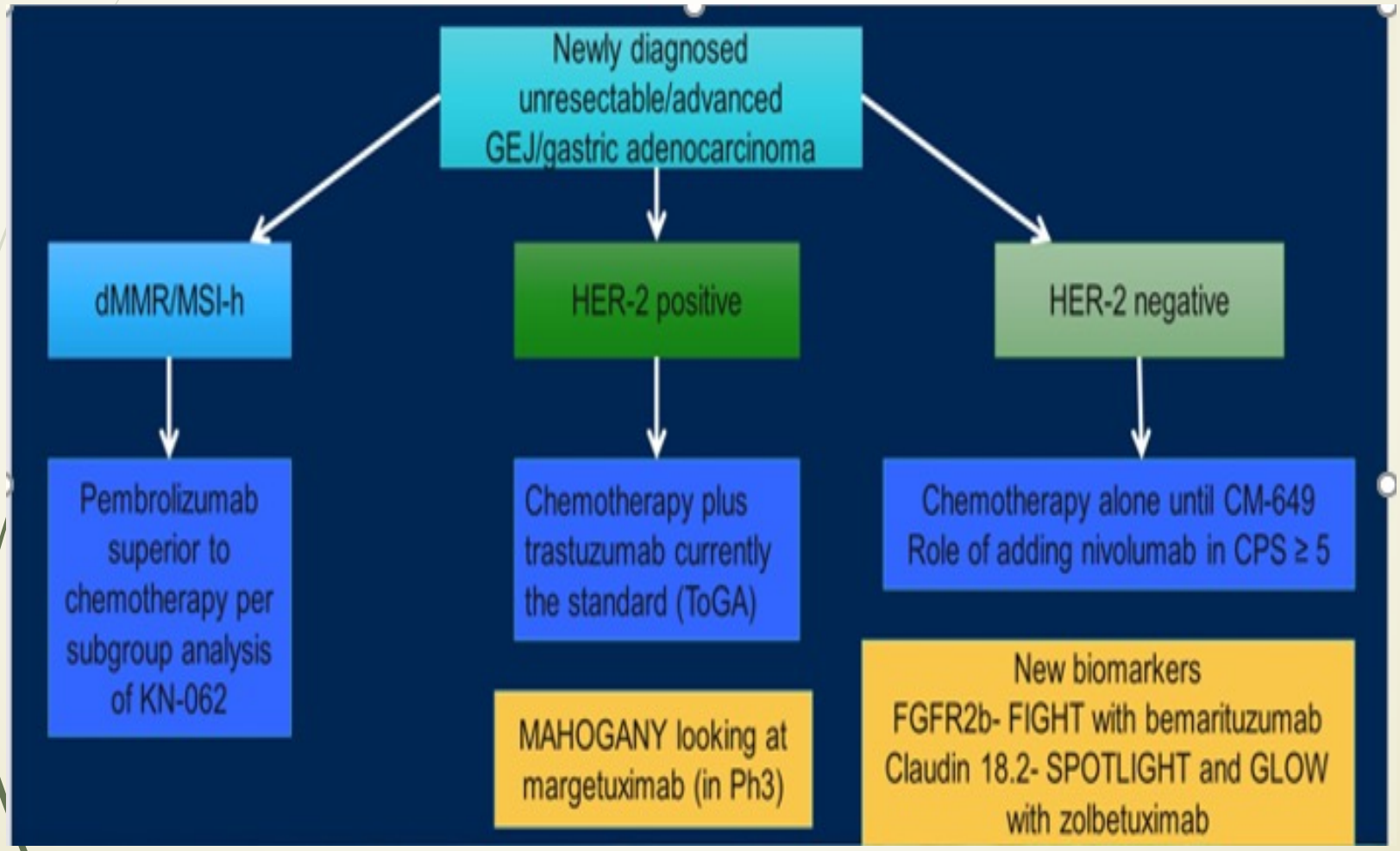
- **Case 2: Adam**
- **28 y/o male Cardio fellow presented dyspepsia, wight loss**
- **EGD: Gastric adenoCa**
- **CT scan/MRI: 3 liver mets in segmt IV**
- **PET scan: increase uptake in Gastric wall/ Liver**
- **Path: Heur 2 (-),**
- **PDL1 CPS 2**

CONTINUUM OF CARE …..
FOR ADVANCED ESOPH/GASTRIC CA

PACLITAXEL/RAMUCIRUMAB
IRINOTECAN
DOCETAXEL
FAM-TRASTUZUMAB DERUXETAN

TRIFLURIDINE/TIPIACIL
PEMBRO … TMB>10
DOSTARLIMAB… dMMR/MSI-H
NTRK INHIB

Management of Advanced Esoph. & Gastric Cancer



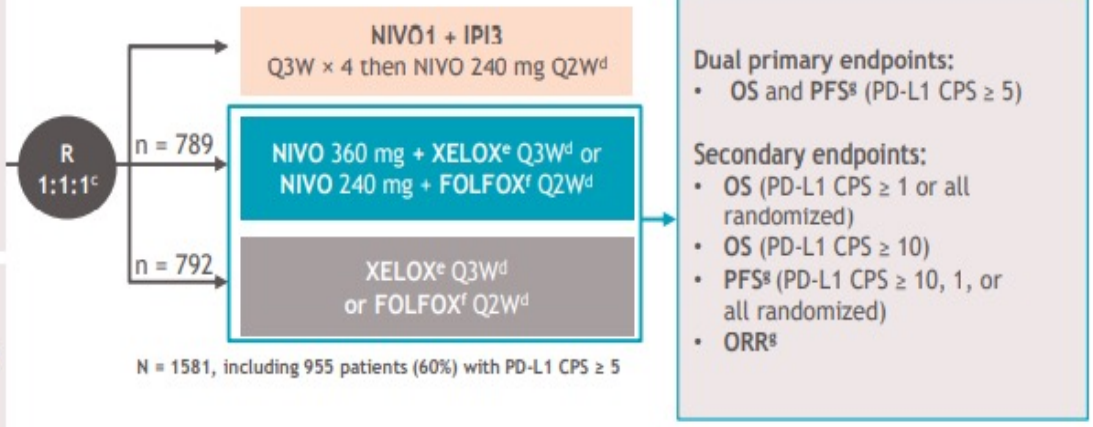
IMMUNOTHERPAY IN ESOPH & GASTRIC CANCERS

CheckMate 649 study design

- CheckMate 649 is a randomized, open-label, phase 3 study[a]

Key eligibility criteria
- Previously untreated, unresectable, advanced or metastatic gastric/GEJ/ esophageal adenocarcinoma
- No known HER2-positive status
- ECOG PS 0-1

Stratification factors
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[b])
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemo (XELOX vs FOLFOX)



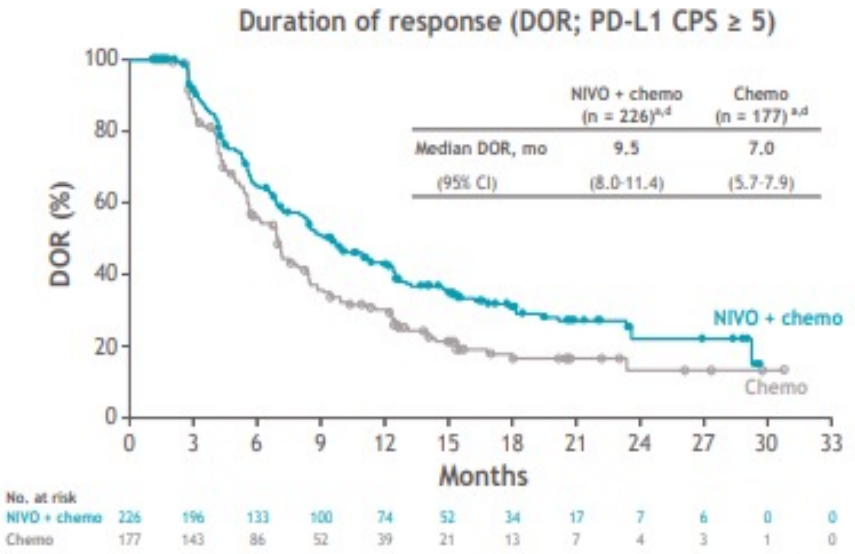
- At data cutoff (May 27, 2020), the minimum follow-up was 12.1 months[h]

[a]ClinicalTrials.gov number, NCT02872116; [b]< 1% includes indeterminate tumor cell PD-L1 expression; determined by PD-L1 IHC 28-8 pharmDx assay (Dako); [c]After NIVO + chemo arm was added and before new patient enrollment in the NIVO1+IPI3 group was closed; [d]Until documented disease progression (unless consented to treatment beyond progression for NIVO + chemo), discontinuation due to toxicity, withdrawal of consent, or study end. NIVO is given for a maximum of 2 years; [e]Oxaliplatin 130 mg/m^2 IV (day 1) and capecitabine 1000 mg/m^2 orally twice daily (days 1-14); [f]Oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2, and FU 400 mg/m^2 IV (day 1) and FU 1200 mg/m^2 IV daily (days 1-2); [g]BICR assessed; [h]Time from concurrent randomization of the last patient to NIVO + chemo vs chemo to data cutoff.

CHECKMATE 649

Response and duration of response

	PD-L1 CPS ≥ 5	
	NIVO + chemo (n = 378)[a]	Chemo (n = 391)[a]
ORR, %	60	45
95% CI	55-65	40-50
P value[b]	< 0.0001	
Best overall response,[c] %		
Complete response	12	7
Partial response	48	38
Stable disease	28	34
Progressive disease	7	11
Not evaluable	6	10
Median TTR (range), months	1.5 (0.8-10.2)	1.5 (1.0-7.1)



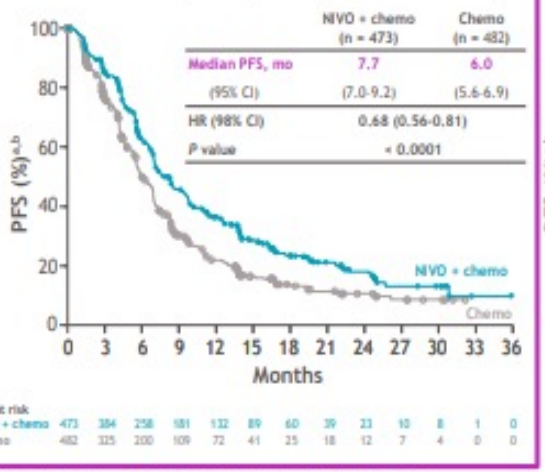
- ORR was higher with NIVO + chemo versus chemo, and responses were more durable

[a]Randomized patients who had target lesion measurements at baseline per BICR assessment; [b]ORR was not formally tested, the pre-specified *P* value is descriptive; [c]Percentages may not add up to 100% due to rounding; [d]Number of responders.

CHECKMATE 649

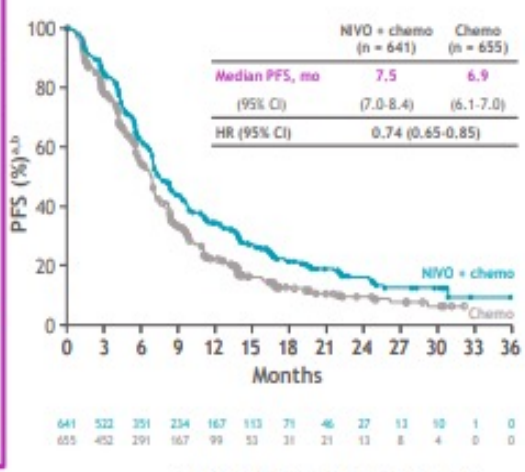
Progression-free survival

Primary endpoint (PD-L1 CPS ≥ 5)



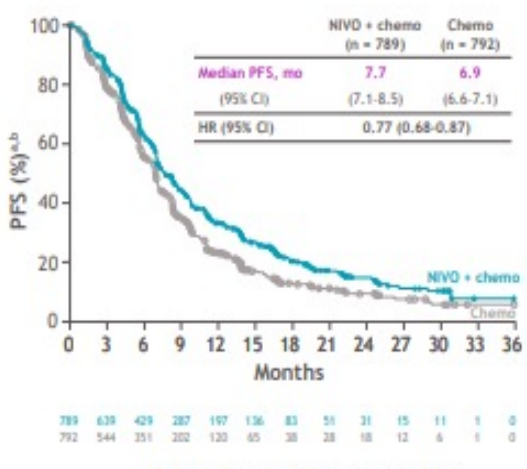
12-mo rate: NIVO + chemo, 36%; chemo, 22%

PD-L1 CPS ≥ 1



NIVO + chemo, 34%; chemo, 22%

All randomized



NIVO + chemo, 33%; chemo, 23%

- Superior PFS, 32% reduction in the risk of progression or death with NIVO + chemo versus chemo in patients whose tumors expressed PD-L1 CPS ≥ 5
- PFS benefit with NIVO + chemo versus chemo in PD-L1 CPS ≥ 1 and all randomized patients

[a]Per BICR assessment; [b]Minimum follow-up 12.1 months.

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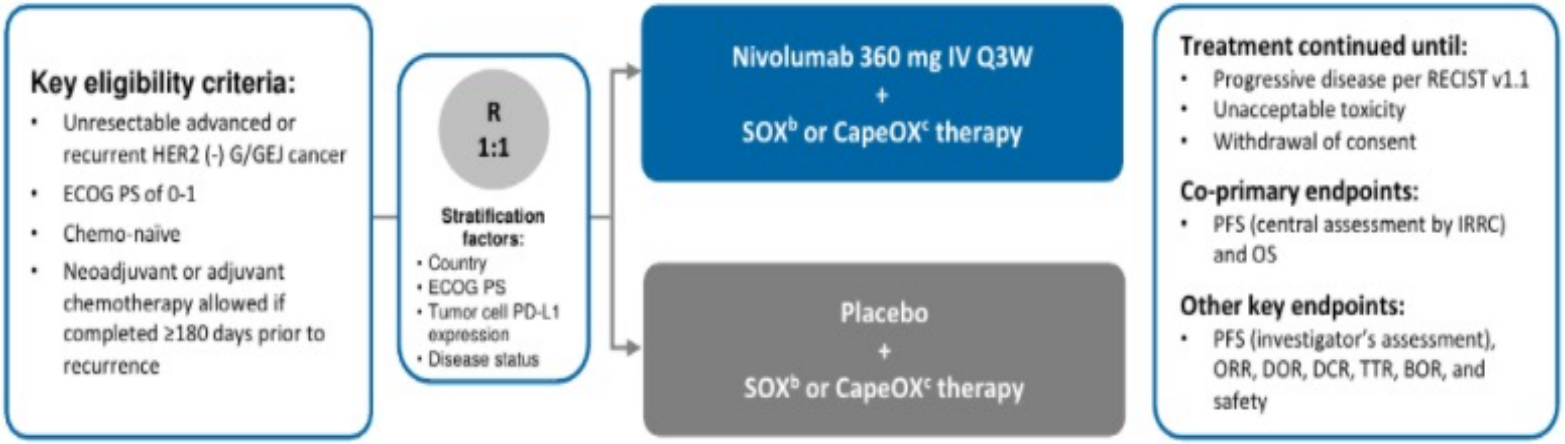
Phase 3 part of ATTRACTION-4: Study Design

- Phase 3 part of ATTRACTION-4 is a double-blind, randomized controlled study conducted at 130 centers in Japan, Korea, and Taiwan[a]



- At data cutoff for interim analysis of PFS (31 Oct 2018), the median follow-up period was 11.6 months
- At data cutoff for final analysis of OS (31 Jan 2020), the median follow-up period was 26.6 months
- A total of 724 patients were randomized between Mar 2017 and May 2018

[a]ClinicalTrials.gov Identifier: NCT02746796,
[b]SOX : S-1 (tegafur-gimeracil-oteracil potassium) 40 mg/m^2 orally twice daily (days 1–14) and Oxaliplatin 130 mg/m^2 IV (day 1), q3w
[c]CapeOX : Capecitabine 1000 mg/m^2 orally twice daily (days 1–14) and Oxaliplatin 130 mg/m^2 IV (day 1), q3w

ATTRACTION 4 TRIAL

ATTRACTION-4

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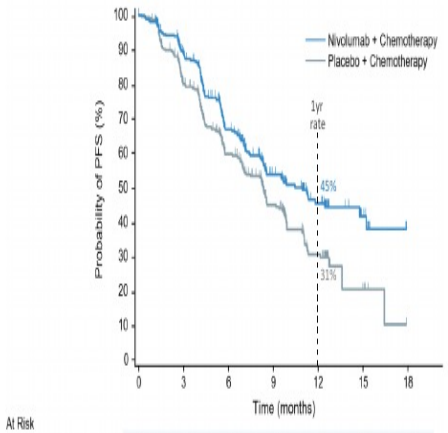
Progression-Free Survival (Interim Analysis)



	Nivolumab + Chemotherapy N = 362	Placebo + Chemotherapy N = 362
Median PFS, months (95% CI)	10.45 (8.44-14.75)	8.34 (6.97-9.40)
Hazard ratio (98.51% CI)	0.68 (0.51-0.90)	
P value	0.0007	
1yr PFS rate (%)	45.4	30.6

At Risk							
Nivolumab + Chemotherapy	362	274	168	94	46	13	0
Placebo + Chemotherapy	362	259	160	80	30	5	0

Data cut off : 31 Oct 2018 at interim analysis

9

ATTRACTION-4

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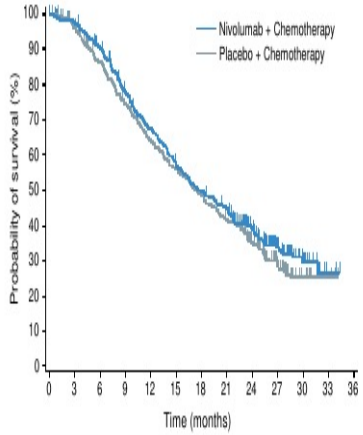
Overall Survival (Final Analysis)

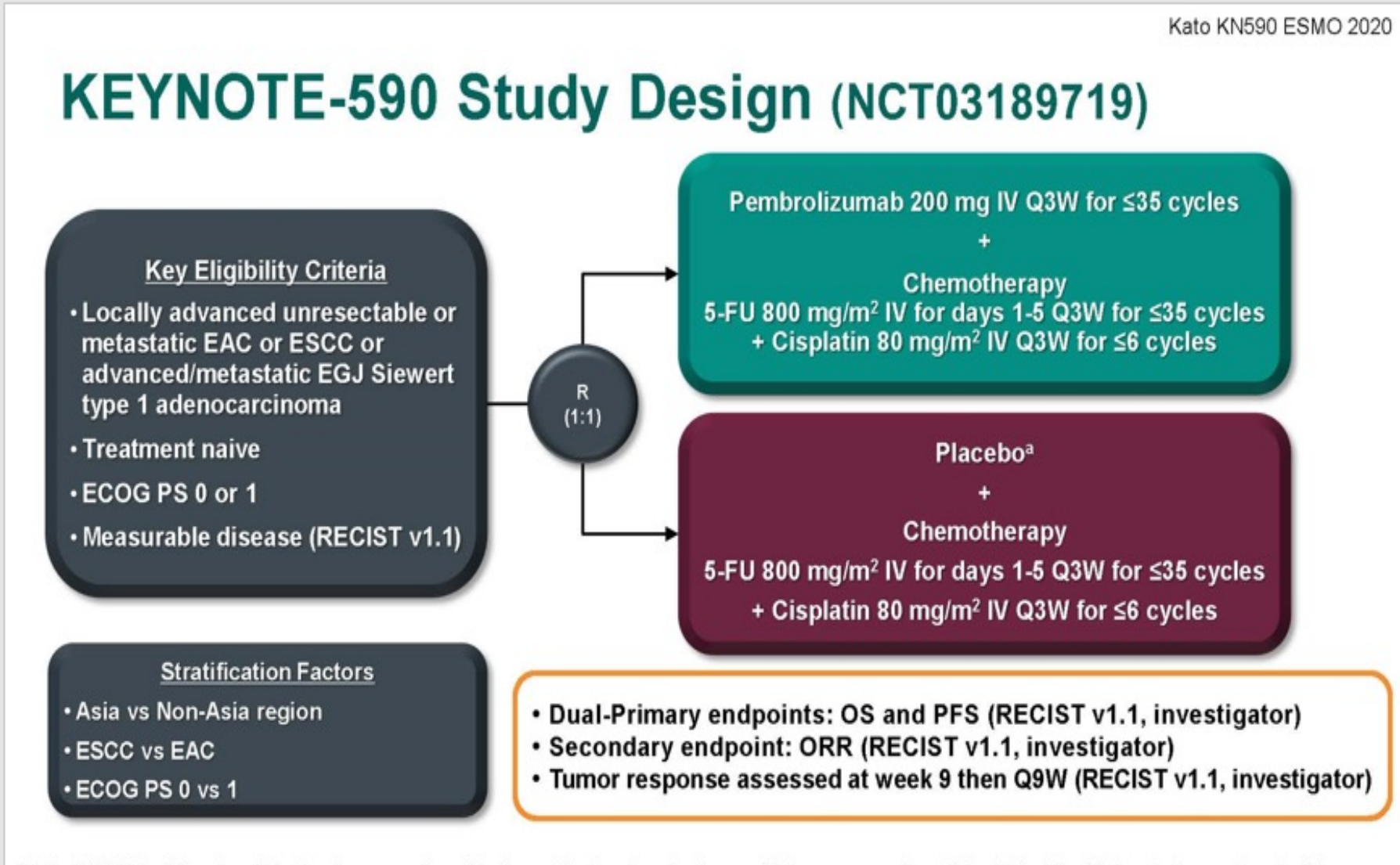


	Nivolumab + Chemotherapy N = 362	Placebo + Chemotherapy N = 362
Median OS, months (95% CI)	17.45 (15.67-20.83)	17.15 (15.18-19.65)
Hazard ratio (95% CI)	0.90 (0.75-1.08)	
P value	0.257	

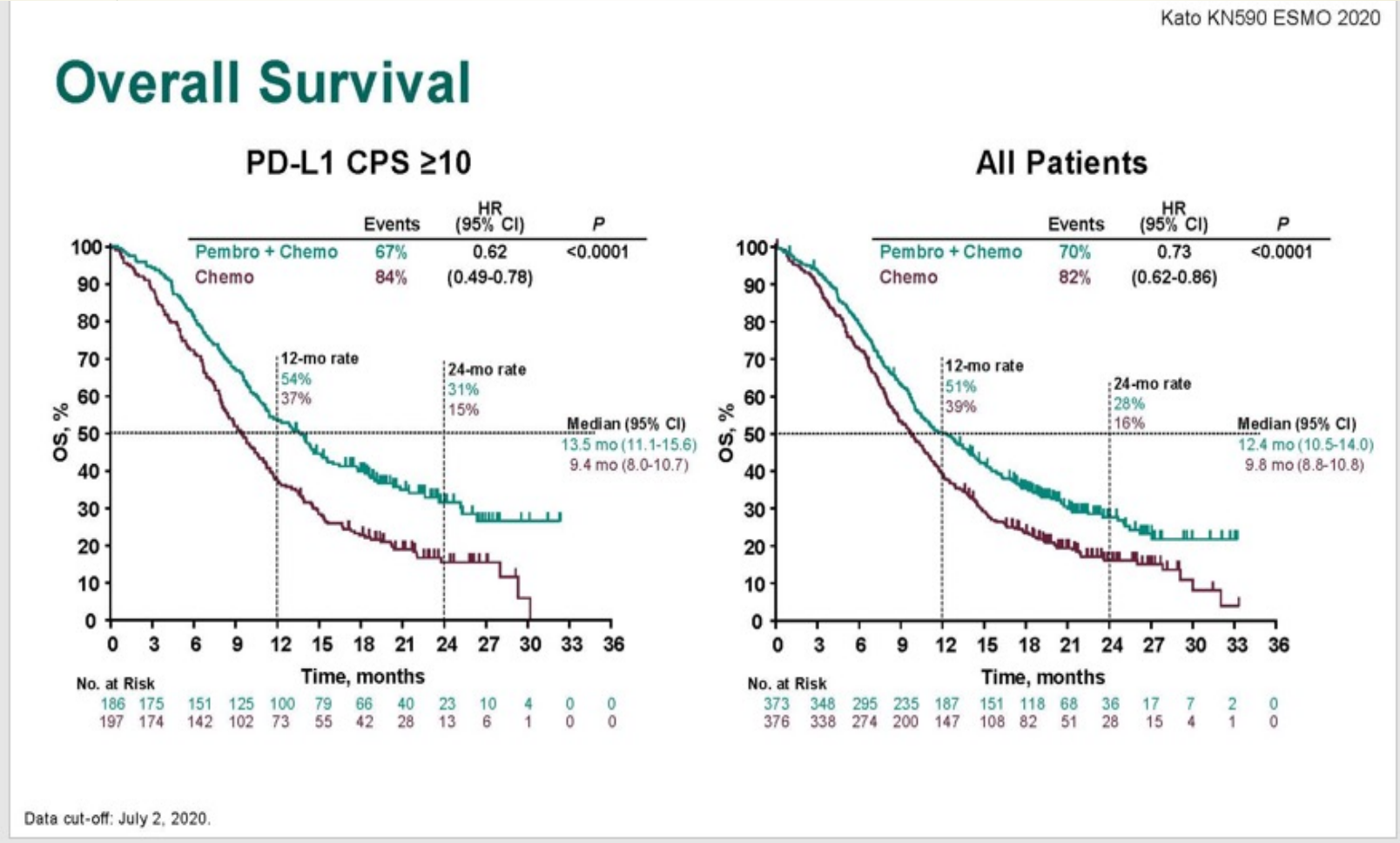
At Risk												
Nivolumab + Chemotherapy	362	346	318	269	232	193	169	150	102	58	23	2	0
Placebo + Chemotherapy	362	342	301	259	219	192	167	141	97	48	16	5	0

Data cut off : 31 Jan 2020 at final analysis

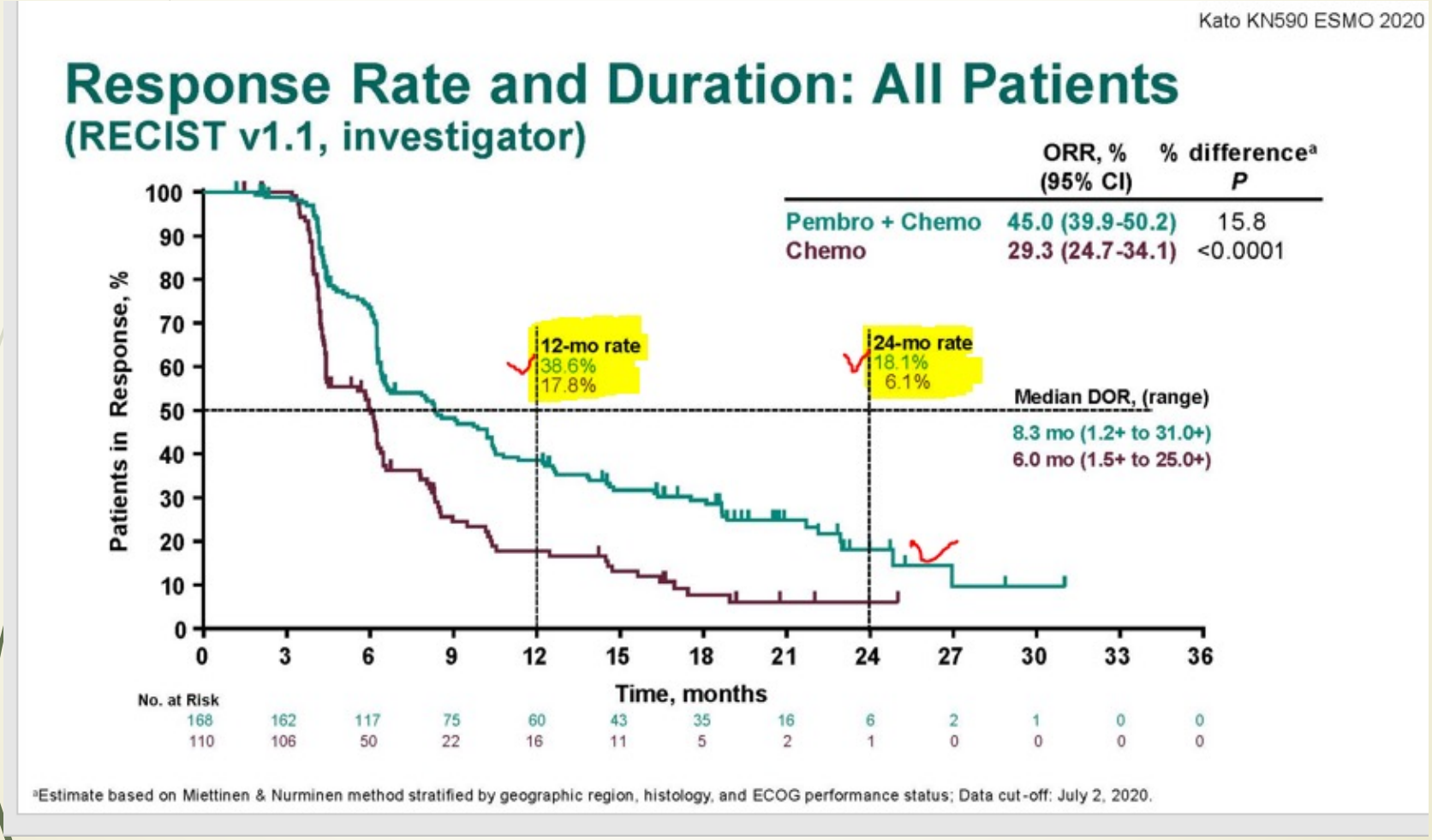
IMMUNOTHERPAY IN ESOPH & GASTRIC CANCERS



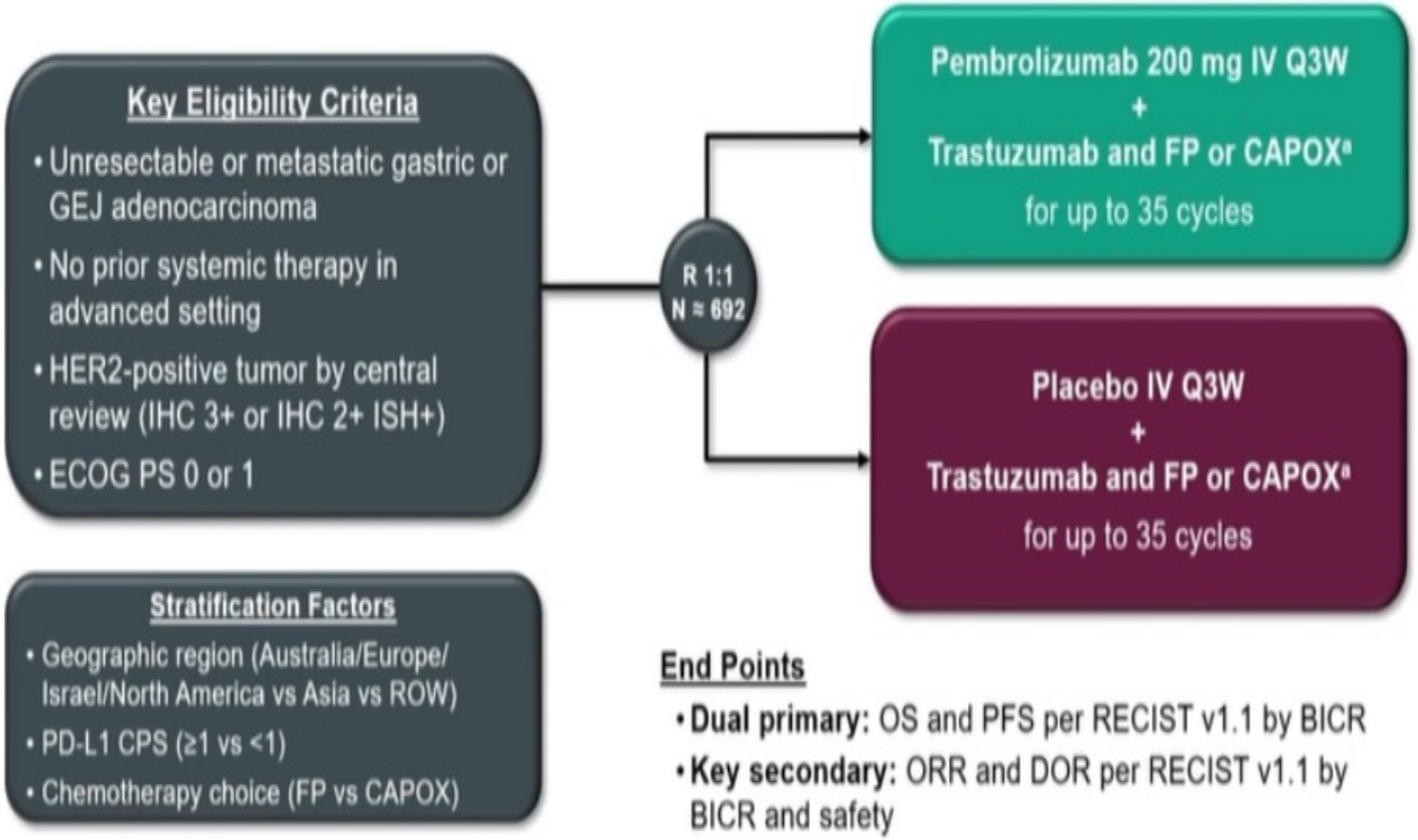
KEYNOTE 590


Kato KN590 ESMO 2020
Overall Survival
PD-L1 CPS ≥10
Events
HR (95% CI)
P
Pembro + Chemo 67% 0.62 <0.0001
Chemo 84% (0.49-0.78)
12-mo rate
54%
37%
24-mo rate
31%
15%
Median (95% CI)
13.5 mo (11.1-15.6)
9.4 mo (8.0-10.7)
OS, %
Time, months
No. at Risk
186 175 151 125 100 79 66 40 23 10 4 0 0
197 174 142 102 73 55 42 28 13 6 1 0 0
All Patients
Events
HR (95% CI)
P
Pembro + Chemo 70% 0.73 <0.0001
Chemo 82% (0.62-0.86)
12-mo rate
51%
39%
24-mo rate
28%
16%
Median (95% CI)
12.4 mo (10.5-14.0)
9.8 mo (8.8-10.8)
OS, %
Time, months
No. at Risk
373 348 295 235 187 151 118 68 36 17 7 2 0
376 338 274 200 147 108 82 51 28 15 4 1 0
Data cut-off: July 2, 2020.

KEYNOTE 590

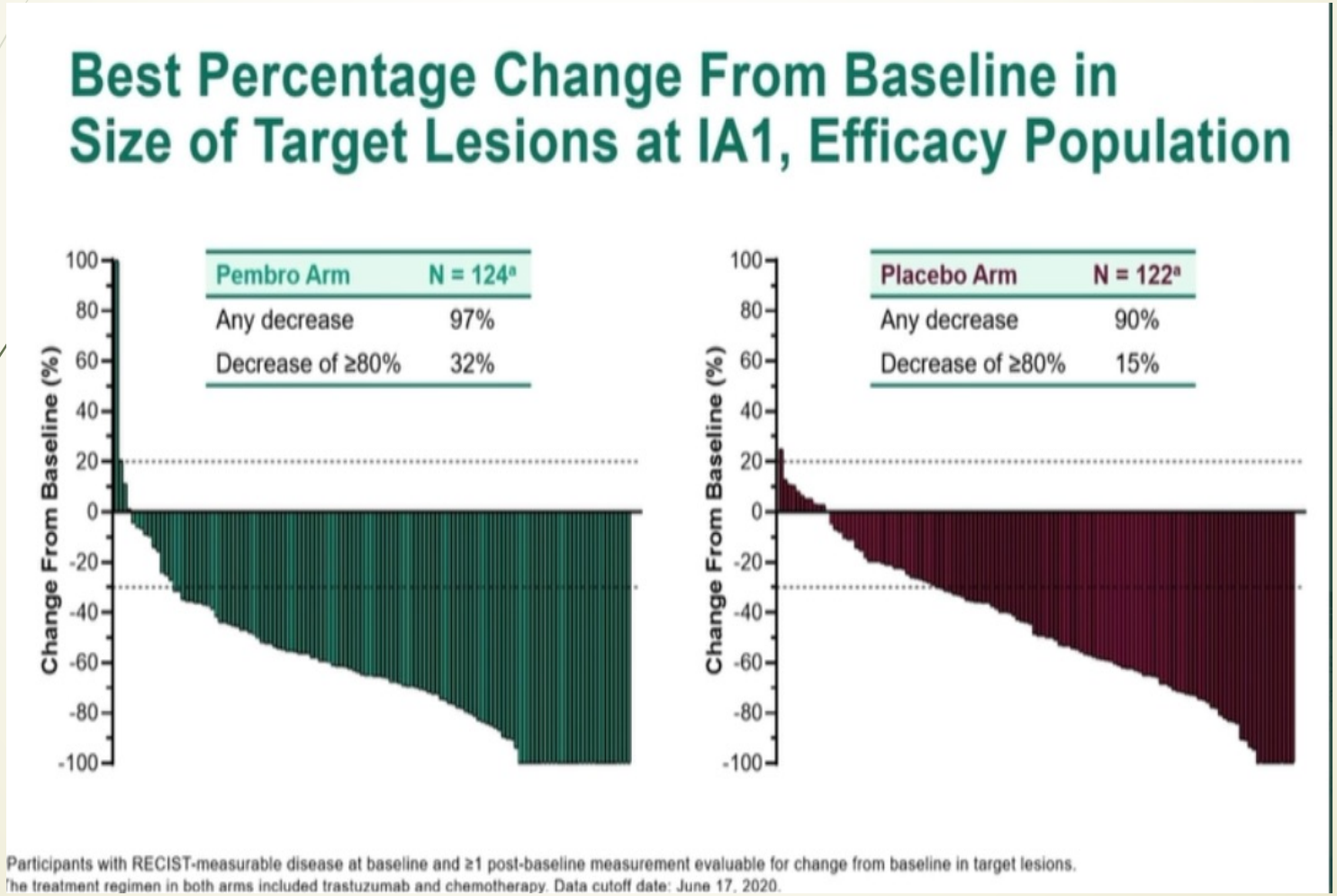

Kato KN590 ESMO 2020
Response Rate and Duration: All Patients
(RECIST v1.1, investigator)
ORR, % (95% CI)
% difference[a] P
Pembro + Chemo 45.0 (39.9-50.2) 15.8
Chemo 29.3 (24.7-34.1) <0.0001
12-mo rate
38.6%
17.8%
24-mo rate
18.1%
6.1%
Median DOR, (range)
8.3 mo (1.2+ to 31.0+)
6.0 mo (1.5+ to 25.0+)
Patients in Response, %
100
90
80
70
60
50
40
30
20
10
0
0 3 6 9 12 15 18 21 24 27 30 33 36
Time, months
No. at Risk
168 162 117 75 60 43 35 16 6 2 1 0 0
110 106 50 22 16 11 5 2 1 0 0 0 0
[a]Estimate based on Miettinen & Nurminen method stratified by geographic region, histology, and ECOG performance status; Data cut-off: July 2, 2020.

KEYNOTE-811 Global Cohort: Randomized, Double-Blind, Phase 3 Study



KEYNOTE 811

TRASTUZ/ PEMBRO OR PLACEBO AND CHEMORx

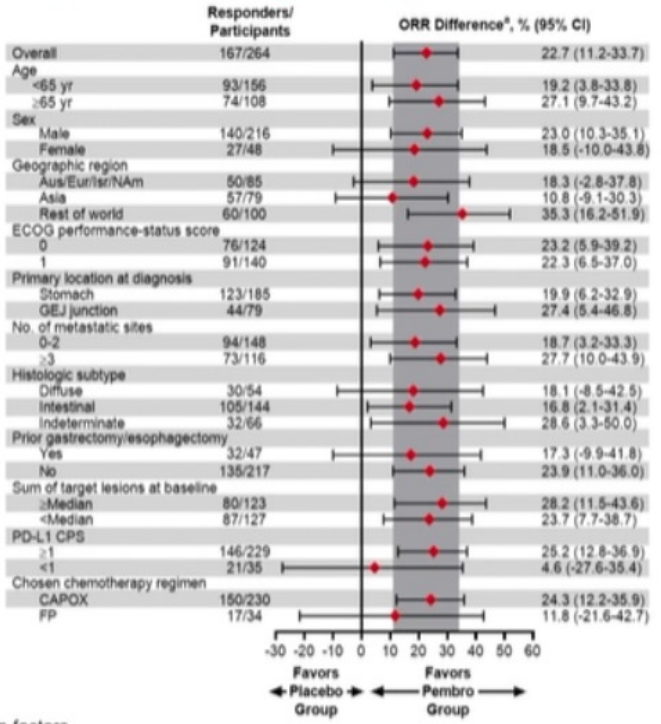


KEYNOTE 811

TRASTUZ/ PEMBRO OR PLACEBO AND CHEMORx

Confirmed Response at IA1, Efficacy Population

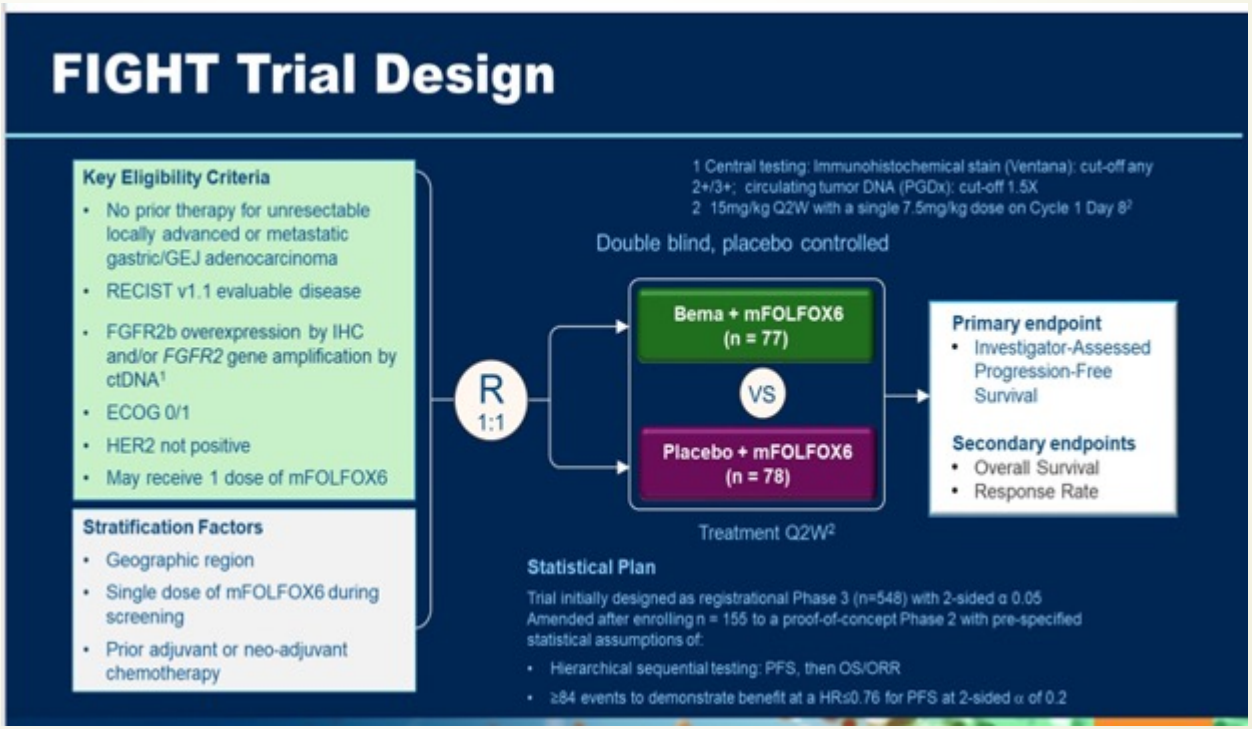
% (95% CI)	Pembro Arm (N = 133)	Placebo Arm (N = 131)
ORR	74.4% (66.2-81.6)	51.9% (43.0-60.7)
ORR difference[a]	22.7% (11.2-33.7) *P* = 0.00006	
DCR	96.2% (91.4-98.8)	89.3% (82.7-94.0)



Calculated using the Miettinen and Nurminen method stratified by the randomization stratification factors.
The treatment regimen in both arms included trastuzumab and chemotherapy. Data cutoff date: June 17, 2020.

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)

Zev A Wainberg, Peter Enzinger, Yoon-Koo Kang, Kensai Yamaguchi, Shukui

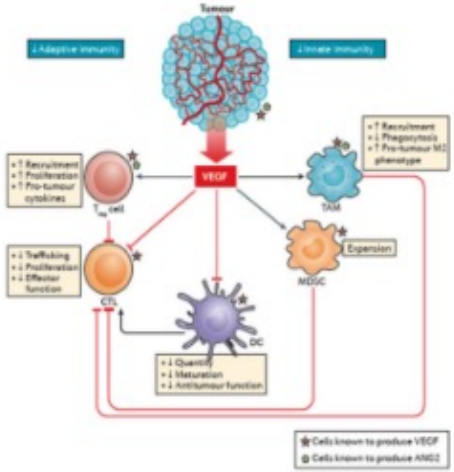


Novel Concepts for IO in GE/ Gastric Cancers

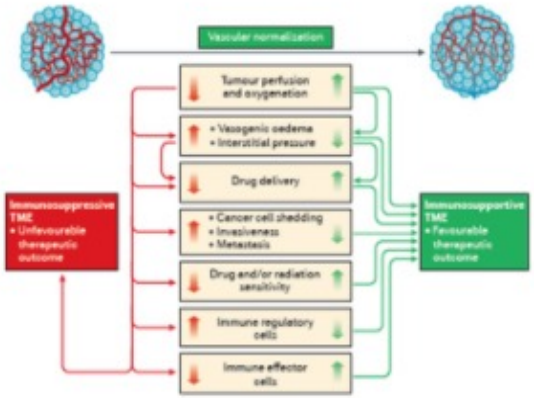
Immune suppression of angiogenesis in TME

- VEGF signaling leads to immunosuppressive state in TME
- Angiogenesis inhibitors normalize tumor vasculature, leading to immune stimulatory status and promotes differentiation and function of immune cells

VEGF signaling effects



Anti-VEGF effects

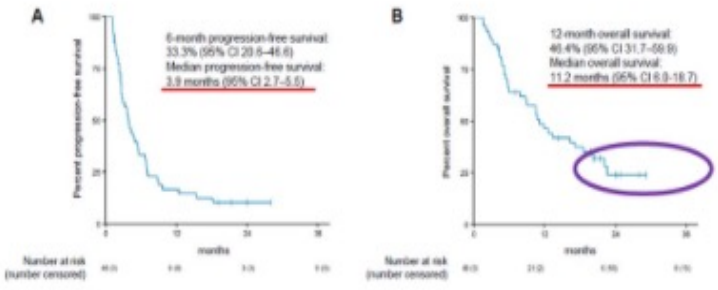


Fukumura D et al. Nat Rev Clin Oncol 2018

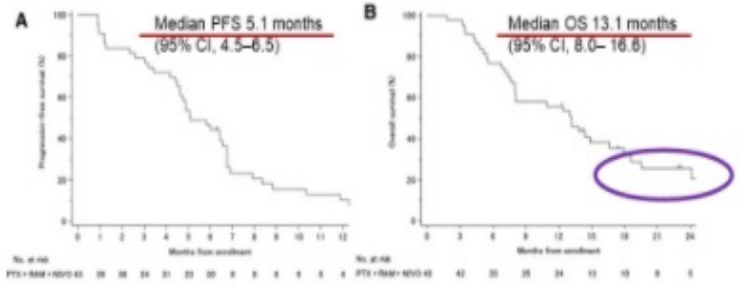
Novel Concepts for IO in GE/ Gastric Cancers

IO + angiogenesis inhibitor (II) in 2nd line

phase I/II Paclitaxel + Nivolumab (n=48)



phase I/II Paclitaxel + Ramucirumab + Nivolumab (n=43)



- Paclitaxel + Ramucirumab in Rainbow trial: mPFS 4.4months(95% CI 4.2-5.3), mOS 9.6months(95% CI 8.5-10.8)
- Adding Nivolumab showed long term survivors!!
- Triplet regimen with Ramucirumab is tolerable and improves survival!

Wilke et al, Lancet Oncology 2014
Lee et al, AACR 2021
Nakajima TE et al, CCR 2021,

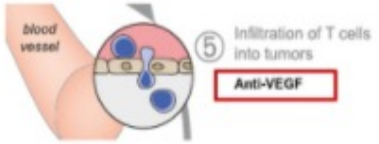
ASCO Gastrointestinal Cancers Symposium #GI22

PRESENTED BY: Sun Young RHA, Moving checkpoint inhibitors forward in combination strategies

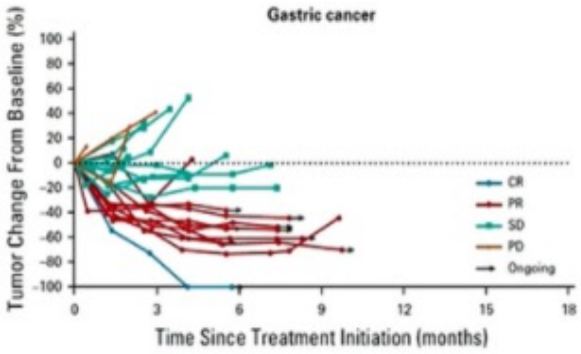
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Novel Concepts for IO in GE / Gastric Cancers

IO + angiogenesis inhibitor (III): VEGFR TKIs



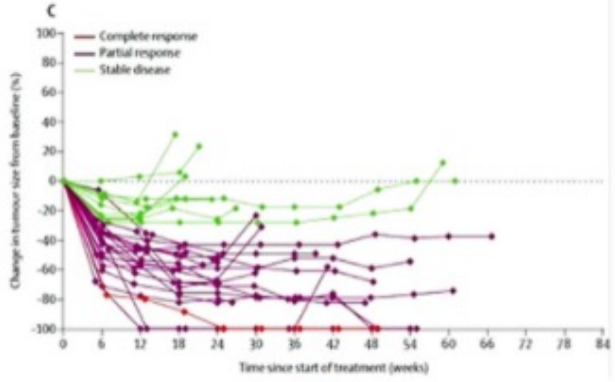
Regorafenib + Nivolumab



Ongoing phase III Integrate IIb trial, late line

Regorafenib + Nivolumab vs SOC chemotherapy

Lenvatinib + Pembrolizumab



Ongoing phase III LEAP-015 trial, 1st line

Lenvatinib + Pembrolizumab + chemo vs chemo

Fukuoka S, JCO, 2021, Kawazoe A, Lancet Oncol 2020, Chung et al ASCO 2021

CONCLUSION

- The treatment Paradigm for gastric & Gastroesophageal cancer is an evolving Process
- Locally Advanced Gastric Ca/ GE adenoCa choosing wisely Perioperative chemoRx
- Esophageal SCC/ AdenoCa selected (Siewart1, ChemoRx is not option) combined Modality is better approach
- Adjuvant Immunotherapy with Nivolumab when R0, Residual disease (>T1,>N1)
- The Alliance Trial with PET Directed combined modality with a greater OS reaching 50.3 m with FOLFOX→FOLFOX/ XRT
- Pembro + Trastuzumab and ChemoRX as new standard for Heur 2+ GE/Gastric Adenoca
- Great Need for targeted Therapy against newer pathways/ receptors