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ADVANCES IN Cancer IMMUNOTHERAPY™

40th ANNIVERSARY

WEST CANCER CENTER & RESEARCH INSTITUTE

partner of OneOncology

Immunotherapy for the Treatment of Gastrointestinal Cancers

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AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

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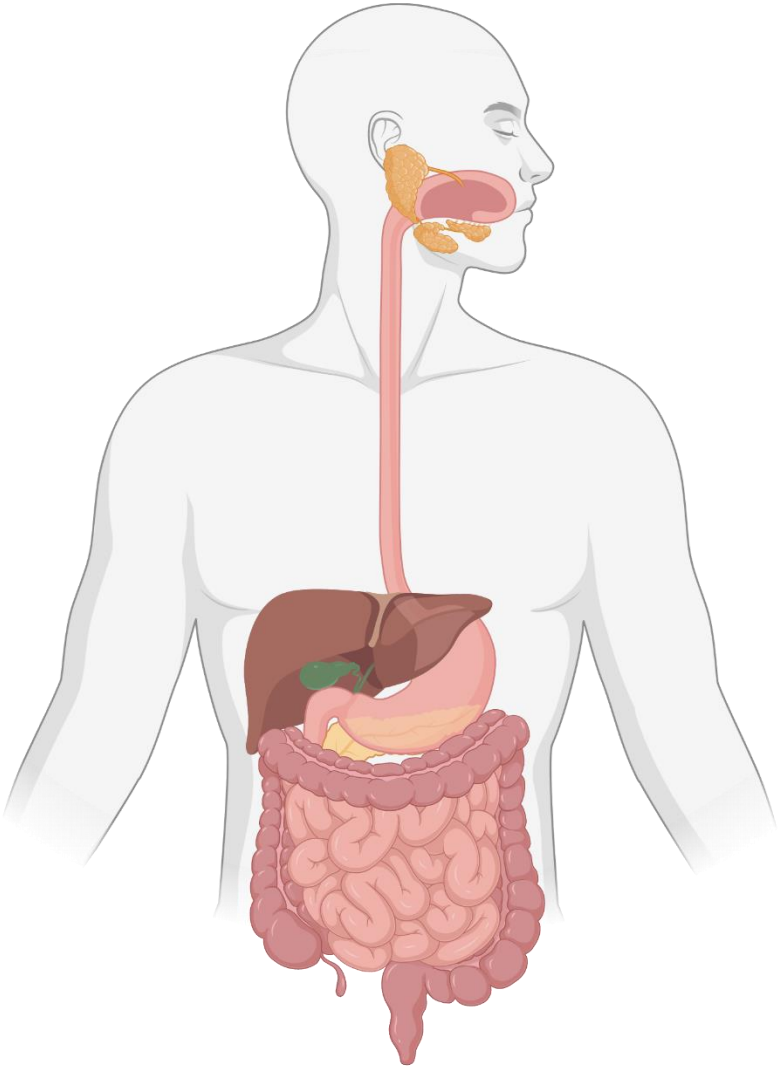
Disclosures

- No relevant financial relationships to disclose
- I will be discussing non-FDA approved indications during my presentation.

Outline

- Gastro-esophageal cancer
- Hepatocellular carcinoma
- Colorectal cancer



March 2021: FDA Approval of IO Agents in GI Cancers

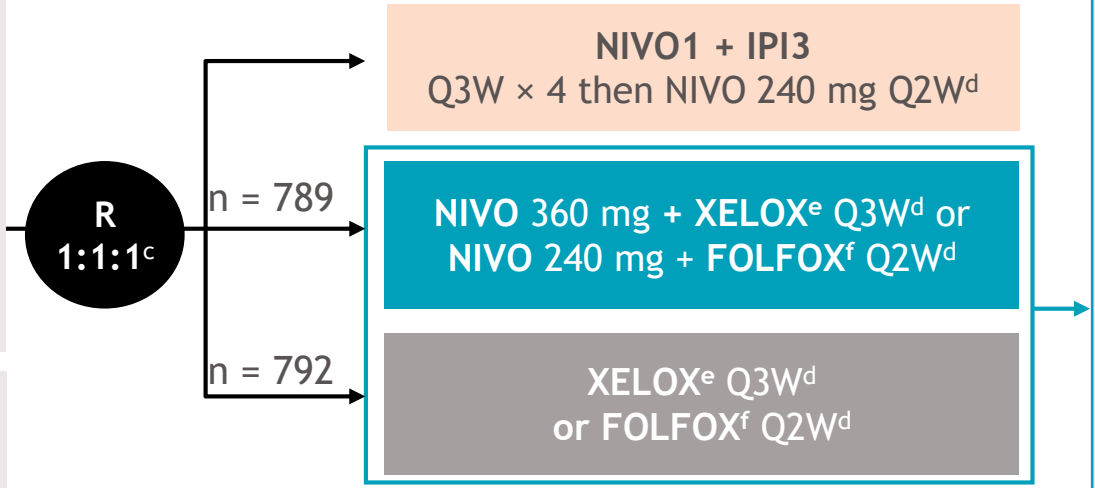
	1st Line	2nd Line	3rd Line	Comments
Esophageal SCC		Pembro for PD-L1 CPS ≥10		
Gastroesophageal ACA			Pembro for PD-L1 CPS ≥1	Nivo approved in Asia based on ATTRACTION-2
Pancreas Ca				
Hepatocellular Ca	Atezolizumab+ BEV	Pembrolizumab Nivolumab		Pembro and Nivo approval based on non-randomized studies
Biliary Ca				
Colorectal Ca	Pembro for MSI-H/ MMR-D		Nivo +/- Ipi and Pembro for MSI-H/ MMR-D	
Anal SCC				
MSI-H/ MMR-D Ca			Pembrolizumab	Tumor-entity independent approval
TMB 10+ (Foundation)			Pembrolizumab	Tumor-entity independent approval

CheckMate 649 – Phase 3 GEC

- 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)



N = 1581, including 955 patients (60%) with PD-L1 CPS ≥ 5

Dual primary endpoints:
- **OS** and **PFS**[g] (PD-L1 CPS ≥ 5)

Secondary endpoints:
- **OS** (PD-L1 CPS ≥ 1 or all randomized)
- **OS** (PD-L1 CPS ≥ 10)
- **PFS**[g] (PD-L1 CPS ≥ 10, 1, or all randomized)
- **ORR**[g]

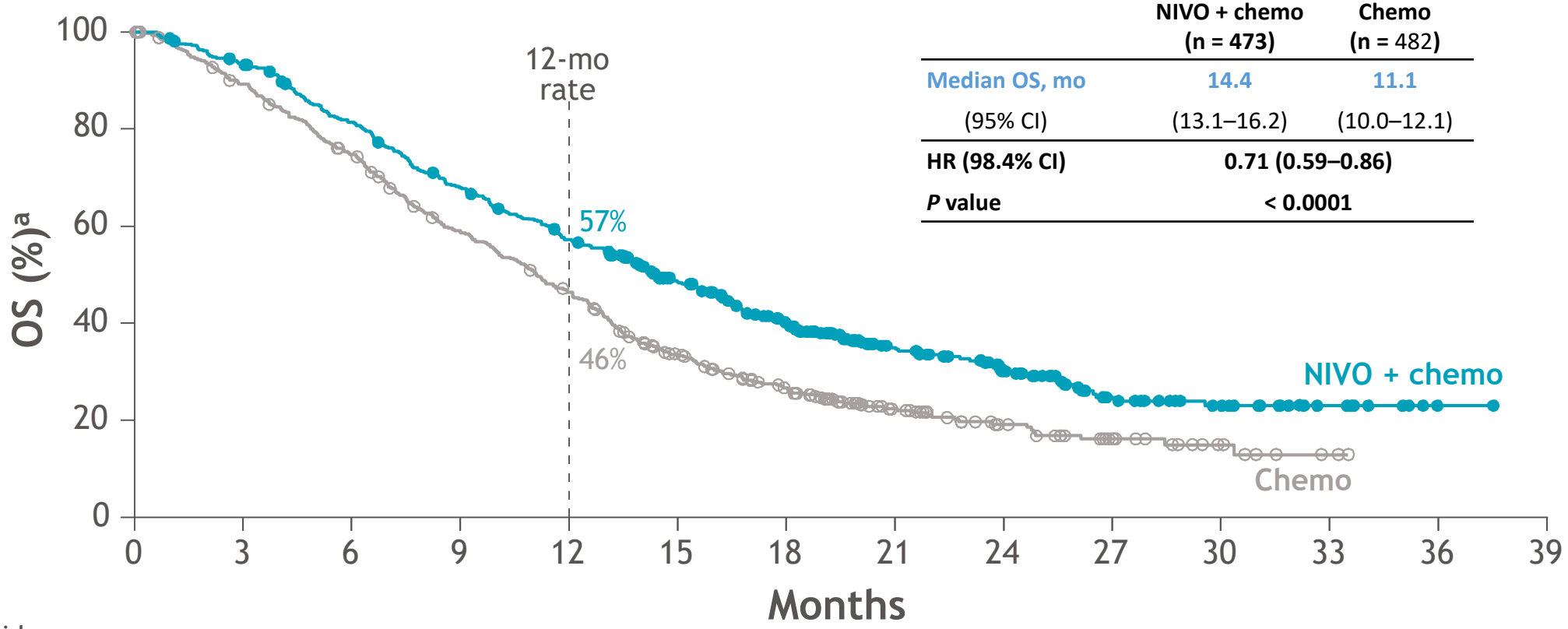
- At data cutoff (May 27, 2020), the minimum follow-up was 12.1 months[h]

[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.

Moehler et al., ESMO 2020

Overall survival

Primary endpoint (PD-L1 CPS ≥ 5)



	NIVO + chemo (n = 473)	Chemo (n = 482)
Median OS, mo	14.4	11.1
(95% CI)	(13.1–16.2)	(10.0–12.1)
HR (98.4% CI)	**0.71 (0.59–0.86)**	
***P* value**	**< 0.0001**	

No. at risk														
NIVO + chemo	473	438	377	313	261	198	149	96	65	33	22	9	1	0
Chemo	482	421	350	271	211	138	98	56	34	19	8	2	0	0

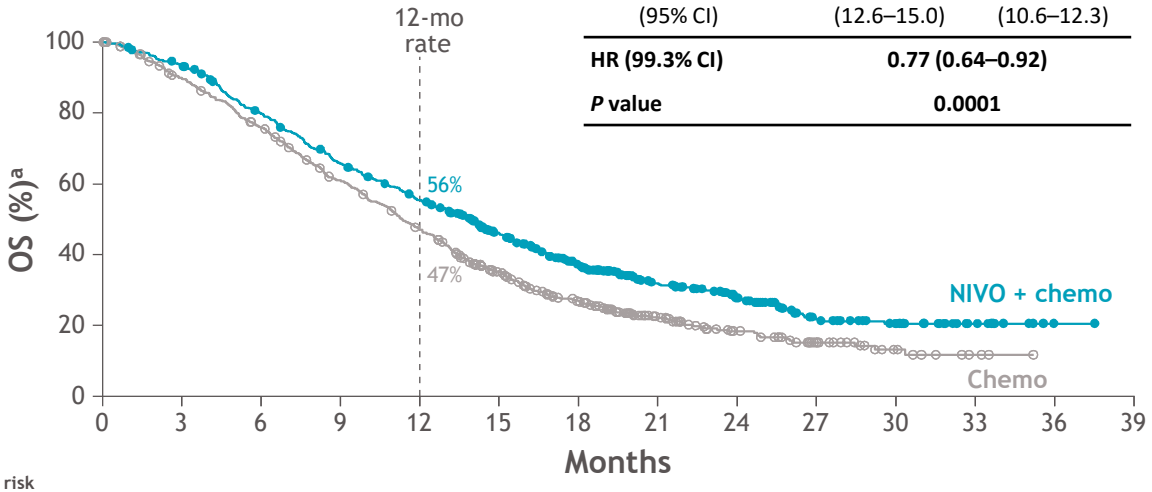
- Superior OS, 29% reduction in the risk of death, and a 3.3-month improvement in median OS with NIVO + chemo versus chemo in patients whose tumors expressed PD-L1 CPS ≥ 5

aMinimum follow-up 12.1 months.

Overall survival

PD-L1 CPS ≥ 1

	NIVO + chemo (n = 641)	Chemo (n = 655)
Median OS, mo	14.0	11.3
(95% CI)	(12.6–15.0)	(10.6–12.3)
HR (99.3% CI)	0.77 (0.64–0.92)	
P value	0.0001	

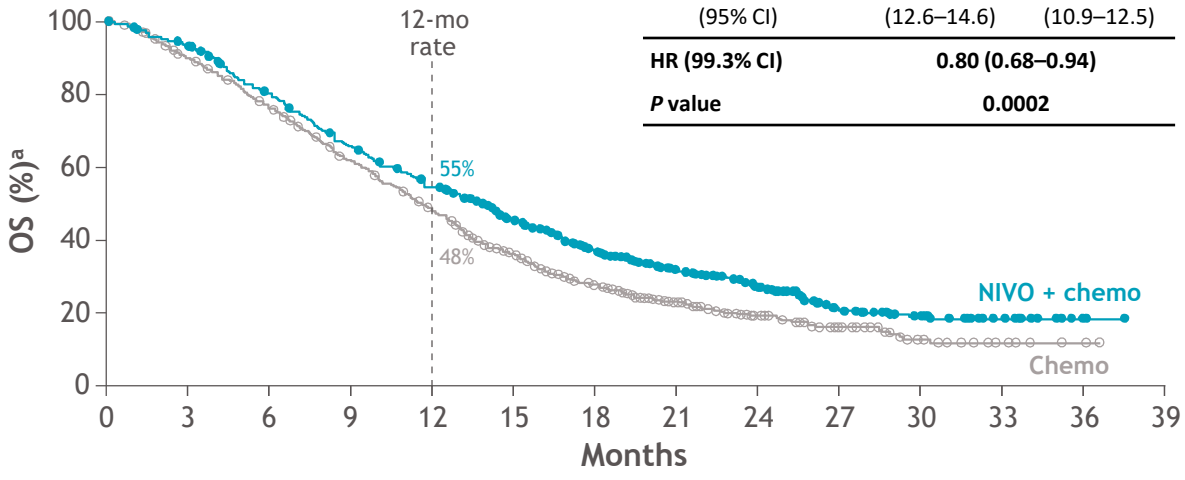


No. at risk

NIVO + chemo	641	595	502	412	344	254	183	118	80	40	28	11	1	0
Chemo	655	575	483	383	292	194	131	77	45	25	10	3	0	0

All randomized

	NIVO + chemo (n = 789)	Chemo (n = 792)
Median OS, mo	13.8	11.6
(95% CI)	(12.6–14.6)	(10.9–12.5)
HR (99.3% CI)	0.80 (0.68–0.94)	
P value	0.0002	



NIVO + chemo	789	731	621	506	420	308	226	147	100	49	34	14	2	0
Chemo	792	697	586	469	359	239	160	94	59	35	15	7	2	0

HR attenuation: 0.71 -> 0.77 -> 0.80 (from CPS ≥5 -> 1 -> all)

- Superior OS benefit in PD-L1 CPS ≥ 1 and all randomized patients with NIVO + chemo versus chemo

[a]Minimum follow-up 12.1 months.

TAKE HOME MESSAGE

- **Patients with PD-L1 CPS ≥ 5 gastric cancer treated with oxaliplatin/fluoropyrimidine and nivolumab can expect a median overall survival of >14 months, a milestone for non-Asian patients, and a new SOC**
- **Other PD-L1 CPS cutoffs will likely be evaluated by FDA**

KEYNOTE-590 Study Design (NCT03189719)

Key Eligibility Criteria

- Locally advanced unresectable or metastatic EAC or ESCC or advanced/metastatic EGJ Siewert type 1 adenocarcinoma
- Treatment naive
- ECOG PS 0 or 1
- Measurable disease (RECIST v1.1)

Stratification Factors

- Asia vs Non-Asia region
- ESCC vs EAC
- ECOG PS 0 vs 1

R (1:1)

Pembrolizumab 200 mg IV Q3W for ≤35 cycles
+
Chemotherapy
5-FU 800 mg/m^2 IV for days 1-5 Q3W for ≤35 cycles
+ Cisplatin 80 mg/m^2 IV Q3W for ≤6 cycles

Placebo[a]
+
Chemotherapy
5-FU 800 mg/m^2 IV for days 1-5 Q3W for ≤35 cycles
+ Cisplatin 80 mg/m^2 IV Q3W for ≤6 cycles

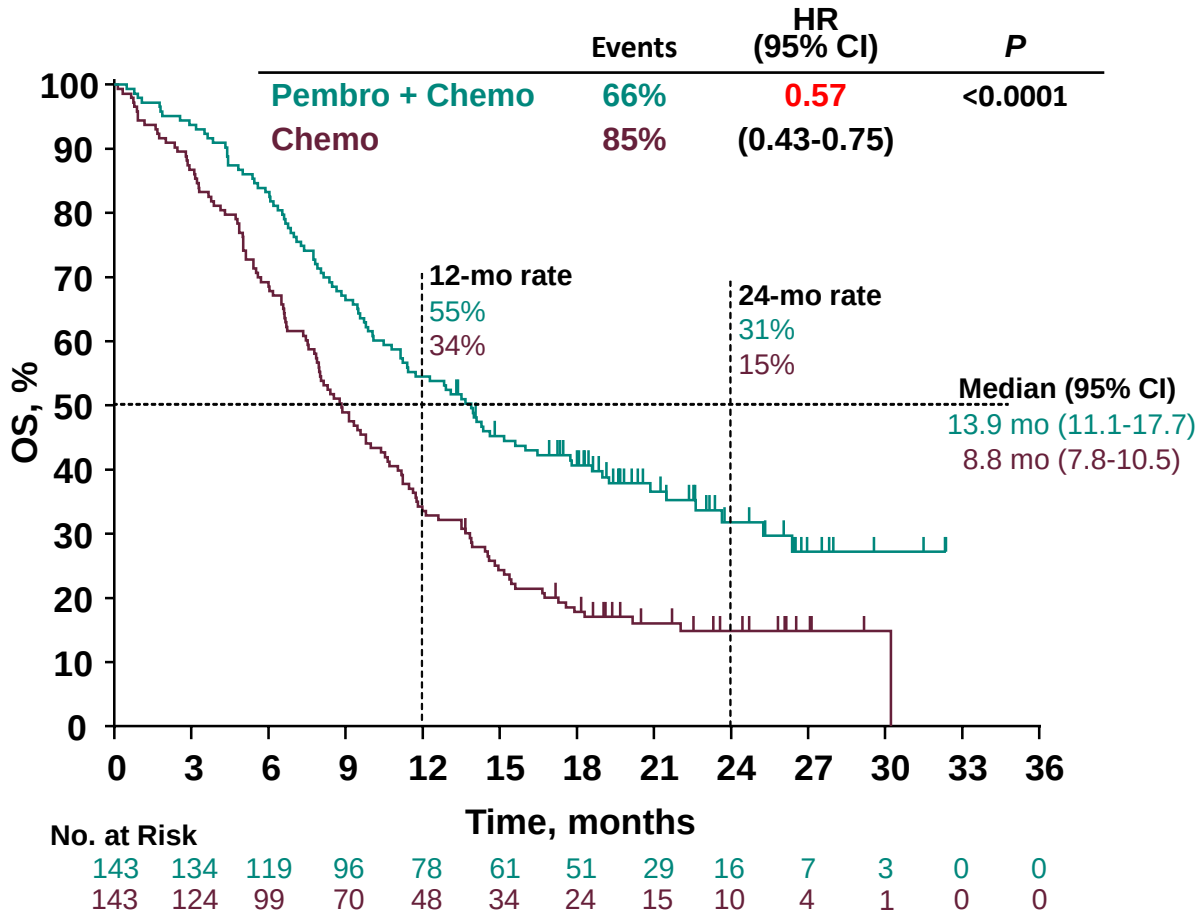
- Dual-Primary endpoints: OS and PFS (RECIST v1.1, investigator)
- Secondary endpoint: ORR (RECIST v1.1, investigator)
- Tumor response assessed at week 9 then Q9W (RECIST v1.1, investigator)

Kato et al., ESMO 2020

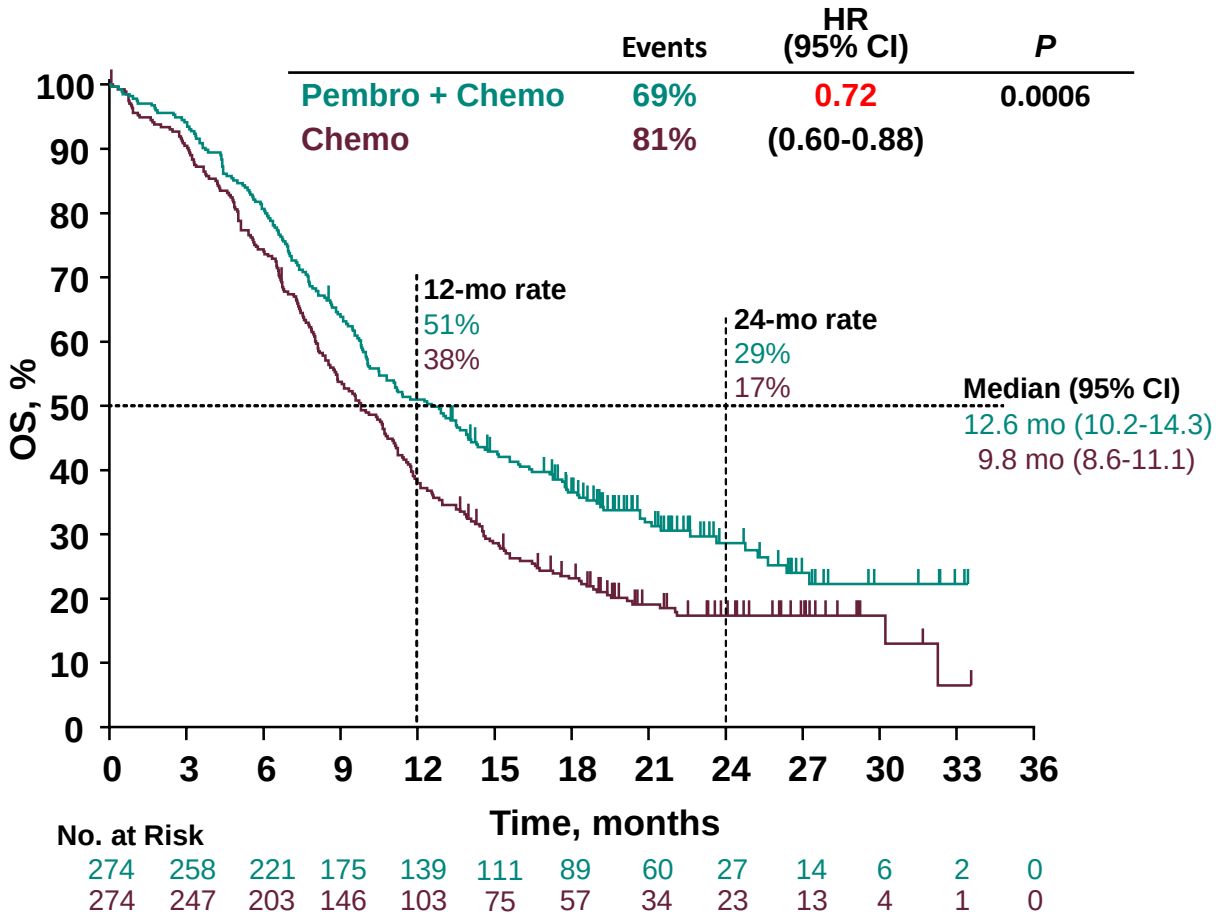
[a]Saline IV Q3W for ≤35 cycles. All treatments were continued for the specified number of cycles or until disease progression, intolerable toxicity, withdrawal of consent, or physician decision; EAC, esophageal adenocarcinoma; EGJ, esophagogastric junction, ESCC, esophageal squamous cell carcinoma.

Overall Survival -ESCC

ESCC PD-L1 CPS ≥10



ESCC

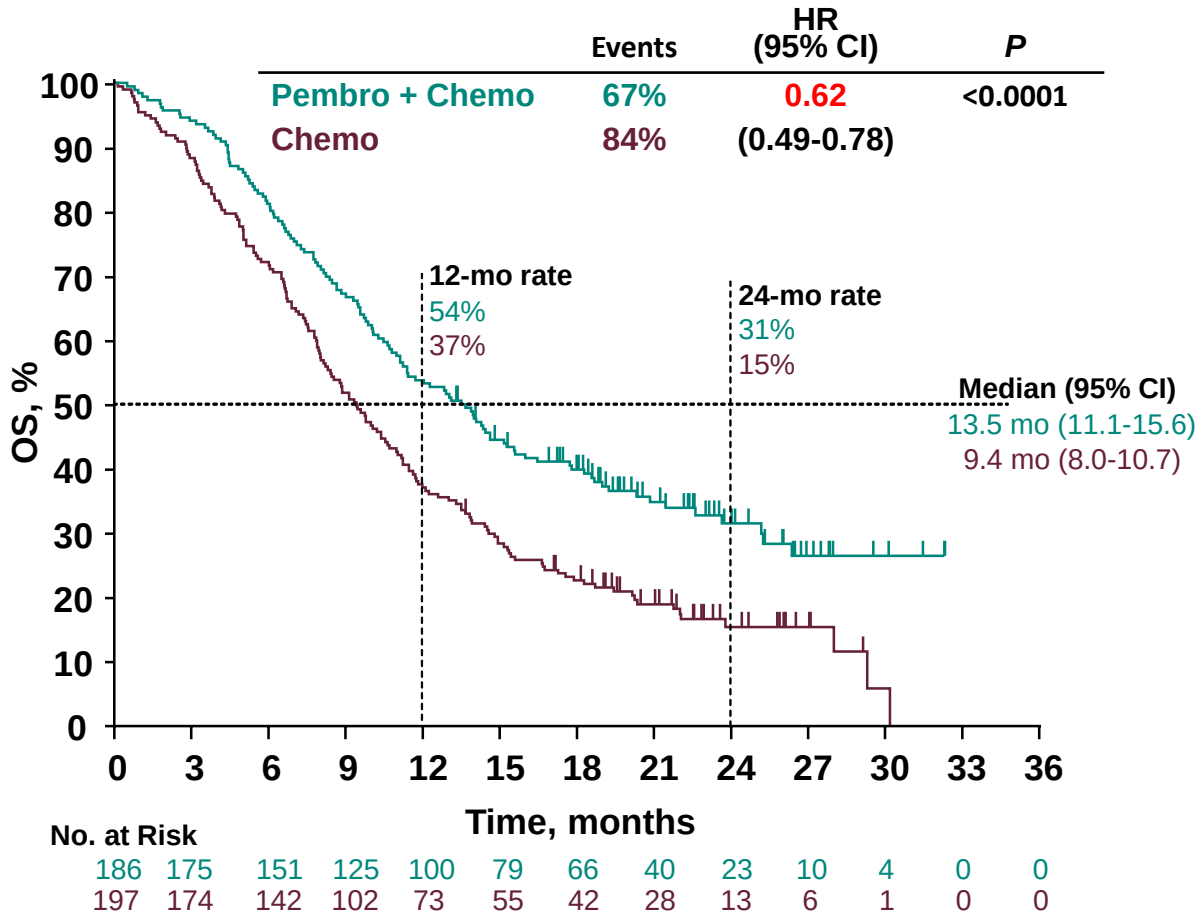


Kato et al., ESMO 2020

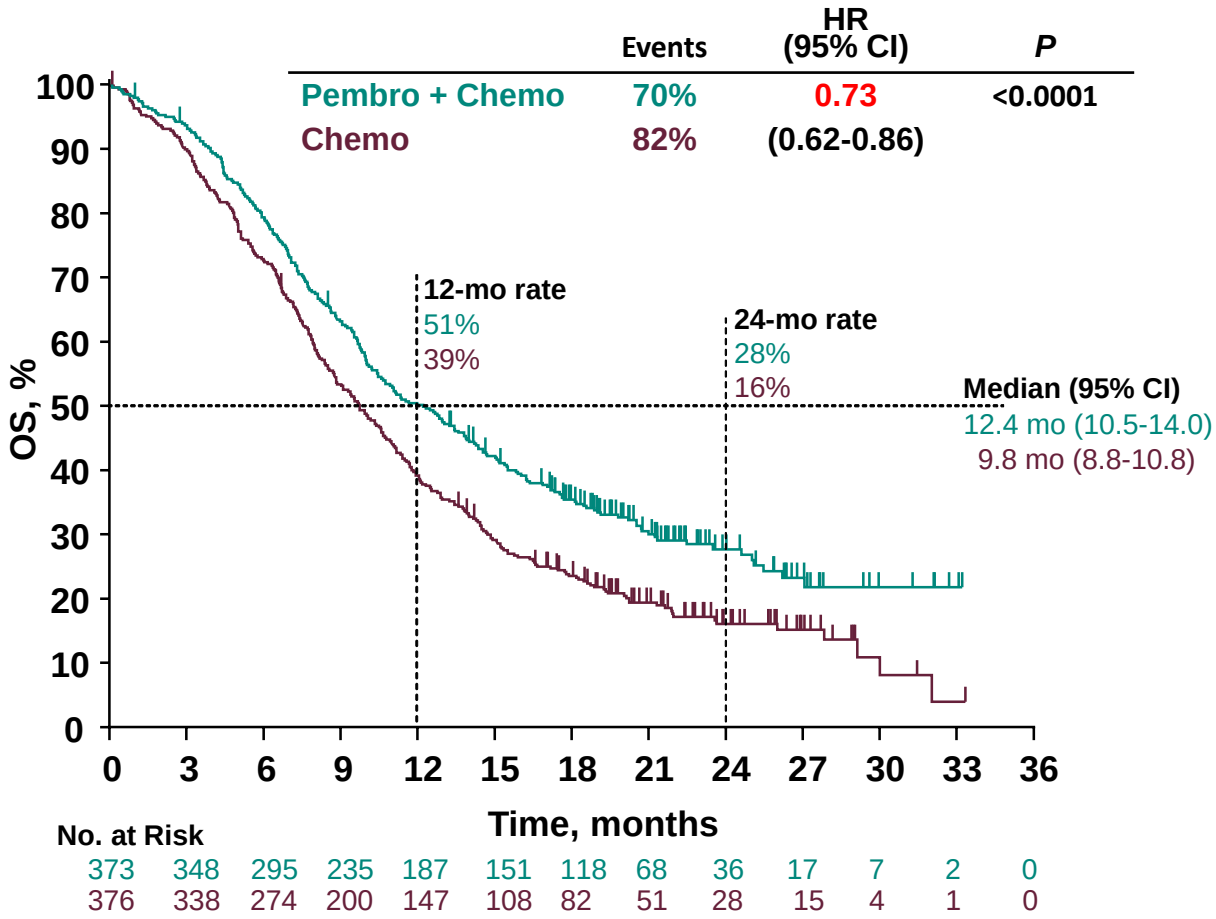
Data cut-off: July 2, 2020.

Overall Survival – ESCC + ACA

PD-L1 CPS ≥10



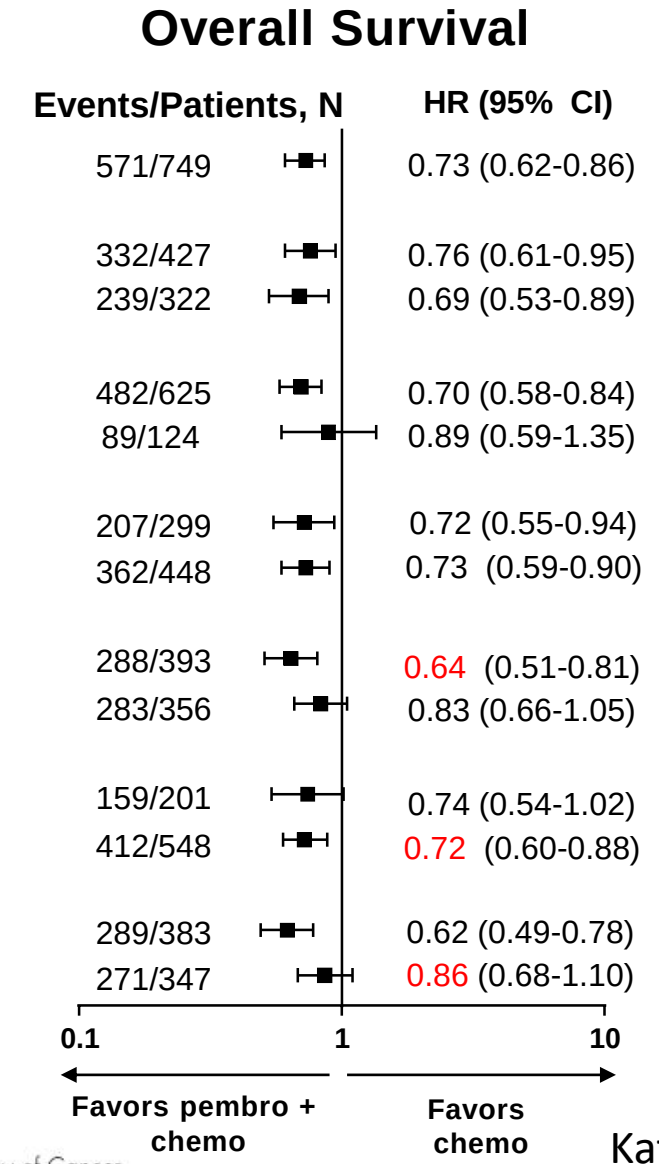
All Patients

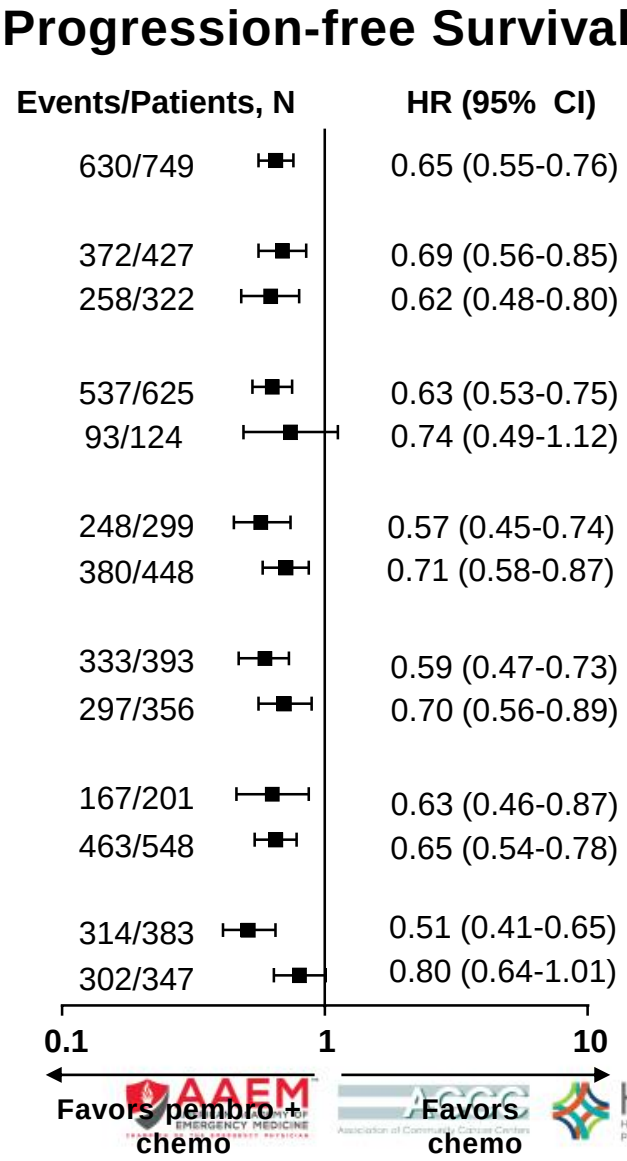


Kato et al., ESMO 2020

Data cut-off: July 2, 2020.

Survival in Key Subgroups: All Patients





Data cut-off: July 2, 2020.

Kato et al., ESMO 2020

CheckMate 577 – adjuvant Ph 3

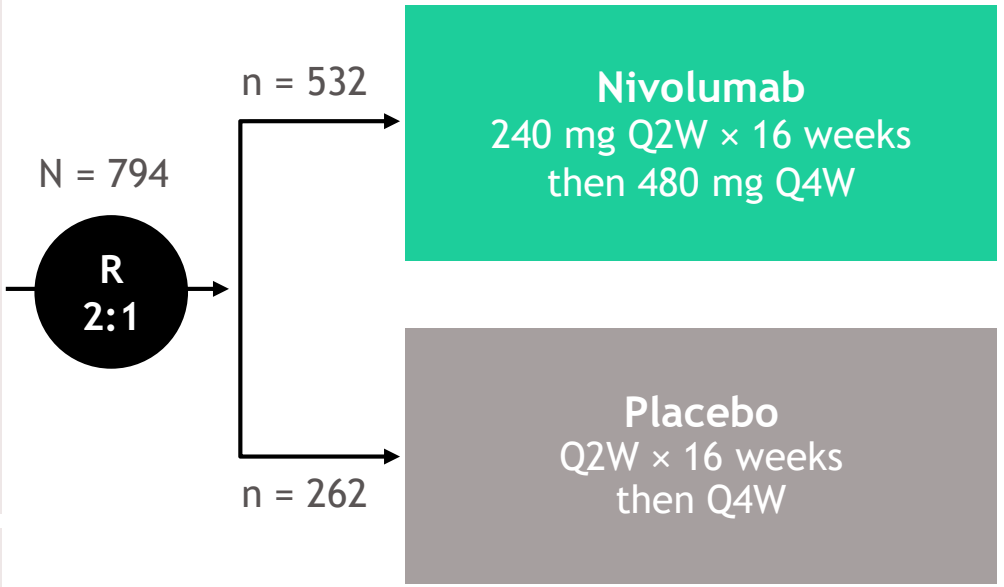
- CheckMate 577 is a global, phase 3, randomized, double-blind, placebo-controlled trial[a]

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])



Total treatment duration of up to 1 year[d]

Primary endpoint:

- DFS[e]

Secondary endpoints:

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

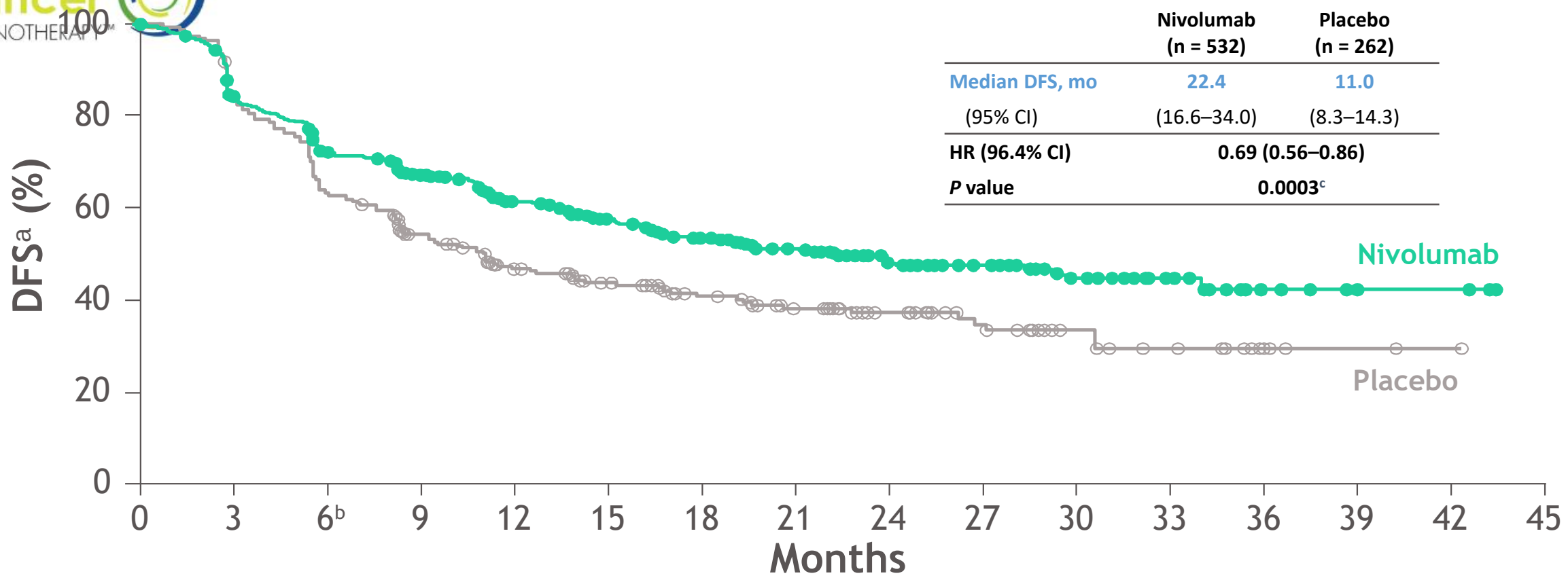
- Median follow-up was 24.4 months (range, 6.2–44.9)[g]
- Geographical regions: Europe (38%), US and Canada (32%), Asia (13%), rest of the world (16%)

[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).

Kelly et al., ESMO 2020

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.

Kelly et al., ESMO 2020

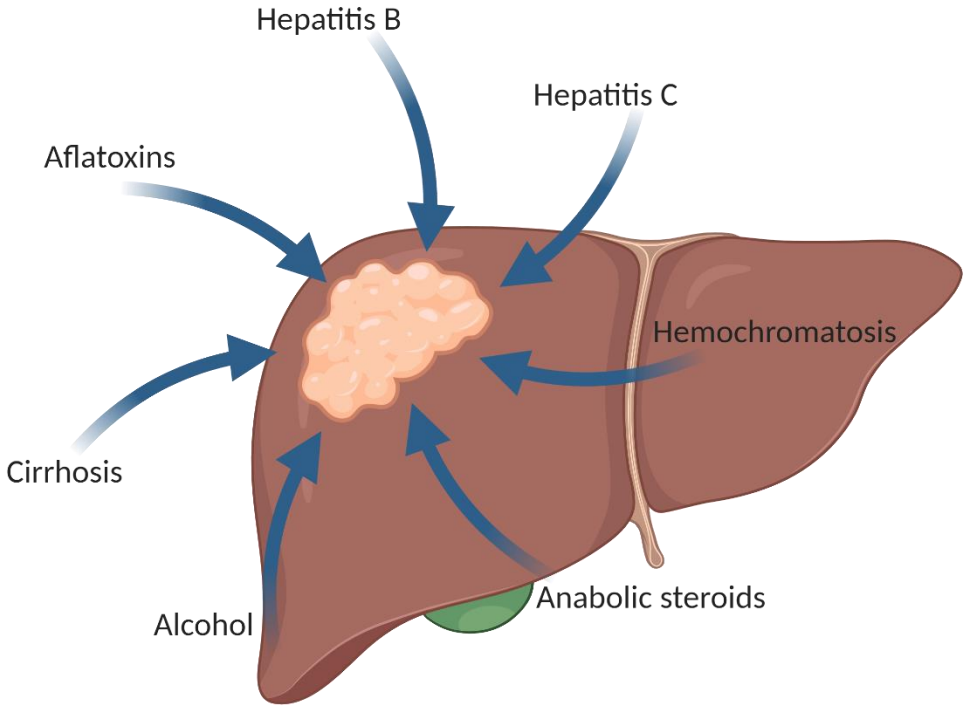
TAKE HOME MESSAGE

- In advanced/ metastatic esophageal cancer CPS ≥10 (but potentially also lower CPS), pembrolizumab plus platinum/ FP is now SOC for SCC *and* ACA

- Patients with stage 2/3 esophago-gastric cancers s/p radio-chemotherapy and resection with residual cancer, adjuvant nivolumab can be considered SOC

Hepatocellular carcinoma

- HCC is the most common type of primary liver cancer
- 3rd leading cause of cancer death worldwide
- Treatment options:
  - Curative: orthotopic liver transplantation, surgical resection
  - Chemoembolization, radiofrequency ablation, microwave ablation, radiation, chemotherapy, targeted therapy
- Many patients are ineligible for surgery/transplant/RFA – there's a need for systemic therapies in HCC



Approved checkpoint inhibitors for HCC

Drug	Approved	Indication	Dose
Nivolumab	2017	Second line	240 mg Q2W or 480 mg Q4W
Pembrolizumab	2018	Second line	200 mg Q3W or 400 mg Q6W
Nivolumab + ipilimumab	2020	Second line	Nivo 1 mg/kg + Ipi 3 mg/kg for 4 doses, then nivo maintenance
Atezolizumab + bevacizumab	2020	First line	Atezolizumab 1200 mg Q3W + bevacizumab 15 mg/kg Q3W

Efficacy of ICIs in sorafenib-experienced HCC

Study	Patient population	Treatment arm(s)	ORR	Landmark OS
CheckMate 040	Advanced HCC with previous sorafenib	Nivolumab	20%	9-month: 74%
		Nivolumab 1 mg/kg + ipilimumab 3 mg/kg Q3W	32%	24-month: 48%
		Nivolumab 3 mg/kg + ipilimumab 1 mg/kg Q3W	31%	24-month: 30%
		Nivolumab 3 mg/kg Q2W + ipilimumab 1 mg/kg Q6W	31%	24-month: 42%
KEYNOTE-240	Advanced HCC with previous sorafenib	Pembrolizumab + BSC	18.3%	Median: 13.9 months
		Placebo + BSC	4.4%	Median: 10.6 months
Study 22	Advanced HCC with previous sorafenib	Durvalumab	10.6	Median: 13.57 months
		Tremelimumab	7.2	Median: 15.11 months
		Tremelimumab (300 mg x 1) + durvalumab 1500 mg Q4W	24.0	Median: 18.73 months
		Tremelimumab (75 mg x 4) + durvalumab 1500 mg Q4W	9.5	Median: 11.30 months

Yau, ESMO 2019; El-Khoueiry, Lancet 2017; Finn, J Clin Oncol 2020; Yau, ASCO 2019; Finn, N Engl J Med 2020; Kelley ASCO 2020.

Efficacy of ICIs in untreated HCC

Study	Patient population	Treatment arm(s)	ORR	Landmark OS
CheckMate 459	Advanced, untreated HCC	Nivolumab	57%	Median: 16.4 months
		Sorafenib	26%	Median: 14.7 months
IMbrave150	Unresectable, untreated HCC	Atezolizumab + bevacizumab	-	12-month: 67.2%
		Sorafenib	-	12-month: 54.6%

In development: Other immunotherapy strategies for HCC

- Combinations with existing immune checkpoint inhibitors
- Alternative immune checkpoints
- Cellular therapies

In development: Combination therapy with ICIs in HCC

Pembrolizumab plus lenvatinib

Untreated HCC

n=100 patients

Pembro 200 mg IV Q3W plus len 12 mg (≥60 kg) or 8 mg (<60kg)

Phase 1b trial results

Median OS 22 mo

Median PFS 8.6 mo

ORR 36%

TRAEs 95% (grade ≥3 67%, grade ≥4 4%)

Phase 3 trial ongoing

FDA did not grant accelerated approval request: did not represent "meaningful advantage" over currently available options

Zhu, ASCO 2020

In development: Selected phase III trials of checkpoint inhibitors

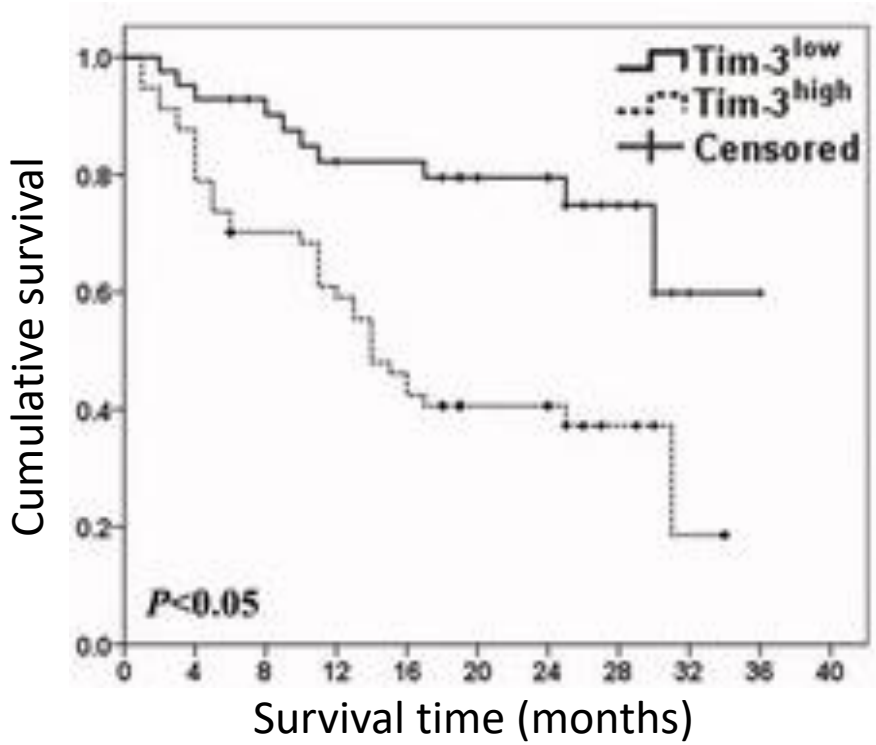
Trial ID	Targets	Drug arms	Status	N	Estimated completion
NCT03794440 (ORIENT-32)	PD-1, VEGF	• Sintilimab + bevacizumab biosimilar • Sorafenib	Active	566	Dec 2022
NCT03298451 (HIMALAYA)	CTLA-4, PD-L1	• Tremelimumab + durvalumab • Sorafenib	Active	1310	Jun 2021
NCT02576509 (Checkmate 459)	PD-1	• Nivolumab • Sorafenib	Result pending	726	July 2020
NCT03755739	PD-1	• Pembrolizumab • Peripheral vs hepatic infusion after TACE	Active	200	Nov 2021
NCT03062358 (KEYNOTE-394)	PD-1	• Pembrolizumab • Placebo	Active	450	Jan 2022
NCT03713593 (LEAP-002)	PD-1, VEGFR	• Pembrolizumab + Lenvatinib • Lenvatinib	Active	750	July 2022
NCT03847428 (EMERALD-2)	PD-L1, VEGF	• Durvalumab + bevacizumab • Combination with resection/MWA vs resection/MWA alone	Not yet recruiting	888	June 2023
NCT03764293	PD-1, TKI	• Camrelizumab + apatinib • Sorafenib	Not yet recruiting	510	Jan 2022
NCT03434379 (IMbrave150)	PD-L1, VEGF	• Atezolizumab + bevacizumab • Sorafenib	Active	480	June 2022

Johnston, World J Gastroenterology 2019.

In development: Other immunotherapy strategies for HCC

- Combinations with existing immune checkpoint inhibitors
- Alternative immune checkpoints
- Cellular therapies

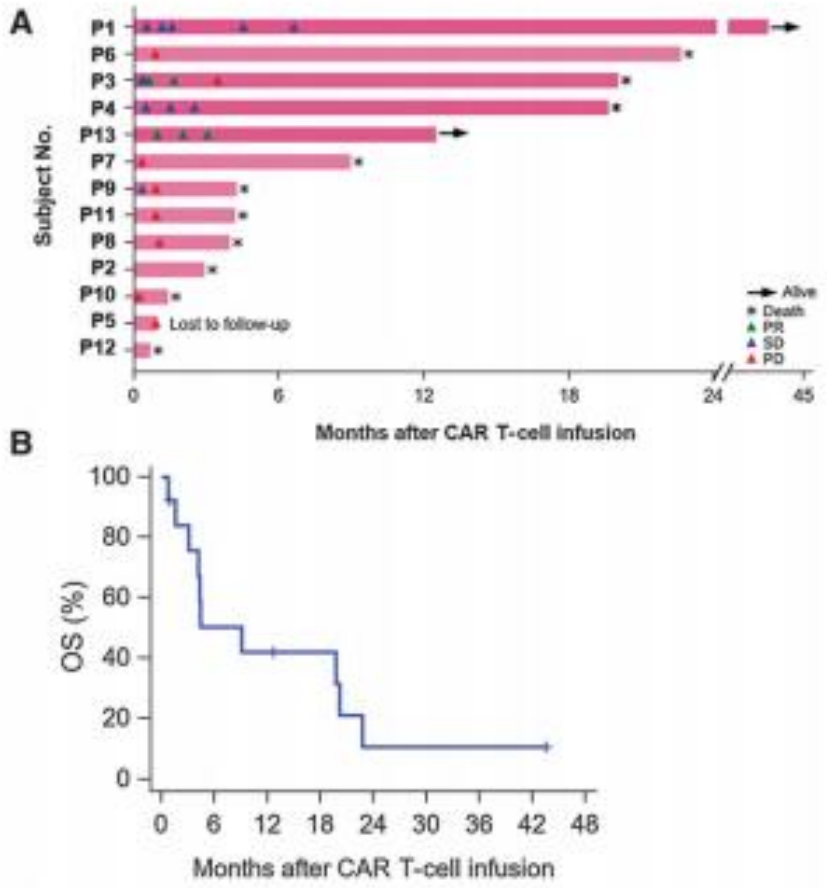
Trial	Intervention	Phase
NCT03680508	TSR-022 + TSR-042 (anti-TIM-3 + anti-PD-1)	2
NCT03652077	INCAGN02390 (anti-TIM-3)	1



Li, Hepatology 2012.

In development: Other immunotherapy strategies for HCC

- Combinations with existing immune checkpoint inhibitors
- Alternative immune checkpoints
- Cellular therapies
  - CAR-GPC3 T-cell therapy in patients with GPC+ HCC (Child Pugh A)
  - Other T-cell therapies in early phase clinical trials
    - Targeting NY-ESO-1, AFP, CD133, EpCAM, etc.



Shi, Clinical Cancer Research 2020

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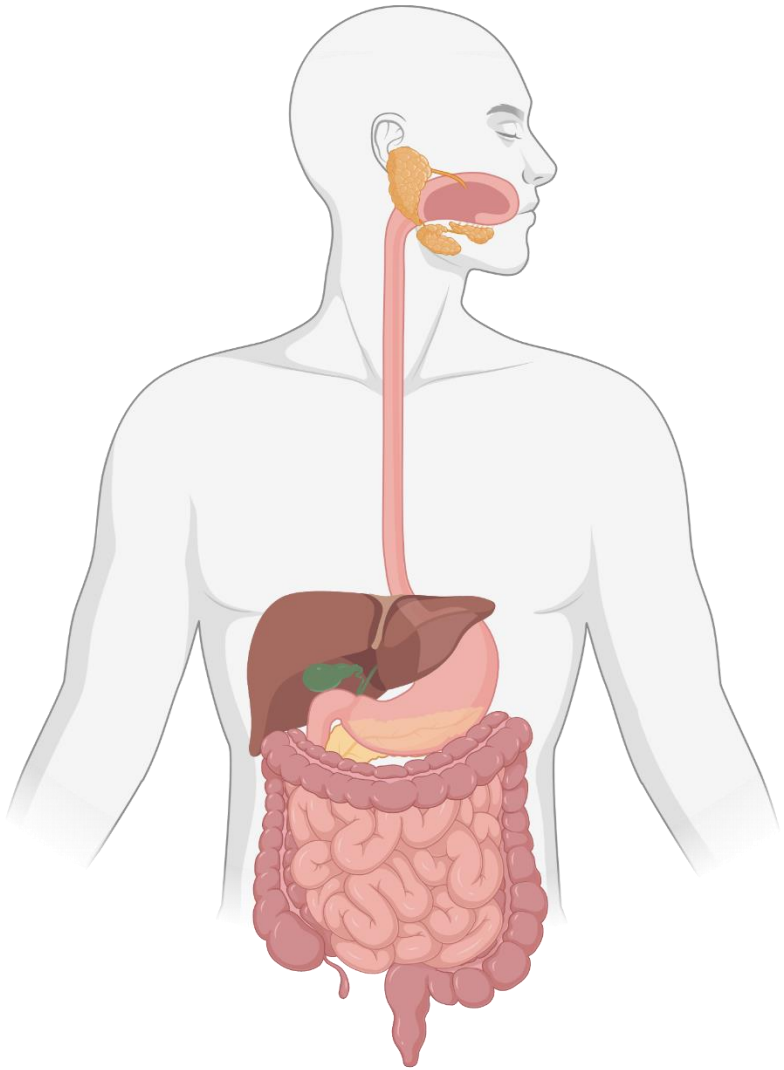
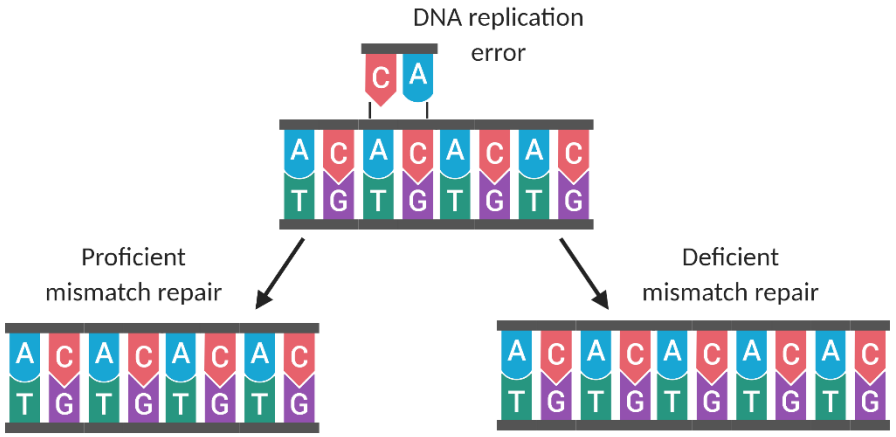
Outline

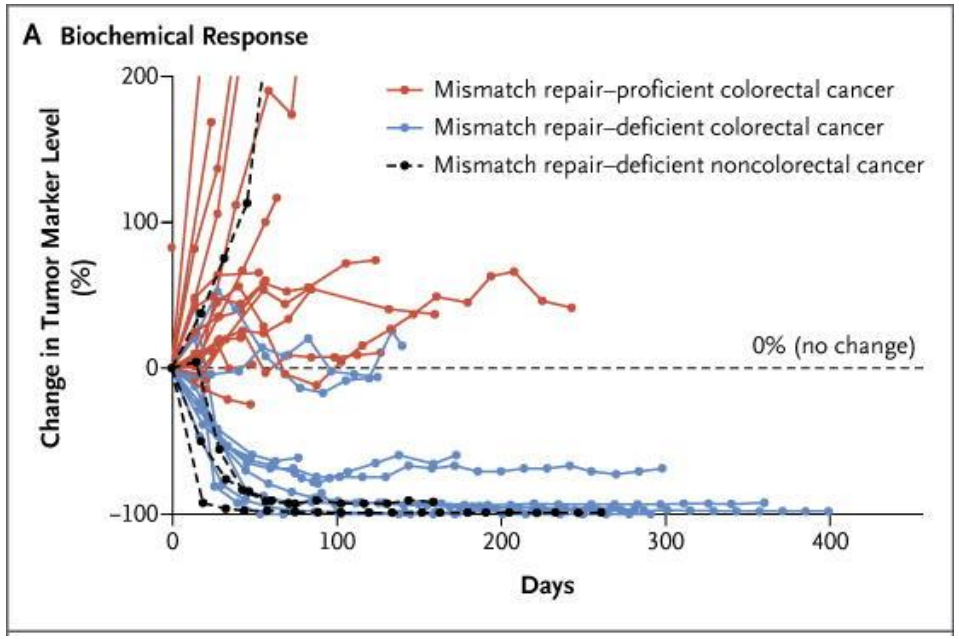
- Hepatocellular carcinoma
- Colorectal cancer
- Other GI malignancies



Colorectal cancer

- Categorized by microsatellite instability/mismatch repair status:
  - MSI-high/MMR-deficient: 15% (but 2-4% of metastatic CRC)
  - MSI-low/MMR-proficient: 85%





Le, N Engl J Med 2015

FDA approvals for colorectal cancer

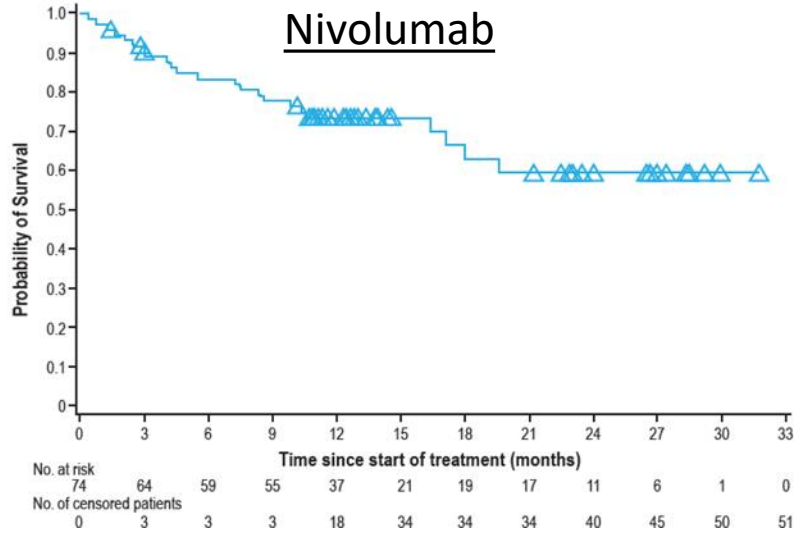
Drug	Approved	Indication	Dose
Nivolumab	2017	MSI-high/dMMR relapsed colorectal cancer following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan	240 mg Q2W or 480 mg Q4W
Nivolumab + ipilimumab	2018	MSI-high/dMMR relapsed/refractory colorectal cancer following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan	Nivo 3 mg/kg + ipi 1 mg/kg for 4 doses, then nivo maintenance
Pembrolizumab	2020	First-line MSI-high/dMMR colorectal cancer	200 mg Q3W or 400 mg Q6W

To date, all ICI approvals for CRC are for those with mismatch repair or microsatellite instability.

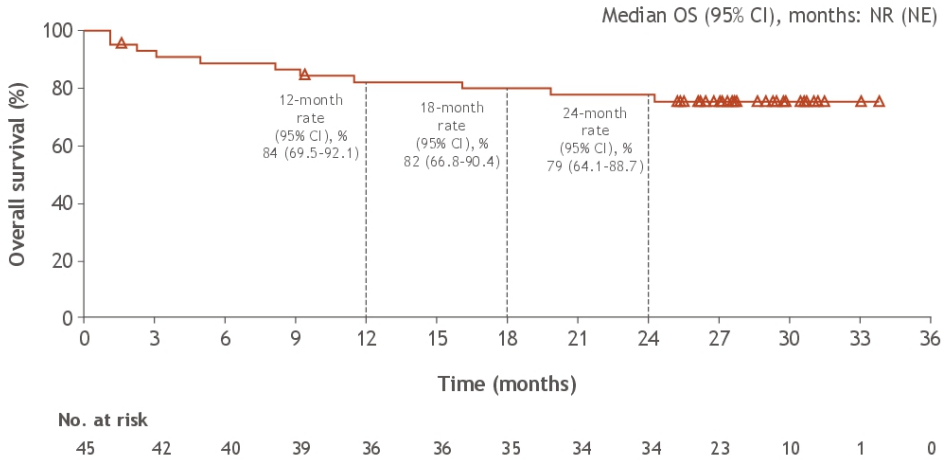
Efficacy of approved ICIs in CRC

Trial	Patient population	Treatment arm(s)	ORR	Landmark PFS	Landmark OS
CheckMate 142	MSI-H/dMMR CRC with progression on prior treatment	Nivolumab	31.1%	12-month: 50.4%	12-month: 73.4%
	MSI-H/dMMR CRC with progression on prior treatment	Nivolumab + ipilimumab	58%	24-month: 60%	24-month: 74%

Nivolumab



Nivolumab + ipilimumab



Andre, ASCO 2020; Overman, Lancet Oncol 2017; Overman, ASCO-GI 2019.

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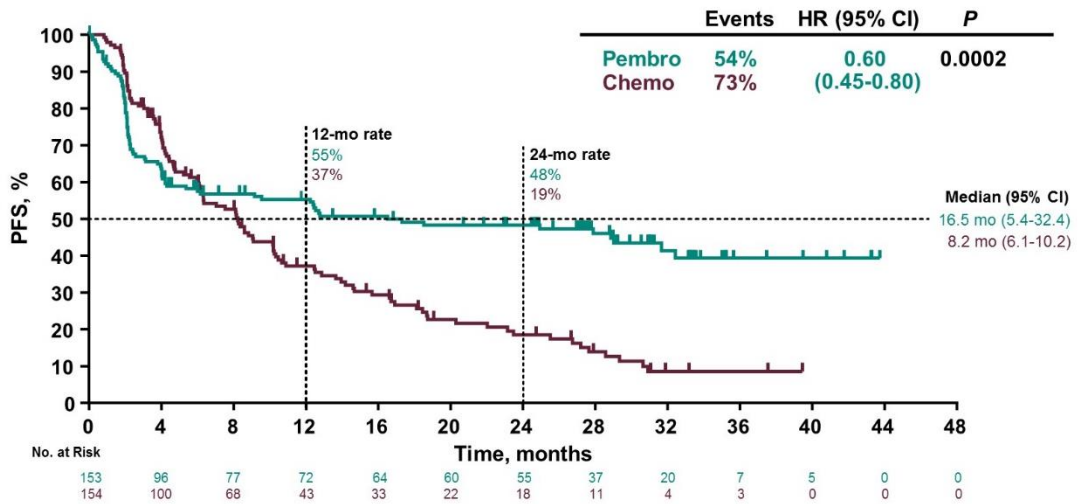
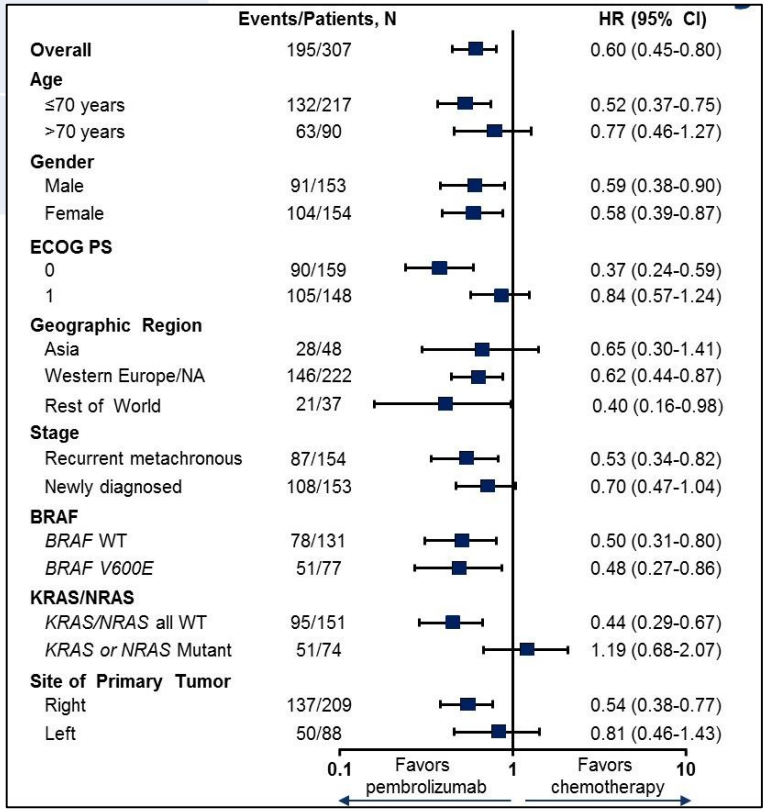
Efficacy of approved ICIs in CRC

Trial	Patient population	Treatment arm(s)	ORR	Landmark PFS	Landmark OS
KEYNOTE-177	Untreated, unresectable/metastatic MSI-H/dMMR CRC	Pembrolizumab	43.8 %	Median: 16.5 months	-
		Investigator's choice	33.1 %	Median: 8.2 months	-





Andre, ASCO 2020; Overman, Lancet Oncol 2017; Overman, ASCO-GI 2019.

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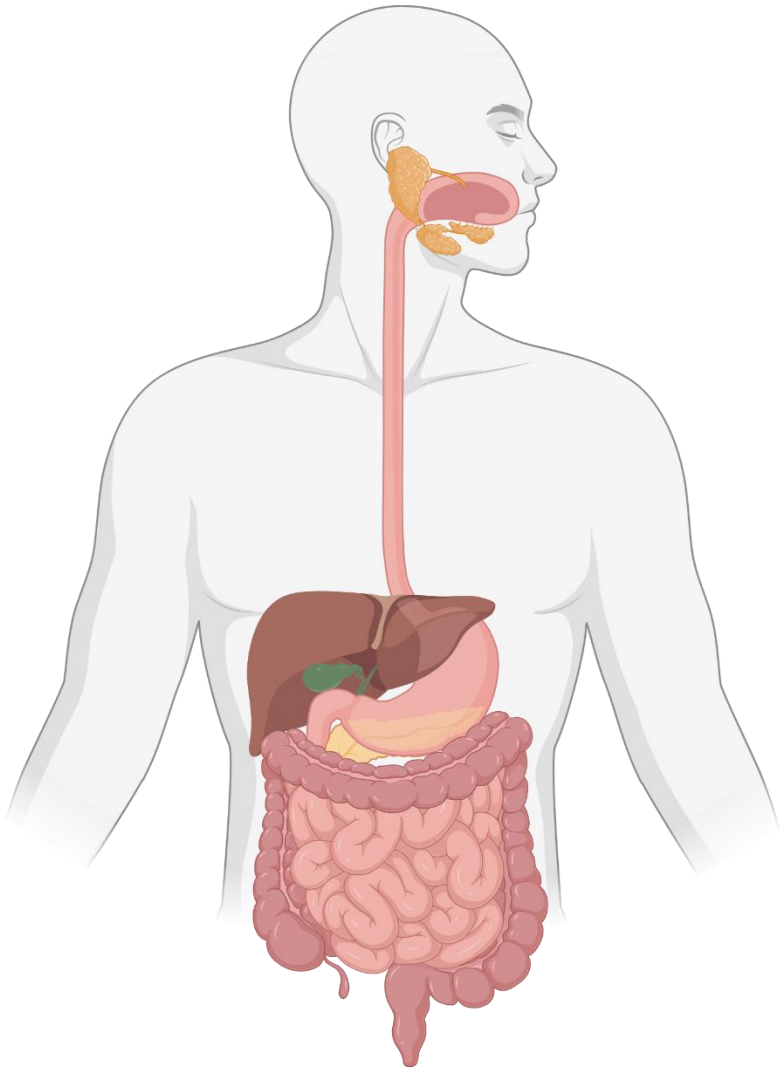
In development: Immunotherapy for MSS/pMMR CRC

Clinical trial number	Patient population	Treatment(s)	Treatment type(s)
NCT04262687	1st-line MSS/pMMR, high immune infiltrate, metastatic CRC	Pembrolizumab + XELOX + bevacizumab	Anti-PD-1 + chemotherapy + anti-angiogenic
NCT04108481	Liver-predominant, MSS/pMMR CRC with 2 prior therapies	Durvalumab + ^{90}Y embolization	Anti-PD-L1 + radiotherapy
NCT03832621	MSS, MGMT-silenced metastatic CRC	Nivolumab + ipilimumab + temozolamide	Anti-PD-1 + anti-CTLA-4 + chemotherapy
NCT03993626	Previously treated MSS CRC	CXD101 + nivolumab	HDAC inhibitor + anti-PD-1
NCT04044430	Previously treated MSS, BRAF V600E metastatic CRC	Nivolumab + encorafenib + binimetinib	Anti-PD-1 + MEK inhibitor + BRAF inhibitor
NCT04301011	MSS CRC with progression on prior therapies	Pembrolizumab + TBio-6517	Anti-PD-1 + oncolytic virus
NCT03639714	MSS CRC with progression on prior therapy	Nivolumab + ipilimumab + GRT-C901 + GRT-R902	Anti-PD-1 + anti-CTLA-4 + neoantigen vaccines
NCT04126733	MSS CRC with progression on prior therapy	Nivolumab + regorafenib	Anti-PD-1 + multi-kinase inhibitor

Outline

- Hepatocellular carcinoma
- Colorectal cancer
- Other GI malignancies



FDA approvals for other GI cancers

Drug	Approved	Indication	Dose
Pembrolizumab	2017	Previously treated PD-L1+ advanced/recurrent **gastric or gastroesophageal junction cancer**	200 mg Q3W or 400 mg Q6W
Pembrolizumab	2019	Previously treated PD-L1+ recurrent/advanced/metastatic **squamous cell carcinoma of the esophagus**	200 mg Q3W or 400 mg Q6W
Nivolumab	2020	**Esophageal squamous cell carcinoma** after previous chemotherapy	240 mg Q2W or 480 mg Q4W

Efficacy of approved checkpoint inhibitors

Trial	Patient population	Treatment arm(s)	ORR	Median PFS (months)	Median OS (months)
KEYNOTE-059	Previously treated gastric/gastroesophageal cancer	Pembrolizumab	ITT: 11.6% PD-L1+: 15.5%	ITT: 2.0 PD-L1+: 2.1	ITT: 5.6 PD-L1+: 5.8
KEYNOTE-180	Advanced/metastatic esophageal squamous cell carcinoma after 2 prior therapies	Pembrolizumab	ITT: 14.3% PD-L1+: 20%	2.1	6.8
KEYNOTE-181	Advanced/metastatic esophageal squamous cell carcinoma after 1 prior therapy	Pembrolizumab	22%	3.2	ITT: 8.2 PD-L1+: 10.3
		Chemotherapy	7%	2.3	ITT: 7.1 PD-L1+: 6.7
ATTRACTION-3	Advanced/metastatic esophageal squamous cell carcinoma after prior therapy	Nivolumab	19.3%	HR: 1.1	10.9
		Chemotherapy	21.5%		8.4

Fuchs, JAMA Oncol 2018; Shah, JAMA Oncol 2018; Metges, ESMO GI 2019; Kato, Lancet Oncol 2019.

Conclusions

- Immune checkpoint inhibitors are beginning to fill the need for systemic therapies in hepatocellular carcinoma
- To date, only MSI-high/MMR-deficient colorectal cancers have approved immunotherapy options
- For gastric, gastroesophageal, and esophageal cancers, PD-L1 expression is important for checkpoint inhibitor responses
- Future directions for all indications include combination therapies

Acknowledgements

- Some figures created using biorender.com

Case Studies

Case: MSI-H Colon Cancer

- 90 yo female in excellent performance status and without major comorbidities.
- November 2018: Presented with iron deficient anemia. Colonoscopy revealed ascending colon mass, biopsy confirms invasive adenocarcinoma. CT staging without distant metastases.
- December 20, 2018: Right hemicolectomy. Pathology revealed 4.6 cm moderately differentiated adenocarcinoma of the cecum with visceral peritoneal invasion. Negative margins. LVI identified. 5/26 lymph nodes involved with malignancy. 3 tumor deposits on the small bowel noted and resected. pT4a pN2a pM1b. Molecular studies reveal MSI-H/dMMR, BRAF V600E mutation.
- January 28, 2019: CT scans without evidence of residual disease.

Case: MSI-H Colon Cancer

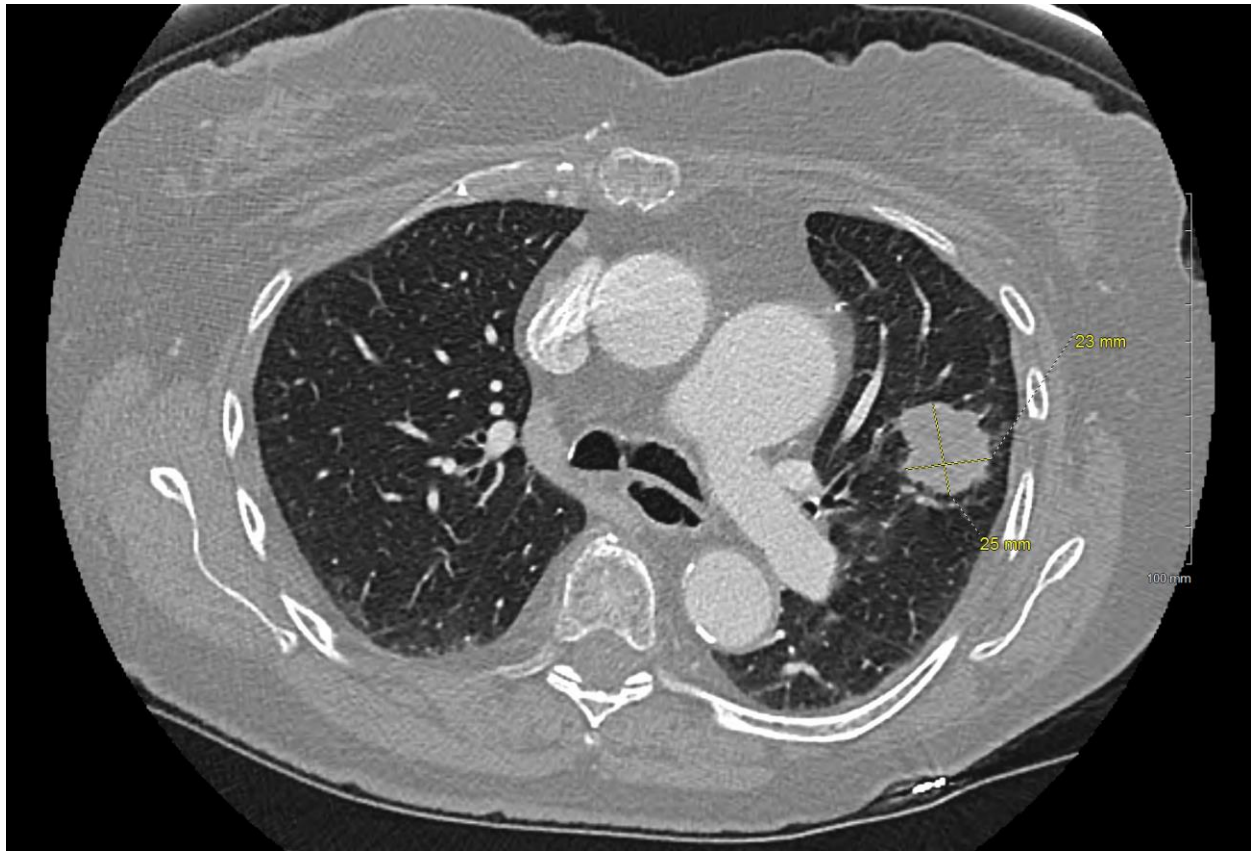
Questions to consider:

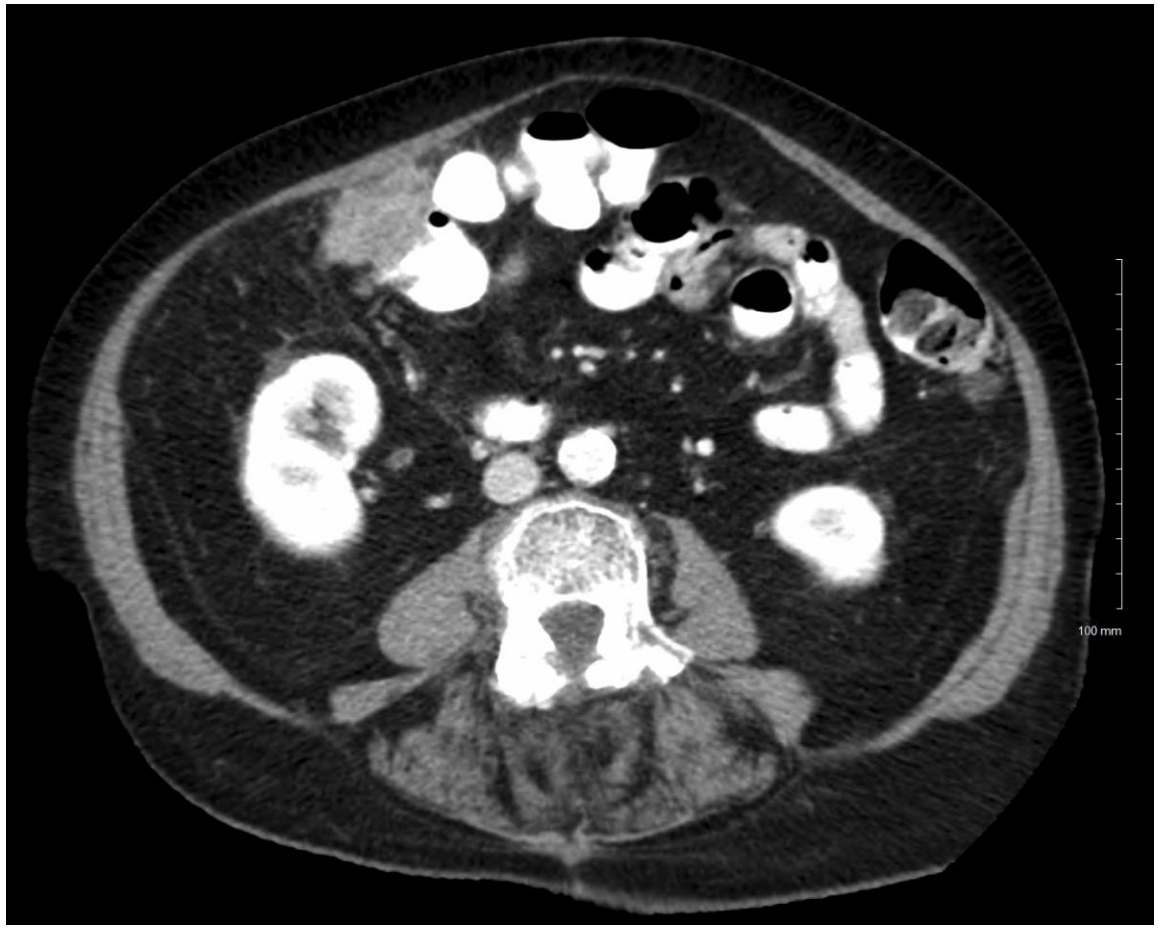
- Adjuvant therapy?
  - Fluoropyrimidine alone of low value in MSI-H/dMMR cancers
  - Oxaliplatin-based therapy in a 90 yo patient?
  - Are we truly talking about “adjuvant therapy” to begin with since it is truly resected stage 4 disease?
- Is there a role for immunotherapy at this point in time?
- Can the recurrence risk be assessed by ctDNA and can ctDNA as marker of MRD help in the surveillance phase?

Case: MSI-H Colon Cancer

- January 28, 2019: CT scans without evidence of residual disease. Start adjuvant capecitabine
- June 7, 2019: Colvera test negative
- July 17, 2019: Finished 6 months of adjuvant capecitabine
- September 14, 2020: Signatera positive (9.9 MTM/mL)
- October 26, 2020: CT CAP with 2.6 x 2.6 x 2.2 cm LUL nodule, 4 x 2.7 x 3.4 cm ascending colon mass, omental metastasis and 8-9 mm liver lesion, potentially hemangioma.
- November 9, 2020: First presentation at West Cancer Center. CEA 51.3

October 26, 2020 – outside CT scan





Case: MSI-H Colon Cancer

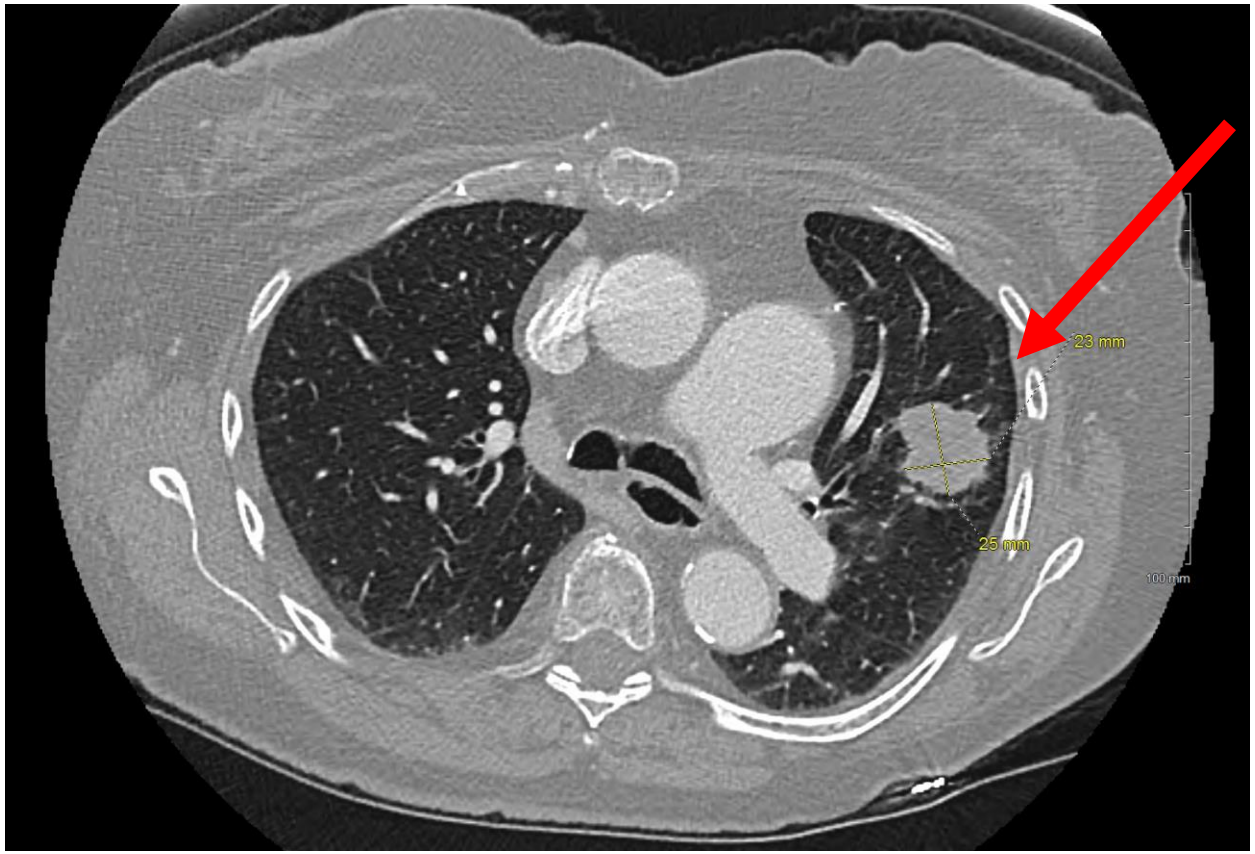
Questions to consider:

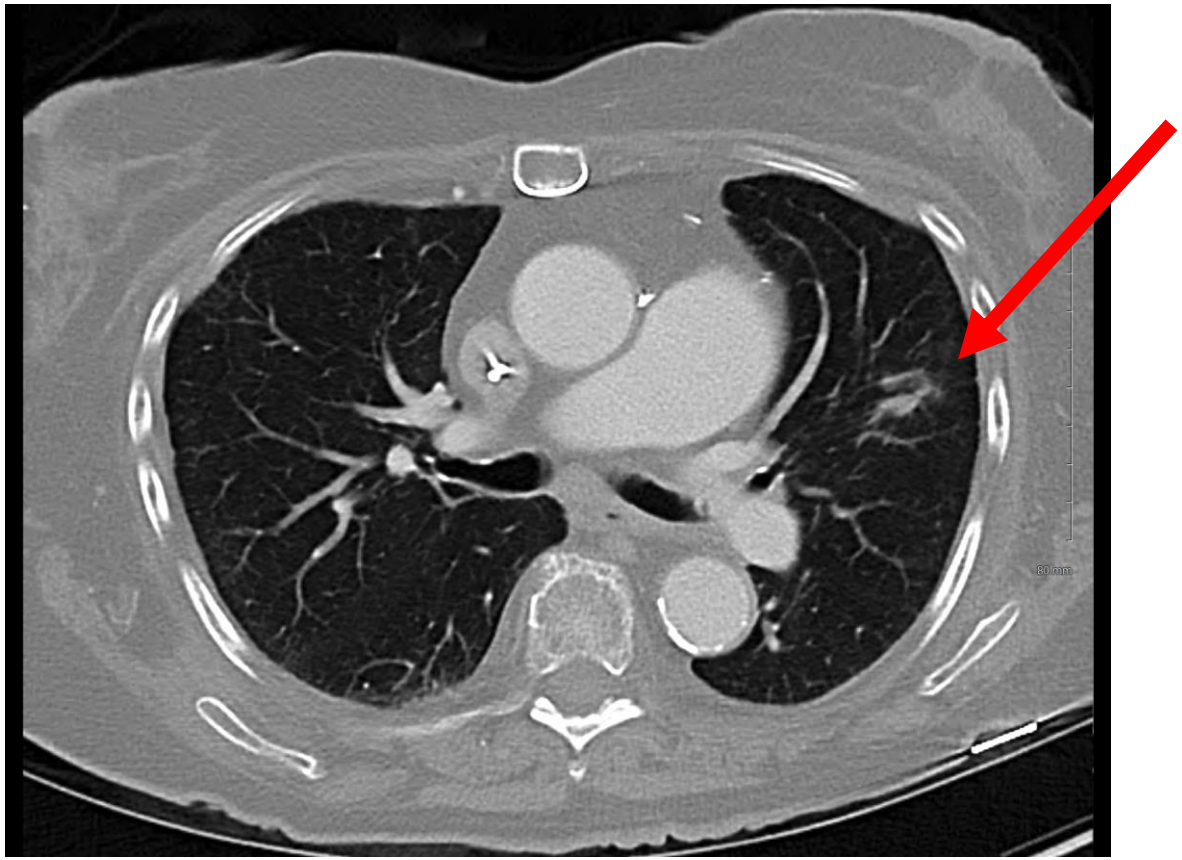
- Best first-line therapy?
  - Chemotherapy?
  - Targeting BRAF mutation (BEACON)?
  - IO therapy?
    - Pembrolizumab single agent
    - Nivolumab/ Ipilimumab

Case: MSI-H Colon Cancer

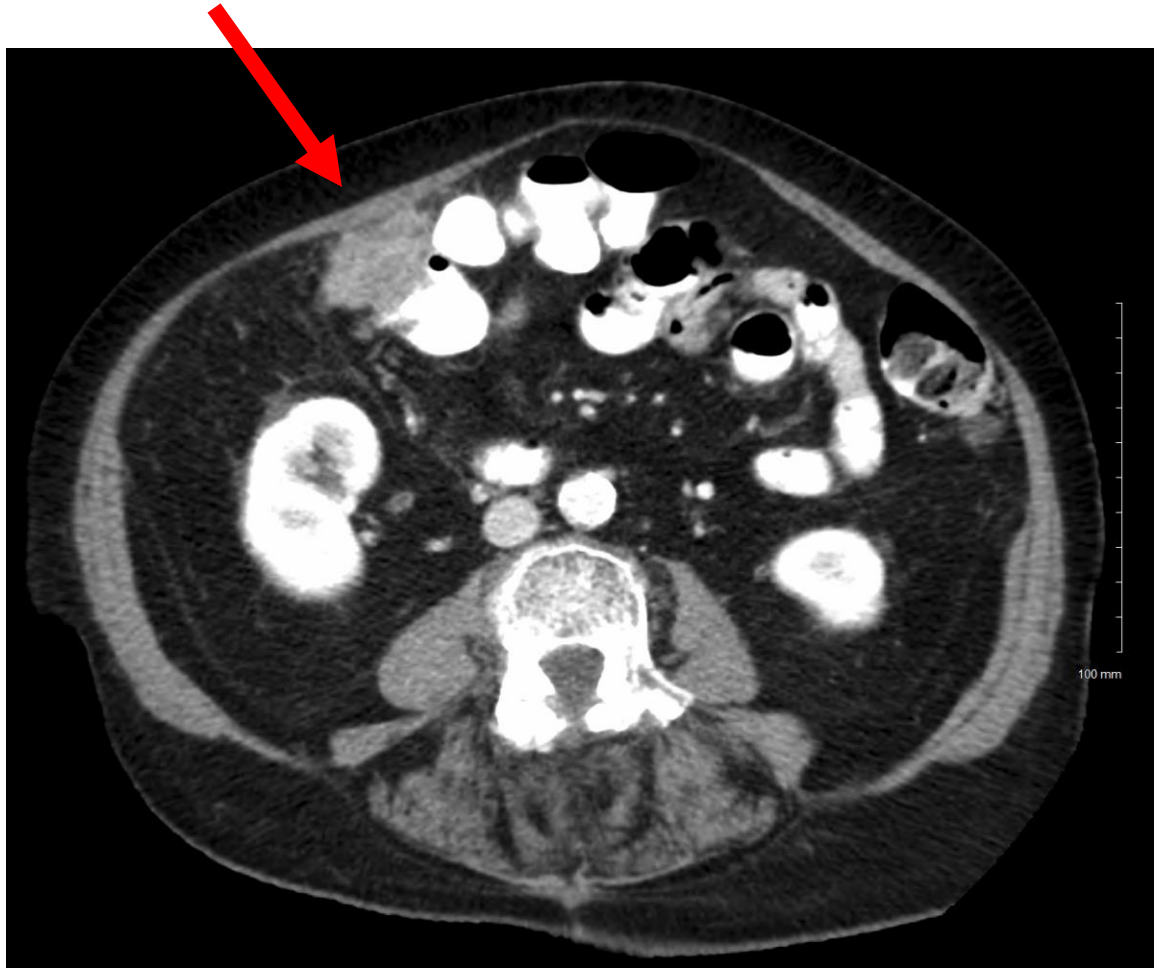
- November 9, 2020: First presentation at West Cancer Center.
- December 8, 2020: Start systemic therapy with pembrolizumab single agent,
  200 mg every 3 weeks. CEA 60.9

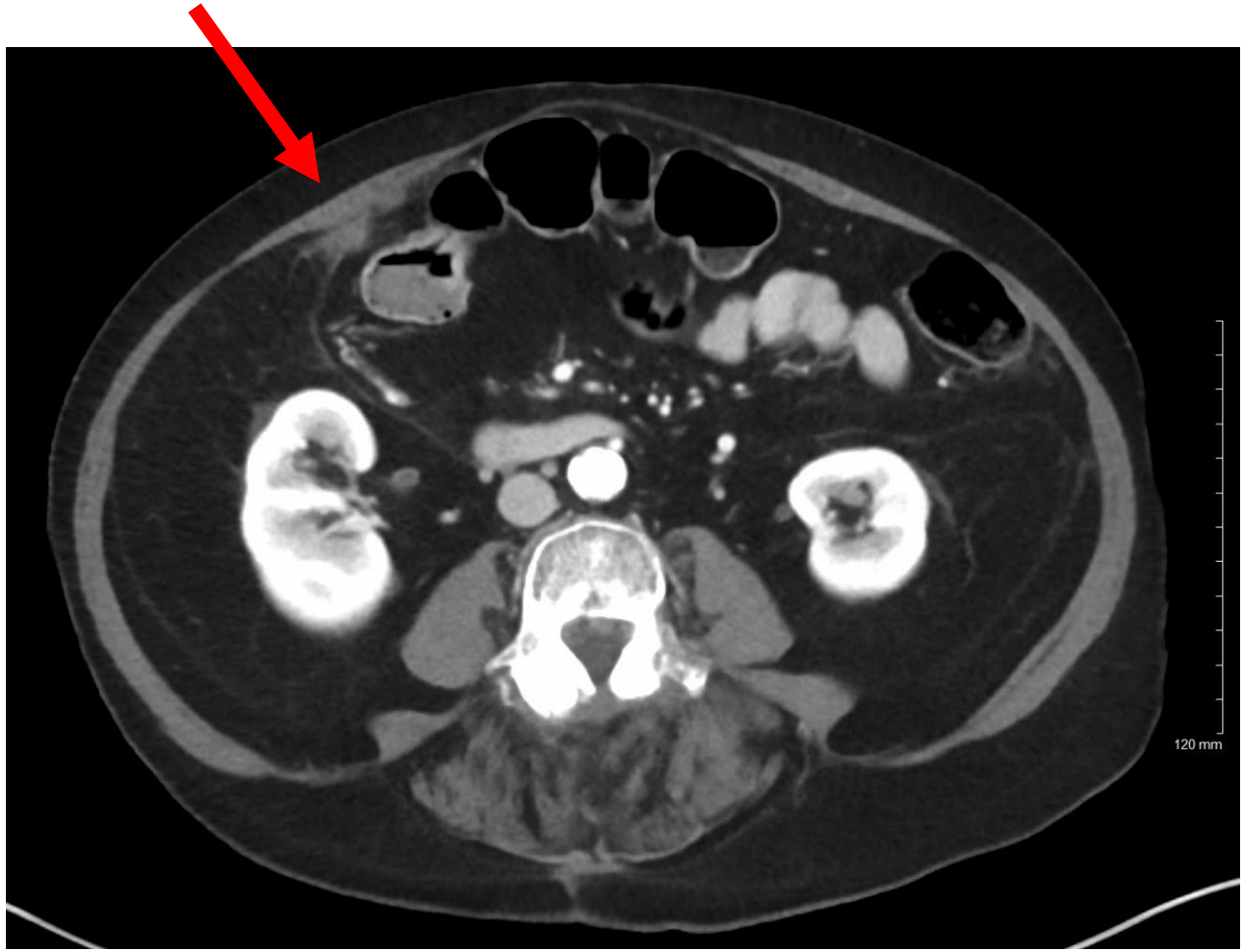
October 2020 -> February 2021





October 2020 -> February 2021





Case: MSI-H Colon Cancer

- December 8, 2020: Start systemic therapy with pembrolizumab single agent,
  200 mg every 3 weeks. CEA 60.9
- February 10, 2021: CT scan of the chest, abdomen, and pelvis reveals a 50 to 70% decrease in the left upper lobe metastases, 70 to 90% decrease in omental metastases and evidence of disease response in the liver as well. CEA 11.6
- Excellent tolerability of therapy – no side-effects