Novel and Emerging Therapeutic Strategies in the Management of Select Gastrointestinal Cancers

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Disclosures

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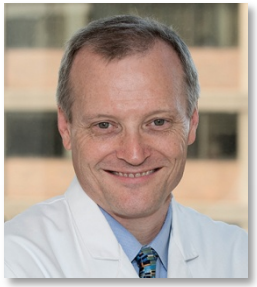

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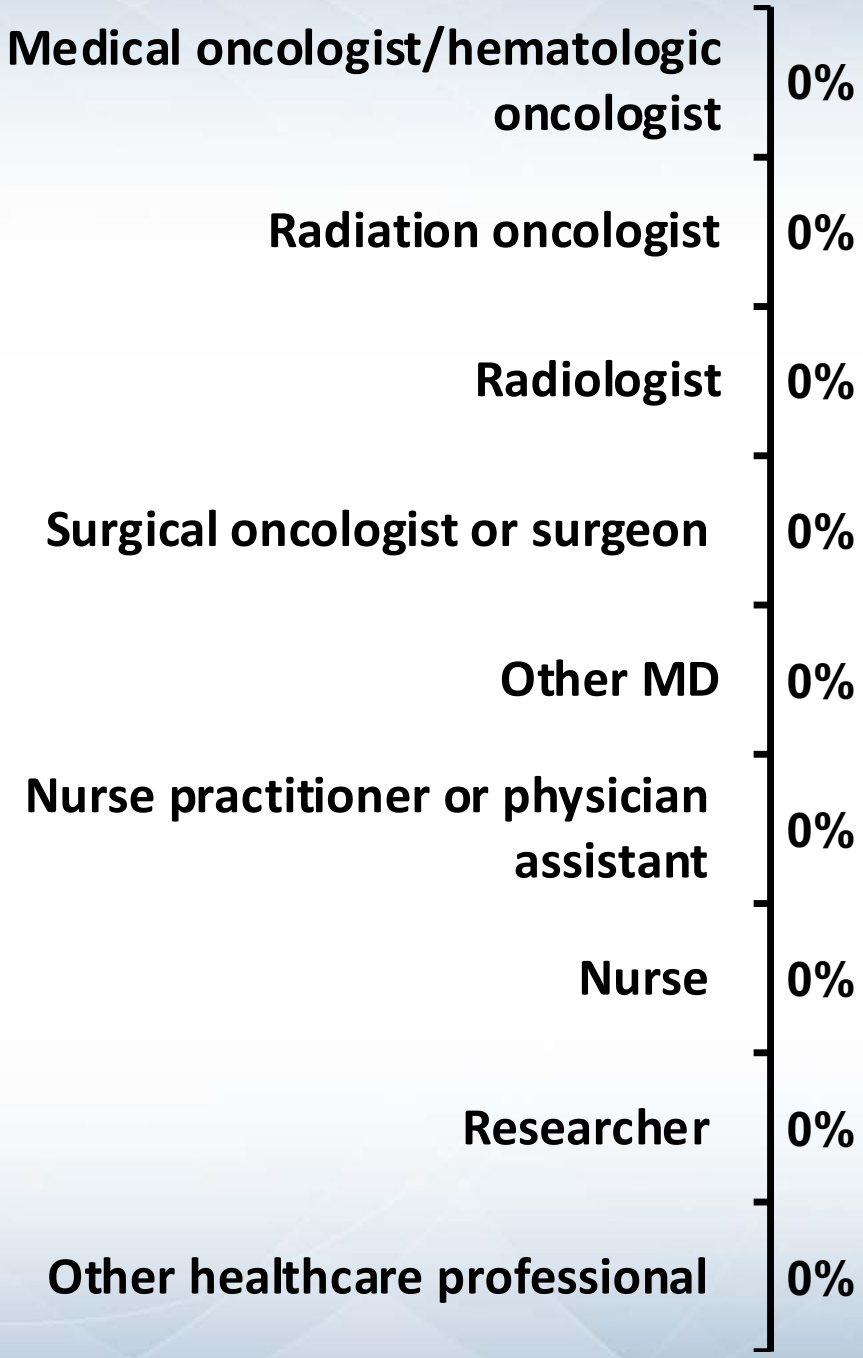
Which of the following best represents your clinical background?

1. Medical oncologist/hematologic oncologist
2. Radiation oncologist
3. Radiologist
4. Surgical oncologist or surgeon
5. Other MD
6. Nurse practitioner or physician assistant
7. Nurse
8. Researcher
9. Other healthcare professional



Novel and Emerging Therapeutic Strategies in the Management of Select Gastrointestinal Cancers

Module 1: Colorectal Cancer

- Primary tumor sidedness and selection of first-line therapy
- Sequencing of available therapies in the second line and beyond
- Novel targeted approaches

Module 2: Hepatocellular Carcinoma

- First-line systemic treatment: Sorafenib versus lenvatinib
- Beyond first-line therapy: Cabozantinib, ramucirumab, regorafenib and anti-PD-1/PD-L1 antibodies

Module 3: Pancreatic Cancer

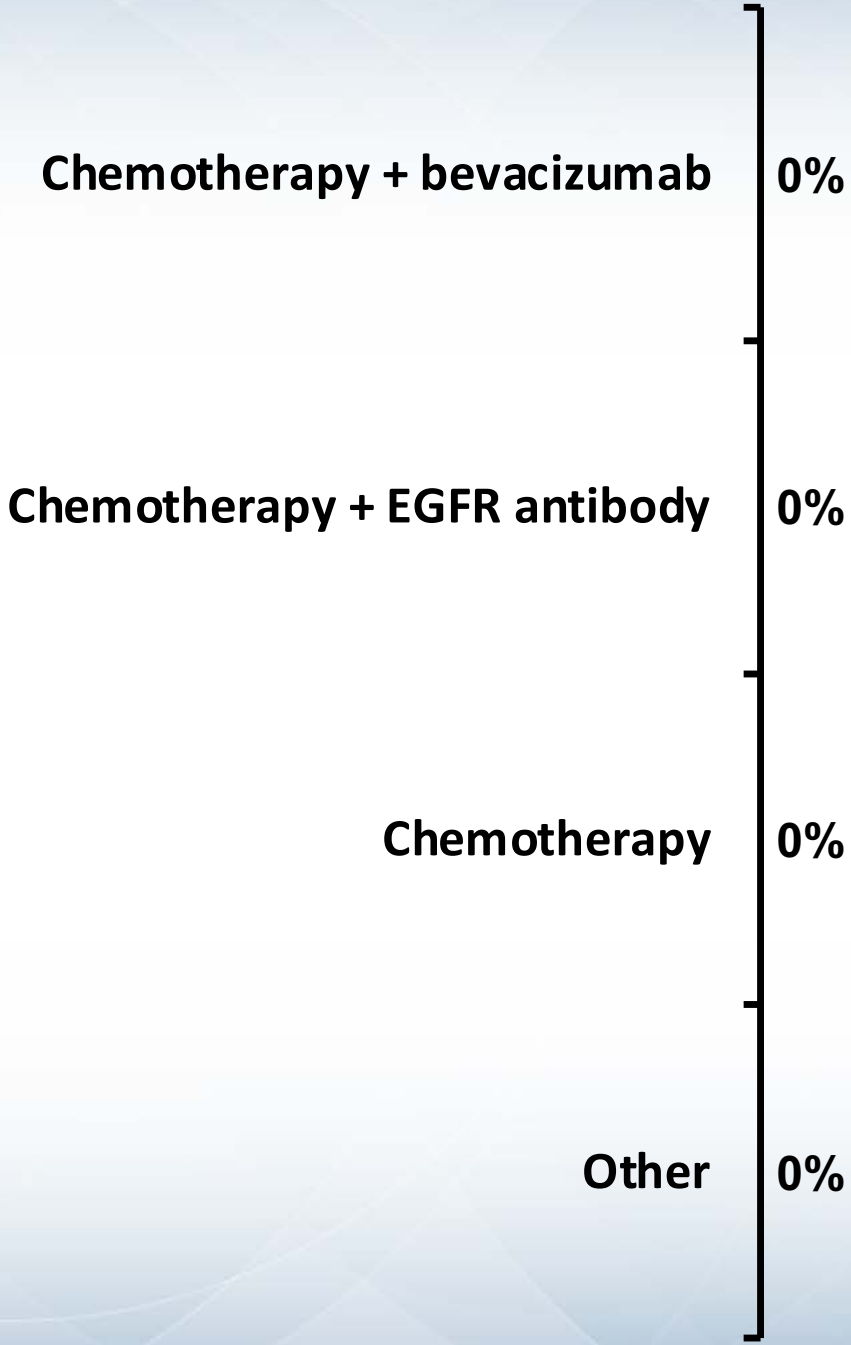
- Neoadjuvant and adjuvant therapy approaches
- Management of metastatic disease and integration of nanoliposomal irinotecan
- BRCA mutations and PARP inhibition

Module 4: Gastric/Gastroesophageal Junction (GEJ)/Esophageal Cancer

- Pembrolizumab for the treatment of recurrent or advanced gastric, GEJ and esophageal cancer
- Efficacy and safety of TAS-102 for recurrent metastatic gastric or GEJ adenocarcinoma

What is your usual first-line treatment strategy for a 65-year-old patient with left-sided, microsatellite-stable (MSS), pan-RAS wild-type metastatic colorectal cancer (mCRC)?

1. **Chemotherapy + bevacizumab**
2. **Chemotherapy + EGFR antibody**
3. **Chemotherapy**
4. **Other**



What is your usual first-line treatment strategy for a 65-year-old patient with left-sided, microsatellite-stable (MSS), pan-RAS wild-type metastatic colorectal cancer (mCRC)?

 TANIOS BEKAII-SAAB, MD	FOLFIRI + bevacizumab
 JOHANNA BENDELL, MD	FOLFIRI + EGFR antibody
 HOWARD S HOCHSTER, MD	FOLFOX + bevacizumab
 JOHN L MARSHALL, MD	CAPOX + bevacizumab
 EILEEN M O'REILLY, MD	FOLFOXIRI + bevacizumab
 PHILIP A PHILIP, MD, PHD	Chemotherapy + bevacizumab
 ALAN P VENOOK, MD	FOLFIRI *or* FOLFOXIRI ± bevacizumab

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How would you compare the global antitumor efficacy of chemotherapy/bevacizumab and chemotherapy/EGFR antibody as first-line therapy for left-sided, MSS, pan-RAS wild-type mCRC?

Do you administer EGFR antibodies to patients with right-sided mCRC?

	Efficacy of chemo/bev vs chemo/EGFR Ab	EGFR Ab for right-sided mCRC?
 TANIOS BEKAII-SAAB, MD	Chemo/EGFR Ab somewhat more efficacious	Yes, 3rd line and beyond
 JOHANNA BENDELL, MD	Chemo/EGFR Ab somewhat more efficacious	Yes, 3rd line and beyond
 HOWARD S HOCHSTER, MD	Efficacy about the same	No
 JOHN L MARSHALL, MD	Chemo/EGFR Ab somewhat more efficacious	Yes, 3rd line and beyond
 EILEEN M O'REILLY, MD	Chemo/EGFR Ab somewhat more efficacious	Yes, 3rd line and beyond
 PHILIP A PHILIP, MD, PHD	Chemo/EGFR Ab somewhat more efficacious	Yes, 2nd line
 ALAN P VENOOK, MD	Chemo/EGFR Ab somewhat more efficacious	No

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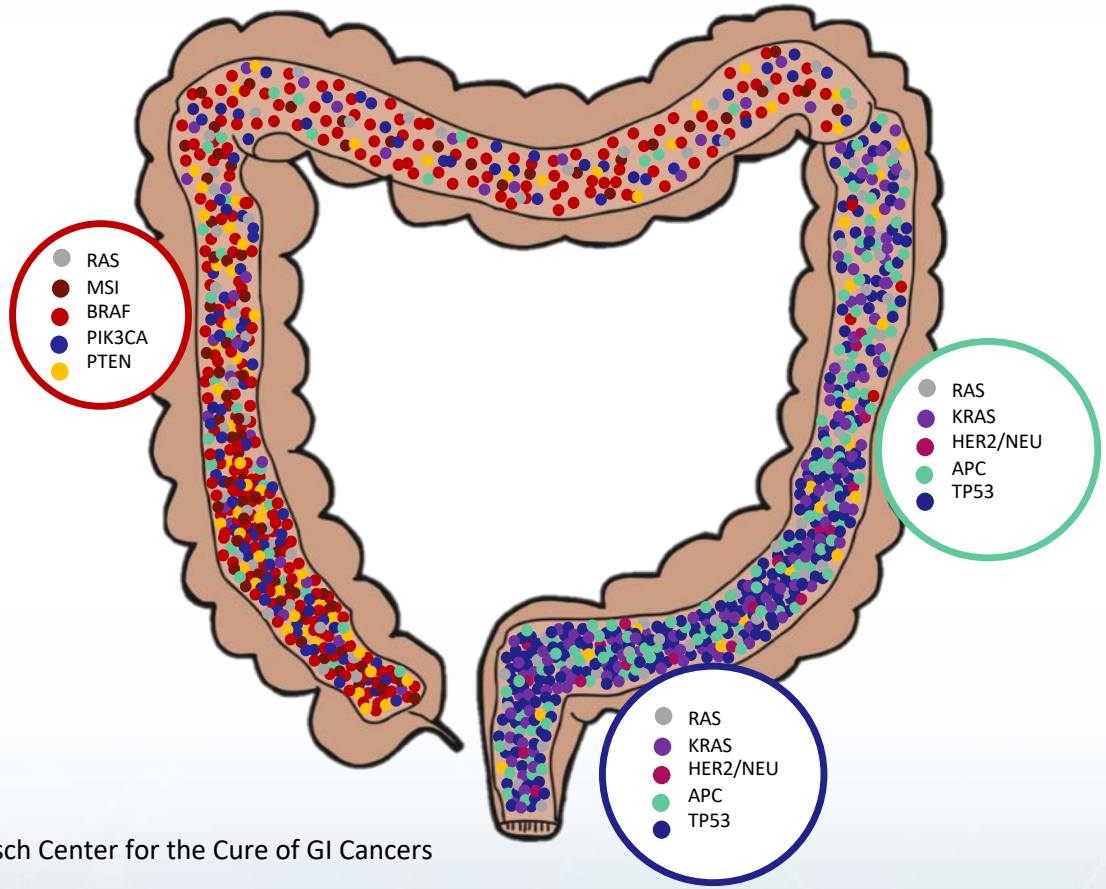
Tumor Sidedness Associated with Genetic Alterations



Venook A et al. *Proc ASCO* 2016;Abstract 3504.

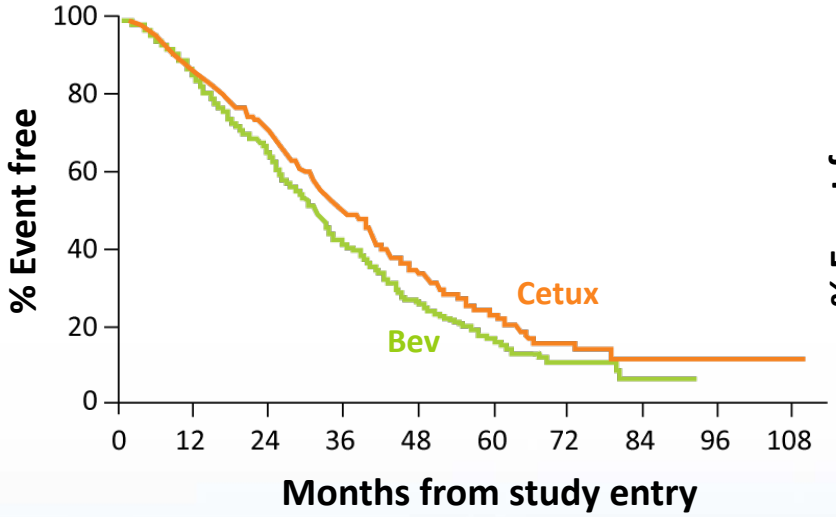
CALGB/SWOG-80405: Overall Survival by Biologic Agent and Primary Tumor Sidedness

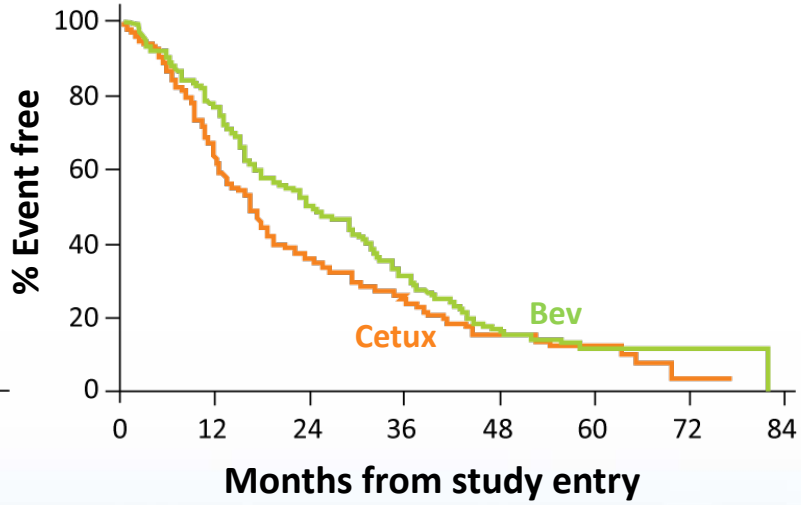
Left-sided primary

Agent	N	Median	HR	*p*-value
Bev	356	31.4 mo	0.817	0.018
Cetux	376	36.0 mo		

Right-sided primary

Agent	N	Median	HR	*p*-value
Bev	150	24.2 mo	1.269	0.065
Cetux	143	16.7 mo		





Venook A et al. *Proc ASCO* 2016;Abstract 3504.

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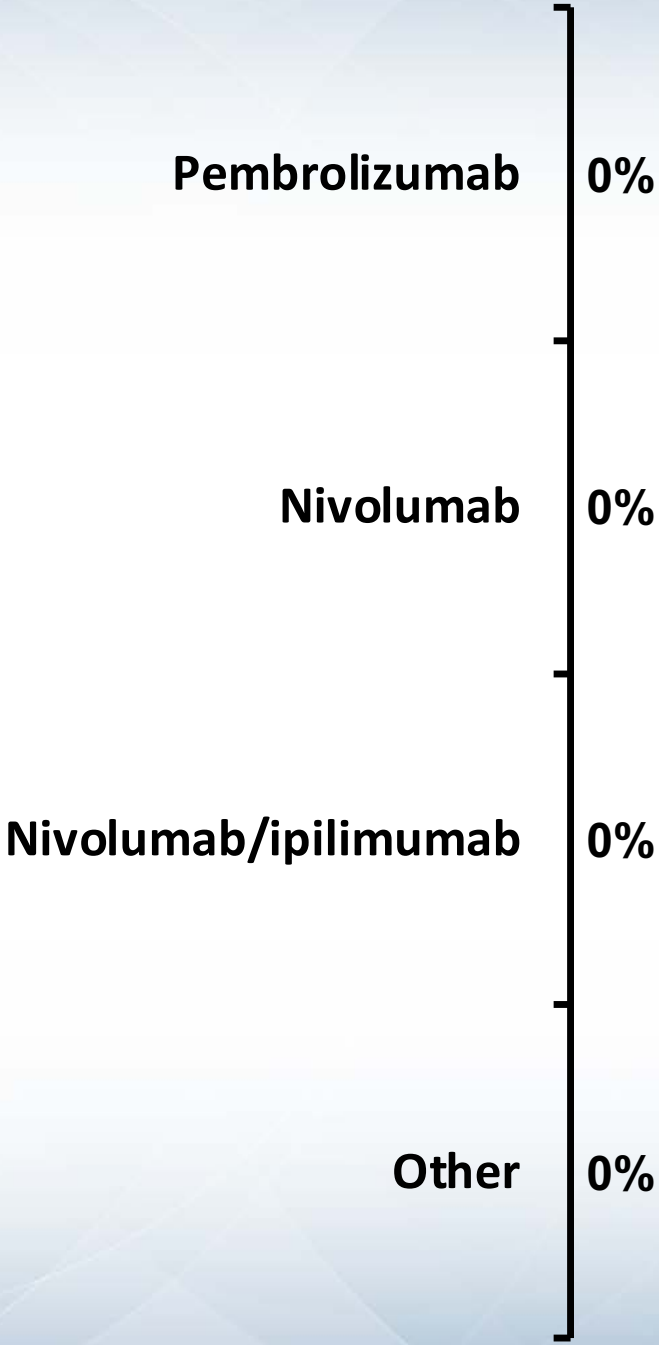
For a younger, otherwise healthy patient with MSI-high mCRC for whom you are planning to administer immune checkpoint inhibitor therapy, which agent or regimen would you most likely recommend?

1. **Pembrolizumab**
2. **Nivolumab**
3. **Nivolumab/ipilimumab**
4. **Other**



For a younger, otherwise healthy patient with MSI-high mCRC for whom you are planning to administer immune checkpoint inhibitor therapy, which agent or regimen would you most likely recommend?

In which line of therapy would you like to use an anti-PD-1/PD-L1 antibody?

	Agent or regimen	Preferred line
 TANIOS BEKAII-SAAB, MD	Pembrolizumab	First line
 JOHANNA BENDELL, MD	Nivolumab/ipilimumab	First line
 HOWARD S HOCHSTER, MD	Nivolumab/ipilimumab	Second line
 JOHN L MARSHALL, MD	Pembrolizumab	First line
 EILEEN M O'REILLY, MD	Nivolumab/ipilimumab	First line
 PHILIP A PHILIP, MD, PHD	Nivolumab/ipilimumab	Second Line
 ALAN P VENOOK, MD	Nivolumab	Second line

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FDA Approvals and Indications for MSI-H or dMMR Solid Tumors or mCRC

Agent, approval date	Indication	Objective response rate
Pembrolizumab May 23, 2017	Adult and pediatric patients with unresectable or metastatic, MSI-H or dMMR solid tumors that have progressed after treatment who have no satisfactory alternative treatment options OR with MSI-H or dMMR mCRC that has progressed after treatment with a fluoropyrimidine, oxaliplatin and irinotecan	39.6%
Nivolumab July 31, 2017	Patients 12 years and older with dMMR and MSI-H mCRC that has progressed after treatment with a fluoropyrimidine, oxaliplatin and irinotecan	28%
Nivolumab + ipilimumab July 10, 2018	Patients 12 years and older with dMMR and MSI-H mCRC that has progressed after treatment with a fluoropyrimidine, oxaliplatin and irinotecan	46%

MSI-H = microsatellite instability high; dMMR = deficient mismatch repair

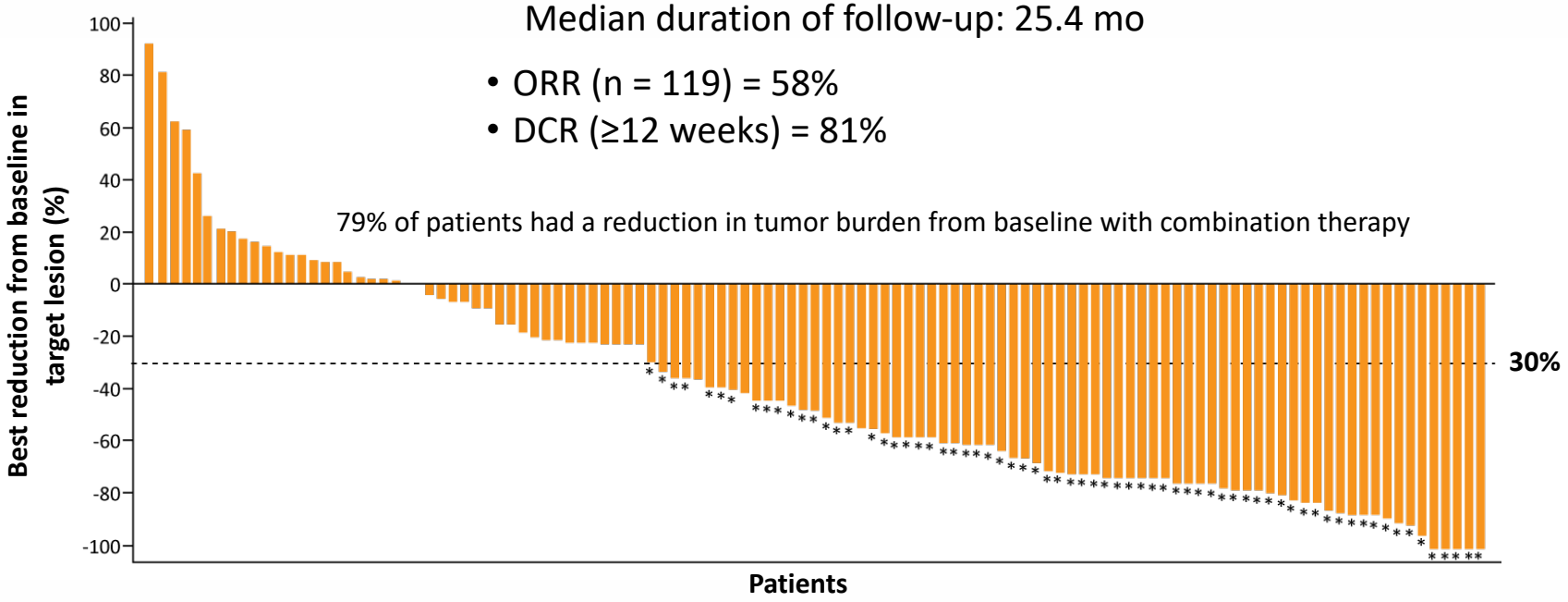
https://www.accessdata.fda.gov; Accessed July 10, 2019.

CheckMate 142: Long-Term Follow-Up of Nivolumab + Low-Dose Ipilimumab in Previously Treated dMMR/MSI-H mCRC

Nivo (3 mg/kg) + ipi (1 mg/kg) q3w x 4, then nivo (3 mg/kg) q2w until disease progression

Median duration of follow-up: 25.4 mo

- ORR (n = 119) = 58%
- DCR (≥12 weeks) = 81%



Patients had target lesion at baseline and at least 1 on-treatment tumor assessment.

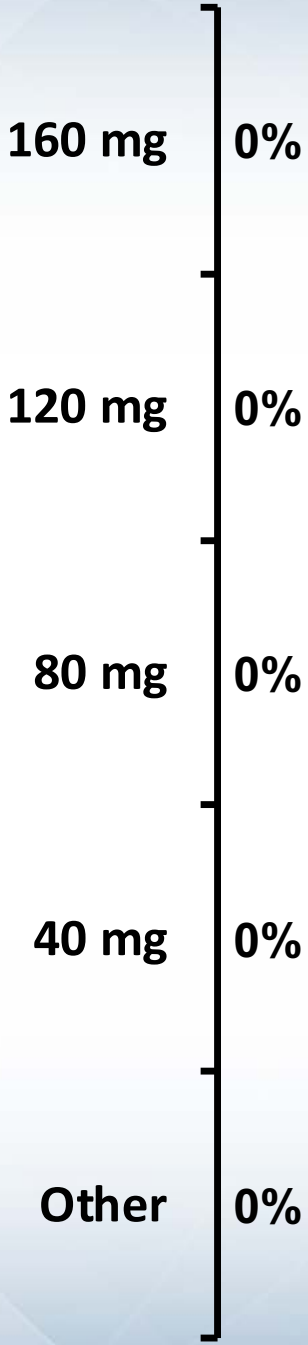
* Confirmed response per investigator assessment

- Select Grade 3/4 treatment-related AEs:
  - Elevated AST (8%), diarrhea (3%), pruritus (2%), fatigue (2%)

Overman MJ et al. Gastrointestinal Cancers Symposium 2019;Abstract 635.

In general, for a younger patient with mCRC, what is your usual starting dose of regorafenib?

1. 160 mg
2. 120 mg
3. 80 mg
4. 40 mg
5. Other



In general, for a younger patient with mCRC, what is your usual starting dose of regorafenib?

 TANIOS BEKAII-SAAB, MD	80 mg
 JOHANNA BENDELL, MD	120 mg
 HOWARD S HOCHSTER, MD	80 mg
 JOHN L MARSHALL, MD	80 mg
 EILEEN M O'REILLY, MD	120 mg
 PHILIP A PHILIP, MD, PHD	120 mg
 ALAN P VENOOK, MD	120 mg

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What would be your third-line treatment recommendation for a 65-year-old patient with right-sided, MSS, pan-RAS wild-type mCRC who is experiencing disease progression after first-line FOLFOX/bev and second-line FOLFIRI/bev (PS 0)?

If the patient had a RAS mutation and PS 0 or PS 1-2?

	Pan-RAS WT, PS 0	RAS mutation, PS 0	RAS mutation, PS 1-2
 TANIOS BEKAII-SAAB, MD	Regorafenib	Regorafenib	Regorafenib or TAS 102 – coin flip
 JOHANNA BENDELL, MD	Regorafenib	Regorafenib or TAS 102 – coin flip	TAS-102
 HOWARD S HOCHSTER, MD	Irinotecan + panitumumab	Regorafenib	TAS-102
 JOHN L MARSHALL, MD	Regorafenib	Regorafenib	TAS-102 (often w/ bev)
 EILEEN M O'REILLY, MD	Regorafenib	Regorafenib	Regorafenib or TAS 102 – coin flip
 PHILIP A PHILIP, MD, PHD	Irinotecan + panitumumab	TAS-102	TAS-102
 ALAN P VENOOK, MD	Irinotecan + panitumumab	Regorafenib or TAS 102 – coin flip	Regorafenib or TAS 102 – coin flip

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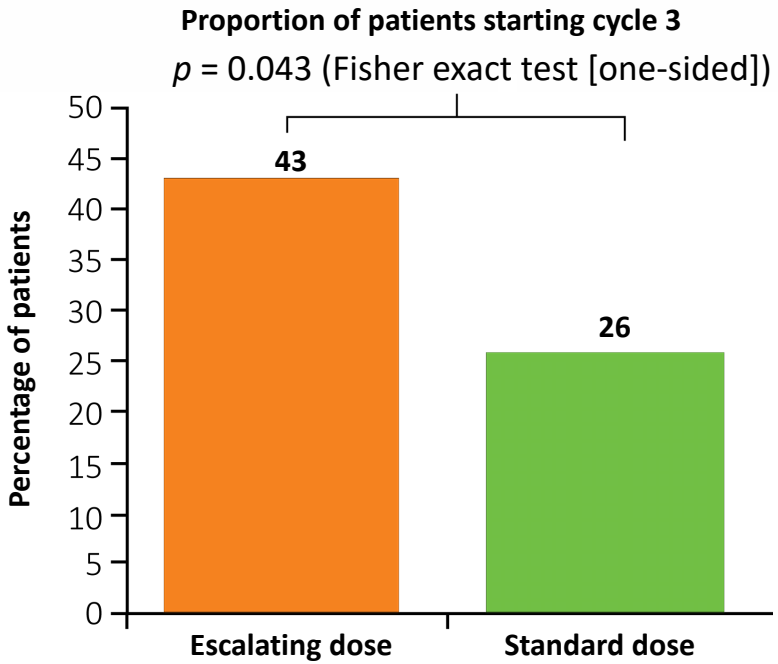
Regorafenib Dose Optimization Study (ReDOS): A Phase II Trial to Evaluate Dosing of Regorafenib for Refractory mCRC



Survival	Esc dose (n = 54)	Std dose (n = 62)	HR	*p*-value
Median OS	9.8 mo	6.0 mo	0.72	0.12
Median PFS	2.8 mo	2.0 mo	0.84	0.38

- Multiple QoL parameters were favorable with the escalating dose versus standard dose strategy primarily at week 2 of cycle 1

Bekaii-Saab TS et al. *Lancet Oncol* 2019;[Epub ahead of print].

RE-ARRANGE: A Phase II Randomized Trial Comparing Different Regorafenib Doses During the First Cycle of Treatment for mCRC

Eligibility

- Stage IV CRC
- Progression on/after approved standard therapies, which must include fluoropyrimidine, oxaliplatin, irinotecan, an anti-VEGF and an anti-EGFR (if RAS WT)

R

Standard Dose (SD)
Regorafenib 160 mg/day 3w on/1w off

Reduced Dose (RD)
Regorafenib 120 mg/day 3w on/1w off
1st cycle; 160 mg/day 3w on/1w off
2nd cycle on

Intermittent Dose (ID)
Regorafenib 160 mg/day 1w on/1w off
1st cycle; 160 mg/day 3w on/1w off
2nd cycle on

	SD Arm (n = 100)	RD Arm (n = 98)	ID Arm (n = 99)
Grade 3 or 4 AEs	60%	56%	55%

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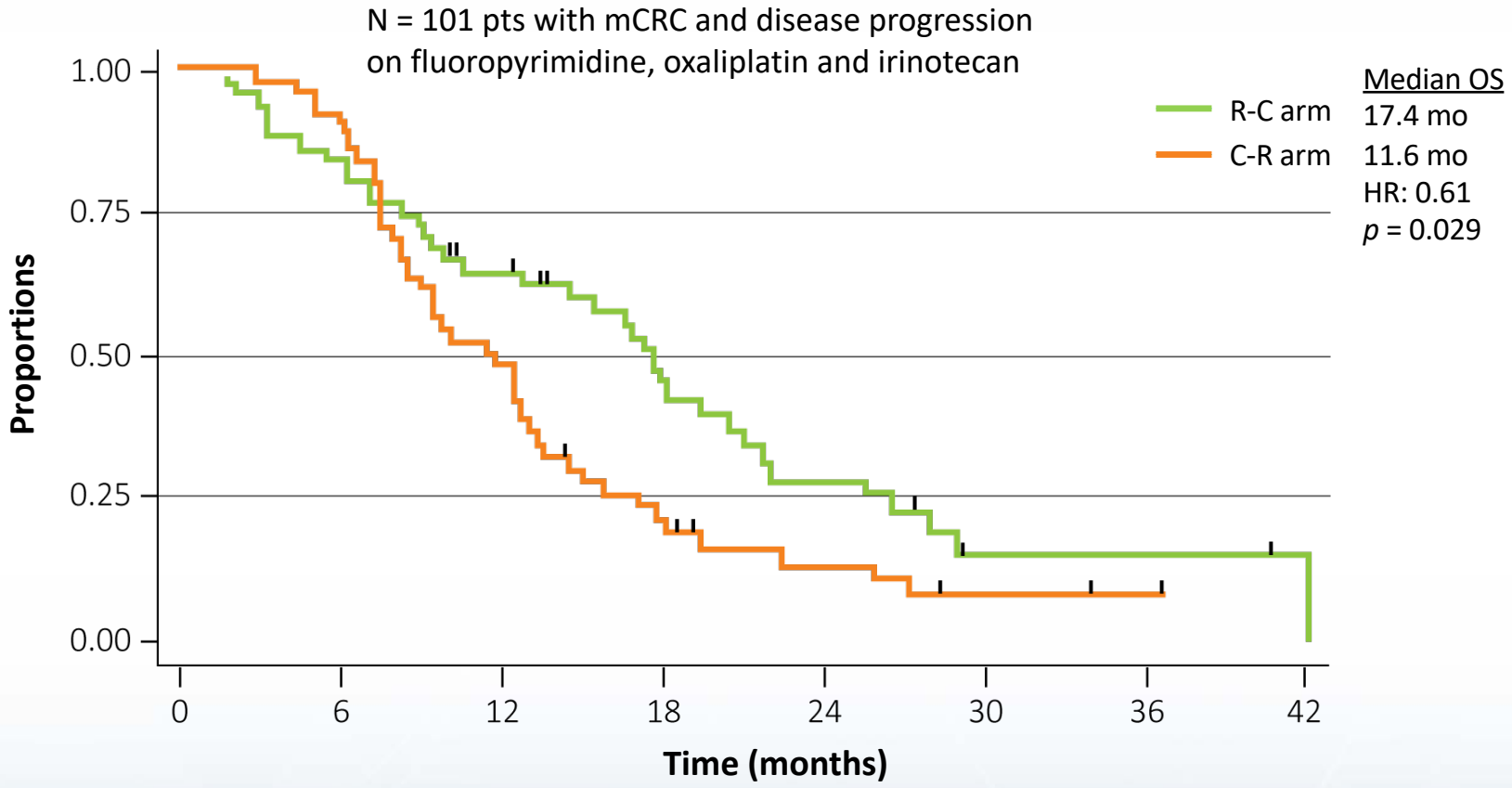
Argiles G et al. *Proc ESMO World Congress GI* 2019;Abstract O-026.

REVERCE: Overall Survival with Regorafenib Followed by Cetuximab versus the Reverse Sequence



Shitara K et al. *Ann Oncol* 2019;30:259-65.

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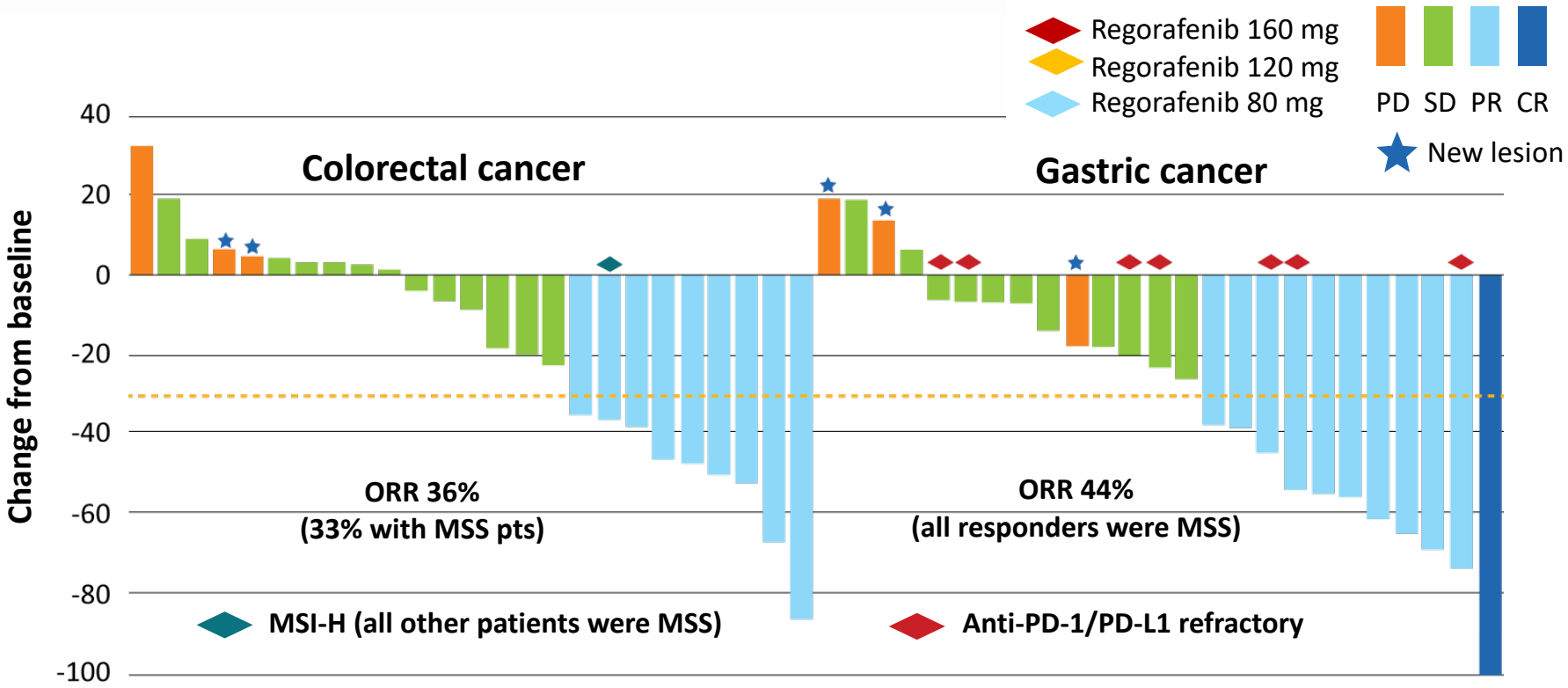
REGONIVO: A Phase Ib Study of Regorafenib with Nivolumab for CRC or Advanced Gastric Cancer (GC)



- Dose of regorafenib reduced to 80 mg due to skin toxicities
- Select Grade ≥3 treatment-related AEs (TRAEs) in all patients: 40%
- Select Grade ≥3 TRAEs in patients given regorafenib 80 mg: 27%
  - Proteinuria (9%)
  - Liver dysfunction (9%)
- One treatment-related death due to diabetic ketoacidosis

Fukuoka S et al. ASCO 2019;Abstract 2522.

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TAS-102 with Bevacizumab for Chemorefractory mCRC

- Randomized study with N = 93 patients with chemorefractory mCRC

	TAS-102/ bevacizumab	TAS-102	HR	*p*-value
Median PFS	4.6 mo	2.6 mo	0.45	0.001
Median OS	9.4 mo	6.7 mo	0.55	0.03

- Adverse events were as expected
- Grade 3 or 4 neutropenia (TAS-102/bev vs TAS-102): 67% vs 38% ($p < 0.05$)
- Serious adverse events (TAS-102/bev vs TAS-102): 19 patients vs 21 patients

Pfeiffer P et al. *Proc ESMO World Congress GI* 2019;Abstract O-014.

In addition to pan-RAS status, which of the following items do you routinely assess in patients with mCRC?

 TANIOS BEKAII-SAAB, MD	HER2 status, BRAF status, MSI, multigene panel (NGS)
 JOHANNA BENDELL, MD	HER2 status, BRAF status, MSI, multigene panel (NGS)
 HOWARD S HOCHSTER, MD	HER2 status, BRAF status, MSI
 JOHN L MARSHALL, MD	HER2 status, BRAF status, MSI, multigene panel (NGS)
 EILEEN M O'REILLY, MD	HER2 status, BRAF status, MSI, multigene panel (NGS)
 PHILIP A PHILIP, MD, PHD	Multigene panel (next-generation sequencing)
 ALAN P VENOOK, MD	HER2 status, BRAF status, MSI

MSI = microsatellite instability; NGS = next-generation sequencing

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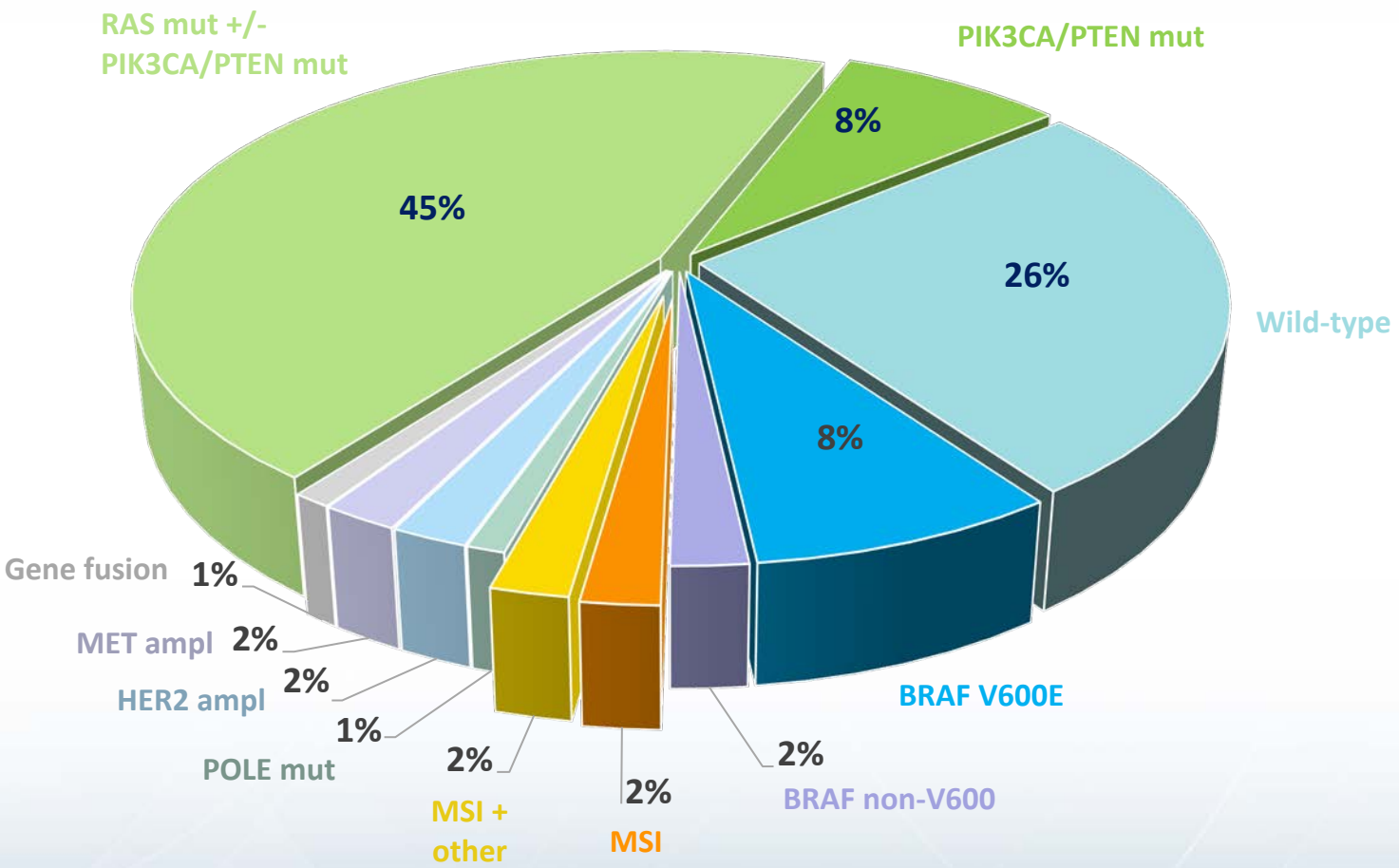
Prevalence of Molecular Alterations in Colorectal Cancer (CRC)



Cervantes A et al. *Medicographia* 2018;40:101-8.

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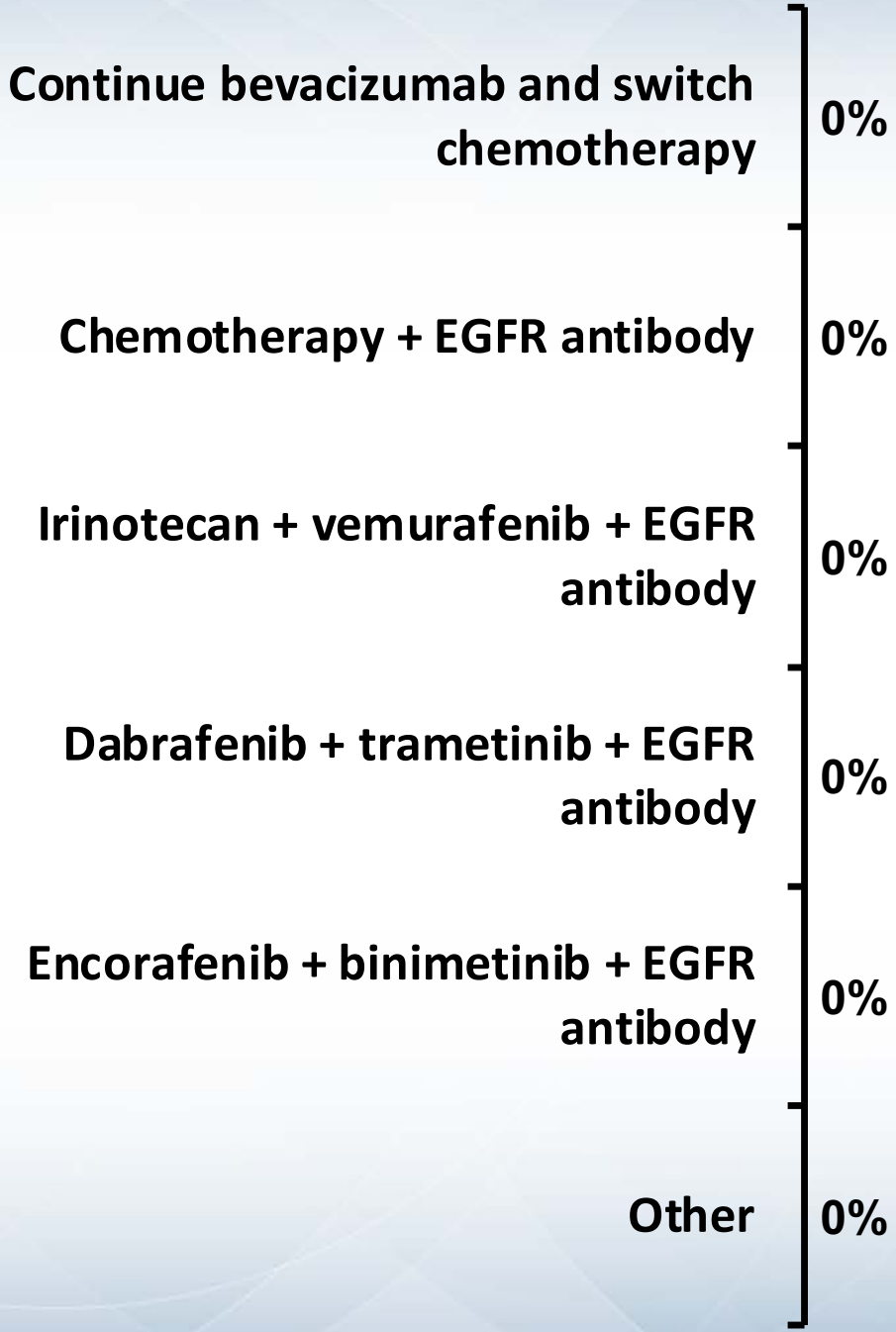
Reimbursement and regulatory issues aside, what would be your most likely second-line treatment recommendation for a 65-year-old patient with left-sided, MSS, pan-RAS wild-type mCRC with a BRAF V600E mutation who received first-line FOLFOXIRI/bevacizumab and experienced disease progression 8 months later (PS 0)?

1. Continue bevacizumab and switch chemotherapy
2. Chemotherapy + EGFR antibody
3. Irinotecan + vemurafenib + EGFR antibody
4. Dabrafenib + trametinib + EGFR antibody
5. Encorafenib + binimetinib + EGFR antibody
6. Other



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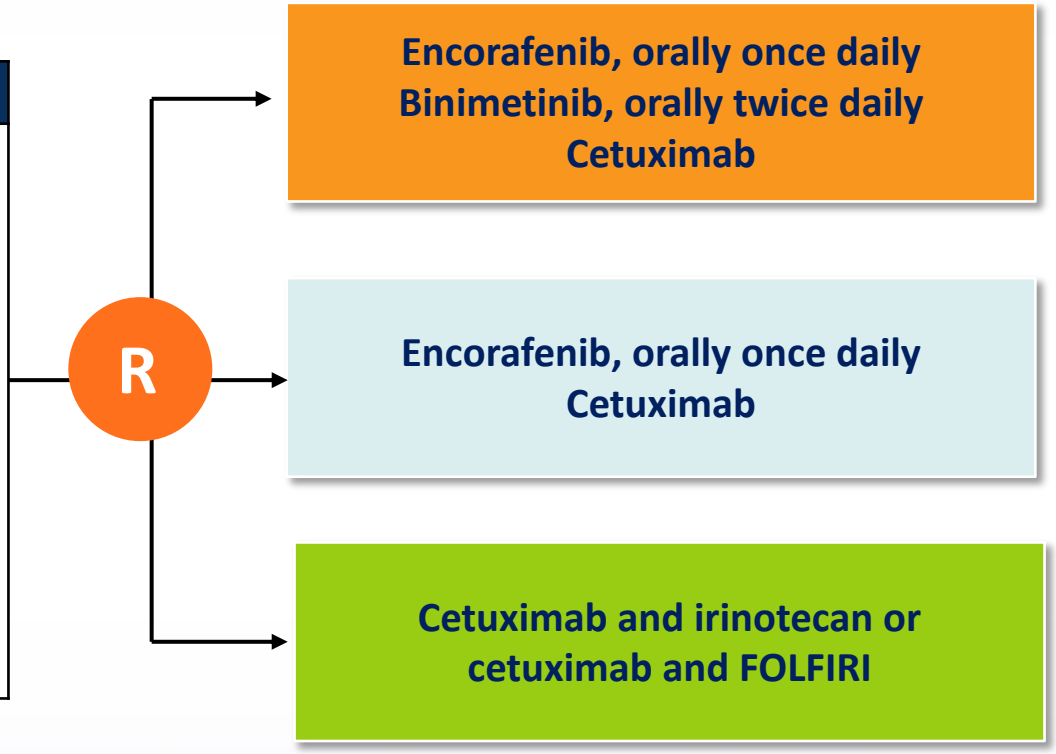
 TANIOS BEKAII-SAAB, MD	Encorafenib + binimetinib + EGFR antibody
 JOHANNA BENDELL, MD	Encorafenib + binimetinib + EGFR antibody
 HOWARD S HOCHSTER, MD	Encorafenib + binimetinib + EGFR antibody
 JOHN L MARSHALL, MD	Encorafenib + binimetinib + EGFR antibody
 EILEEN M O'REILLY, MD	Encorafenib + binimetinib + EGFR antibody
 PHILIP A PHILIP, MD, PHD	Encorafenib + binimetinib + EGFR antibody
 ALAN P VENOOK, MD	Encorafenib + binimetinib + EGFR antibody

BEACON CRC: A Phase III Trial of Encorafenib and Cetuximab with or without Binimetinib for mCRC with BRAF V600E Mutation

Trial Identifier: NCT02928224

Eligibility

- Histologically or cytologically confirmed metastatic CRC
- Disease progression after 1 or 2 regimens in the metastatic setting
- BRAF V600E mutation in tumor tissue as previously determined by a local assay at any time prior to screening or by the central laboratory



Primary endpoint: OS and ORR (by blinded central review) comparing the triplet to the control arm.

Kopetz S et al. *NEJM* 2019;[Epub ahead of print]. Tabernero J et al. *Proc ESMO* 2019;Abstract LBA32.

BEACON CRC: Encorafenib and Cetuximab with or without Binimetinib for mCRC with BRAF V600E Mutation

	ENCO/CETUX/BINI (n = 224)	ENCO/CETUX (n = 220)	Control – Irinotecan or FOLFIRI + cetuximab (n = 221)
Confirmed ORR	26%	20%	2%*
Median OS	9.0 mo	8.4 mo	5.4 mo
Hazard ratio (*p*-value)	0.52 (<0.001)	0.60 (<0.001)	Ref

*$p < 0.001$

Adverse events were as anticipated based on prior trials with each combination.

Kopetz S et al. *NEJM* 2019;[Epub ahead of print]. Tabernero J et al. *Proc ESMO* 2019;Abstract LBA32.

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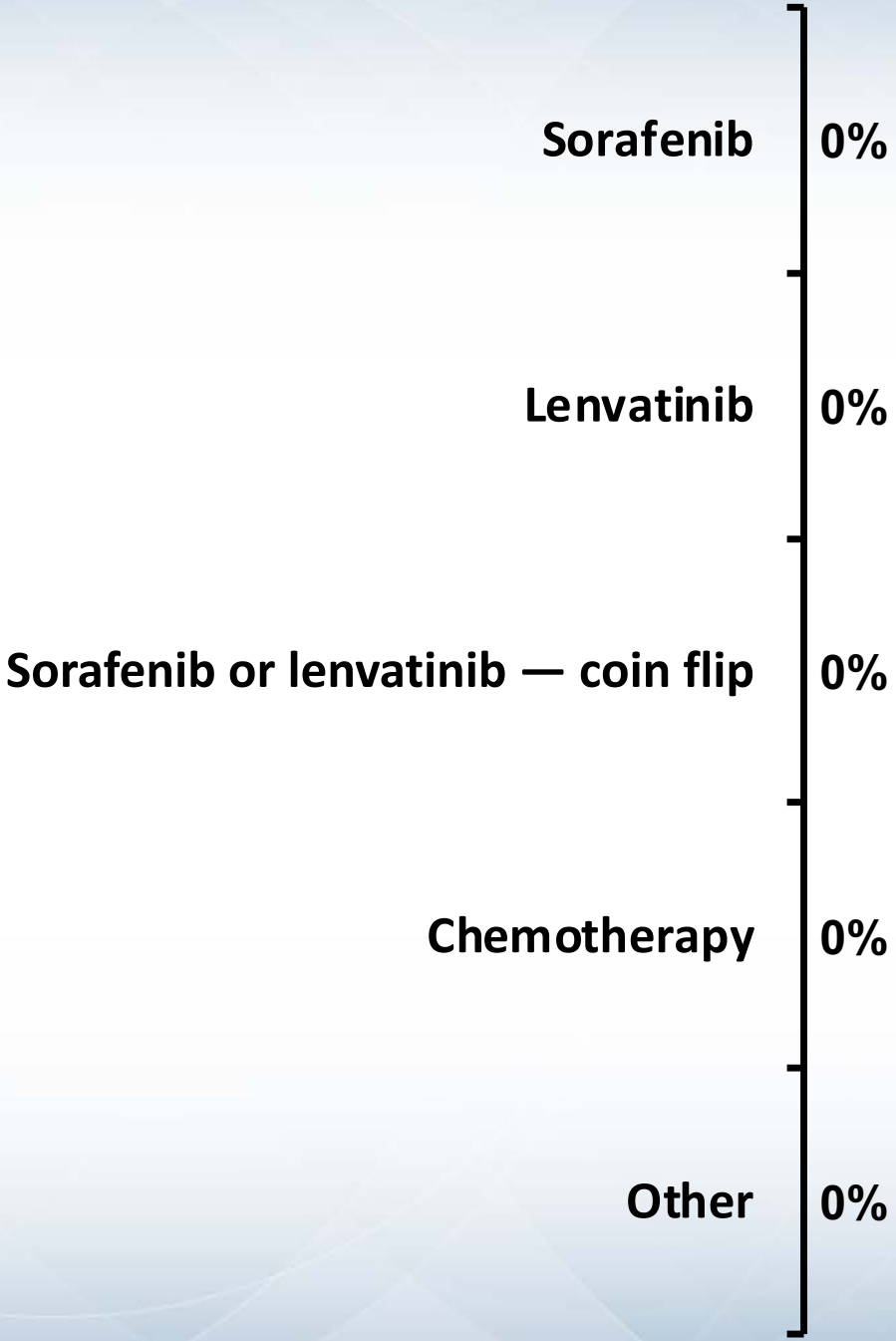
- Management of metastatic disease and integration of nanoliposomal irinotecan
- BRCA mutations and PARP inhibition

Module 4: Gastric/Gastroesophageal Junction (GEJ)/Esophageal Cancer

- Pembrolizumab for the treatment of recurrent or advanced gastric, GEJ and esophageal cancer
- Efficacy and safety of TAS-102 for recurrent metastatic gastric or GEJ adenocarcinoma

What would be your most likely first-line systemic treatment for a 65-year-old patient with hepatocellular carcinoma (HCC), a Child-Pugh A score and a PS of 0?

1. Sorafenib
2. Lenvatinib
3. Sorafenib or lenvatinib — coin flip
4. Chemotherapy
5. Other



What would be your most likely first-line systemic treatment for a 65-year-old patient with…

	Child-Pugh A HCC		Child-Pugh B7 HCC	
	PS 0	Painful bone mets	PS 0	PS 1
 TANIOS BEKAII-SAAB, MD	Sorafenib	Lenvatinib	Sorafenib or lenvatinib – coin flip	Sorafenib or lenvatinib – coin flip
 JOHANNA BENDELL, MD	Lenvatinib	Lenvatinib	Lenvatinib	Lenvatinib
 HOWARD S HOCHSTER, MD	Sorafenib or lenvatinib – coin flip	Sorafenib or lenvatinib – coin flip	Lenvatinib	Lenvatinib
 JOHN L MARSHALL, MD	Sorafenib	Lenvatinib	Sorafenib or lenvatinib – coin flip	Sorafenib
 EILEEN M O'REILLY, MD	Lenvatinib	Lenvatinib	Sorafenib	Sorafenib or lenvatinib – coin flip
 PHILIP A PHILIP, MD, PHD	Lenvatinib	Lenvatinib	Lenvatinib	Lenvatinib
 ALAN P VENOOK, MD	Sorafenib or lenvatinib – coin flip	Sorafenib or lenvatinib – coin flip	Sorafenib or lenvatinib – coin flip	Sorafenib or lenvatinib – coin flip

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Based on current clinical trial data and your personal experience, how would you compare the global antitumor efficacy and tolerability profile of sorafenib and lenvatinib as first-line therapy for HCC?

	Efficacy	Tolerability
 TANIOS BEKAII-SAAB, MD	About the same	Sorafenib has somewhat more toxicity
 JOHANNA BENDELL, MD	Lenvatinib is somewhat more efficacious	Sorafenib has somewhat more toxicity
 HOWARD S HOCHSTER, MD	About the same	About the same
 JOHN L MARSHALL, MD	Lenvatinib is somewhat more efficacious	Lenvatinib has somewhat more toxicity
 EILEEN M O'REILLY, MD	Lenvatinib is somewhat more efficacious	About the same
 PHILIP A PHILIP, MD, PHD	Lenvatinib is somewhat more efficacious	Lenvatinib has somewhat more toxicity
 ALAN P VENOOK, MD	About the same	About the same

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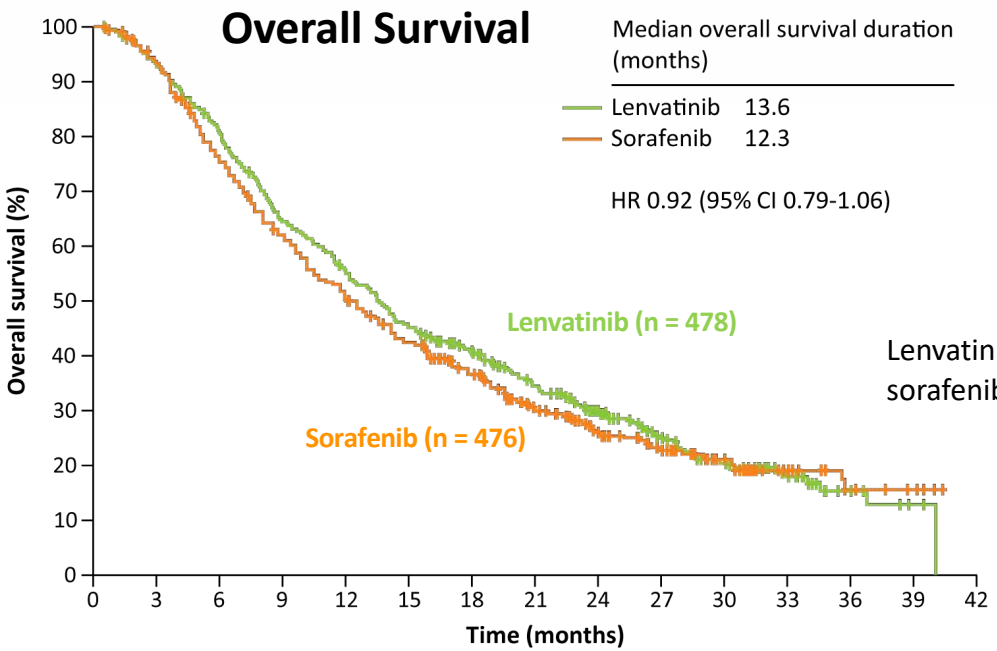
REFLECT: A Phase III Trial of Lenvatinib versus Sorafenib as First-Line Treatment for Unresectable HCC



Lenvatinib showed noninferiority to sorafenib in terms of OS

Outcomes	Lenvatinib (n = 478)	Sorafenib (n = 476)	HR or OR	*p*-value
Median PFS	7.4 mo	3.7 mo	HR 0.66	<0.0001
Median time to progression	8.9 mo	3.7 mo	HR 0.63	<0.0001
Objective response rate	24.1%	9.2%	OR 3.13	<0.0001

HR = hazard ratio; OR = odds ratio

The safety and tolerability profiles of lenvatinib were consistent with those previously observed.

Kudo M et al. *Lancet* 2018;391(10126):1163-73.

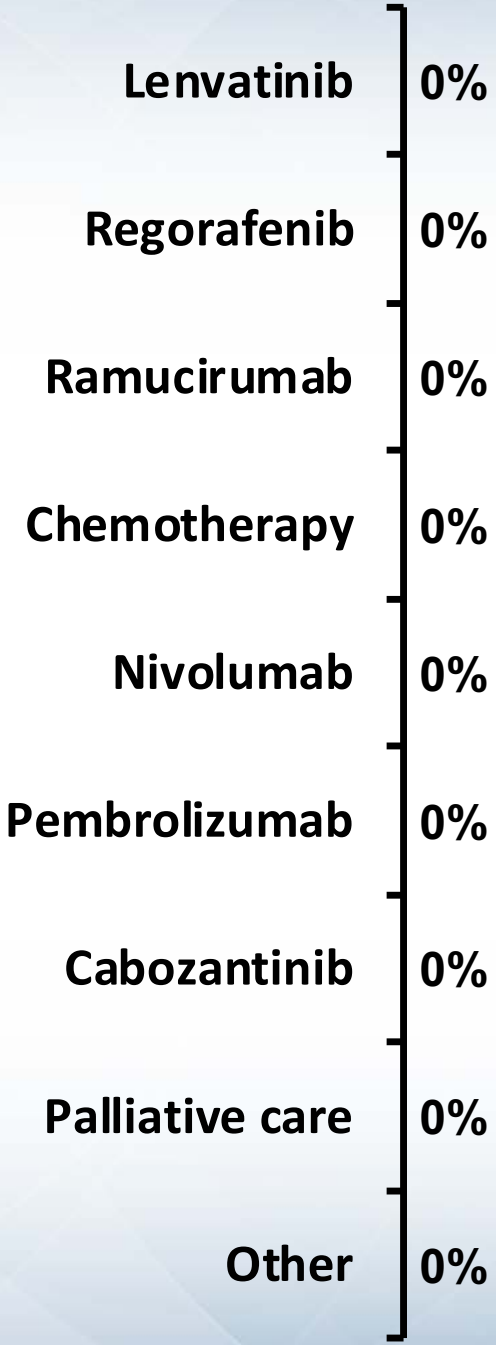
REFLECT: Select Treatment-Emergent AEs

Adverse event, n (%)	Lenvatinib (n = 476)		Sorafenib (n = 475)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Hypertension	201 (42)	111 (23)	144 (30)	68 (14)
Diarrhea	184 (39)	20 (4)	220 (46)	20 (4)
Decreased appetite	162 (34)	22 (5)	127 (27)	6 (1)
Decreased weight	147 (31)	36 (8)	106 (22)	14 (3)
Fatigue	141 (30)	18 (4)	119 (25)	17 (4)
Palmar-plantar erythrodysesthesia	128 (27)	14 (3)	249 (52)	54 (11)
Proteinuria	117 (25)	27 (6)	54 (11)	8 (2)
Dysphonia	113 (24)	1 (0)	57 (12)	0 (0)
Nausea	93 (20)	4 (1)	68 (14)	4 (1)
Decreased platelet count	87 (18)	26 (6)	58 (12)	16 (3)
Vomiting	77 (16)	6 (1)	36 (8)	5 (1)

Kudo M et al. *Lancet* 2018;391(10126):1163-73; Cheng AL et al. *Proc ASCO* 2017;Abstract 4001.

What would be your most likely second-line systemic therapy for a 65-year-old patient with HCC, a Child-Pugh A score and a PS of 0 who received first-line standard-dose sorafenib with minimal toxicity, had stable disease for 14 months and then experienced disease progression (alpha-fetoprotein [AFP] 2,500 ng/mL)?

1. Lenvatinib
2. Regorafenib
3. Ramucirumab
4. Chemotherapy
5. Nivolumab
6. Pembrolizumab
7. Cabozantinib
8. Palliative care
9. Other



What would be your most likely second-line systemic therapy for a 65-year-old patient with HCC who received first-line standard-dose sorafenib with minimal toxicity, had stable disease for 14 months and then experienced disease progression?

	Child-Pugh A, PS 0		Child-Pugh B7, PS 1	
	AFP 2,500 ng/mL	AFP 300 ng/mL	AFP 2,500 ng/mL	AFP 300 ng/mL
 TANIOS BEKAII-SAAB, MD	Regorafenib	Regorafenib	Ramucirumab	Pembrolizumab
 JOHANNA BENDELL, MD	Cabozantinib	Cabozantinib	Cabozantinib	Cabozantinib
 HOWARD S HOCHSTER, MD	Regorafenib	Regorafenib	Regorafenib	Regorafenib
 JOHN L MARSHALL, MD	Regorafenib	Regorafenib	Pembrolizumab	Pembrolizumab
 EILEEN M O'REILLY, MD	Regorafenib	Regorafenib or nivolumab	Ramucirumab	Nivolumab
 PHILIP A PHILIP, MD, PHD	Regorafenib	Regorafenib	Ramucirumab	Regorafenib
 ALAN P VENOOK, MD	Nivolumab	Nivolumab	Nivolumab	Nivolumab

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What would be your most likely second-line systemic therapy for a 65-year-old patient with HCC who received first-line sorafenib and required a dose reduction to 400 mg daily, had stable disease for 5 months and then experienced disease progression?

	Child-Pugh A, PS 0		Child-Pugh B7, PS 1	
	AFP 2,500 ng/mL	AFP 300 ng/mL	AFP 2,500 ng/mL	AFP 300 ng/mL
 TANIOS BEKAII-SAAB, MD	Cabozantinib	Cabozantinib	Ramucirumab	Cabozantinib
 JOHANNA BENDELL, MD	Ramucirumab	Cabozantinib	Ramucirumab	Cabozantinib
 HOWARD S HOCHSTER, MD	Regorafenib	Regorafenib	Ramucirumab	Nivolumab
 JOHN L MARSHALL, MD	Pembrolizumab	Pembrolizumab	Pembrolizumab	Pembrolizumab
 EILEEN M O'REILLY, MD	Nivolumab	Nivolumab	Nivolumab	Nivolumab
 PHILIP A PHILIP, MD, PHD	Ramucirumab	Regorafenib	Ramucirumab	Cabozantinib
 ALAN P VENOOK, MD	Nivolumab	Nivolumab	Nivolumab	Nivolumab

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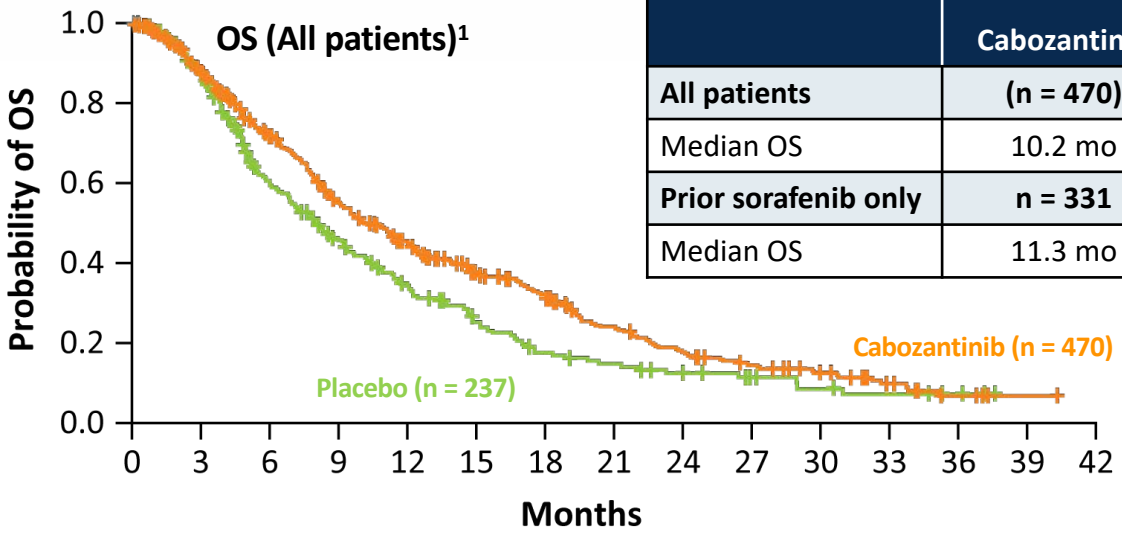
CELESTIAL: A Phase III Trial of Cabozantinib versus Placebo for Advanced HCC



	Cabozantinib	Placebo	HR	*p*-value
All patients	**(n = 470)**	**(n = 237)**	0.76	0.005
Median OS	10.2 mo	8.0 mo		
Prior sorafenib only	**n = 331**	**n = 164**	0.70	NR
Median OS	11.3 mo	7.2 mo		

OS in cabozantinib group by AFP response*[2]	Median OS	No. of deaths
AFP response (N = 117)	16.1 mo	81
No AFP response (N = 119)	9.1 mo	85

* ≥20% decrease in AFP level from baseline at week 8

[1] Abou-Alfa GK et al. *N Engl J Med* 2018;379(1):54-63; [2] Merle P et al. *Proc ESMO GI* 2018;Abstract O-011.

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FDA Grants Approval to Ramucirumab for HCC

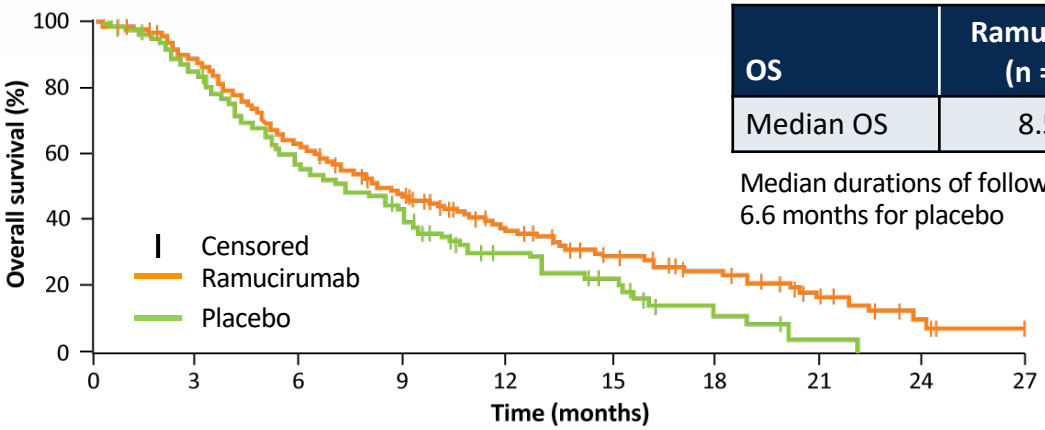
Press Release – May 10, 2019

"The Food and Drug Administration approved ramucirumab as a single agent for hepatocellular carcinoma (HCC) in patients who have an alpha fetoprotein (AFP) of ≥400 ng/mL and have been previously treated with sorafenib.

Approval was based on REACH-2 (NCT02435433), a multinational, randomized, double-blind, placebo-controlled, multicenter study in 292 patients with advanced HCC with AFP ≥400 ng/mL who had disease progression on or after sorafenib or who were intolerant."

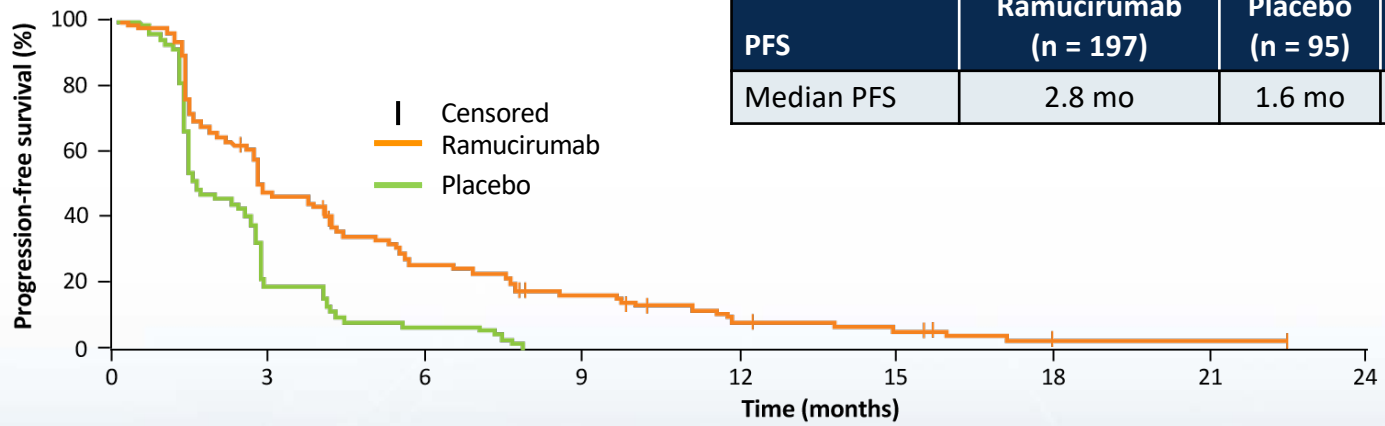
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ramucirumab-hepatocellular-carcinoma

REACH-2: A Phase III Trial of Ramucirumab After Sorafenib for Patients with Advanced HCC and Increased AFP



OS	Ramucirumab (n = 197)	Placebo (n = 95)	HR	*p*-value
Median OS	8.5 mo	7.3 mo	0.710	0.0199

Median durations of follow-up were 7.9 months for ramucirumab, 6.6 months for placebo



PFS	Ramucirumab (n = 197)	Placebo (n = 95)	HR	*p*-value
Median PFS	2.8 mo	1.6 mo	0.452	<0.0001

Grade ≥3 AEs associated with ramucirumab included hypertension and hyponatremia.

Zhu AX et al. *Proc ASCO* 2018;Abstract 4003; *Lancet Oncol* 2019;20(2):282-96.

RESORCE: A Phase III Trial of Regorafenib for Patients with HCC Who Experienced Disease Progression on Sorafenib

	Regorafenib (n = 379)	Placebo (n = 194)	HR	*p*-value
Median PFS[1]	3.1 mo	1.5 mo	0.46	<0.0001
Median OS (primary analysis)[1]	10.6 mo	7.8 mo	0.63	<0.0001
Median OS (updated analysis)[2,3]	10.7 mo	7.9 mo	0.62	<0.0001
ORR (mRECIST)[1]	11%	4%	—	0.0047
Disease control rate[1]	65%	36%	—	<0.0001

- Common clinically relevant Grade 3/4 TEAEs: Hypertension (15% vs 5%), hand-foot skin reaction (13% vs 1%), fatigue (9% vs 5%) and diarrhea (3% vs 0%)[1]
  - Data cutoff for primary analysis: February 29, 2016
  - Data cutoff for updated OS analysis: January 23, 2017

[1] Bruix J et al. *Lancet* 2017;389(10064):56-66; [2] Bruix J et al. *Proc ESMO 2017 World Congress GI*;Abstract O-009; [3] Bruix J et al. *Proc ILCA* 2018;Abstract O-023.

CheckMate 040: A Phase I/II Dose Escalation and Expansion Trial of Nivolumab for Advanced HCC

Dose-Expansion Phase (3 mg/kg)

Efficacy	All patients (n = 214)	Uninfected untreated/ intolerant (n = 56)	Uninfected progressor (n = 57)	HCV infected (n = 50)	HBV infected (n = 51)
Objective response rate	20%	23%	21%	20%	14%
Median DOR	9.9 mo	8.4 mo	NYR	9.9 mo	NYR
9-mo overall survival	74%	82%	63%	81%	70%

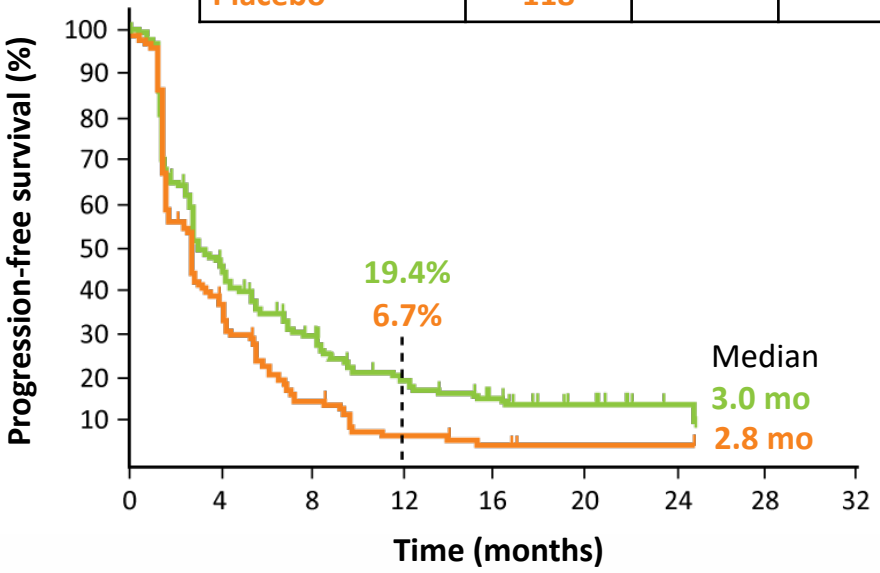
HCV = hepatitis C virus; HBV = hepatitis B virus; DOR = duration of response; NYR = not yet reached

On September 22, 2017, the Food and Drug Administration granted accelerated approval to nivolumab for the treatment of HCC in patients who have previously received sorafenib.

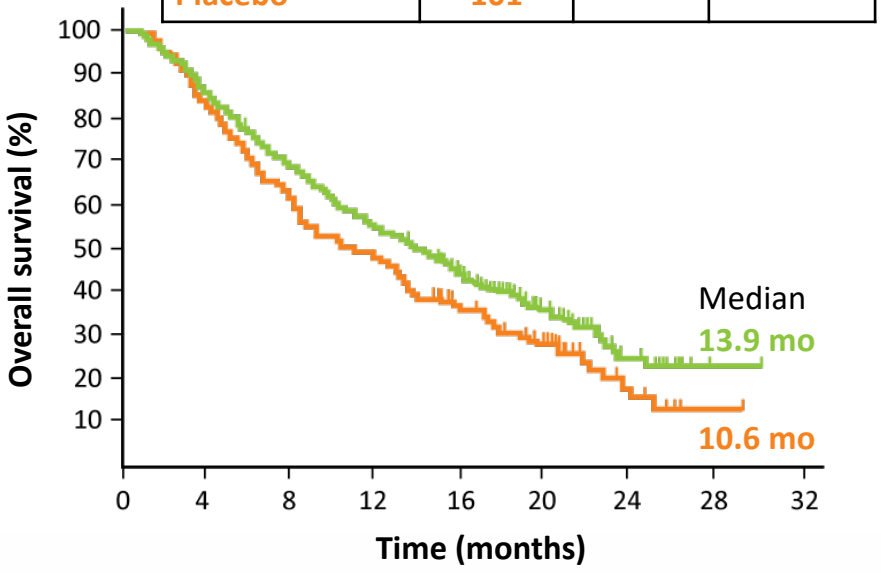
El-Khoueiry AB et al. *Lancet* 2017;389(10088):2492-502;
https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm577166.htm.

Phase III KEYNOTE-240 Trial: Pembrolizumab versus Best Supportive Care as Second-Line Therapy for Advanced HCC

PFS final analysis			
	Events	HR	*p*-value
Pembrolizumab	214	0.718	0.0022
Placebo	118		



Overall survival			
	Events	HR	*p*-value
Pembrolizumab	183	0.781	0.0238
Placebo	101		



- Accelerated approval for pembrolizumab granted in 2018 based on Phase II KEYNOTE-224 study
- Confirmatory KEYNOTE-240 trial: Numerical but not statistical advantage in PFS and OS
- Results of Phase III KEYNOTE-394 are pending

Finn R et al. *Proc ASCO* 2019;Abstract 4004; https://investors.merck.com/news/press-release-details/2019/Merck-Provides-Update-on-KEYNOTE-240-a-Phase-3-Study-of-KEYTRUDA-pembrolizumab-in-Previously-Treated-Patients-with-Advanced-Hepatocellular-Carcinoma/default.aspx

Ongoing Phase III Studies of Checkpoint Inhibitors in Advanced HCC

Study identifier	Target accrual	Eligibility	Randomization
LEAP-002 (NCT03713593)	750	First line, advanced HCC	• Lenvatinib + Pembrolizumab • Lenvatinib
IMbrave150 (NCT03434379)	480	First line, locally advanced or advanced HCC	• Atezolizumab + Bevacizumab • Sorafenib
HIMALAYA (NCT03298451)	1,310	First line, advanced HCC	• Durvalumab • Durvalumab + Tremelimumab (2 regimens) • Sorafenib
COSMIC-312 (NCT03755791)	640 (6:3:1)	First line, advanced HCC	• Cabozantinib + Atezolizumab • Sorafenib • Cabozantinib

www.clinicaltrials.gov, Accessed July 2019

What would be your most likely third-line systemic therapy recommendation for an otherwise healthy 65-year-old patient with HCC who experienced disease progression on first-line sorafenib and second-line nivolumab (AFP 2,500 ng/mL)? If their AFP was 300 ng/mL?

	AFP 2,500 ng/mL	AFP 300 ng/mL
 TANIOS BEKAII-SAAB, MD	Cabozantinib	Cabozantinib
 JOHANNA BENDELL, MD	Cabozantinib	Cabozantinib
 HOWARD S HOCHSTER, MD	Palliative care	Palliative care
 JOHN L MARSHALL, MD	Ramucirumab	Regorafenib
 EILEEN M O'REILLY, MD	Ramucirumab	Cabozantinib
 PHILIP A PHILIP, MD, PHD	Ramucirumab	Cabozantinib
 ALAN P VENOOK, MD	Cabozantinib	Cabozantinib

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Novel and Emerging Therapeutic Strategies in the Management of Select Gastrointestinal Cancers

Module 1: Colorectal Cancer

- Primary tumor sidedness and selection of first-line therapy
- Sequencing of available therapies in the second line and beyond
- Novel targeted approaches

Module 2: Hepatocellular Carcinoma

- First-line systemic treatment: Sorafenib versus lenvatinib
- Beyond first-line therapy: Cabozantinib, ramucirumab, regorafenib and anti-PD-1/PD-L1 antibodies

Module 3: Pancreatic Cancer

- Neoadjuvant and adjuvant therapy approaches
- Management of metastatic disease and integration of nanoliposomal irinotecan
- BRCA mutations and PARP inhibition

Module 4: Gastric/Gastroesophageal Junction (GEJ)/Esophageal Cancer

- Pembrolizumab for the treatment of recurrent or advanced gastric, GEJ and esophageal cancer
- Efficacy and safety of TAS-102 for recurrent metastatic gastric or GEJ adenocarcinoma

Phase II Studies of (Neo)Adjuvant Chemotherapy for Resectable Pancreatic Adenocarcinoma

NEONAX: Neoadjuvant and adjuvant or adjuvant gemcitabine/*nab* paclitaxel

Outcome	Arm A (n = 25) (perioperative)	Arm B (n = 23) (adjuvant)
Tumor resection: Yes No	80% 20%	91.3% 8.7%
Postoperative complications	45%	42.8%

Grade ≥3 adverse events increased in the perioperative arm, but this was manageable and did not result in peri- or postoperative mortality.

SWOG-S1505: Neoadjuvant mFOLFIRINOX versus gemcitabine/*nab* paclitaxel

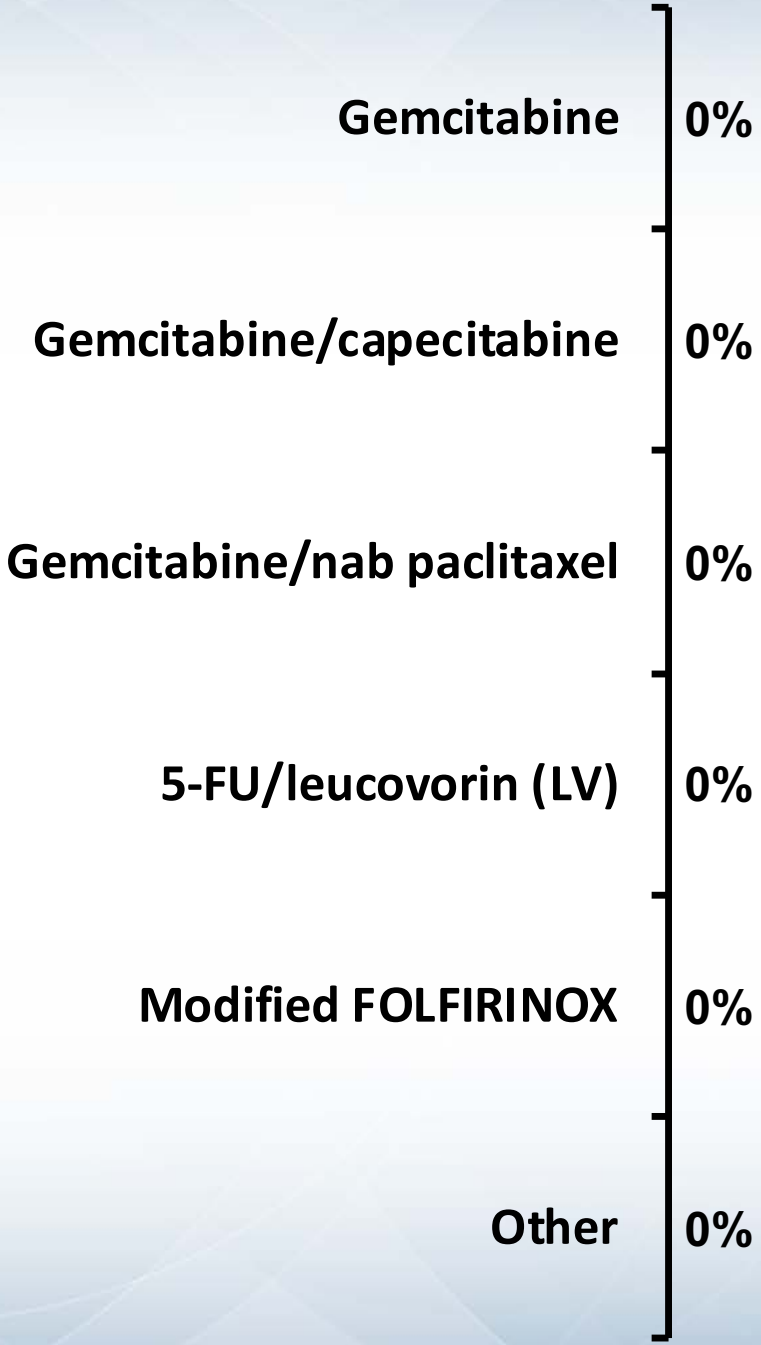
Outcome	Total (n = 99)
Reached protocol surgery: Yes No	77% 23%

Preoperative chemotherapy was safe and feasible.

Uhl W et al. *Proc ASCO* 2019;Abstract 4128; Sohal D et al. *Proc ASCO* 2019;Abstract 4137.

What is your likely adjuvant systemic therapy recommendation for an otherwise healthy 75-year-old patient after surgical resection of pancreatic cancer?

1. Gemcitabine
2. Gemcitabine/capecitabine
3. Gemcitabine/*nab* paclitaxel
4. 5-FU/leucovorin (LV)
5. Modified FOLFIRINOX
6. Other



What is your likely adjuvant systemic therapy recommendation for an otherwise healthy 75-year-old patient after surgical resection of pancreatic cancer?

Would you administer *nab* paclitaxel/gemcitabine as adjuvant therapy for a patient with pancreatic cancer?

	Adjuvant therapy	*Nab* paclitaxel/gemcitabine as adjuvant therapy?
 TANIOS BEKAII-SAAB, MD	Modified FOLFIRINOX	No
 JOHANNA BENDELL, MD	Modified FOLFIRINOX	No
 HOWARD S HOCHSTER, MD	Modified FOLFIRINOX	No
 JOHN L MARSHALL, MD	Modified FOLFIRINOX	No
 EILEEN M O'REILLY, MD	Modified FOLFIRINOX	No
 PHILIP A PHILIP, MD, PHD	Modified FOLFIRINOX	Not a candidate or refuses FFX Good performance status
 ALAN P VENOOK, MD	Modified FOLFIRINOX	Yes, patient w/ poor PS or hyperbilirubinemia

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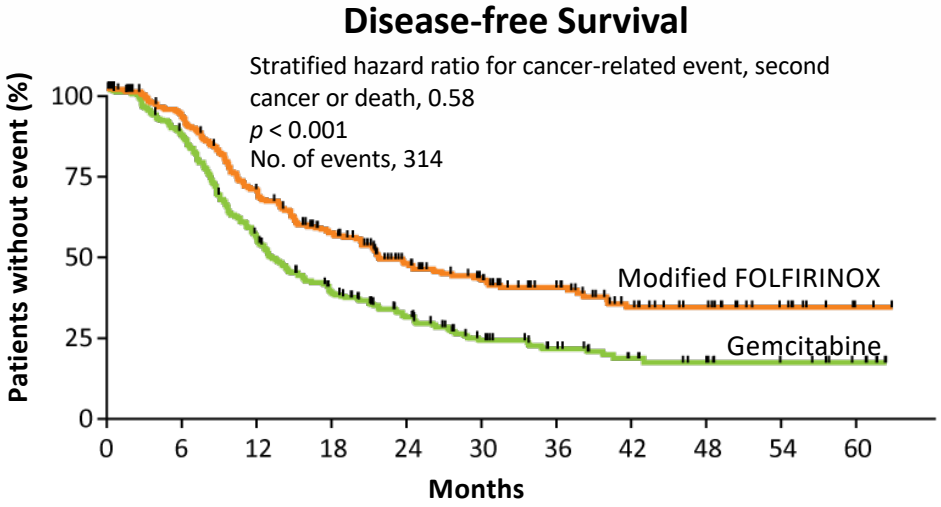
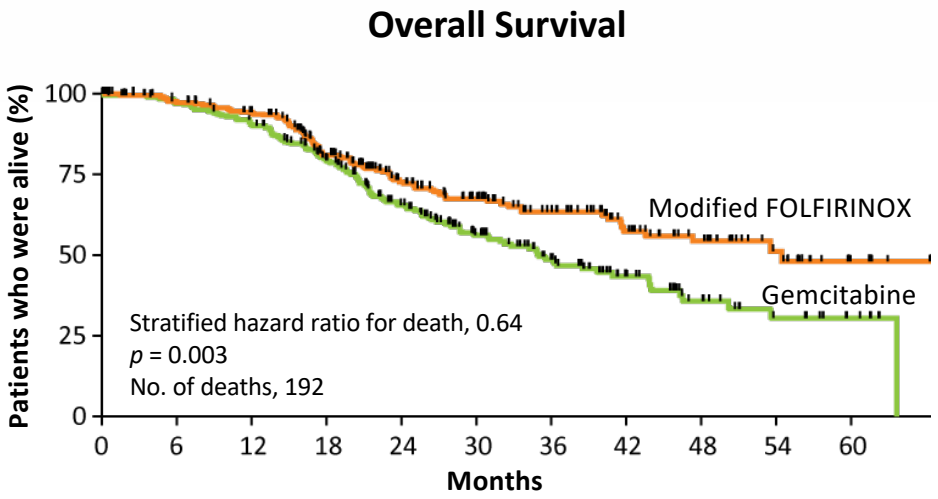
PRODIGE 24/CCTG PA.6: Survival and Safety with FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer



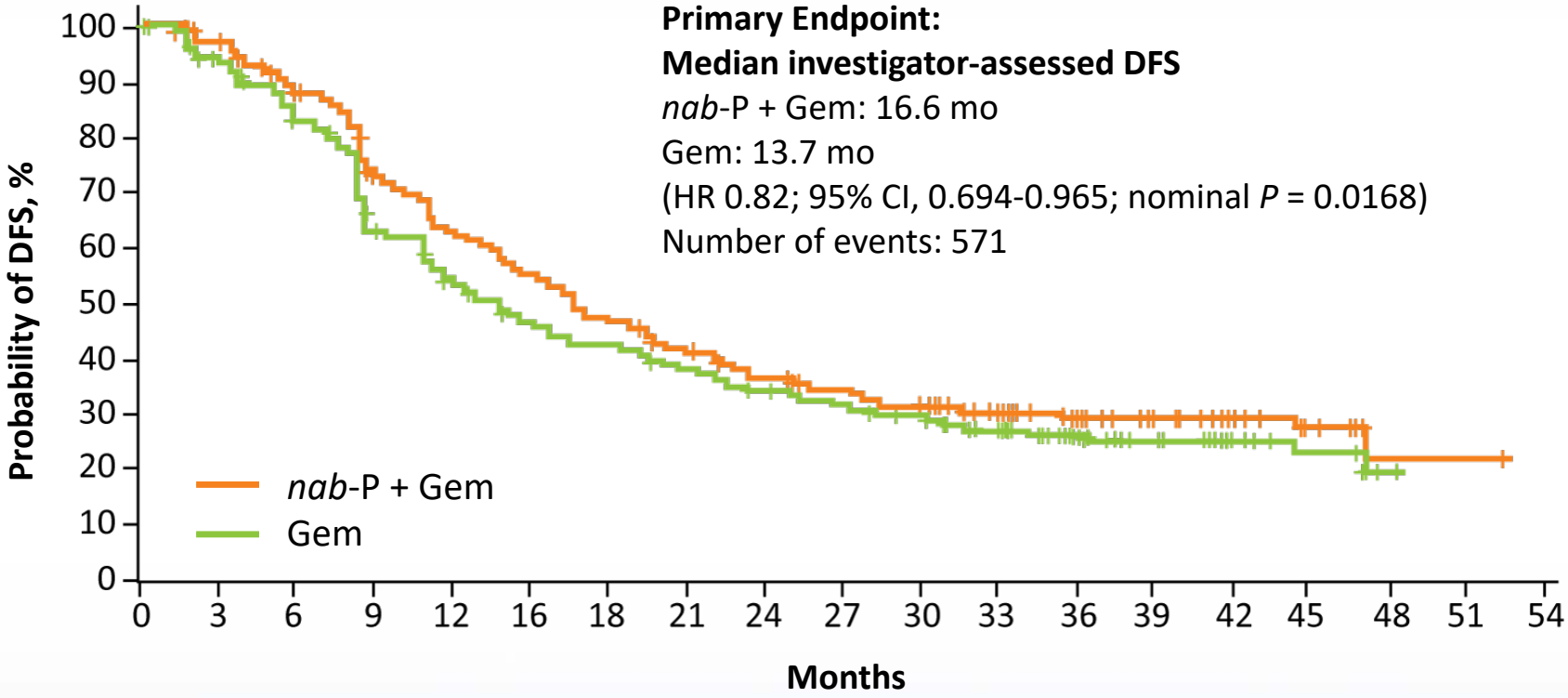


Outcome	mFOLFIRINOX (n = 247)	Gem (n = 246)	HR	*p*-value
Median DFS	21.6 mo	12.8 mo	0.58	<0.001
Median OS	54.4 mo	35.0 mo	0.64	0.003

- Grade 3/4 AEs: mFOLFIRINOX, 75.9%; gemcitabine, 52.9%
- Grade 3/4 AEs higher in mFOLFIRINOX arm: diarrhea, paresthesia, fatigue, peripheral neuropathy, vomiting, abdominal pain, mucositis
- Grade 3/4 AEs higher in the gemcitabine arm: thrombocytopenia

Conroy T et al. *N Engl J Med* 2018;379(25):2395-406.

Phase III APACT Trial of Adjuvant Gemcitabine/*Nab* Paclitaxel for Surgically Resected Pancreatic Adenocarcinoma



Primary Endpoint:
Median investigator-assessed DFS
nab-P + Gem: 16.6 mo
Gem: 13.7 mo
(HR 0.82; 95% CI, 0.694-0.965; nominal *P* = 0.0168)
Number of events: 571

- The primary endpoint was not met.
- Interim-analysis OS was improved for *nab*-P + Gem compared to Gem (40.5 mo vs 36.2 mo; HR 0.82, nominal *P* = 0.045).

Tempero M et al. *Proc ASCO* 2019;Abstract 4000;
Reni M et al. *Proc ESMO World Congress GI* 2019;Abstract O-001.

Phase II LAPACT Trial of *Nab* Paclitaxel and Gemcitabine for Unresectable Locally Advanced Pancreatic Cancer: Survival, Response and Safety Results

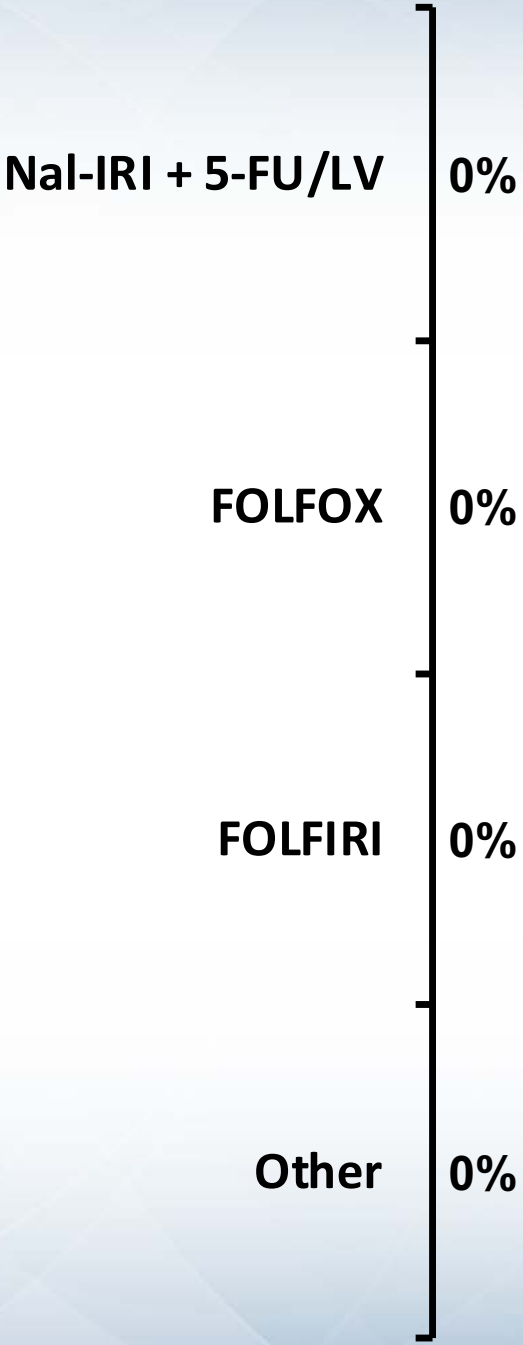
Outcome (all patients)	N = 107
Objective response rate	32.7%
Partial response rate	32.7%
Disease control rate (SD ≥24 weeks)	65.4%
Median PFS	10.8 mo
Estimated 1-y OS (interim analysis)	72%

Nab paclitaxel/gemcitabine was tolerable and QoL was maintained for most patients.

Hammel P et al. Gastrointestinal Cancers Symposium 2018;Abstract 204.

What second-line therapy would you recommend to a 75-year-old who is not a candidate for FOLFIRINOX and who receives first-line gemcitabine/*nab* paclitaxel for metastatic pancreatic cancer and experiences disease progression after 5 months?

1. **Nal-IRI + 5-FU/LV**
2. **FOLFOX**
3. **FOLFIRI**
4. **Other**



What second-line therapy would you recommend to a 75-year-old who is not a candidate for FOLFIRINOX and who receives first-line gemcitabine/*nab* paclitaxel for metastatic pancreatic cancer and experiences disease progression after 5 months?

 TANIOS BEKAII-SAAB, MD	Nal-IRI + 5-FU/LV
 JOHANNA BENDELL, MD	Nal-IRI + 5-FU/LV
 HOWARD S HOCHSTER, MD	FOLFIRI
 JOHN L MARSHALL, MD	Nal-IRI + 5-FU/LV
 EILEEN M O'REILLY, MD	Nal-IRI + 5-FU/LV
 PHILIP A PHILIP, MD, PHD	Nal-IRI + 5-FU/LV
 ALAN P VENOOK, MD	FOLFIRI

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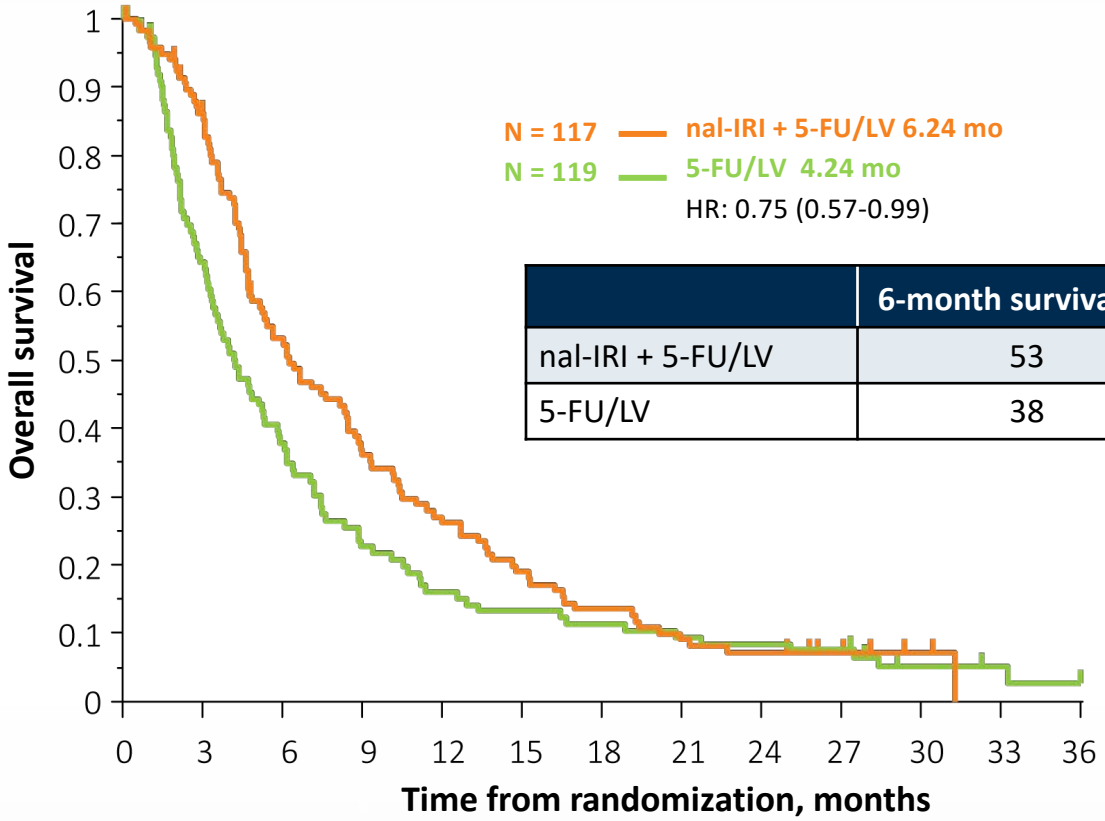
NAPOLI-1: Final Overall Survival and Tolerability with Nal-IRI/5-FU/LV vs 5-FU/LV as Second-Line Therapy

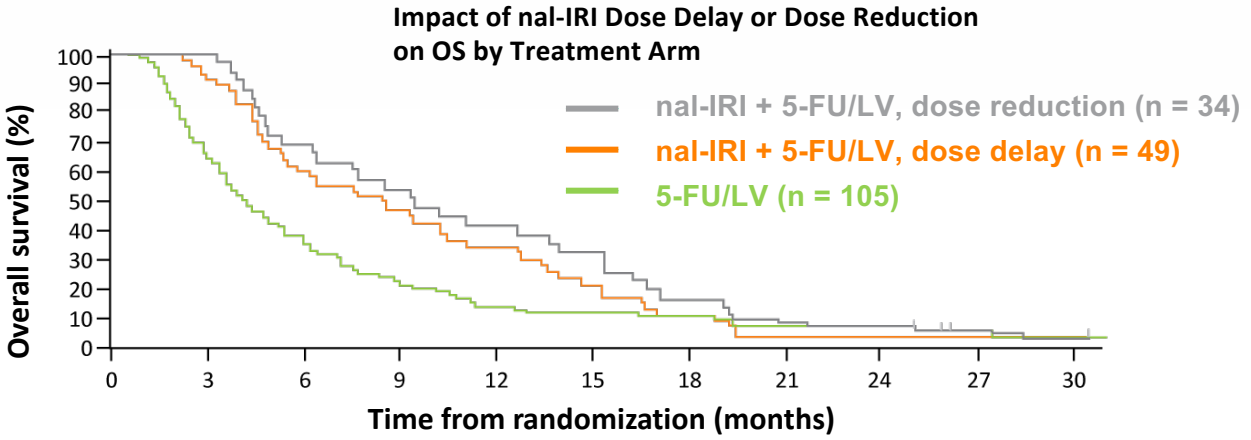


	6-month survival (%)	1-year survival (%)
nal-IRI + 5-FU/LV	53	26
5-FU/LV	38	16

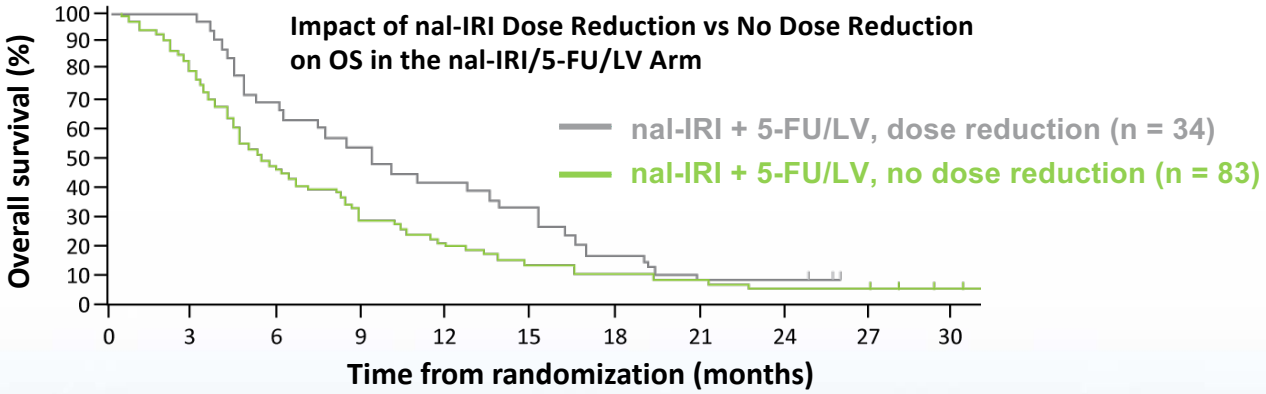
- Grade 3 and 4 adverse events with nal-IRI + 5-FU/LV included neutropenia (15.4%), diarrhea (9.4%), vomiting (6.0%) and fatigue (6.8%)
- Health-related quality of life was maintained with nal-IRI + 5-FU/LV

Wang-Gillam A et al. *Eur J Cancer* 2019;108:78-87;
Hubner RA et al. *Eur J Cancer* 2019;106:24-33; *Lancet* 2016;387:545-57.

NAPOLI-1: Impact on OS of Dose Modifications or Dose Delays of Nal-IRI + 5-FU/LV



OS was greater with nal-IRI/5-FU/LV vs 5-FU/LV only



No significant impact of dose reduction or dose delay on OS in the nal-IRI/5-FU/LV arm

Wang-Gillam A et al. Gastrointestinal Cancers Symposium 2018;Abstract 388.

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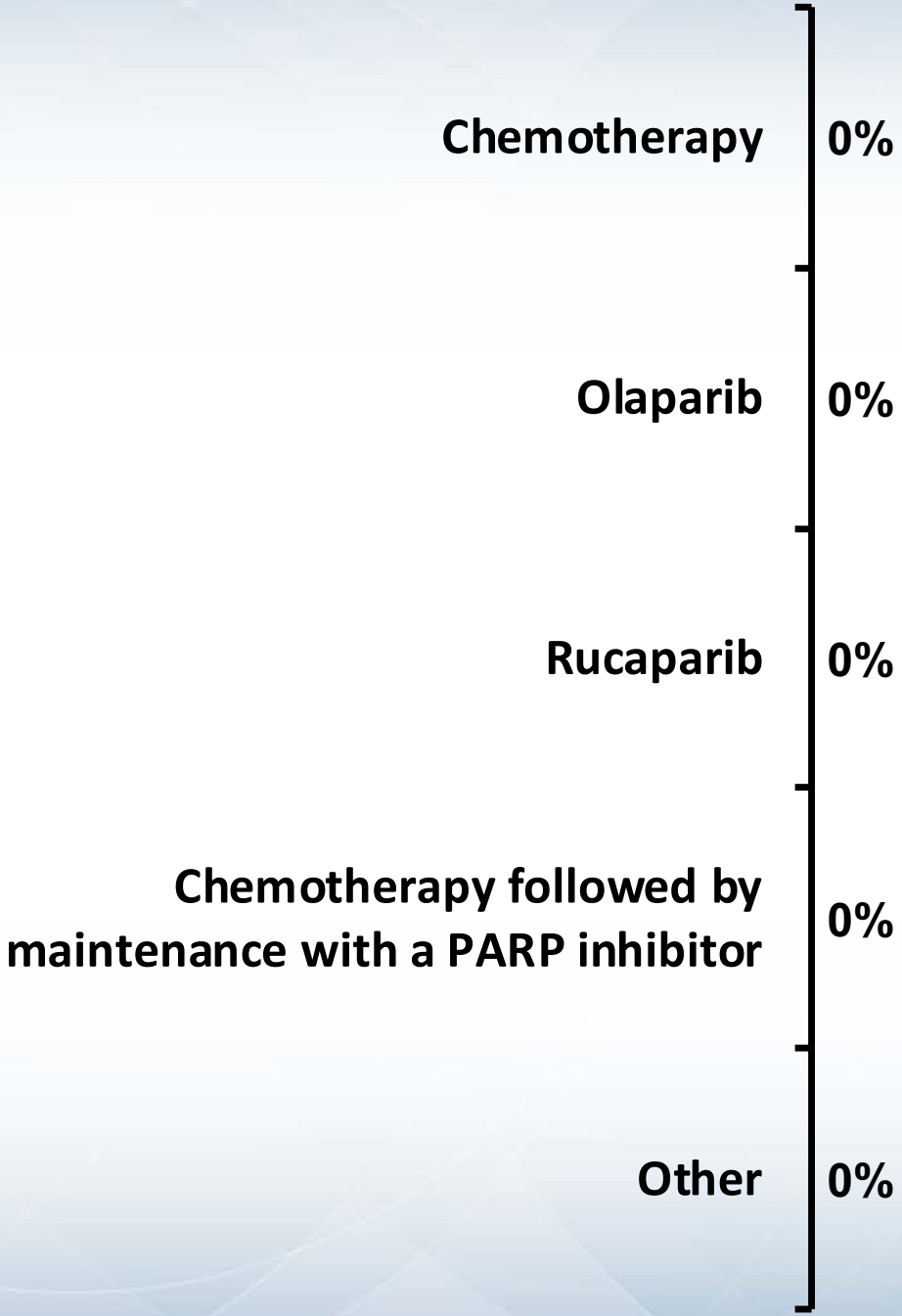
Regulatory and reimbursement issues aside, which treatment would you recommend to a 65-year-old patient who is diagnosed with unresectable metastatic pancreatic cancer with a deleterious germline BRCA2 mutation?

1. Chemotherapy
2. Olaparib
3. Rucaparib
4. Chemotherapy followed by maintenance with a PARP inhibitor
5. Other



Regulatory and reimbursement issues aside, which treatment would you recommend to a 65-year-old patient who is diagnosed with unresectable metastatic pancreatic cancer with a deleterious germline BRCA2 mutation?

Do you test for germline BRCA mutation status in your patients with metastatic pancreatic cancer and no significant family history of cancer?

	Tx for de novo mPCa with BRCA mutation	Test for BRCA mutations?
 TANIOS BEKAII-SAAB, MD	mFOLFIRINOX	Yes (Invitae assay)
 JOHANNA BENDELL, MD	FOLFIRINOX → maintenance olaparib	Yes (Foundation Medicine)
 HOWARD S HOCHSTER, MD	FOLFIRINOX → maintenance olaparib	No
 JOHN L MARSHALL, MD	FOLFOX → maintenance olaparib	No (somatic and WES)
 EILEEN M O'REILLY, MD	mFOLFIRINOX → maintenance olaparib	Yes (multigene panel)
 PHILIP A PHILIP, MD, PHD	modified FFX → Olaparib	Yes (germline and NGS)
 ALAN P VENOOK, MD	FOLFIRINOX	Yes (UCSF500 assay)

WES = whole exome sequencing

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DNA Damage Response (DDR) Tumor Mutations in Pancreatic Cancer

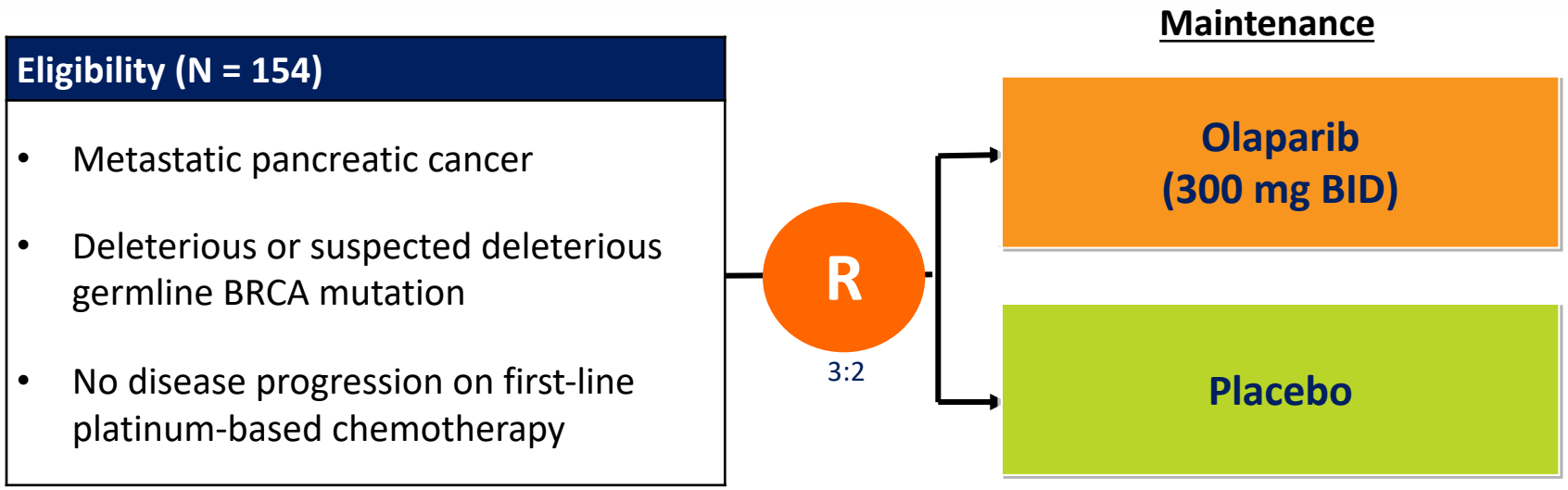
- 17%-25% of pancreatic adenocarcinomas harbor mutations in DDR genes, including those involved with homologous recombination

Gene (≥1% Detection)	KYT (N = 616)	Caris (N = 833)
ATM	4.5%	3.60%
BRCA2	2.9%	3.33%
SMARCA4	1.6%	NR
BAP1	1.3%	0.48%
BRCA1	1.3%	1.41%
BRIP1	1.0%	0.48%
PALB2	0.8%	1.2%

Know Your Tumor® (KYT) Data Set; Caris Database Review

Adapted from Michael Pishvaian, MD, PhD

POLO: A Phase III Trial of Maintenance Olaparib for Metastatic Adenocarcinoma of the Pancreas

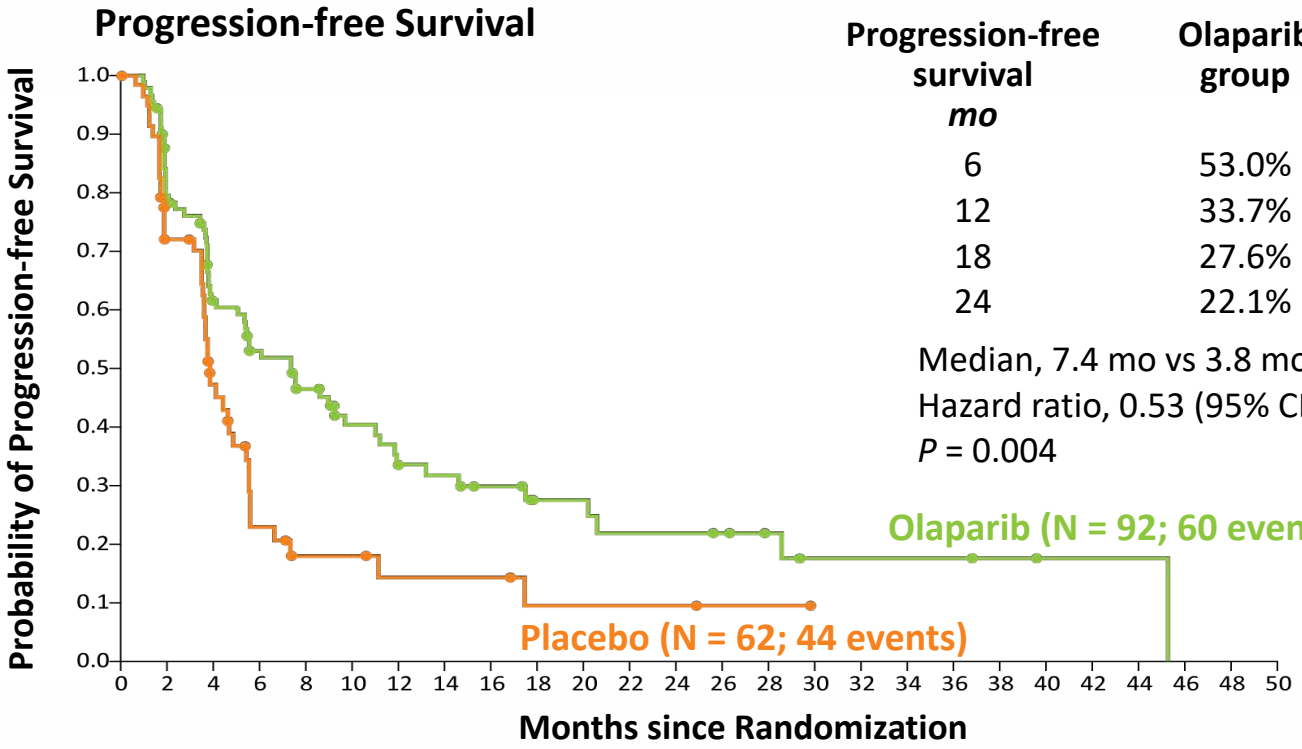


Primary endpoint: Progression-free survival

Key secondary endpoints include overall survival, time to second disease progression, response rate and health-related quality of life, disease control rate

www.clinicaltrials.gov (NCT02184195); https://www.astrazeneca.com/media-centre/press-releases/2019/lynparza-significantly-delayed-disease-progression-as-1st-line-maintenance-treatment-in-germline-brca-mutated-metastatic-pancreatic-cancer-26022019.html.

POLO: A Phase III Trial of Maintenance Olaparib for Metastatic Pancreatic Cancer with BRCA Mutation



Progression-free survival *mo*	Olaparib group	Placebo group
6	53.0%	23%
12	33.7%	14.5%
18	27.6%	9.6%
24	22.1%	9.6%

Median, 7.4 mo vs 3.8 mo
Hazard ratio, 0.53 (95% CI, 0.35-0.82)
P = 0.004

- An interim analysis of overall survival showed no difference between olaparib and placebo (median 18.9 mo vs 18.1 mo, HR 0.91, *p* 0.68)
- The adverse-effect profile of maintenance olaparib was similar to that observed in other tumor types

Golan T et al. *N Engl J Med* 2019;381(4):317-27.

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Phase II Interim Analysis of Maintenance Rucaparib for Patients with Advanced Pancreatic Cancer and BRCA1/2 or PALB2 Mutations

Outcome	n = 24
PFS	9.1 mo
Overall response rate	36.8%
Disease control rate	89.5%

- Patients with advanced pancreatic cancer and pathogenic germline or somatic mutation in BRCA1/2 or PALB2 were enrolled
- Treatment with rucaparib was well tolerated without dose-limiting toxicities
- Most common adverse events: nausea, dysgeusia, fatigue

Binder KR et al. *Proc AACR* 2019;Abstract CT234.

Novel and Emerging Therapeutic Strategies in the Management of Select Gastrointestinal Cancers

Module 1: Colorectal Cancer

- Primary tumor sidedness and selection of first-line therapy
- Sequencing of available therapies in the second line and beyond
- Novel targeted approaches

Module 2: Hepatocellular Carcinoma

- First-line systemic treatment: Sorafenib versus lenvatinib
- Beyond first-line therapy: Cabozantinib, ramucirumab, regorafenib and anti-PD-1/PD-L1 antibodies

Module 3: Pancreatic Cancer

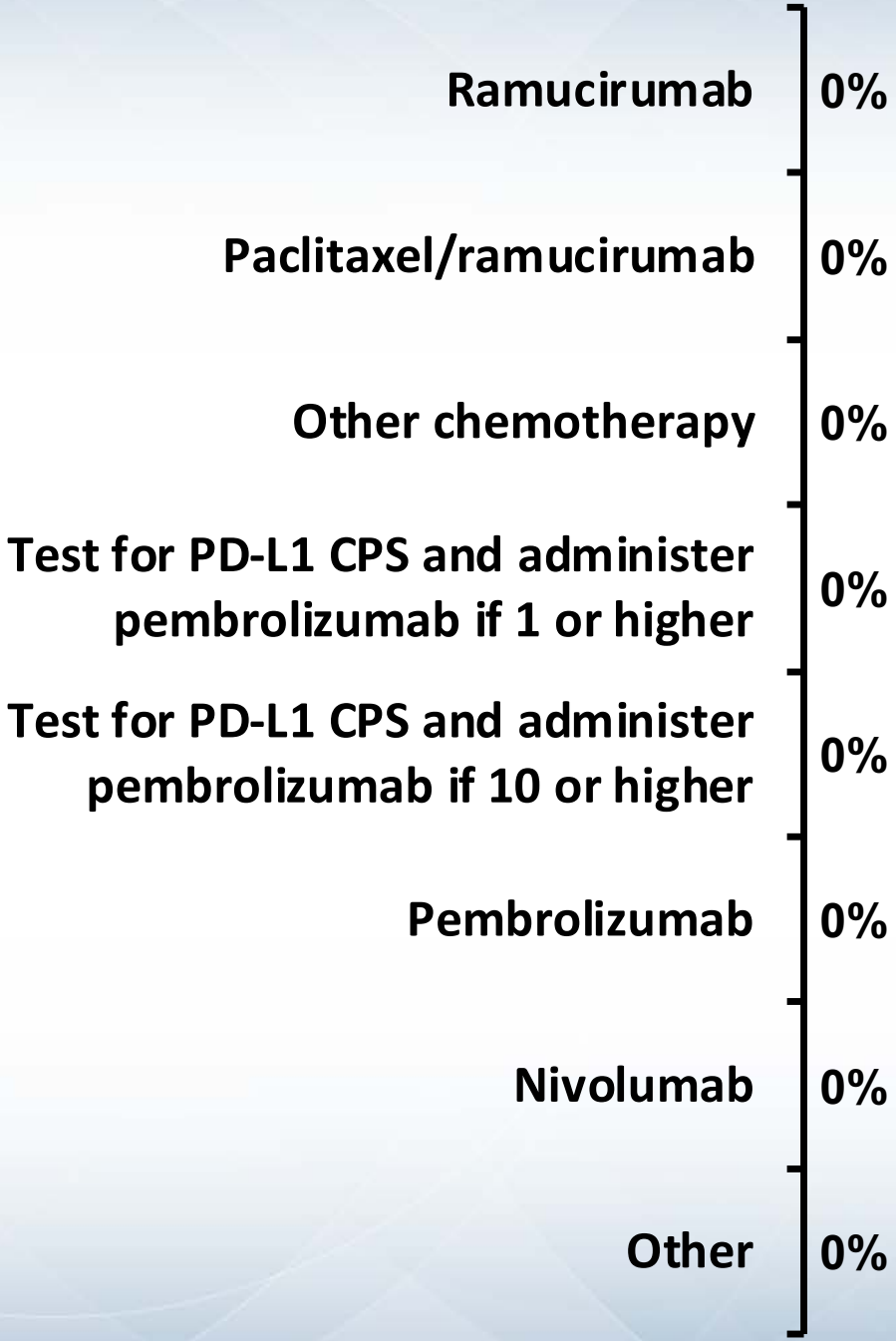
- Neoadjuvant and adjuvant therapy approaches
- Management of metastatic disease and integration of nanoliposomal irinotecan
- BRCA mutations and PARP inhibition

Module 4: Gastric/Gastroesophageal Junction (GEJ)/Esophageal Cancer

- Pembrolizumab for the treatment of recurrent or advanced gastric, GEJ and esophageal cancer
- Efficacy and safety of TAS-102 for recurrent metastatic gastric or GEJ adenocarcinoma

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-negative, MSS gastric cancer who has experienced disease progression on first-line FOLFOX?

1. Ramucirumab
2. Paclitaxel/ramucirumab
3. Other chemotherapy
4. Test for PD-L1 CPS and administer pembrolizumab if 1 or higher
5. Test for PD-L1 CPS and administer pembrolizumab if 10 or higher
6. Pembrolizumab
7. Nivolumab
8. Other



Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-negative, MSS gastric cancer who has experienced disease progression on first-line FOLFOX?

 TANIOS BEKAII-SAAB, MD	Test for PD-L1 CPS, administer pembrolizumab if ≥10
 JOHANNA BENDELL, MD	Paclitaxel/ramucirumab
 HOWARD S HOCHSTER, MD	Test for PD-L1 CPS, administer pembrolizumab if ≥10
 JOHN L MARSHALL, MD	Paclitaxel/ramucirumab
 EILEEN M O'REILLY, MD	Test for PD-L1 CPS, administer pembrolizumab if ≥10
 PHILIP A PHILIP, MD, PHD	Test for PD-L1 CPS, administer pembrolizumab if ≥10
 ALAN P VENOOK, MD	Test for PD-L1 CPS, administer pembrolizumab if ≥1

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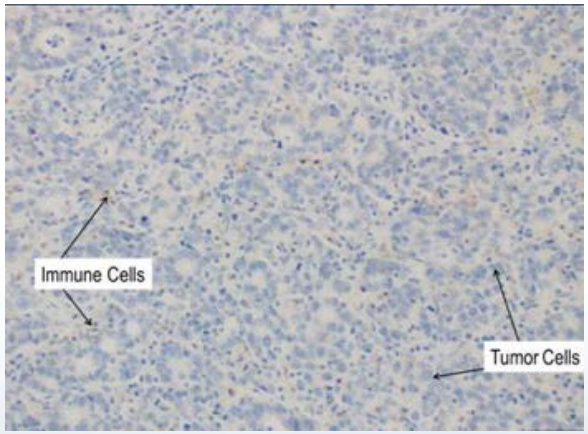
KEYNOTE-059 Trial Cohort 1: PD-L1 Expression and Combined Positive Score (CPS)

- PD-L1 expression is determined by the CPS

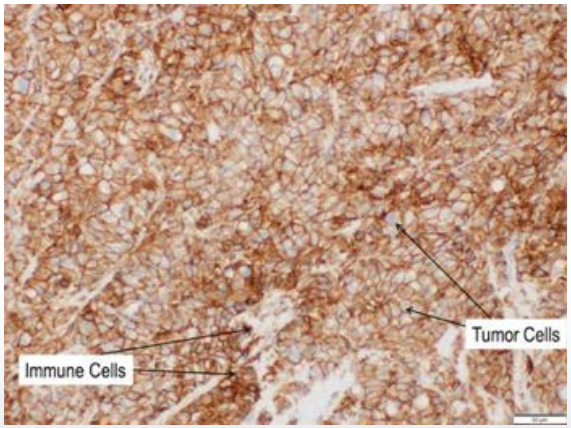
$$\text{CPS} = \frac{\text{Number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages)}}{\text{Total number of viable tumor cells}} \times 100$$

- A specimen is considered to have positive PD-L1 expression if CPS ≥1%

PD-L1-negative



PD-L1-positive



Fuchs CS et al. *Proc ASCO* 2017;Abstract 4003.

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Pembrolizumab in Advanced Gastric or Gastroesophageal Cancer

- Accelerated approval of pembrolizumab monotherapy as third- or later-line therapy was based on the Phase II KEYNOTE-059 study
  - ORR: 11.6% (all patients); 15.5% (PD-L1-positive); 57% (MSI-high)
- Phase III KEYNOTE-061 trial of pembrolizumab versus paclitaxel as second-line therapy did not meet its primary endpoint of OS in patients with CPS ≥1
  - Median OS: Pembrolizumab 9.1 mo, paclitaxel 8.3 mo (HR 0.82; $p = 0.042$)
- Phase III KEYNOTE-062 trial evaluates pembrolizumab with or without chemotherapy versus chemotherapy as first-line therapy

Fuchs C et al. *JAMA Oncol* 2018;4(5):e180013; Shitara K et al. *Lancet* 2018;392(10142):123-33; Tabernero J et al. *Proc ASCO* 2019;Abstract LBA4007. Shitara K et al. *Proc ESMO* 2019;Abstract LBA44.

KEYNOTE-062: A Phase III Trial of Pembrolizumab with and without Chemotherapy as First-Line Treatment for Advanced Gastric or GEJ Adenocarcinoma

CPS ≥1	Pembro + chemo (n = 257)	Pembro (n = 256)	Chemo (n = 250)
Median OS	12.5 mo	10.6 mo	11.1 mo
HR, *p*-value	0.85, 0.046	0.91, 0.91	Ref
MSI-H	**Pembro + chemo (n = 17)**	**Pembro (n = 14)**	**Chemo (n = 19)**
Median OS	Not reached	Not reached	8.5 mo
HR	0.37	0.29	Ref

- Pembrolizumab was noninferior to chemotherapy for OS in patients with CPS ≥1, and a clinically meaningful improvement in OS was reported with pembro versus chemo for patients with CPS ≥10 (17.4 mo vs 10.8 mo, HR 0.69)
- Pembrolizumab + chemotherapy did not show superior OS or PFS for patients with CPS ≥1 or OS for CPS ≥10.

Shitara K et al. *Proc ESMO* 2019;Abstract LBA44.

Pembrolizumab Approved as Monotherapy for Recurrent Locally Advanced or Metastatic Squamous Cell Carcinoma of the Esophagus

Press Release – July 31, 2019

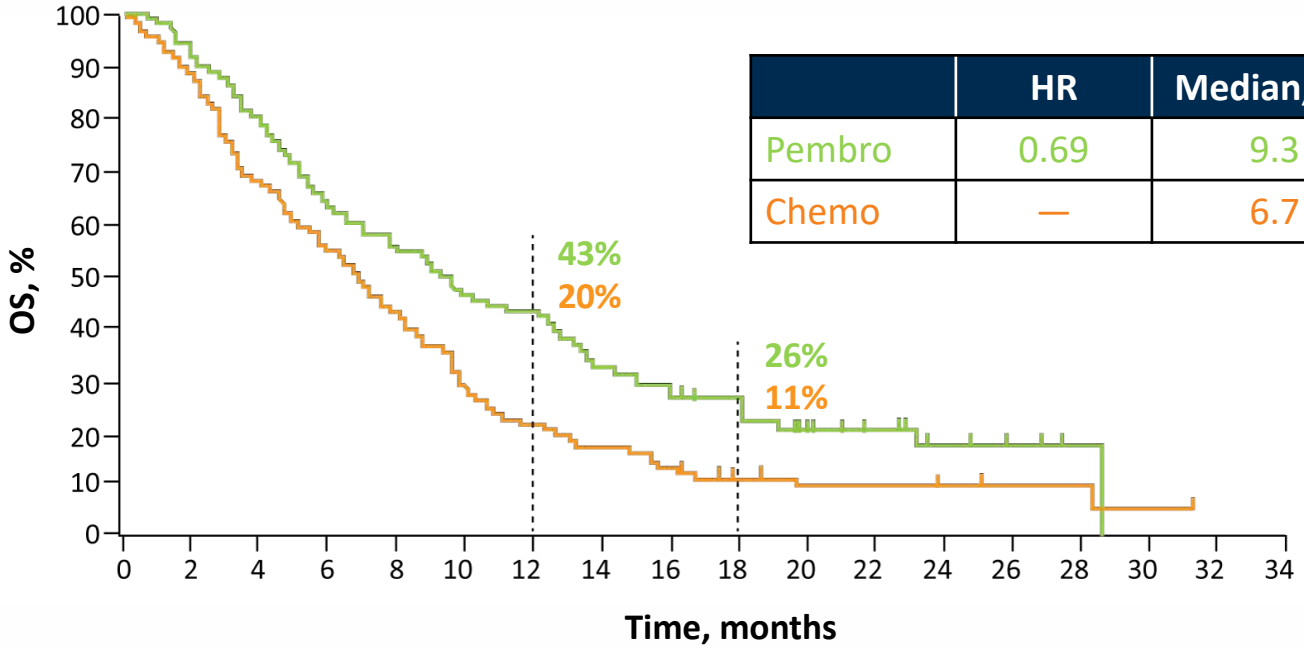
"The US Food and Drug Administration has approved pembrolizumab as monotherapy for the treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus whose tumors express PD-L1 (**Combined Positive Score [CPS] ≥10**) as determined by an FDA-approved test, with disease progression after one or more prior lines of systemic therapy.

The approval was based on data from KEYNOTE-181, a multicenter, randomized, open-label, active-controlled trial [for] patients with recurrent locally advanced or metastatic esophageal cancer who progressed on or after one prior line of systemic treatment for advanced disease."

https://www.businesswire.com/news/home/20190731005305/en/FDA-Approves-New-Monotherapy-Indication-Merck%E2%80%99s-KEYTRUDA%C2%AE

KEYNOTE-181: A Phase III Trial of Second-Line Pembrolizumab Compared to Chemotherapy for Advanced Esophageal Cancer

Overall Survival (PD-L1 CPS ≥10) for Patients with Squamous Cell Carcinoma



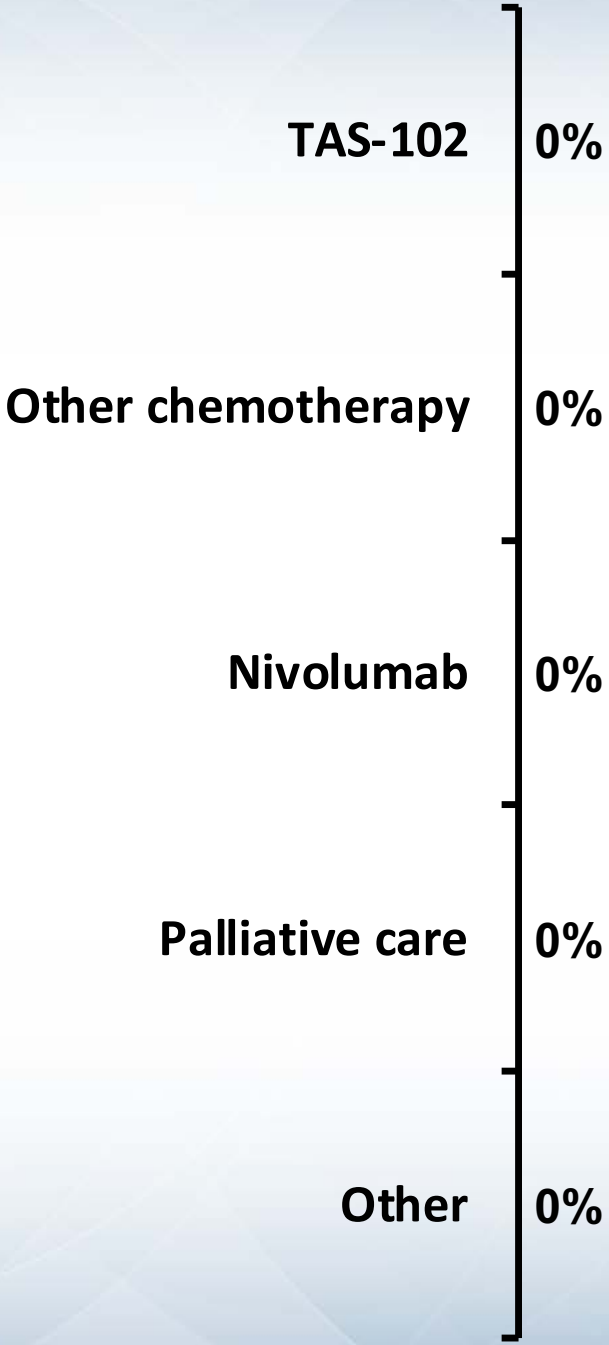
	HR	Median, mo	*p*-value
Pembro	0.69	9.3	0.0074
Chemo	—	6.7	

- ORR higher with pembrolizumab than with chemotherapy for patients with CPS ≥10 (21.5% vs 6.1%)
- Lower frequency of Grade 3-5 treatment-related adverse events with pembrolizumab than with chemotherapy (18.2% vs 40.9%); no new safety signals observed

Kojima T et al. Gastrointestinal Cancers Symposium 2019;Abstract 2;
Metges J et al. *Proc ESMO World GI Congress* 2019;Abstract O-012.

What is your usual third-line treatment for a patient with metastatic HER2-negative, MSS gastric cancer (PD-L1 CPS lower than 1) who has experienced disease progression on FOLFOX and paclitaxel/ramucirumab?

1. TAS-102
2. Other chemotherapy
3. Nivolumab
4. Palliative care
5. Other



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 TANIOS BEKAII-SAAB, MD	TAS-102
 JOHANNA BENDELL, MD	Irinotecan
 HOWARD S HOCHSTER, MD	TAS-102
 JOHN L MARSHALL, MD	TAS-102
 EILEEN M O'REILLY, MD	Nivolumab
 PHILIP A PHILIP, MD, PHD	FOLFIRI
 ALAN P VENOOK, MD	TAS-102

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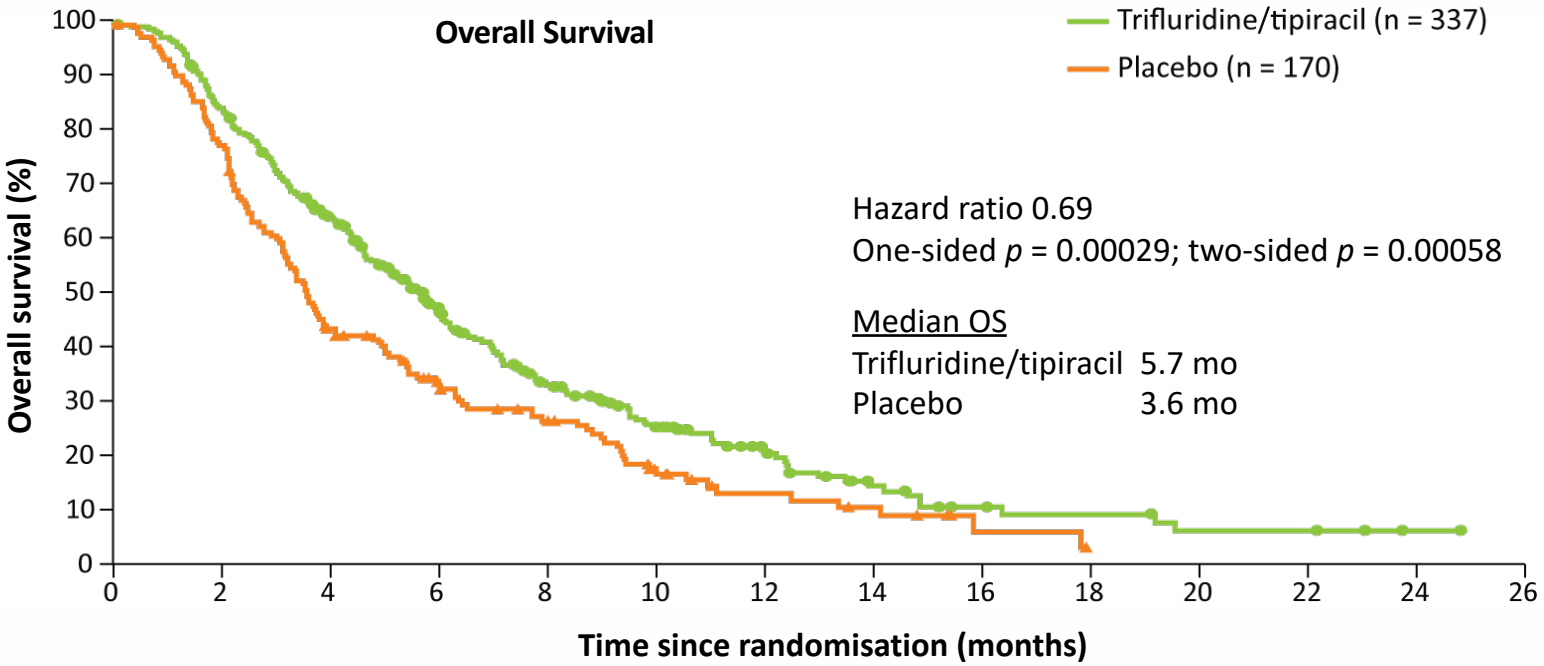
Phase III TAGS Trial of Trifluridine/Tipiracil for Patients with Heavily Pretreated Metastatic Gastric Cancer: Outcome Summary



Clinical variable	Trifluridine/tipiracil	Placebo	HR	*p*-value
Median PFS	2.0 mo	1.8 mo	0.57	<0.0001
ORR	4.0%	2.0%	—	0.28

Shitara K et al. *Lancet Oncol* 2018;19(11):1437-48.

Questions?

To view the slides please visit
www.ResearchToPractice.com/Meetings/Slides

Novel and Emerging Therapeutic Strategies in the Management of Select Gastrointestinal Cancers

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