CHALLENGING CASES

Colon Cancer

Prepared by: Cornerstone Specialty Network

Challenging Cases Conducted: July 15 and September 24, 2025

Participating Practices

Challenging Cases in… Colon Cancer

Program conducted:

July–September 2025

Note: Aggregated results and high-level summary based on 2 practices (≤13 HCPs) and do not necessarily reflect the views and opinions of the moderator or Cornerstone Specialty Network unless otherwise stated. Clinical data, NCCN Guidelines, and FDA approvals current at time of presentation.

Report completed: December 2025

- **Fort Wayne Oncology & Hematology (n=4)** **July 15, 2025**
- **Northwest Georgia Oncology Centers (n=9)** **September 24, 2025**

Overall Program Impact and Future Considerations

Colon cancer management is guided by multidisciplinary input and ctDNA testing via Signatera and Guardant, with FOLFOX + atezolizumab commonly used post-surgery; emerging interest in perioperative immunotherapy for dMMR disease, with progression managed by re-testing and dual immunotherapy favored for first-line metastatic treatment

- Multidisciplinary teams (MDT) are commonly utilized to support decision-making, while those who do not have an official MDT rely on connections with specialists to help manage patients with colon cancer
- ctDNA testing is commonly utilized to guide treatment decisions, with Natera (Signatera) and Guardant as the main vendors
- Majority recommend FOLFOX + Atezolizumab as treatment after surgery
- Advisors would prefer dual IO or single agent IO in the neoadjuvant setting if approved for dMMR colon cancer
- Retesting is frequently performed at first metastatic progression to inform subsequent treatments
- Upon tumor progression, most recommend either dual immunotherapy or FOLFOX ± bevacizumab for first-line metastatic treatment
- ***Recommended actions:*** *Provide education, real-world data, and support tools to guide treatment decisions based on ctDNA testing with Signatera and Guardant for evidence of molecular residual disease (MRD), educate on the benefit of early use of immunotherapy for dMMR colon cancer, and evidence-based sequencing at progression*

Challenging Cases in Colon Cancer

Colon Cancer

Patient Case: dMMR colon cancer

- *What is the optimal treatment strategy for patients with dMMR tumors?*
- *What impact will new clinical data have on your treatment decisions?*
- *Awareness of recent FDA approvals?*

1st-line Neo/Adjuvant Therapy Decision

Patient History

72-year-old woman

- *2-month history of bloating and abdominal discomfort*
- *Prior colonoscopy (2-years ago): negative*
- *Unintentional weight loss*
- *Hysterectomy*
- *High blood pressure*
- *No family history*

Metastatic Diagnosis

CBCs: Hg 8.4 g/dL with elevated CEA of 6 ng/mL

Colonoscopy: 3.8-cm mass ascending colon

Biopsy: adenocarcinoma

Mismatch repair-deficient (dMMR), KRAS, NRAS, HER2, and BRAF wild type

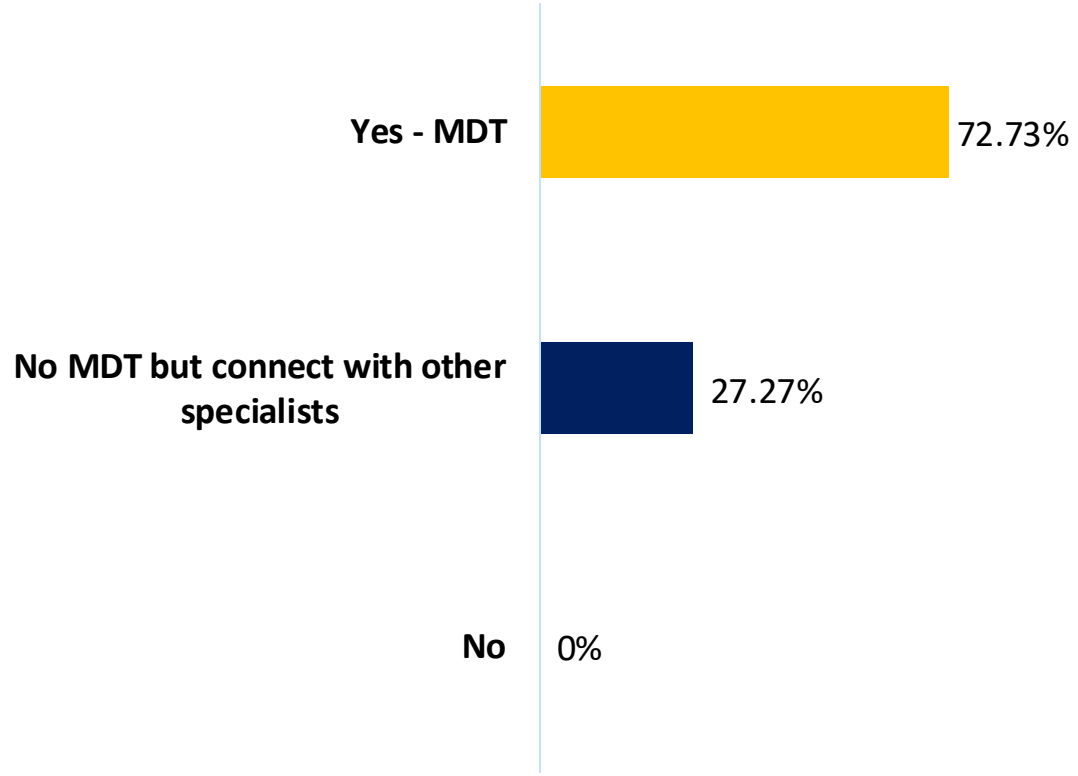
CT scan: LN positive

ECOG PS 1

Stage III: T1-3, N1, M0

ARS Results from HCP Participants

Do you have a multidisciplinary team (MDT) to help manage patients with colon cancer?



Answered: 11

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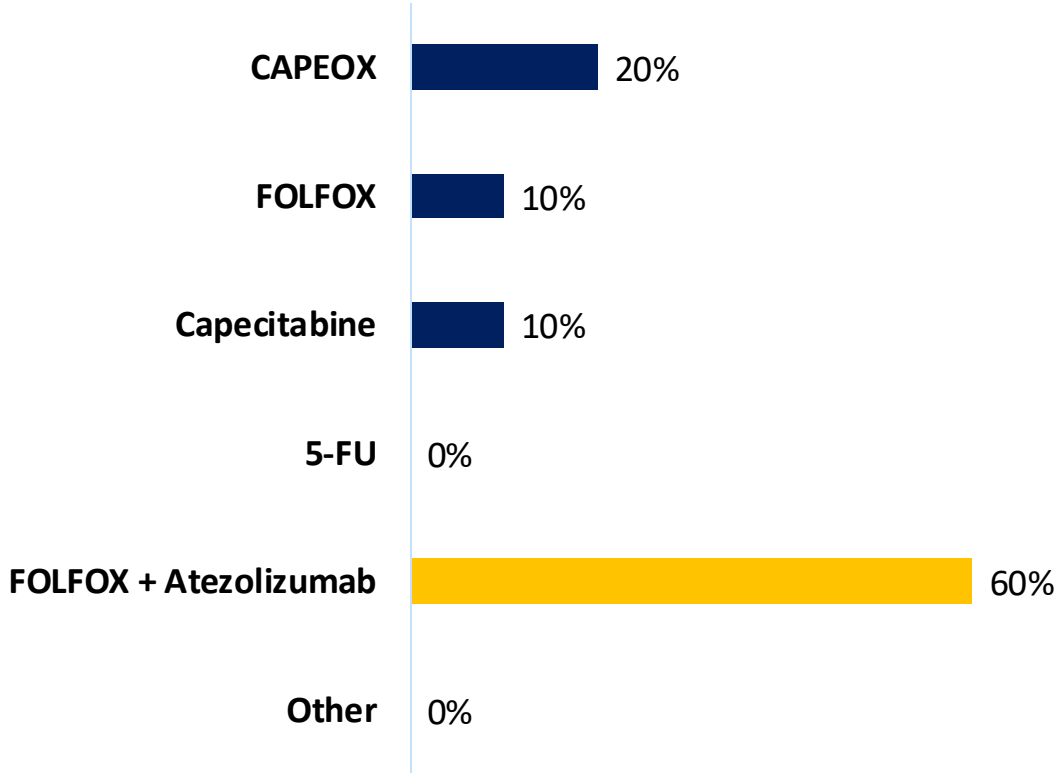
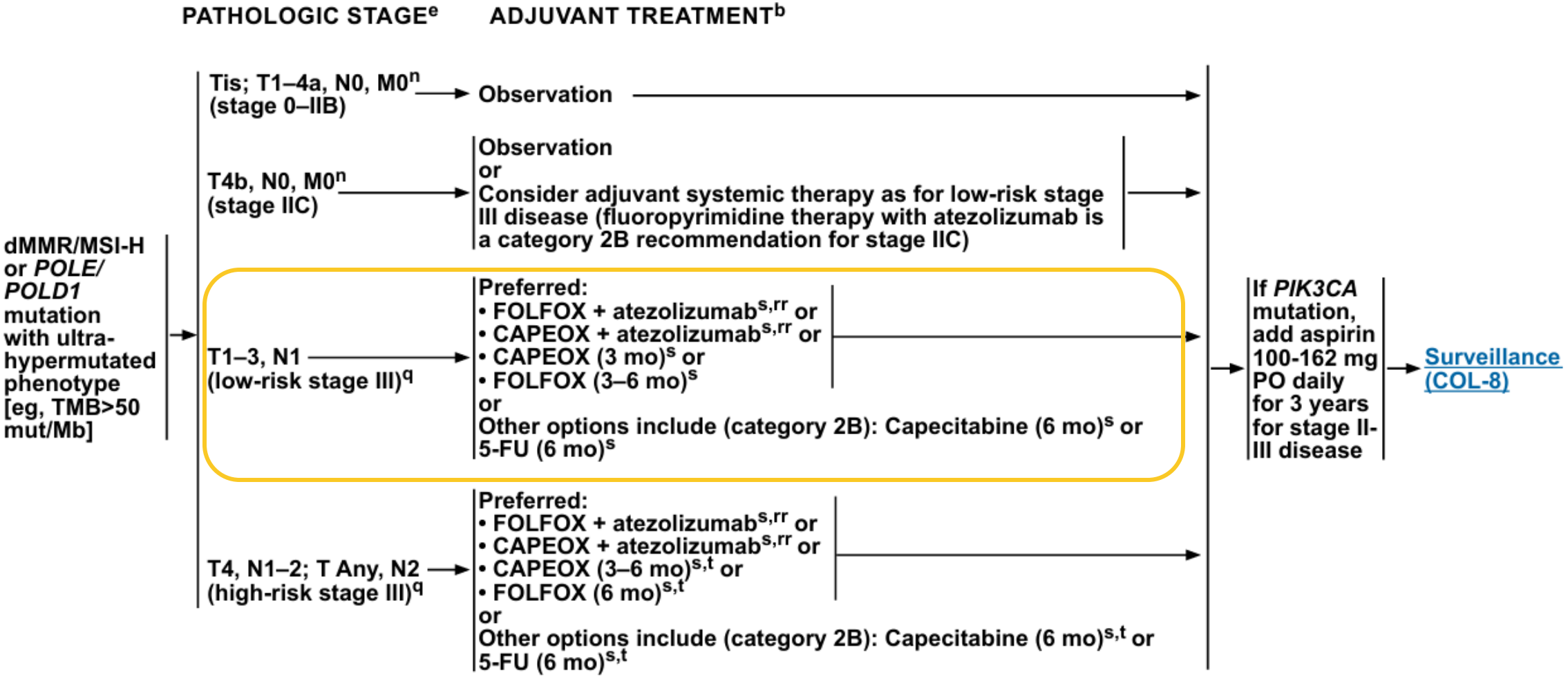
What is your treatment recommendation after surgery?

ARS Results from HCP Participants

What is your treatment recommendation after surgery?



Answered: 10

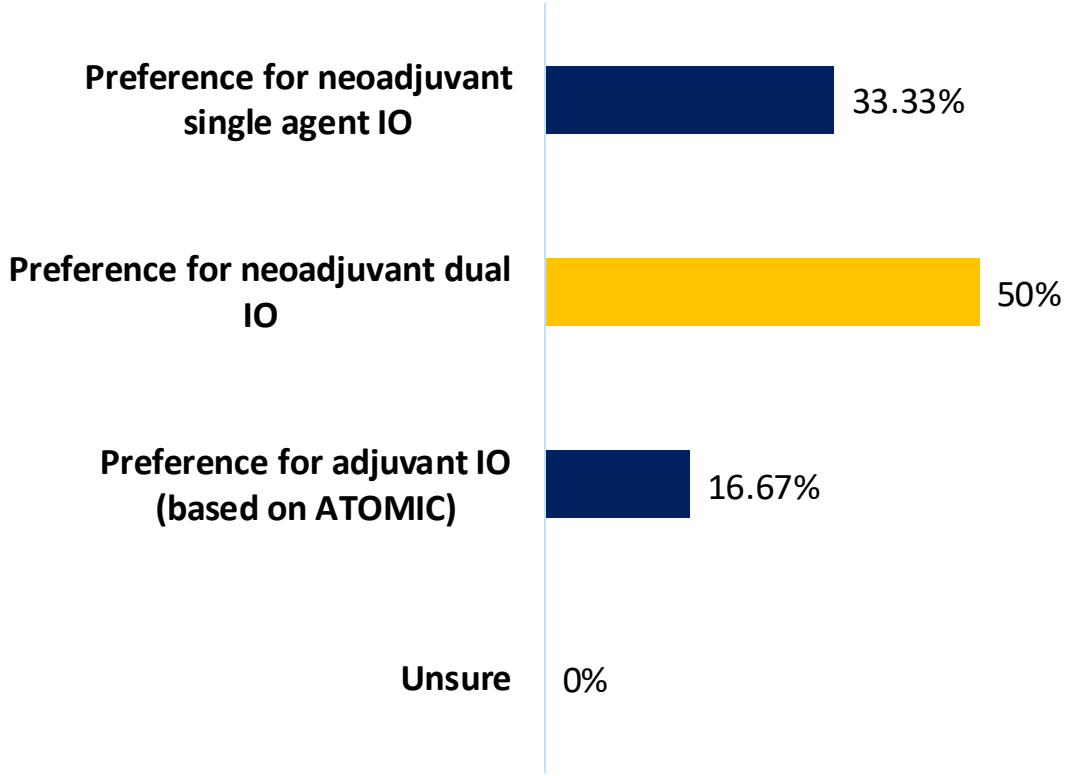


Efficacy of Neoadjuvant IO In dMMR Colon Cancer

Study	Treatment Regimen	Treatment duration	No. of patients	pCR or cCR rate	Grade 3-4 adverse events
NICHE-2 *N Engl J Med.* 2024;390(21):1949-1958.	NIVO + IPI	4 weeks	115	68%	5%
Xu et al., ASCO 2024	Sintilimab ± IBI310	6 weeks	101	78% vs 47%	10% (mono) 6% (dual)
NICHE-3 *Nat Med.* 2024;30(11):3284-3290.	NIVO + relatlimab	8 weeks	59	68%	10%
PICC *Lancet Gastroenterol Hepatol.* 2022;7(1):38-48.	Toripalimab + celecoxib	12 weeks	34	88%	3%
PICC *Lancet Gastroenterol Hepatol.* 2022;7(1):38-48.	Toripalimab *(w/o celecoxib)*	12 weeks	34	65%	3%
NEOPRISM	Pembro	6 Weeks	32	58%	6%
IMHOTEP *Ann Oncol.* 2024;35(suppl 2):S429.	Pembro	4-8 Weeks	77	47% (1 cycle) 68% (2 cycles)	13%
N Engl J Med 2025;392:2297-2308	Dostarlimab	6 months	22	82%	6%

ARS Results from HCP Participants

If neoadjuvant or adjuvant IO was approved for dMMR colon cancer what would be your treatment preference?



Answered: 6

2nd case: 1st-line mBC Therapy Decision

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Metastatic Diagnosis

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dMMR, KRAS, NRAS, HER2,and BRAF wild type

CT scan: liver lesions

ECOG PS 1

Stage IV colon cancer

Do you retest at first metastatic progression?

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ARS Results from HCP Participants

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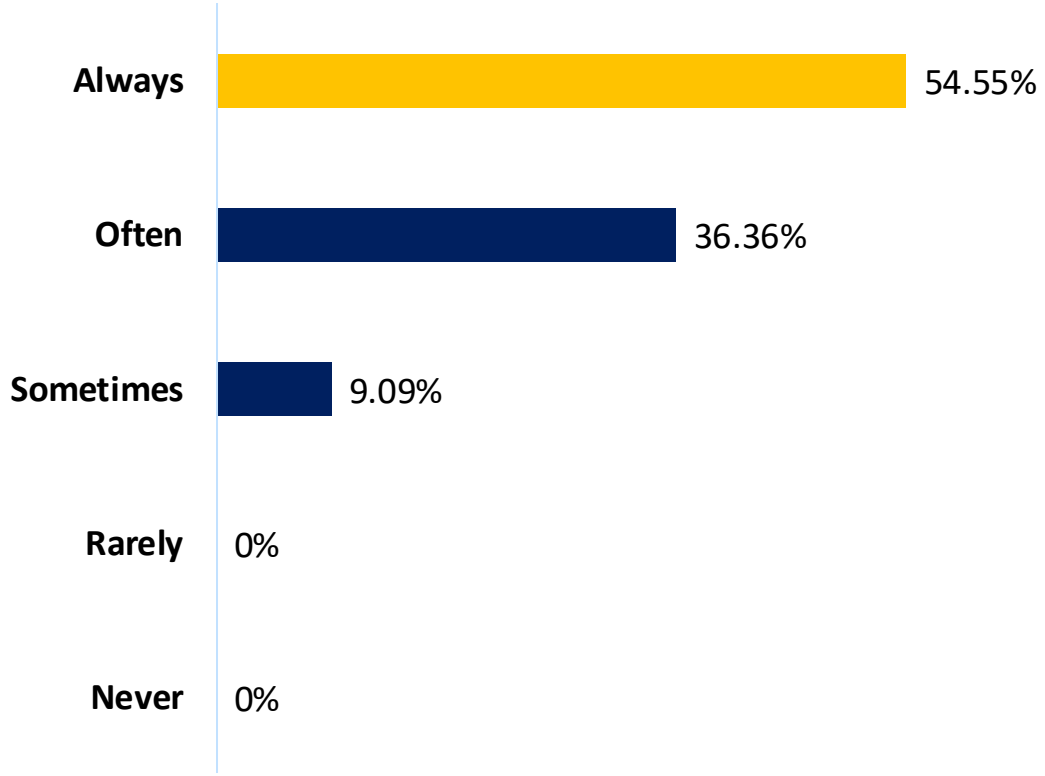

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dMMR, KRAS, NRAS, and BRAF wild type

CT scan: liver lesions

ECOG PS 1

Stage IV colon cancer

What is your first line metastatic treatment recommendation on tumor progression?

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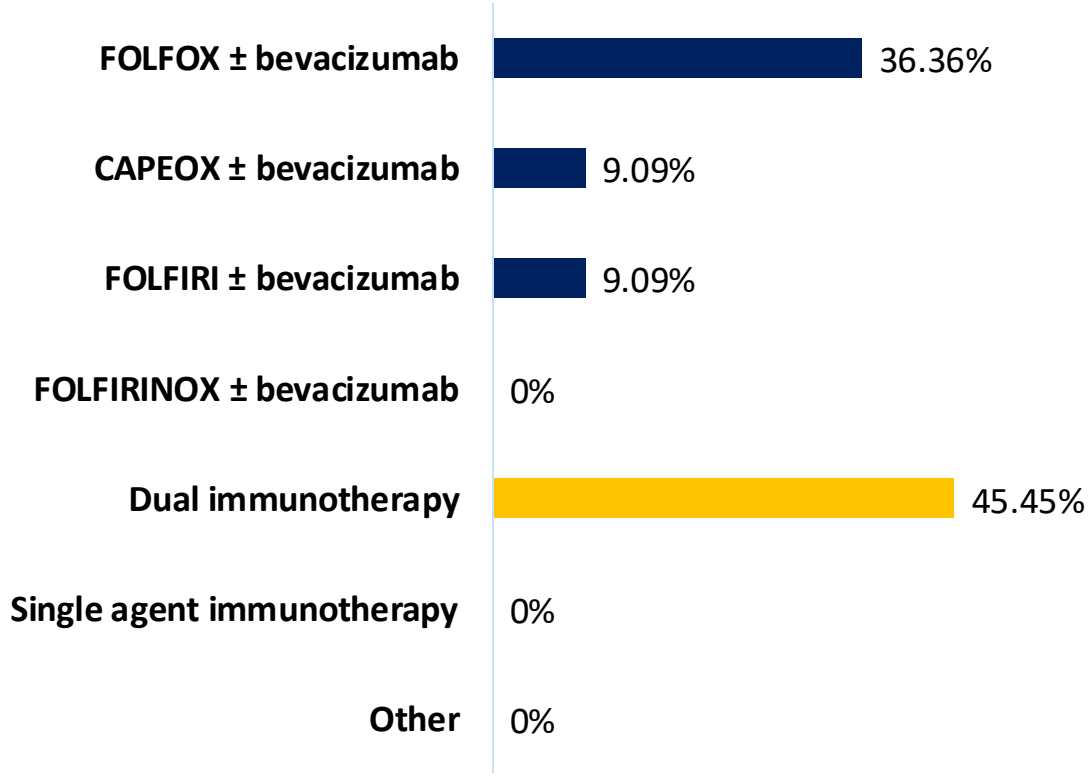
ARS Results from HCP Participants

What is your first line metastatic treatment recommendation on tumor progression?



Answered: 11

CONTINUUM OF CARE - SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE[a,b,c]

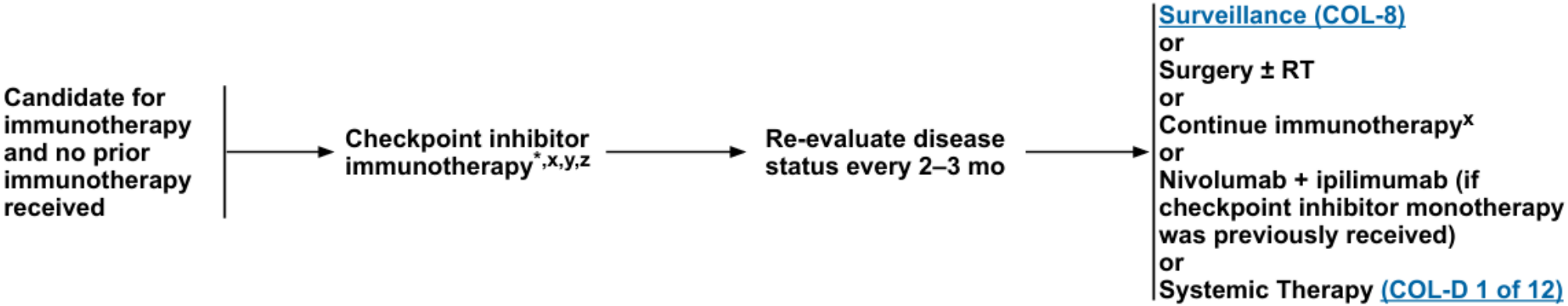
pMMR/MSS (or dMMR/MSI-H or *POLE/POLD1* mutation with ultra-hypermutated phenotype [eg, TMB>50 mut/Mb] that is ineligible for or progressed on checkpoint inhibitor immunotherapy)

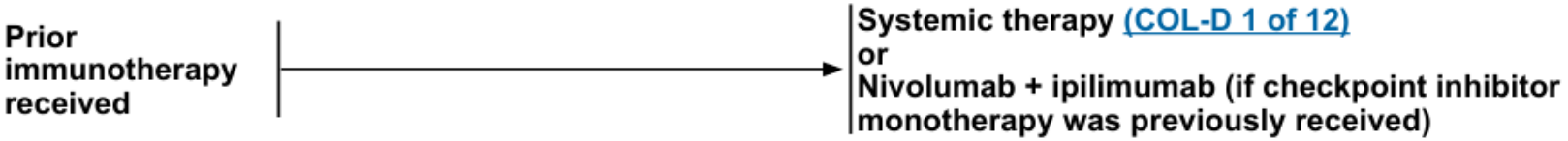
INITIAL THERAPY[d]	
Intensive Therapy Recommended	**Intensive Therapy NOT Recommended**
• FOLFOX[e] ± bevacizumab • CAPEOX[e] ± bevacizumab • FOLFIRI[f] ± bevacizumab • FOLFIRINOX[e,f,g,h] ± bevacizumab • *KRAS/NRAS/BRAF* WT[i] and left-sided tumors only: ▸ FOLFOX[e] + (cetuximab or panitumumab)[j,k] ▸ CAPEOX[e] + (cetuximab or panitumumab)[j,k] ▸ FOLFIRI[f] + (cetuximab or panitumumab)[j,k] • *BRAF* V600E mutation positive[j]: ▸ Encorafenib + (cetuximab or panitumumab) + FOLFOX[e] • If disease progression, see COL-D 2 of 12	• 5-FU ± leucovorin ± bevacizumab • Capecitabine ± bevacizumab • *KRAS/NRAS/BRAF* WT[i] and left-sided tumors only: ▸ (Cetuximab or panitumumab)[j,k] (category 2B) • HER2-amplified and *RAS and* BRAF WT[j]: ▸ Trastuzumab + [pertuzumab or lapatinib or tucatinib][l] • If disease progression and improvement in functional status: ▸ Consider initial therapy in first column[m] ▸ OR if previous fluoropyrimidine, see COL-D 2 of 12 • If disease progression and no improvement in functional status, see best supportive care (NCCN Guidelines for Palliative Care)

For dMMR/MSI-H or *POLE/POLD1* mutation with ultra-hypermutated phenotype [eg, TMB>50 mut/Mb], see COL-D 3 of 12

CONTINUUM OF CARE - SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE[a,b,c]

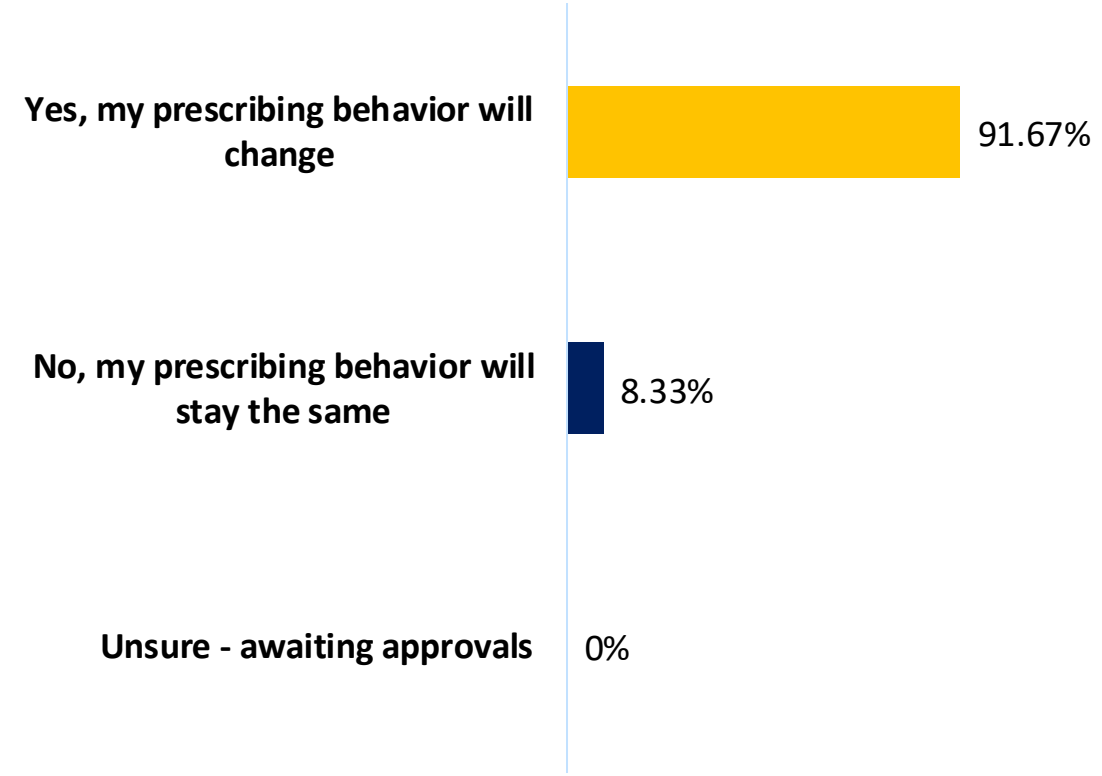
dMMR/MSI-H or *POLE/POLD1* mutation with ultra-hypermutated phenotype [eg, TMB>50 mut/Mb]
Any line of therapy





ARS Results from HCP Participants

Will the challenging case discussed impact your prescribing behavior for patients with dMMR colon cancer?



Answered: 12

Key Takeaways

Colon Cancer

Patient Case: 1st line mBC

- *MMR deficiency is a predictive biomarker for immunotherapy efficacy*
  - *Patient identification is important*
- *Adjuvant IO plus chemotherapy benefits patients with resected stage 3 dMMR (ATOMIC)*
  - *Potentially practice changing but is yet to be approved or added to NCCN Guidelines*
- *Neoadjuvant IO may be more effective with de-escalation of chemotherapy*
  - *Strategy extrapolation from other tumor types?*