Survey of 50 General Medical Oncologists: Colorectal Cancer

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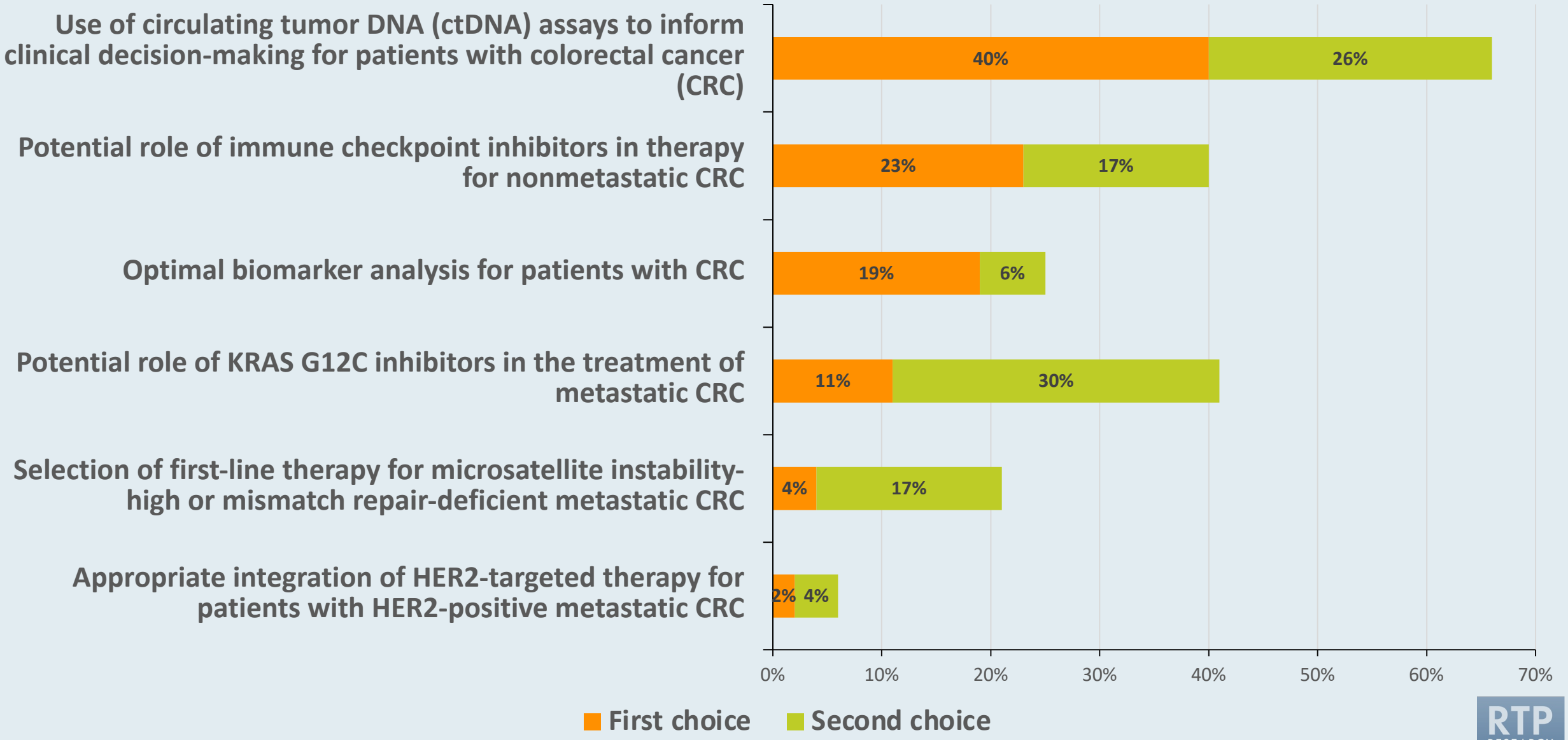
TO PRACTICE

Topics of Interest for Future CME Programs



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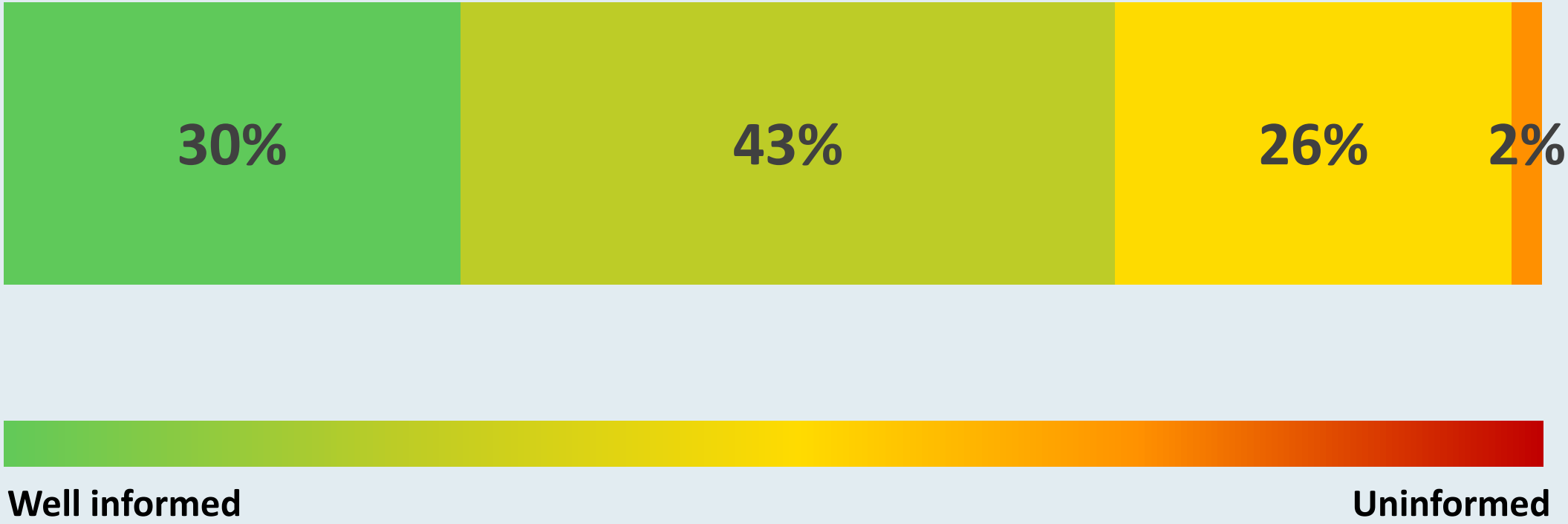
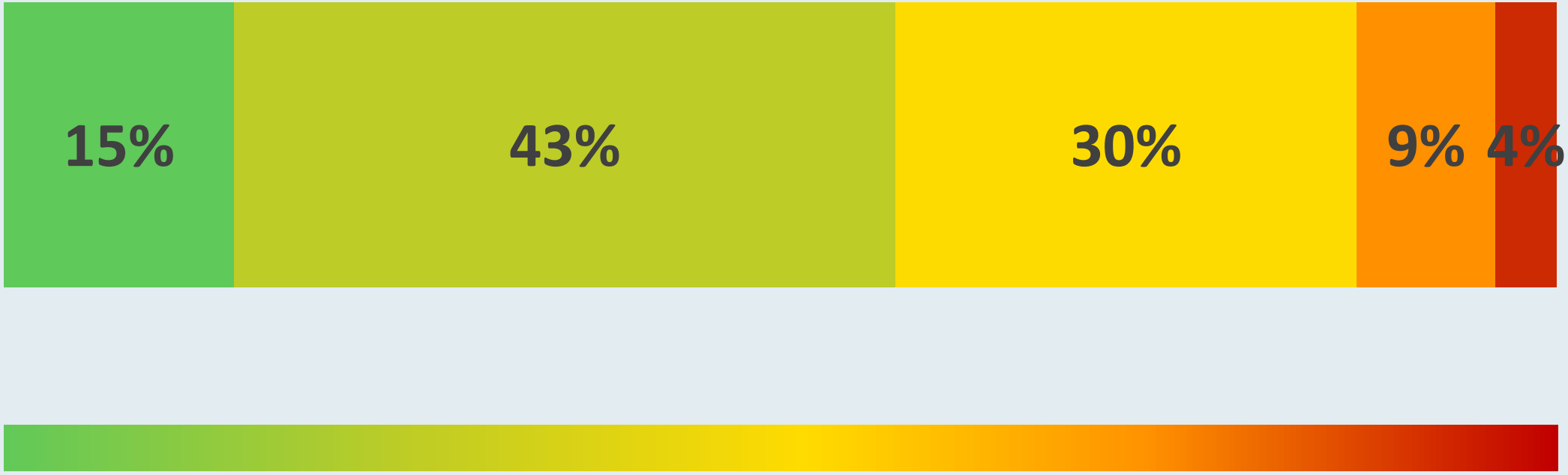
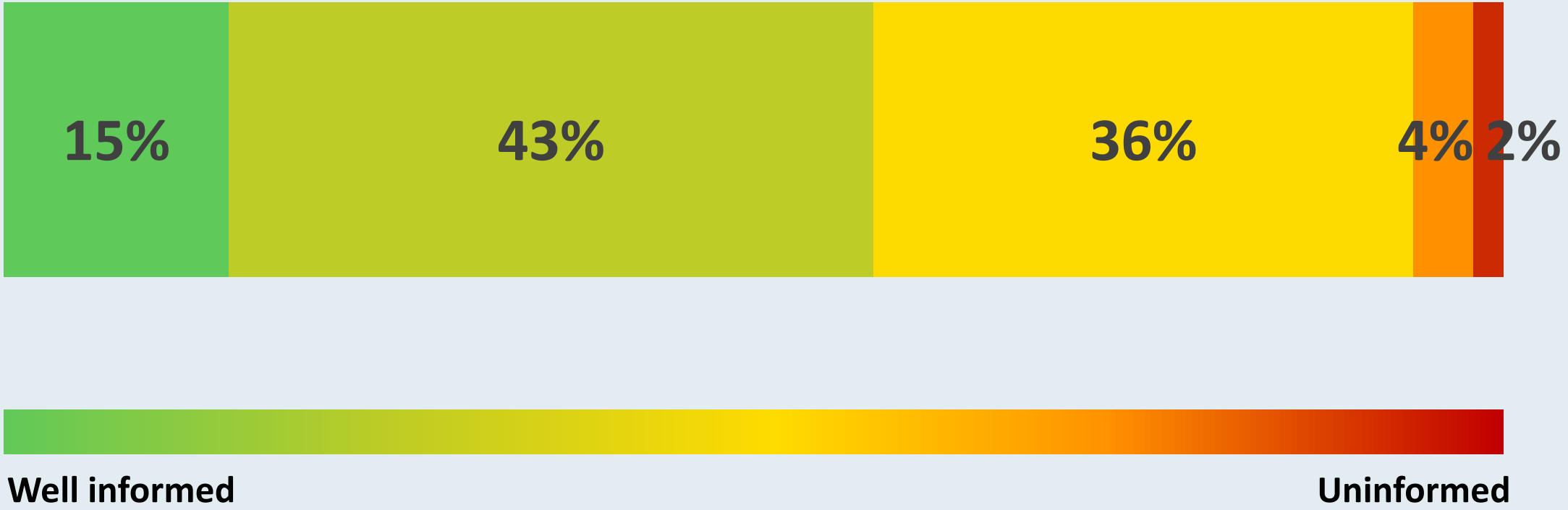
How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to optimal biomarker analysis for patients with CRC?



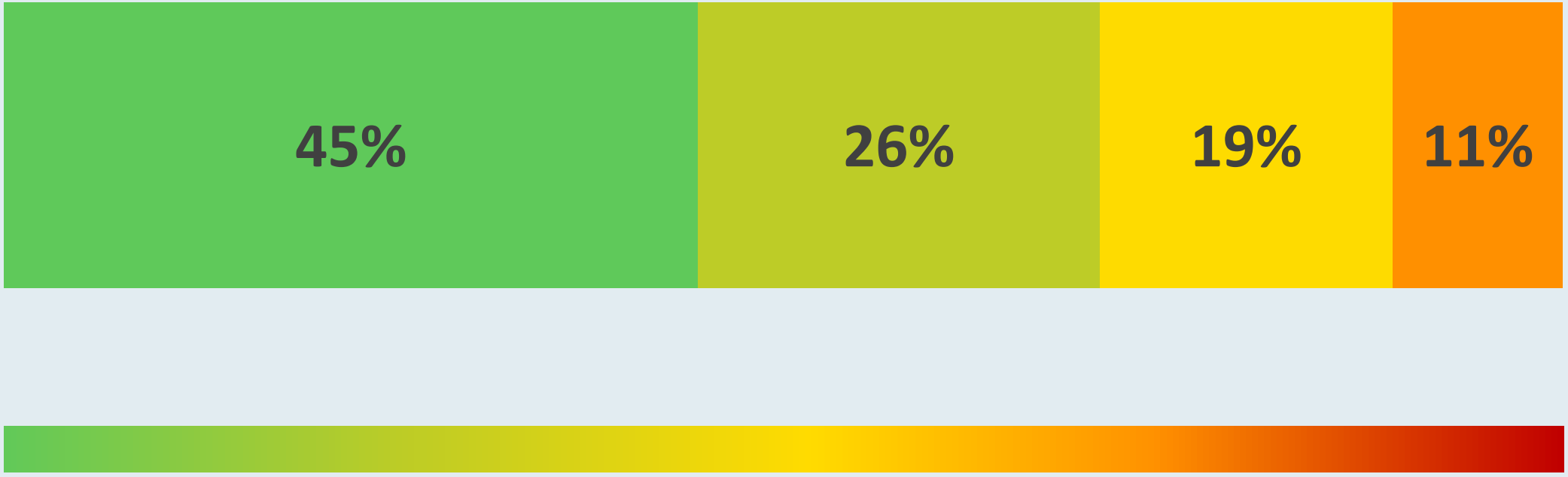
How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the potential role of immune checkpoint inhibitors in therapy for nonmetastatic CRC?



How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the use of circulating tumor DNA assays to inform clinical decision-making for patients with CRC?



How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the selection of first-line therapy for microsatellite instability-high or mismatch repair-deficient metastatic CRC?



How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the appropriate integration of HER2-targeted therapy for patients with HER2-positive metastatic CRC?

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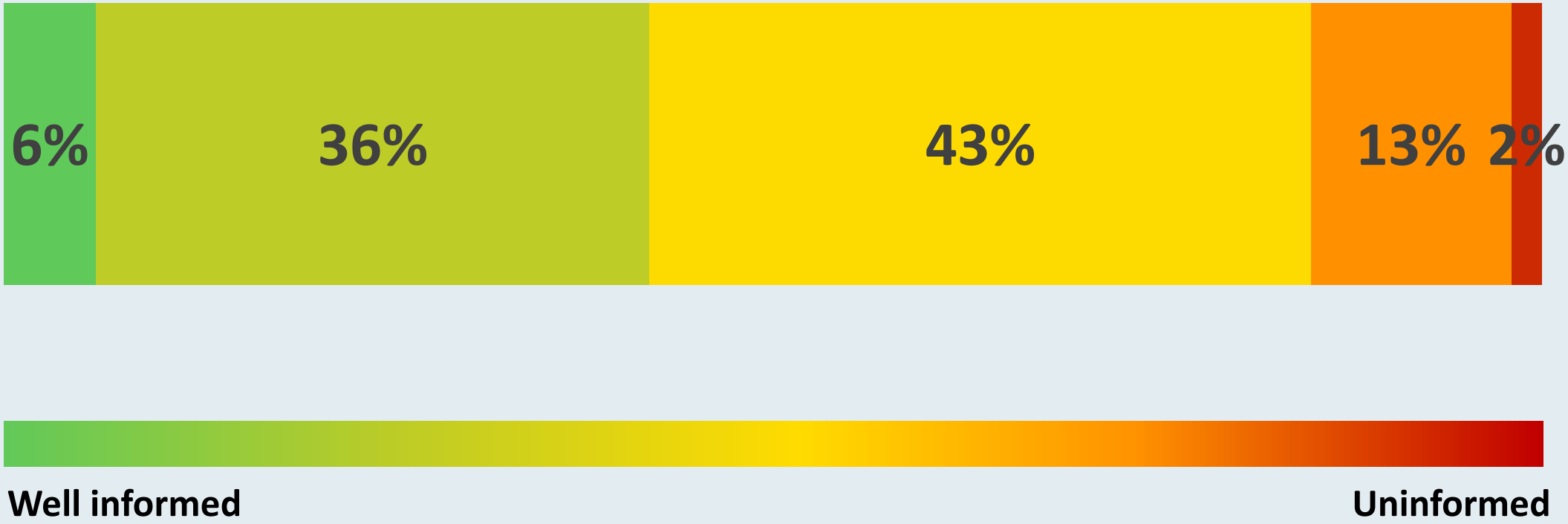
How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the potential role of KRAS G12C inhibitors in the treatment of metastatic CRC?



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Impediments or Barriers to the Delivery of High-Quality Care

- Ability for patients to get to our clinic
- Management of EGFR related side effects
- Time
- None, care delivered with high quality in this patient population
- No barriers
- Many treatments cause GI side effects which can be challenging for these patients
- What is the best sequence of drugs?
- Trial access
- Lack of first line trials
- Insurance

Impediments or Barriers to the Delivery of High-Quality Care (Continued)

- Ineffective therapies for patients with progressive disease, and lack of biomarkers
- Tissue testing availability
- Delay of care due to local hospital not performing molecular testing right away
- Lack of evidence of IO in first line colon cancer for MSI cancers
- Lack of understanding of young onset colorectal cancers' biology of disease
- Timing on getting studies back
- None
- Need better agents for 3rd line and beyond
- More efficacious treatment options

Impediments or Barriers to the Delivery of High-Quality Care (Continued)

- I practice in a retirement town; patient comorbidity is the main concern
- Counseling patients based on ctDNA results; subsequent management upon ctDNA MRD
- Need to learn about kras inhibitors
- Delayed recovery from surgery/ostomy issues
- Ability for multidisciplinary care
- Incorporating ctDNA and immunotherapy
- High risk Stage 2; convincing patient for adjuvant therapy
- Not sure what to do with positive ctDNA in limited stage CRC
- Lack of guidelines for optimal sequencing
- Insurance reasons

Impediments or Barriers to the Delivery of High-Quality Care (Continued)

- Insurance approval
- Difficult to obtain all biomarkers due to insufficient tissue biopsy size
- Insurance coverage for non-FDA approved indications
- Patients are not represented in the trial, due to ECOG 2-3
- Can ctDNA assays help to guide treatment and improve OS?
- Access to novel therapies (e.g., IO)
- Optimal molecular testing quickly
- Patients are too ill to receive multiple lines of therapy
- Unable to have ctDNA testing covered by insurance

Impediments or Barriers to the Delivery of High-Quality Care (Continued)

- Access to treatment or clinical trials
- Insurance
- NGS denial by insurance sometimes
- Oxaliplatin neurotoxicity
- Occasional lack of coverage of ctDNA by insurance
- Treatment complications and frequent hospitalizations lead to fewer patients making it beyond 3rd line
- None

Questions from General Medical Oncologists on the Use of ctDNA Assays for CRC

- What do you do with a rising ctDNA after resection of oligo met in lung and negative scans?
- Please comment on difference regarding Signatera™ and Guardant 360® reveal for ctDNA testing and preference.
- Do you still perform ctDNA if initial specimens before any treatment is negative?
- Lack of practical guidelines on use in Stage 2 or 3 cancers.
- Available data to aid in predictive interventions, that is should we be deciding adjuvant therapies based on ctDNA results yet?
- Patient with Stage 2 colon cancer but liver abscesses after surgery. Signatera (-). How often would you test?
- Would you recommend adjuvant capecitabine for MSS pT3 pN1a (1/19 LNs) and ctDNA negative? What about in a similar patient with MSI-H disease?
- Can quantitative ctDNA be used to monitor chemotherapy response?
- Is this standard of care per NCCN guidelines? If the ctDNA rises, should we start chemo?

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Questions from General Medical Oncologists on the Use of ctDNA Assays for CRC (Continued)

- In a high-risk patient with poor chemo tolerance opted to stop chemo and do ctDNA monitoring, which was initially negative then turned positive 1 year later. Other than more frequent imaging and colonoscopy, what would the experts do if the ctDNA came back positive?
- How do you use ctDNA for decision making?
- Would you use ctDNA to de-escalate or escalate treatment at this time?
- How often should we check this?
- After 6 months of adjuvant FOLFOX, patient remains ctDNA positive but no evidence of disease. Patient is very apprehensive that her disease will invariably recur. What can I offer her or do to reduce the chances of treatment recurrence? Her Caris was negative and had no mutations.
- Will you consider intensifying treatment?
- Is this ready for primetime?
- Positive ctDNA post adjuvant — does it call for longer treatment?

Questions from General Medical Oncologists on the Use of ctDNA Assays for CRC (Continued)

- What is the current role of ctDNA sequentially in a patient whose initial ctDNA post op Stage II is negative?
- Could Stage 3 patients safely omit chemo if ctDNA negative?
- What is the utility of using ctDNA in the adjuvant setting?
- Patient with Stage 3 colon cancer 3 years ago and remains in remission. Do you think she's a candidate for ctDNA monitoring after 3 years?
- In what Stage 2 settings would you opt not to obtain ctDNA to influence management?
- Will insurance cover and what clinical decision to make? Any impact on adding adjuvant chemotherapy?
- What to do with a ctDNA positive result?
- Is there enough data to support routine use of ctDNA testing for these patients?
- False negative rate?
- Like to know more about how to apply into clinical practice?
- Can ctDNA be used to guide adjuvant therapy in Stage III? Is evidence as good as in Stage II?

Questions from General Medical Oncologists on the Use of ctDNA Assays for CRC (Continued)

- Considering the clinical data, when would the use of ctDNA be incorporated into NCCN guidelines?
- Duration of adjuvant therapy in the era of ctDNA studies? Would one be comfortable stopping adjuvant therapy at 6 months if ctDNA is still weakly positive? Role of monitoring post adjuvant therapy for ctDNA?
- What to do if ctDNA in Stage II is positive?
- Role of withholding chemotherapy in elderly patients with Stage 3 CRC?
- When monitoring for recurrence, how often should we be checking ctDNA, does this reduce the need for follow up scans, and how do you incorporate checking tumor markers (cea) with ctDNA?
- Role of ctDNA in Stage III CRC and Stage IV with isolated liver metastasis?
- If ctDNA becomes positive in the adjuvant setting, after a period of negativity and metastatic work up is negative, how do you manage these patients?
- Would you trust ctDNA results and avoid unnecessary chemo?
- Which assay? When to intervene, does intervening sooner really change the eventual trajectory of the disease, just intervene when radiological lay detectable?

Questions from General Medical Oncologists on the Use of Immunotherapy or HER2- or KRAS-Targeted Treatment

- If this patient was HER2 positive and Pan RAS neg, which would you target first?
- Preference for which anti-EGFR with adagrasib?
- More info on second and 3rd options with KRAS mutated?
- What line of therapy for KRAS G12C or HER2 therapy?
- KRAS incorporation first line? What if having GI bleed or concerns for obstruction/fistula — do we worry about AEs similarly as other TKIs or VEGF inhibitors?
- Would you use KRAS targeted therapy alone or in combination? What line of treatment?
- I have not yet treated KRAS G12C metastatic colon cancer and would like to learn more about the treatment options.
- Optimal treatment strategy?
- Don’t know role of immunotherapy in HER2 and KRAS mutation positive disease?
- Do you take into account POLE or POLD mutation when deciding about immune therapy use?

Questions from General Medical Oncologists on the Use of Immunotherapy or HER2- or KRAS-Targeted Treatment (Continued)

- Would it make sense to integrate HER2 or KRAS targeted therapy in frontline treatment?
- I've recommended tucatinib with trastuzumab. Would you recommend T-DXd ahead of it or keep it on for later?
- How long will you consider treatment when patient achieves CR?
- Switch to MOUNTAINEER upon progression on trastuzumab deruxtecan?
- How do you look for HER2 — tumor or blood?
- What do I use now, KRAS related TKI combination or T-DXd?
- KRAS G12C, optimal first line therapy?
- What is your preferred first line therapy for HER2 positive CRC, metastatic disease?
- If the patient has both low HER2 and KRAS G12C, which targeted therapy should I choose first?
- Are there data for sequencing in 1L prior to HER2 or KRAS-targeted therapies?
- Response rate and what line to introduce?

Questions from General Medical Oncologists on the Use of Immunotherapy or HER2- or KRAS-Targeted Treatment (Continued)

- What is the best scenario to use a KRAS inhibitor?
- When is the optimal line to use immunotherapy?
- Not used in my practice, would like to learn more.
- Is HER2 mutation a target?
- Which KRAS G12C inhibitor is most effective?
- In which line would you sequence HER2 targeted therapy? And what about KRAS-directed therapy?
- If patient fails front line HER2 therapy what is the next therapy to use?
- Have you seen KRAS inhibitors cause hypoglycemia?
- When would you introduce targeted therapy, which line?
- How long to wait to sequence?