

Colorectal Cancer



Tests usually made in routine

- Sequencing of KRAS, NRAS and BRAF for anti-EGFR therapies (cetuximab and panitumumab)
- MSI or MMR for poor prognosis to fluorouracil treatment



How to treat metastatic CRC?

- Conventional chemotherapies including 5-FU, leucovorin, irinotecan, capecitabine and oxaliplatin
- Targeted therapies including bevacizumab, regorafenib, cetuximab, panitumumab, ramucirumab and aflibercept

HOW CAN ONCODNA BE USEFUL?

• For approved treatments



OncoSTRAT&GO™



DNA / RNA



KRAS and NRAS - extended mutations testing (codons 12, 13, 59, 61, 117, 146)

To predict resistance to EGFR-targeted monoclonal antibodies (cetuximab and panitumumab) (38-60% incidence).

EGFR - extended mutations testing (extra cellular domain)

To predict specific resistance to EGFR-targeted monoclonal antibodies (cetuximab and panitumumab) (10% incidence).

BRAF - extended mutations testing

To predict poor prognosis to EGFR-targeted monoclonal antibodies (cetuximab and panitumumab) (11% incidence).

cMET - copy number testing

To predict (1) poor prognosis/resistance to EGFR-targeted monoclonal antibodies (cetuximab and panitumumab) and (2) response to crizotinib*, cabozantinib* (9-18 % incidence).

ERBB2 (HER2) - copy number testing

To predict (1) poor prognosis/resistance to EGFR-targeted monoclonal antibodies (cetuximab and panitumumab) and (2) response to trastuzumab* (4-20 % incidence).

APC - extended mutations testing

To predict good prognosis to anti-angiogenic treatments (bevacizumab, ramucirumab and zaltrap) (30 % incidence).

PROTEINS



ERCC1 - over-expression

To predict poor prognosis to platinum-based therapies.

TS - over-expression

To predict poor prognosis to 5-FU and capecitabine.

TOPO1 - positive expression

To predict good prognosis to irinotecan.

VEGFR2 - over-expression

To predict good prognosis to anti-VEGFR2 treatment (ramucirumab).

PROTEINS + DNA



MSI - testing + POLE & POLD1 - mutations & copy number testing + Tumor Burden - testing + PD-L1 & CD8 - over-expression

To predict (1) poor response to 5-FU and capecitabine and (2) good prognosis to anti-PDL1 / anti-PD1 treatments (pembrolizumab, nivolumab* and atezolizumab*).



CDK4 / CDK6 / RB1 / CDKN2A - mutations & copy number testing + pRB1 - expression

To predict good prognosis to anti-CDK4/6 treatments (palbociclib and ribociclib)*.

* : Drugs FDA approved for other indications.

** : Drugs in development



• For Drugs in Development

DNA / RNA



FGFR1/2/3 - *extended mutations, copy number and translocation testing*

To predict good prognosis to anti-FGFRx treatments (AZD4547).

NTRK1/2/3 - *translocation testing*

To predict good prognosis for anti-NTRKx treatments (entrectinib and LOXO-101).

PROTEINS



IGF1R - *positive expression*

To predict good prognosis to anti-IGF1R treatment (dalotuzumab) and poor prognosis to anti-EGFR treatments (cetuximab and panitumumab).

* : Drugs FDA approved for other indications.

WHY AND WHEN A PERSONALIZED LIQUID BIOPSY COULD BE MADE ?



• Neoadjuvant Settings

The evaluation of the response to anti-tumor therapies for solid tumors is based on the monitoring of the size of lesions and must be accurately measured in at least one dimension (longest in plane diameter is to be recorded) (RECIST criteria).

LIMITATIONS OF THIS APPROACH:

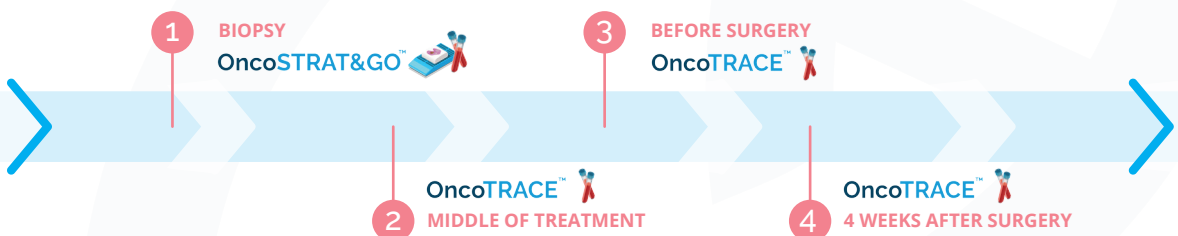
- ✗ Early evaluation after treatment start is difficult because tumor shrinkage can only be detected after several therapeutic cycles.
- ✗ Response is non-evaluable when disease is not measurable (liquid effusion, follow-up post complete tumor resection...)

OUR SUGGESTED ALTERNATIVE:

ctDNA can be used as a non-invasive tool to monitor the disease evolution during treatment. But which mutations must be followed and how many ?

Our solutions are able to:

- ✓ Predict a relapse sooner than conventional imaging technologies
- ✓ Detect resistance mutations to anticipate therapy changes
- ✓ Predict sensitivity to new therapies



• Adjuvant / Systemic settings



2 weeks before the scheduled visit with the patient.

