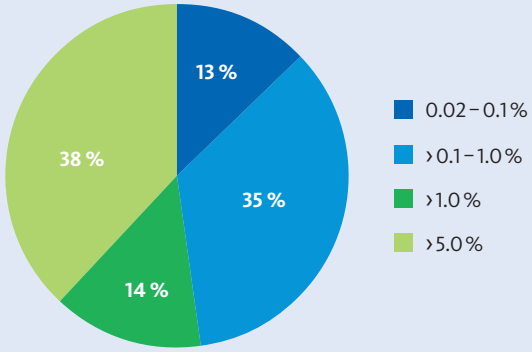
# OncoBEAM RAS CRC

## Optimising therapy selection in metastasized CRC (mCRC)

Precision medicine using anti-EGFR therapy is a well-established part of mCRC management. However, it requires reliable and timely RAS mutation analysis as recommended by international guidelines (ESMO, NCCN, ASCO). Liquid biopsies revolutionised precision medicine, overcoming limitations of tissue biopsy like tumour heterogeneity, samples accessibility and turnaround time. Especially for monitoring therapy response, liquid biopsy facilitates fast adaption of therapies according to clonal tumour evolution, so further improving mCRC management. Since almost half of RAS mutant mCRC patients present with a mutant allele fraction lower than 1% (Fig. 1) highly sensitive technologies are mandatory. The eligibility of the OncoBEAM RAS CRC IVD kit was proven in various clinical studies as summarised and listed below (Fig. 2).

**Distribution of RAS Mutant Allele Fraction in mCRC patients**




References: Schmiegel *et al.* 2016, Saunders *et al.*, 2016, Vidal *et al.*, 2017

*'Determining RAS in serial liquid biopsies lets you monitor the clonal dynamics of tumours, detect the emergence of resistance early on, and select the right treatment at all times.'*

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**Figure 1**

## Meta-analysis of concordance studies between OncoBEAM and tissue biopsy

| | Tissue RAS result | | |
|---|---|---|---|
| **OncoBEAM RAS CRC plasma result** | **Mutation detected** | **No mutation detected** | **Total** |
| Mutation detected | 112 | 7 | 119 |
| No mutation detected | 9 | 110 | 119 |
| Total | 121 | 117 | 238 |

- **Overall percent agreement = 93.3 % (222 / 238)**
- Positive percent agreement = 92.6 % (112 / 121)
- Negative percent agreement = 94.0 % (110 / 117)
- OncoBEAM RAS CRC stage IV mutant population = 50.0 % (119/238)
- Tissue stage IV mutant population = 50.8 % (121/238)

References: Schmiegel *et al.* 2016, Saunders *et al.*, 2016, Vidal *et al.*, 2017

**Figure 2**

# OncoBEAM RAS CRC liquid biopsy for reliable therapy selection and monitoring in mCRC

## Selected publications


[1] ***Garcia-Foncillas J et al.*** *(2017): Incorporating BEAMing technology as a liquid biopsy into clinical practice for the management of colorectal cancer patients: an expert taskforce review. Annals of Oncology. 0(0):1 – 7.*

***Key message:*** *BEAMing posseses the potential to replace tissue biopsy for the detection and monitoring of RAS mutations and enables precision and cost-effective CRC patient management by individualising treatment plans.*

[2] ***Toledo R et al.*** *(2017): Clinical validation of prospective liquid biopsy monitoring in patients with wild-type RAS metastatic colorectal cancer treated with FOLFIRI-cetuximab. Oncotarget. 8(21):35289 – 35300.*

***Key message:*** *This prospective trial confirms BEAMing as a high-efficiency method for tumour genotyping and its monitoring and demonstrated for the first time that continued detection of wt circulating DNA points out to a prolonged tumour response to anti-EGFR therapy.*

[3] ***Grasselli J et al.*** *(2017): Concordance of blood- and tumor-based detection of RAS mutations to guide anti-EGFR therapy in metastatic colorectal cancer. Annals of Oncology. 28(6):1294 – 1301.*

***Key message:*** *High proportion of patients (48 %) show low mutant allele frequencies in cell free DNA between 0.01 % and 1 %, which requires highly sensitive diagnostics to predict treatment benefit in RAS wild-type mCRC patients receiving anti-EGFR therapy.*

[4] ***Vidal J et al.*** *(2017): Plasma ctDNA RAS mutation analysis for the diagnosis and treatment monitoring of metastatic colorectal cancer patients. Ann. Oncol. 28(6):1325 – 1332.*

***Key message:*** *OncoBEAM RAS CRC assay shows high overall agreement in RAS mutations status between plasma and tissue (93.0 %) and is useful for monitoring the dynamics of RAS mutations during anti EGFR therapy to detect emergence of resistance.*

[5] ***Schmiegel W et al.*** *(2017): Blood-based detection of RAS mutations to guide anti-EGFR therapy in colorectal cancer patients: concordance of results from circulating tumor DNA and tissue-based RAS testing. Molecular Oncology. 11:208 – 219.*

***Key message:*** *The high overall concordance (91.8 %) between plasma RAS testing and tissue RAS mutation testing in this study demonstrates that BEAMing is comparable to tissue-based detection testing and is eligible to select mCRC patients for anti-EGFR therapy.*

[6] ***Tabernero J et al.*** *(2015): Analysis of Circulating DNA and Protein Biomarkers to Predict the Clinical Activity of Regorafenib and Assess Prognosis in Patients with Metastatic Colorectal Cancer: A Retrospective, Exploratory Analysis of the CORRECT Trial. The Lancet Oncology 16(8):937 – 948.*

***Key message:*** *Regorafenib showed clinical benefit across several subgroups of mCRC patients and assessing baseline cell free tumour (ct) DNA concentration by BEAMing showed promise as a prognostic indicator for clinical outcomes in mCRC patients.*

[7] ***Siravegna G et al.*** *(2015): Clonal Evolution and Resistance to EGFR Blockade in the Blood of Colorectal Cancer Patients. Nature Medicine 21(7):795 – 801.*

***Key message:*** *Liquid instead of tissue biopsy can be used to closely monitor the dynamic molecular evolution of metastatic colorectal tumours during anti-EGFR therapy in order to identify those patients that benefit from anti-EGFR.*

[8] ***Morelli MP et al.*** *(2015): Characterizing the Patterns of Clonal Selection in Circulating Tumor DNA from Patients with Colorectal Cancer Refractory to Anti-EGFR Treatment. Annals of Oncology. 26(4):731 – 36.*

***Key message:*** *Newly detected KRAS mutations in mCRC patients resistant to anti-EGFR treatment derive from rare, pre-existing clones in the primaries and could be followed up by highly sensitive liquid biopsy assays enabling the quick adaption of treatment strategies.*

[9] ***Misale S et al.*** *(2014): Blockade of EGFR and MEK Intercepts Heterogeneous Mechanisms of Acquired Resistance to Anti-EGFR Therapies in Colorectal Cancer. Science Translational Medicine. 6(224):224ra26.*

***Key message:*** *Liquid biopsies used for monitoring RAS mutations of mCRC patients on anti-EGFR therapy enable early initiation of combination therapies with MEK inhibitors in order to optimise the therapy success and delay disease progression.*

[10] ***Diehl F. et al.*** *(2008): Circulating Mutant DNA to Assess Tumor Dynamics. Nature Medicine 14(9):985–90.*

***Key message:*** *BEAMing technology is a highly sensitive approach for quantifying ctDNA in patients undergoing multimodality therapy for CRC leading to a personalised genomics approach that could be used to noninvasively monitor tumour burden.*



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