Sysmex OncoBEAM™ RAS CRC Kit and CyFlow® Cube 6i System (desktop flow cytometer and autoloader)

The OncoBEAM™ RAS CRC Platform provides proven clinical blood-based testing in your laboratory:

Our Test Menu

OncoBEAM™ RAS CRC Kit CE-IVD (16 KRAS mutations and 18 NRAS mutations) Sysmex Catalog No: ZR150100	**KRAS 16** Exon 2: Codons 12 & 13 Exon 3: Codons 59 & 61 Exon 4: Codons 117 & 146	**NRAS 18** Exon 2: Codons 12 & 13 Exon 3: Codons 59 & 61 Exon 4: Codons 117 & 146

Bibliography

[1] ***Grasselli, J et al.*** *(2016): Circulating tumor DNA extended RAS mutational analysis as a surrogate of mutational status of tumor samples in metastatic colorectal cancer and its impact on patient selection for anti-EGFR therapy. Study presented at the meeting of ESMO 18th World Congress on Gastrointestinal Cancer, Barcelona, Spain. Ann Oncol 27 (suppl_2): ii127, O – 024*

[2] *NCCN Clinical Practice Guidelines in Oncology™: Colon Cancer. National Comprehensive Cancer Network. V2, 2017.*

[3] ***Van Cutsem, E et al.*** *(2016): ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol 27(8):1386 – 1422.*

[4] ***Allegra, J et al.*** *(2016): Extended RAS gene mutation testing in metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy: American Society of Clinical Oncology Provisional Clinical Opinion Update 2015. J Clin Oncol 34(2):179 – 185.*

[5] ***Sorich, MJ et al.*** *(2015): Extended RAS mutations and anti-EGFR monoclonal antibody survival benefit in metastatic colorectal cancer: a meta-analysis of randomized, controlled trials. Ann Oncol 26(1):13 – 21.*

[6] *OncoBEAM™ RAS CRC Kit Instructions for Use, OBMRASIVD.*

[7] ***Vidal Barrull, J et al.*** *(2016): Accuracy of plasma RAS mutation testing for therapy selection and monitoring of colorectal cancer patients. ESMO 2016. Ann Oncol 27 (suppl_6): Abstract 533P.*

[8] ***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. Mol Oncol 11(2):208 – 219.*

[9] ***Saunders, MP et al.*** *(2016): Performance assessment of blood based RAS mutation testing: concordance of results obtained from prospectively collected samples. ESMO 2016. Ann Oncol 27 (suppl_6): Abstract 526P.*

[10] ***Vidal Barrull, J et al.*** *(2017): Clinical applications of extended ctDNA RAS mutation determination in metastatic colorectal cancer. ASCO Gastrointestinal Cancers Symposium 2017. J Clin Oncol 35 (suppl 4S; Abstract 607).*

Distributor: Sysmex Europe GmbH
Bornbarch 1, 22848 Norderstedt, Germany · Phone +49 40 52726-0 · Fax +49 40 52726-100 · info@sysmex-europe.com · **www.sysmex-europe.com**

Manufacturer: Sysmex Inostics GmbH
Falkenried 88, 20251 Hamburg, Germany · Phone +49 40 325907-0 · Fax +49 040 325907-6699 · info@sysmex-inostics.com · **www.sysmex-inostics.com**

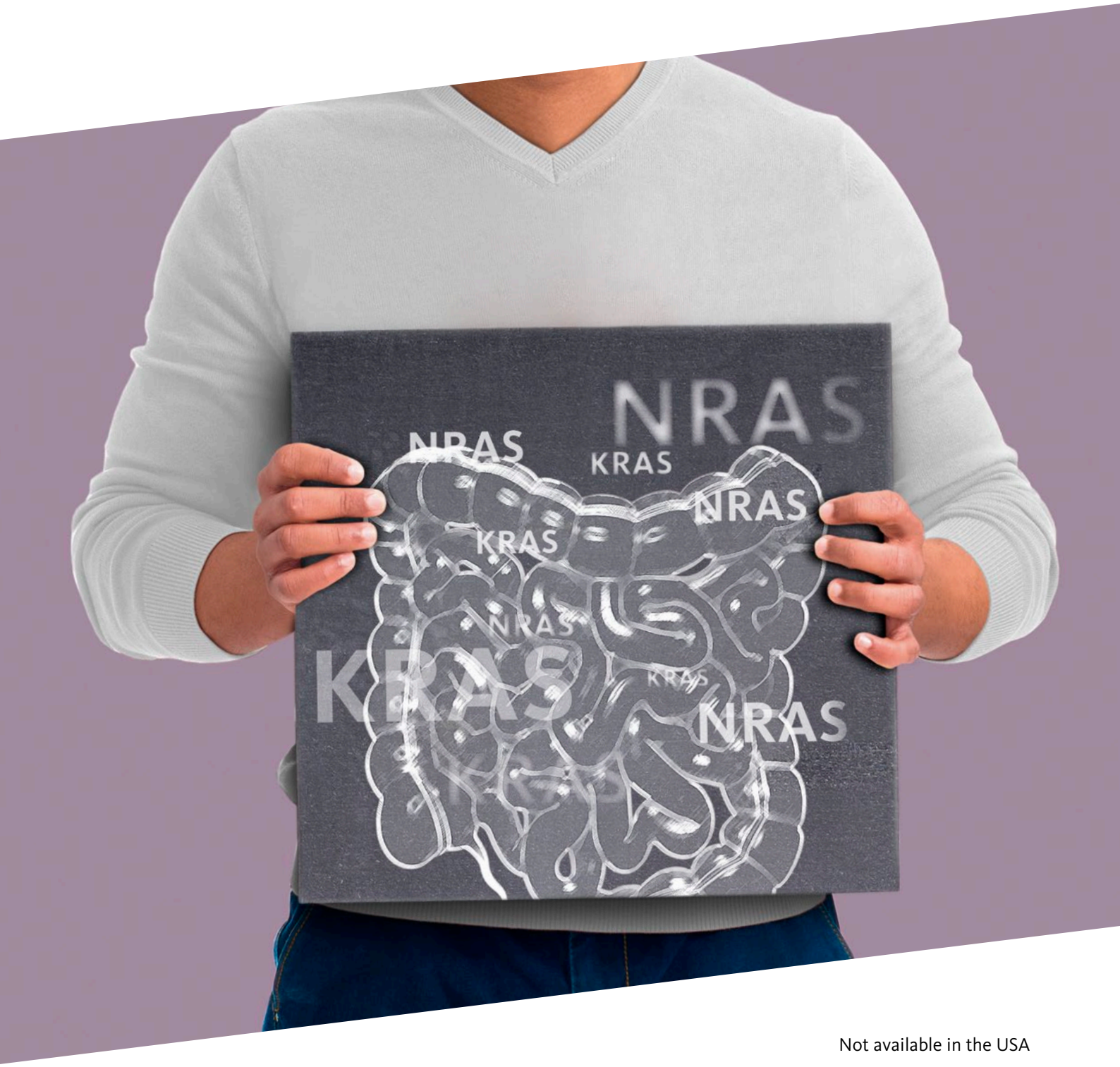
Sysmex Corporation
1-5-1 Wakinohama-Kaigandori, Chuo-ku, Kobe 651-0073, Japan · Phone +81 78 265-0500 · Fax +81 78 265-0524 · **www.sysmex.co.jp**

You will find your local Sysmex representative's address under www.sysmex-europe.com/contacts

ZE001373.EN.C.05/17

OncoBEAM™ RAS CRC Platform

High Sensitivity – Proven Clinical Value[1]

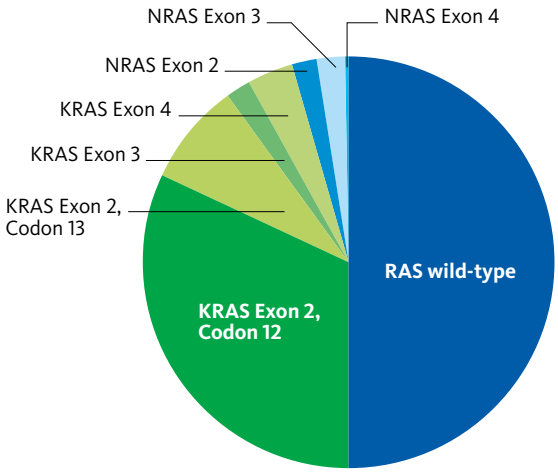


Not available in the USA

www.sysmex-europe.com/RAS

Go Beyond Biopsy with Blood

OncoBEAM™ RAS Platform Meets Current RAS Testing Guidelines



- In 2015, CRC clinical practice guidelines were updated to recommend expanded RAS testing prior to use of an anti-EGFR treatment.[2,3,4]
- A meta-analysis of nine randomized controlled trials was conducted on the prevalence of RAS mutations, for both KRAS Exon 2 and new KRAS and NRAS mutations, in metastatic colorectal cancer (mCRC). Patients with tumors exhibiting one of the new RAS mutations were found unlikely to significantly benefit from anti-EGFR monoclonal antibody therapy in mCRC.[5]
- The frequency of KRAS and NRAS mutations in Exons 2, 3 and 4 in the trials reviewed in the meta-analysis formed the basis for our OncoBEAM™ RAS CRC Kit. Using proven BEAMing technology, our platform offers a comprehensive panel of 34 mutations in the KRAS and NRAS oncogenes.

High Concordance with Tissue

Blood-based OncoBEAM™ RAS CRC Kit demonstrates high concordance with standard of care tissue testing[6]

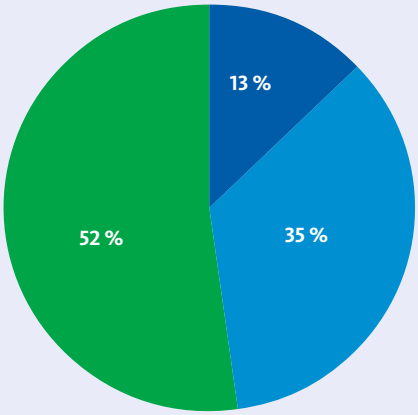
	Tissue RAS Result		
OncoBEAM™ RAS CRC Plasma Result	**Mutation Detected**	**No Mutation Detected**	**Total**
Mutation Detected	112	7	119
No Mutation Detected	9	110	119
Total	121	117	238

- **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)

High Sensitivity

The OncoBEAM™ RAS CRC Platform has the sensitivity required to detect low RAS percent mutant fractions in blood.

Mutant-Allele Fractions



48 % of the analyzed mCRC patients showed ctDNA at <1 % fraction

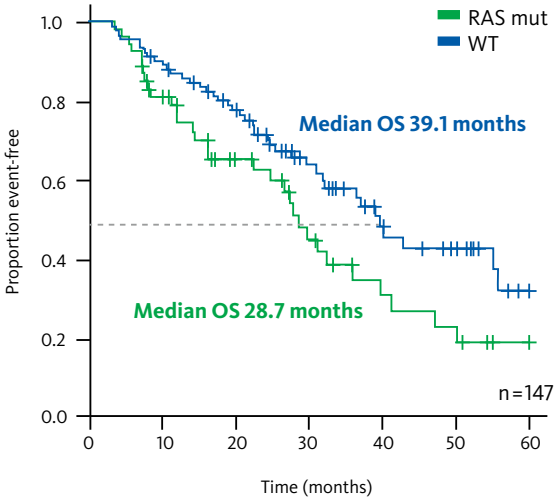
- OncoBEAM™ RAS CRC Platform is able to detect low levels of RAS mutations shown to be relevant for therapy selection and response to treatment.[7]
- A meta-analysis of data generated with the OncoBEAM™ CRC assay showed that 48 % of the analyzed mCRC patients had a mutant allele fraction (MAF) between 0.02 % – 1.0 %.[8,9,10]
- This data indicates that to properly select metastatic colorectal cancer patients eligible for anti-EGFR therapy using a blood sample, the OncoBEAM™ RAS CRC assay's high sensitivity is required.

0.02 – 0.1 % › 0.1 – 1.0 % › 1.0 %

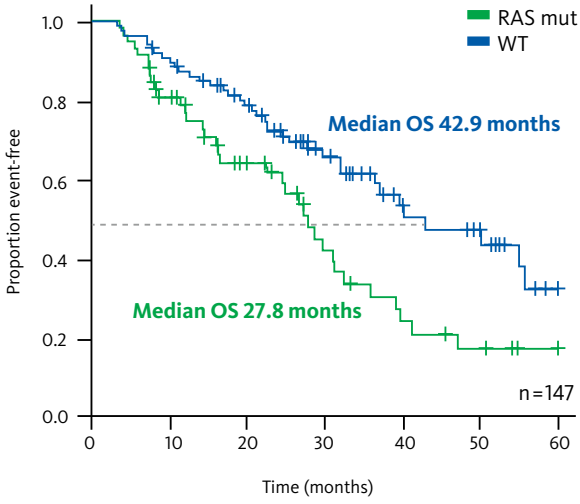
Equivalent Clinical Performance to Standard of Care Tissue Testing

No Significant Differences in Overall Survival Between Blood and Tissue Testing

Overall Survival (OS) in Metastatic CRC Patient Population by Tissue Tumor Testing[1]



Overall Survival (OS) in Metastatic CRC Patient Population by BEAMing Testing[1]



OncoBEAM™ technology leverages the advantages of a minimally invasive blood-based test while retaining the accuracy of a tissue based test for selecting patients that will benefit most from anti-EGFR therapy.