[Oncofocus] Patient Test Report

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Primary site	Colon	**Tumour % (macrodissected)**	80
Tumour subtype	Metastatic Colonic Adenocarcinoma		
Tissue type	Liver		

Comment:
The DNA and RNA extracted from this sample were of optimal quality. The Oncofocus assay on which the sample was run met all assay specific quality metrics.

221 genes were targeted using 2530 unique amplicons covering oncogenes, fusion genes, genes susceptible to copy number variation and tumour suppressors. Actionable genetic variants detected by Oncofocus are linked to 485 anti-cancer targeted therapies.

The following actionable variants were detected:

Variant Summary

Sample Cancer Type: Colorectal Cancer

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

Gene Variant	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials
KRAS p.(G12A) c.35G>C	⊘ (3)	⊘ (2)	⊘ (4)	⊘ (3)	● (32)
RB1 p.(W516Ter) c.1548G>A	✖	✖	✖	✖	● (1)
TP53 p.(R248W) c.742C>T	✖	✖	✖	✖	● (5)
FLT3 amplification	✖	✖	✖	✖	● (2)

EMA: European Medicine Agency, **US-FDA:** United States-Food and Drug Administration, **ESMO:** European Society for Medical Oncology, **US-NCCN:** United States-National Comprehensive Cancer Network. Numbers in parentheses indicate the number of relevant therapies with evidence. Hotspot variants with >10% alternate allele reads, and in >10 unique reads are classified as 'detected' with an assay sensitivity and positive predictive value of 97%. Copy number variants; amplifications of a >5% confidence value of ≥4 after normalization and deletions of ≤1 are classified as present when the tumour% >50%. Gene Fusions are reported when occurring in >20 counts and meeting the thresholds of assay specific internal RNA quality control. With a sensitivity of 99% and PPV of 99%. Supplementary technical information is available upon request.

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

KRAS p.(G12A) c.35G>C

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
cetuximab	⊘	⊘	⊘	⊘	✖
cetuximab + oxaliplatin	⊘	✖	✖	✖	✖
panitumumab + oxaliplatin	⊘	✖	✖	✖	✖
panitumumab	✖	⊘	⊘	⊘	✖
cetuximab + chemotherapy	✖	✖	⊘	✖	● (II)
panitumumab + chemotherapy	✖	✖	⊘	✖	✖
tyrosine kinase inhibitors	✖	✖	✖	⊘	✖
bevacizumab + chemotherapy	✖	✖	✖	✖	● (III)
AKT inhibitor + MEK inhibitor	✖	✖	✖	✖	● (II/III)
aflibercept + chemotherapy	✖	✖	✖	✖	● (II)
MK-1775 + olaparib	✖	✖	✖	✖	● (II)
palbociclib	✖	✖	✖	✖	● (II)
regorafenib, vorinostat + hydroxychloroquine	✖	✖	✖	✖	● (II)
sorafenib	✖	✖	✖	✖	● (II)
sorafenib + chemotherapy	✖	✖	✖	✖	● (II)
afatinib + selumetinib	✖	✖	✖	✖	● (I/II)
BAL-3833	✖	✖	✖	✖	● (I/II)
dacomitinib + PD-0325901	✖	✖	✖	✖	● (I/II)
lapatinib + trametinib	✖	✖	✖	✖	● (I/II)
LNP3794	✖	✖	✖	✖	● (I/II)
palbociclib + PD-0325901	✖	✖	✖	✖	● (I/II)
ribociclib + trametinib	✖	✖	✖	✖	● (I/II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available. See global clinical trials section in the pages to follow.

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Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

KRAS p.(G12A) c.35G>C (continued)

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
atezolizumab + cobimetinib	✖	✖	✖	✖	● (I)
binimetinib + chemotherapy	✖	✖	✖	✖	● (I)
CB-5083	✖	✖	✖	✖	● (I)
crizotinib + PD-0325901	✖	✖	✖	✖	● (I)
HM-95573	✖	✖	✖	✖	● (I)
LXH254	✖	✖	✖	✖	● (I)
MGD007	✖	✖	✖	✖	● (I)
MM-151 + trametinib	✖	✖	✖	✖	● (I)
pembrolizumab + SCH-900353, ridaforolimus + SCH-900353, SCH-900353 + chemotherapy	✖	✖	✖	✖	● (I)
RO-5126766	✖	✖	✖	✖	● (I)
selinexor	✖	✖	✖	✖	● (I)
selumetinib + ciclosporin	✖	✖	✖	✖	● (I)
sEphB4-HSA	✖	✖	✖	✖	● (I)
trametinib + chemotherapy + radiation therapy + surgical intervention	✖	✖	✖	✖	● (I)
trametinib + radiation therapy, trametinib + surgical intervention	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available. See global clinical trials section in the pages to follow.

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Relevant Therapy Summary (continued)

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RB1 p.(W516Ter) c.1548G>A

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
palbociclib	✖	✖	✖	✖	● (II)

TP53 p.(R248W) c.742C>T

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
MK-1775 + olaparib	✖	✖	✖	✖	● (II)
ixazomib + vorinostat	✖	✖	✖	✖	● (I)
MK-1775	✖	✖	✖	✖	● (I)
pembrolizumab + p53MVA	✖	✖	✖	✖	● (I)
SGT-53, SGT-53 + chemotherapy	✖	✖	✖	✖	● (I)

FLT3 amplification

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
ponatinib	✖	✖	✖	✖	● (II)
sorafenib	✖	✖	✖	✖	● (II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available. See global clinical trials section in the pages to follow.

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Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated

EMA information is current as of 2016-10-03. For the most up-to-date information, search www.ema.europa.eu/ema.

KRAS p.(G12A) c.35G>C

⊘ cetuximab, cetuximab + oxaliplatin

Cancer type: Colorectal Cancer **Label as of:** 2015-02-03 **Variant class:** KRAS exon 2 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000558/WC500029119.pdf

⊘ panitumumab + oxaliplatin

Cancer type: Colorectal Cancer **Label as of:** 2016-04-15 **Variant class:** KRAS exon 2 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000741/WC500047710.pdf

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Current US-FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated

US-FDA information is current as of 2016-10-03. For the most up-to-date information, search www.fda.gov.

KRAS p.(G12A) c.35G>C

⊘ cetuximab

Cancer type: Colorectal Cancer **Label as of:** 2015-04-10 **Variant class:** KRAS G12 mutation

Indications and usage:

Erbitux® is an epidermal growth factor receptor (EGFR) antagonist indicated for treatment of:

Head and Neck Cancer

- Locally or regionally advanced squamous cell carcinoma of the head and neck in combination with radiation therapy.
- Recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck in combination with platinum-based therapy with 5-FU.
- Recurrent or metastatic squamous cell carcinoma of the head and neck progressing after platinum-based therapy.

Colorectal Cancer

K-Ras wild-type, EGFR-expressing, metastatic colorectal cancer as determined by FDA-approved tests

- in combination with FOLFIRI for first-line treatment,
- in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
- as a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

Limitation of Use: Erbitux® is not indicated for treatment of *Ras*-mutant colorectal cancer.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125084s262lbl.pdf

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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KRAS p.(G12A) c.35G>C (continued)

⊘ panitumumab

Cancer type: Colorectal Cancer **Label as of:** 2015-03-11 **Variant class:** KRAS G12 mutation

Indications and usage:

Vectibix® is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of wild-type KRAS (exon 2) metastatic colorectal cancer (mCRC) as determined by an FDA-approved test for this use:

- In combination with FOLFOX for first-line treatment.
- As monotherapy following disease progression after prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy.

Limitation of Use: Vectibix® is not indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125147s200lbl.pdf

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Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated

ESMO information is current as of 2016-09-07. For the most up-to-date information, search www.esmo.org.

KRAS p.(G12A) c.35G>C

⊘ cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

⊘ cetuximab + chemotherapy

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

⊘ panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

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KRAS p.(G12A) c.35G>C (continued)

⊘ panitumumab + chemotherapy

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

⊘ cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic disease (Not specified)

Reference: ESMO Clinical Practice Guidelines - Rectal Cancer [Ann Oncol 2013; 24 (Suppl 6): vi81-vi88.]

⊘ panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic disease (Not specified)

Reference: ESMO Clinical Practice Guidelines - Rectal Cancer [Ann Oncol 2013; 24 (Suppl 6): vi81-vi88.]

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Current US-NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated

US-NCCN information is current as of 2016-09-07. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

KRAS p.(G12A) c.35G>C

⊘ cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2016]

⊘ cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 2.2016]

⊘ panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2016]

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KRAS p.(G12A) c.35G>C (continued)

⊘ panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 2.2016]

⊘ tyrosine kinase inhibitors

Cancer type: Non-Small Cell Lung Cancer **Variant class:** KRAS mutation

Summary:

NCCN Guidelines® do not contain a recommendation regarding KRAS mutations and tyrosine kinase inhibitor (TKI) therapy in non-small cell lung cancer, but include the following evidentiary statements:

- "KRAS mutations are associated with intrinsic EGFR TKI resistance, and KRAS gene sequencing could be useful for the selection of patients as candidates for EGFR TKI therapy. KRAS testing may identify patients who may not benefit from further molecular diagnostic testing."
- "KRAS mutations are also predictive of lack of benefit from platinum/vinorelbine chemotherapy or EGFR TKI therapy."
- "TKI therapy is not effective in patients with KRAS mutations and ALK gene rearrangements."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2016]

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Current Global Clinical Trials Information

Global Clinical Trials information is current as of 2016-09-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

KRAS p.(G12A) c.35G>C

NCT02162563
Treatment Strategies in Colorectal Cancer Patients With Initially Unresectable Liver-only Metastases CAIRO5 a Randomized Phase III Study of the Dutch Colorectal Cancer Group (DCCG)

Cancer type: Colorectal Cancer

Variant class: RAS mutation

Other identifiers: CAIRO 5, CAIRO5, DCCG 14-01, EudraCT Number: 2013-005435-24, NL47650.018.14, TrialTroveID-210801

Population segments: Liver mets, Neoadjuvant, Stage IV

Phase: III

Therapy: bevacizumab + chemotherapy

Country: Netherlands

No NCT ID - see other identifier(s)
Molecular selection of therapy in metastatic colorectal cancer: a molecularly stratified randomised controlled trial programme

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: CR13, CRUK/11/054, EudraCT Number: 2012-005111-12, FOCUS-4, FOCUS4, ISRCTN90061546, MREC N° 13/SC/0111, TrialTroveID-187137, UKCRN ID: 14893

Population segments: First line, Stage III, Stage IV

Phase: II/III

Therapy: AKT inhibitor + MEK inhibitor

Country: United Kingdom

NCT02173990
Predictive Value of DCE-US in Patients With Metastatic Colorectal Cancer Treated With First-line Aflibercept-based Treatment. An Exploratory, International, Multicenter, Phase II Study

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: EudraCT number: 2013-004540-33, PULSAR, PULSAR-1303, RECF2410, TrialTroveID-211746

Population segments: First line, Stage IV

Phase: II

Therapy: aflibercept + chemotherapy

Country: France

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KRAS p.(G12A) c.35G>C (continued)

No NCT ID - see other identifier(s)
Phase II study of first-line treatment by FOLFOXIRI+bevacizumab in patients with RAS mutant-type metastatic colorectal cancer

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: JACCRO CC-11, TrialTroveID-218272, UMIN000015152

Population segments: First line, Stage IV

Phase: II

Therapy: bevacizumab + chemotherapy

Country: Japan

No NCT ID - see other identifier(s)
A Phase II trial of irinotecan/ S-1 (IRIS) + alfa (panitumumab/ bevacizumab) as second line chemotherapy for metastatic colorectal cancer (mCRC).

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: IRIS-PB trial -Part B-, IRIS-PB trial -Part P-, TrialTroveID-203951, UMIN000009317, UMIN000009318

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: II

Therapy: bevacizumab + chemotherapy

Country: Japan

No NCT ID - see other identifier(s)
A phase II randomized study evaluating the activity and tolerability of first line treatment with bevacizumab + XELOX 2 than FOLFOX 4 + bevacizumab in patients with advanced colorectal cancer with known K-ras mutated tumor

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: 2802, EudraCT Number: 2010-022091-31, GOIM 2802, TrialTroveID-115430

Population segments: First line, Stage III, Stage IV

Phase: II

Therapy: bevacizumab + chemotherapy

Country: Italy

No NCT ID - see other identifier(s)
Phase II study of combination chemotherapy with TS-1/irinotecan and bevacizumab as second-line therapy in patient with K-RAS mutation-type metastatic colorectal cancer

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: SRIM study, TrialTroveID-156536, UMIN000005900

Population segments: Second line or greater/Refractory/Relapsed, Stage IV

Phase: II

Therapy: bevacizumab + chemotherapy

Country: Japan

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KRAS p.(G12A) c.35G>C (continued)

No NCT ID - see other identifier(s)
Non-resectable colorectal liver metastases of KRAS mutant type treated with oxaliplatin, fluorouracil and L-leucovorin plus bevacizumab induction toward liver R0 resection trial

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: NEXTO-mt, TrialTroveID-179078, UMIN000009530

Population segments: Adjuvant, Liver mets, Neoadjuvant, Stage IV

Phase: II

Therapy: bevacizumab + chemotherapy

Country: Japan

NCT01802645
Open, Randomized, Multicenter Phase II Trial With Cetuximab /5-FU/FA/ Irinotecan or Cetuximab/5-FU/FA / Irinotecan/Oxaliplatin in K-ras/B-raf Wild Type Patients or With Irinotecan/ Oxaliplatin/5-FU/FA With or Without Bevacizumab in K-ras Mutant Patients as Neoadjuvant Treatment in Patients With Non- Resectable Colorectal Liver Metastases.

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: CELIM 2- study, CELIM2, DRKS00010758, EudraCT Number: 2011-003288-31, TrialTroveID-141012, TUD-CELIM2-050

Population segments: Adjuvant, Liver mets, Neoadjuvant, Stage IV

Phase: II

Therapy: bevacizumab + chemotherapy

Country: Germany

NCT01858649
Randomized Phase II Study Comparing Pathological Responses Observed on Colorectal Cancer Metastases Resected After Preoperative Treatment Combining Bevacizumab With FOLFOX or FOLFIRI

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: BEV-ONCO2012, CTBE2013000207, EudraCT Number: 2012-005376-34, TrialTroveID-186955

Population segments: Neoadjuvant, Stage IV

Phase: II

Therapy: bevacizumab + chemotherapy

Country: Belgium

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KRAS p.(G12A) c.35G>C (continued)

NCT01037790
Phase II Trial of the Cyclin-Dependent Kinase Inhibitor PD 0332991 in Patients With Cancer

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: NCI-2009-01467, Study 1006, TrialTroveID-120590, UPCC 03909, UPCC03909

Population segments: HER2 negative, HER2 positive, Metastatic, Second line or greater/Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

Phase: II

Therapy: palbociclib

Country: United States

US State: PA

US Contact: Peter O'Dwyer [855-216-0098; PennCancerTrials@emergingmed.com]

NCT02316340
Modulation of Autophagy: A Clinical Study of Vorinostat Plus Hydroxychloroquine Versus Regorafenib in Refractory Metastatic Colorectal Cancer (mCRC) Patients

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: CTMS 14-2015, CTMS# 14-2015, HSC20150178H, NCI-2015-00175, NCI-2015-00203, TrialTroveID-243207

Population segments: Second line or greater/Refractory/Relapsed, Stage IV

Phase: II

Therapies: regorafenib, vorinostat + hydroxychloroquine

Country: United States

US State: TX

US Contact: Epp Goodwin [210-450-5798; CTRCReferral@uthscsa.edu]

NCT01675999
PRODIGE 22-ECKINOXE: Randomized Phase II Trial of Neoadjuvant FOLFOX 4 Versus FOLFOX 4 With Cetuximab Versus Immediate Surgery in Locally Advanced Colon Cancer ECKINOXE : EXperimental Colon KIRAS-status based Neoadjuvant OXwith or without treatment aliplatin Erbitux

Cancer type: Colorectal Cancer

Variant class: RAS mutation

Other identifiers: ECKINOXE, ECKINOXE # PRODIGE 22, ECKINOXE PRODIGE 22 FFCD 1003, EudraCT Number: 2011-001519-29, P100131, PHRC10_02-42, PRODIGE 22-ECKINOXE, PRODIGY 22 - FFCD 1003, RECF2082, TrialTroveID-173718

Population segments: Adjuvant, Neoadjuvant, Stage II, Stage III

Phase: II

Therapy: cetuximab + chemotherapy

Country: France

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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KRAS p.(G12A) c.35G>C (continued)

NCT02450656
Phase I/II study with the combination of afatinib and selumetinib in advanced KRAS mutant positive and PIK3CA wildtype colorectal, non-small cell lung and pancreatic cancer

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

Other identifiers: EudraCT Number: 2014-001855-22, M14AFS, NL49983.031.14, TrialTroveID-251759

Population segments: KRAS, Second line or greater/Refractory/Relapsed, Stage II, Stage III, Stage IV

Other inclusion criteria: PIK3CA wild type

Phase: I/II

Therapy: afatinib + selumetinib

Country: Netherlands

NCT02039336
Phase I/II Study With the Combination of Dacomitinib and PD-0325901 in Metastatic KRAS Mutation Positive Colorectal, Non-small Cell Lung and Pancreatic Cancer

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

Other identifiers: EudraCT Number: 2013-003299-10, M13DAP, NL45985.031.13, TrialTroveID-200856

Population segments: KRAS, Line of therapy N/A, Stage III, Stage IV

Phase: I/II

Therapy: dacomitinib + PD-0325901

Country: Netherlands

NCT02230553
Phase I/II study with lapatinib plus trametinib in patients with metastatic KRAS mutant colorectal, non-small cell lung and pancreatic cancer

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

Other identifiers: EudraCT Number: 2014-002209-39, M14LTK, NL49551.031.14, TrialTroveID-214278

Population segments: KRAS, Second line or greater/Refractory/Relapsed, Stage IV

Other inclusion criteria: PIK3CA wild type

Phase: I/II

Therapy: lapatinib + trametinib

Country: Netherlands

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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KRAS p.(G12A) c.35G>C (continued)

NCT02703571
A Phase I/II Study of Safety and Efficacy of Ribociclib (LEE011) in Combination With Trametinib (TMT212) in Patients With Metastatic or Advanced Solid Tumors

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: CTMT212X2106, EudraCT Number: 2015-005019-34, TrialTroveID-274520

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I/II

Therapy: ribociclib + trametinib

Countries: Netherlands, United States

US States: AR, FL

US Contact: Novartis Pharmaceuticals [888-669-6682]

NCT02583542
A Phase Ib/IIa Study of AZD2014 in Combination With Selumetinib in Patients With Advanced Cancers.

Cancer type: Colorectal Cancer

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 009896QM, EudraCT Number: 2014-002613-31, IRAS ID 172356, Torcmek, TrialTroveID-265019, UKCRN ID:18725

Population segments: EGFR, FGFR, HER2 negative, HER2 positive, KRAS, Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Country: United Kingdom

NCT01988896
A Phase Ib Study of the Safety and Pharmacology of Atezolizumab Administered With Cobimetinib in Patients With Locally Advanced or Metastatic Solid Tumors

Cancer type: Colorectal Cancer

Variant class: KRAS G12 mutation

Other identifiers: 13-223, 14-301, 20132268, CT672, DFCI: 14-301, EudraCT Number: 2013-003329-27, GP28363, GP28363-V2, HIC: 1403013518, NCI-2014-00166, Octopus, TrialTroveID-197176

Population segments: ALK, EGFR, KRAS, Second line or greater/Refractory/Relapsed, Stage I, Stage II, Stage III, Stage IV

Phase: I

Therapy: atezolizumab + cobimetinib

Countries: Australia, Canada, Germany, Republic of Korea, Singapore, United States

US States: CA, CO, CT, MA, NC, NY, TX, WA

US Contact: Clinical Trials Hoffmann-La Roche [888-662-6728; global.rochegenentechtrials@roche.com]

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

KRAS p.(G12A) c.35G>C (continued)

NCT02510001
A Phase I Study of MEK 1/2 Inhibitor PD-0325901 With cMET Inhibitor PF-03241066 in RASMT and RASWT (With Aberrant c-MET) Colorectal Cancer Patients

Cancer type: Colorectal Cancer

Variant class: KRAS G12 mutation

Other identifiers: 17363, EudraCT Number: 2014-000463-40, ISRCTN18043777, MErCuRIC, MErCuRIC1, OCTO-049, TrialTroveID-217604, UKCRN ID:17363

Population segments: First line, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: crizotinib + PD-0325901

Country: United Kingdom

NCT01740648
A Phase I Trial of MEK Inhibitor Trametinib in Combination With Neoadjuvant 5-Fluorouracil Chemoradiation in the Treatment of KRAS, BRAF, and NRAS-MUTANT Rectal Cancers

Cancer type: Colorectal Cancer

Variant class: KRAS G12 mutation

Other identifiers: 2012C0086, 201403053, NCCNGSK10033, NCI-2012-02158, OSU-12054, TrialTroveID-174199

Population segments: Line of therapy N/A, Neoadjuvant, Stage II, Stage III

Phase: I

Therapy: trametinib + chemotherapy + radiation therapy + surgical intervention

Country: United States

US State: OH

US Contact: Ohio State University Comprehensive Cancer Center [800-293-5066; Jamesline@osumc.edu]

NCT02243917
A Phase 1, Open-Label, Dose Escalation and Dose Expansion Study Evaluating the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Effects of Orally Administered CB-5083 in Subjects With Advanced Solid Tumors

Cancer type: Colorectal Cancer

Variant class: KRAS exon 2 mutation

Other identifiers: 149511, CLC-101, TrialTroveID-216163

Population segments: Second line or greater/Refractory/Relapsed, Stage II, Stage III, Stage IV

Phase: I

Therapy: CB-5083

Country: United States

US States: AZ, CA, CO, GA, PA

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

KRAS p.(G12A) c.35G>C (continued)

NCT02538627
A Phase 1 Study Evaluating the Safety, Pharmacology and Preliminary Activity of the Co-Administration of MM-151 and MM-121 in Heregulin Positive Cancer Patients

Cancer type: Colorectal Cancer

Variant class: KRAS activating mutation

Other identifiers: MM-151-01-01-02, NCI-2015-01527, TrialTroveID-264006, VICCPHI1598

Population segments: Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV

Phase: I

Therapy: MM-151 + trametinib

Country: United States

US States: CO, GA, IL, TN

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT02613650
A Phase Ib Trial of a Combination of FOLFIRI With MEK162 in Patients With Advanced KRAS Positive Metastatic Colorectal Cancers

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: CMEK162AUS12T, HCI87144, MEK162/FOLFIRI, NCI-2016-00331, TrialTroveID-268582

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: binimetinib + chemotherapy

Country: United States

US State: UT

US Contact: Alexis Mollard [801-587-5598; alexis.mollard@hci.utah.edu]

NCT02405065
Phase I Study to Assess the Safety, Tolerability and Pharmacokinetics and Anti-tumor Activity of HM95573 in Solid Tumors

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: HM-RAFI-101, TrialTroveID-220532

Population segments: KRAS, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: HM-95573

Country: Republic of Korea

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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KRAS p.(G12A) c.35G>C (continued)

NCT02248805
A Phase I, First-in-Human, Open Label, Dose Escalation Study of MGD007, A Humanized gpA33 x CD3 Dual-Affinity Re-Targeting (DART) Protein in Patients With Relapsed/Refractory Metastatic Colorectal Carcinoma.

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: 00056149, 14-524, AAAP4552, CP-MGD007-01, J14126, NCI-2015-00188, TrialTroveID-208327

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: MGD007

Country: United States

US States: MA, MD, NC, OR

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

No NCT ID - see other identifier(s)
A Phase I Study to Evaluate the Safety, Tolerability and Efficacy of MK-8353 Combination Therapies in Subjects With Advanced Solid Tumors

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: EudraCT Number: 2012-002695-13, MK8353-010, NL41947.031.12, TrialTroveID-222700

Population segments: KRAS, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapies: pembrolizumab + SCH-900353, ridaforolimus + SCH-900353, SCH-900353 + chemotherapy

Country: Netherlands

NCT02078349
An Investigator Sponsored Phase I Study of the Safety, Pharmacokinetics and Pharmacodynamics of Escalating Doses Followed by Dose Expansion of the Selective Inhibitor of Nuclear Export (SINE) Selinexor (KPT-330) in Asian Patients With Advanced or Metastatic Solid Tumor Malignancies

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: 2013/01034, KPT330-A1, TrialTroveID-203656

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), KRAS, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: selinexor

Country: Singapore

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

KRAS p.(G12A) c.35G>C (continued)

NCT01642342
A First-In-Human Phase I Study of sEphB4-HSA in Patients With Advanced Solid Tumors With Expansion at the Maximum Tolerated Dose (MTD) or Recommended Phase II Dose (RP2D).

Cancer type: Colorectal Cancer

Variant class: KRAS mutation

Other identifiers: 0C-11-3, NCI-2012-00971, TrialTroveID-171511

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: sEphB4-HSA

Country: United States

US State: CA

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT02188264
A Phase IB Study of the Combination of AZD6244 Hydrogen Sulfate (Selumetinib) and Cyclosporin A (CsA) in Patients With Advanced Solid Tumors With an Expansion Cohort in Metastatic Colorectal Cancer

Cancer type: Colorectal Cancer

Variant class: RAS mutation

Other identifiers: 051406, 13-2628, 201409113, 9571, NCI-2014-01484, NCI-9571-CIRB, NCI/CTEP #9571, NCI9571, P9571_A01PAMDREVW01, TrialTroveID-212843

Population segments: Stage IV, Second line or greater/Refractory/Relapsed, Stage III

Exclusion criteria variant class: BRAF mutation

Phase: I

Therapy: selumetinib + ciclosporin

Country: United States

US States: CO, MO, NC, NJ, OH, PA, TX

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD2014 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant classes: KRAS & TP53 mutation

Other identifiers: 1508016363, OLAPCO, TrialTroveID-266161

Population segments: First line, Second line or greater/Refractory/Relapsed, Stage IV

Phase: II

Therapy: MK-1775 + olaparib

Country: United States

US State: CT

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

KRAS p.(G12A) c.35G>C (continued)

NCT02029001
A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: KRAS mutation

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER, TrialTroveID-200294

Population segments: Maintenance/Consolidation, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Exclusion criteria variant class: BRAF V600 mutation

Phase: II

Therapy: sorafenib

Country: France

NCT02747537
Phase II Clinical Trial Treating Relapsed/Recurrent/Refractory Pediatric Solid Tumors With the Genomically-Targeted Agent Sorafenib in Combination With Irinotecan

Cancer type: Unspecified Solid Tumor

Variant class: RAS mutation

Other identifiers: 201605006, NCI-2016-00680, TrialTroveID-277232

Population segments: (N/A), Second line or greater/Refractory/Relapsed

Phase: II

Therapy: sorafenib + chemotherapy

Country: United States

US State: MO

US Contact: Dr. Robert Hayashi [314-454-6018; hayashi_r@kids.wustl.edu]

NCT02022982
Phase I/II Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the MEK Inhibitor PD-0325901 for Patients with KRAS Mutant Non-Small Cell Lung Cancer and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: KRAS mutation

Other identifiers: 13-506, NCI-2014-00940, TrialTroveID-200043

Population segments: KRAS, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I/II

Therapy: palbociclib + PD-0325901

Country: United States

US State: MA

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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KRAS p.(G12A) c.35G>C (continued)

NCT02437227
A Phase 1, First in Man, Dual Centre, Open-label Dose Escalation Study With Expansion to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of CCT3833 (BAL3833), a panRAF Inhibitor, Given Orally in Patients With Advanced Solid Tumours, Including Metastatic Melanoma

Cancer type: Unspecified Solid Tumor

Variant class: RAS mutation

Other identifiers: 4232, PanRAF, TrialTroveID-257046

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I/II

Therapy: BAL-3833

Country: United Kingdom

No NCT ID - see other identifier(s)
A Phase I/II Study of LNP3794 in Patients with Advanced Solid Tumors having RAS/BRAF Mutations

Cancer type: Unspecified Solid Tumor

Variant class: RAS mutation

Other identifier: TrialTroveID-250171

Population segments: Line of therapy N/A, Stage III, Stage IV

Phase: I/II

Therapy: LNP3794

Country: United Kingdom

NCT02407509
A Phase I Trial of RO5126766 (a Dual RAF/MEK Inhibitor) Exploring Intermittent, Oral Dosing Regimens in Patients With Solid Tumours or Multiple Myeloma

Cancer type: Unspecified Solid Tumor

Variant class: KRAS mutation

Other identifiers: CCR3808, DDU RAF/MEK, EudraCT Number: 2012-001040-22, TrialTroveID-206542

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: RO-5126766

Country: United Kingdom

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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KRAS p.(G12A) c.35G>C (continued)

NCT02015117
A Phase 1 Study of Trametinib in Combination With Radiation Therapy for Brain Metastases

Cancer type: Unspecified Cancer

Variant class: KRAS mutation

Other identifiers: 2013C0115, 9458, NCI-2013-02343, OSU 13197, OSU-13197, TrialTroveID-199440

Population segments: CNS mets, First line, Line of therapy N/A, Stage IV

Phase: I

Therapies: trametinib + radiation therapy, trametinib + surgical intervention

Country: United States

US States: IL, OH

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT02607813
A Phase I Dose Finding Study of Oral LXH254 in Adult Patients With Advanced Solid Tumors Harboring MAPK Pathway Alterations

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 2015-0913, CLXH254X2101, EudraCT Number: 2015-003421-33, NCI-2015-02280, REec-2016-2132, TrialTroveID-268216

Population segments: Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: LXH254

Countries: Canada, Germany, Japan, Netherlands, Spain, United States

US States: NY, TX

US Contact: Novartis Pharmaceuticals [888-669-6682]

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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RB1 p.(W516Ter) c.1548G>A

NCT01037790
Phase II Trial of the Cyclin-Dependent Kinase Inhibitor PD 0332991 in Patients With Cancer

Cancer type: Unspecified Solid Tumor

Variant class: G1/S cell cycle pathway

Other identifiers: NCI-2009-01467, Study 1006, TrialTroveID-120590, UPCC 03909, UPCC03909

Population segments: HER2 negative, HER2 positive, Metastatic, Second line or greater/Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

Phase: II

Therapy: palbociclib

Country: United States

US State: PA

US Contact: Peter O'Dwyer [855-216-0098; PennCancerTrials@emergingmed.com]

TP53 p.(R248W) c.742C>T

NCT02432963
A Phase I Study of a p53MVA Vaccine in Combination With Pembrolizumab

Cancer type: Colorectal Cancer

Variant class: TP53 mutation

Other identifiers: 116634, 122284, 122771, 124524, 15002, NCI-2015-00653, TrialTroveID-256830

Population segments: HER2 negative, Second line or greater/Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative, Unresectable

Phase: I

Therapy: pembrolizumab + p53MVA

Country: United States

US State: CA

US Contact: Vincent Chung [800-826-4673]

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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TP53 p.(R248W) c.742C>T (continued)

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD2014 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant classes: KRAS & TP53 mutation

Other identifiers: 1508016363, OLAPCO, TrialTroveID-266161

Population segments: First line, Second line or greater/Refractory/Relapsed, Stage IV

Phase: II

Therapy: MK-1775 + olaparib

Country: United States

US State: CT

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT02042989
A Phase I Study of MLN9708 and Vorinostat to Target Autophagy in Patients With Advanced p53 Mutant Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: 2013-0511, NCI-2014-01091, TrialTroveID-201319

Population segments: Line of therapy N/A, Stage III, Stage IV

Phase: I

Therapy: ixazomib + vorinostat

Country: United States

US State: TX

US Contact: Dr. Siqing Fu [713-563-1930]

NCT02610075
A Phase Ib Study to Determine the Maximum Tolerated Dose (MTD) of AZD1775 Monotherapy in Patients With Locally Advanced or Metastatic Solid Tumours.

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: D6015C00003, REFMAL 398, TrialTroveID- 268385

Population segments: Liver mets, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: MK-1775

Country: United States

US States: CO, TN

US Contact: AstraZeneca Clinical Study Information Center [877-240-9479; information.center@astrazeneca.com]

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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TP53 p.(R248W) c.742C>T (continued)

NCT02354547
A Phase I Study of SGT-53, a TfRscFv-Liposome-p53 Complex, in Children with Refractory or Recurrent Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: 1405-1316, SGT53-01-2, TrialTroveID-251586

Population segments: (N/A), Second line or greater/Refractory/Relapsed

Phase: I

Therapies: SGT-53, SGT-53 + chemotherapy

Country: United States

US State: TX

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

FLT3 amplification

NCT02029001
A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: FLT3 amplification

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER, TrialTroveID-200294

Population segments: Maintenance/Consolidation, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Exclusion criteria variant class: BRAF V600 mutation

Phase: II

Therapy: sorafenib

Country: France

NCT02272998
Phase II Study Of Ponatinib For Advanced Cancers With Genomic Alterations In Fibroblastic Growth Factor Receptor (FGFR) And Other Genomic Targets (KIT, Pdgfra, RET FLT3, ABL1)

Cancer type: Unspecified Solid Tumor

Variant class: FLT3 aberration

Other identifiers: 14078, 2014C0143, NCI-2014-01499, OSU-14078, TrialTroveID-219466

Population segments: Advanced, Second line or greater/Refractory/Relapsed, Stage IV

Phase: II

Therapy: ponatinib

Country: United States

US States: MI, OH

US Contact: The Ohio State University Comprehensive Cancer Center [800-293-5066]

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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Appendix: Evidence Summary by Variant Class

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

KRAS p.(G12A) c.35G>C

Variant Class	Evidence Items
RAS/RAF/MEK/ERK pathway	2
↳ RAS mutation	6
↳ RAS activating mutation	0
↳ KRAS activating mutation	1
↳ KRAS G12 mutation	5
↳ KRAS mutation	31
↳ KRAS activating mutation	1
↳ KRAS G12 mutation	5
↳ KRAS exon 2 mutation	10
↳ KRAS G12 mutation	5

RB1 p.(W516Ter) c.1548G>A

Variant Class	Evidence Items
G1/S cell cycle pathway	1

TP53 p.(R248W) c.742C>T

Variant Class	Evidence Items
TP53 mutation	6

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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Appendix: Evidence Summary by Variant Class (continued)

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

FLT3 amplification

Variant Class	Evidence Items
FLT3 aberration	1
↳ FLT3 amplification	1

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

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Appendix: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
KRAS	p.(G12A)	c.35G>C	COSM522	chr12:25398284	40.60%	NM_033360.3	missense
RB1	p.(W516Ter)	c.1548G>A	.	chr13:48955432	14.00%	NM_000321.2	nonsense
TP53	p.(R248W)	c.742C>T	COSM10656	chr17:7577539	48.12%	NM_000546.5	missense

Copy Number Variations

Gene	Locus	Copy Number
FLT3	chr13:28579521	6.45

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

Report Signed by		Report Checked by	
			
Clinical Scientist	☑		
Pathologist	☐	BMS	☑
BMS (Senior)	☐		

Terms and Conditions

The following paragraph on Liability is an extract from the Oncologica Tests' Terms and Conditions. The extract is to draw your attention to particular terms applicable to you but nothing set out here is intended to supersede or override our Terms and Conditions, which can be found on our website at www.oncologica.com under the title Oncologica Tests' Terms and Conditions. Please read these Oncologica Test Terms and Conditions carefully before you submit an order for the Oncologica Tests, as you will be bound by these Terms and Conditions, once a contract comes into existence as per paragraph 2 of the Oncologica Test's Terms and Conditions.

6. Liability

6.1 Oncologica operates in compliance with international ISO15189:2012 standards and is regulated by UKAS. The Oncologica Tests have not been cleared or approved by the United States Food and Drug Administration; however, such clearance or approval is not required.

6.2 The Patient agrees that the Oncologica Test Report is intended for clinical use and interpretation by a physician who is experienced and skilled in the use and interpretation of clinical test data. The Oncologica Test Report is based on the Sample submitted by the Patient. The Oncologica Test Report should not be considered or its contents applied to any other patient or any other sample. Oncologica does not update an Oncologica Test Report once it has been sent.

6.3 Information compiled in the Oncologica Test Report includes is from publicly available as well as proprietary sources. By updating the source database, Oncologica makes every effort to provide the most accurate and up-to-date information. However, Oncologica does not warrant or represent that the information in the Oncologica Test Report is accurate, timely or complete.

6.4 The Oncologica Test Report contains drug and clinical trial information. However, Oncologica does not warrant or represent that any drug or clinical trial identified by the Oncologica Test will guarantee a therapeutic response for a particular Patient. The drugs listed in an Oncologica Test Report are ranked on clinical evidence as to the predicted efficacy or appropriateness for the Patient. The Patient shall ensure that its physician shall evaluate and interpret the Oncologica Test Report, along with all other available clinical information about the Patient, to determine the best treatment decisions in their own independent medical judgment. Patient management decisions should not be based on a single test, nor solely on the information contained in the Oncologica Test Report.

6.5 Subject to paragraph 6.10, Oncologica shall have no liability for any use made of the information provided in the Oncologica Test Report, including but not limited to any report prepared by Oncologica summarising the results of the Oncologica Tests, any advice supplied by Oncologica, any decisions taken, or for any costs incurred by Patient and/or the Patient's physician and/or the Agent in consequence of such use, advice or decisions. The Oncologica Test and/or the Oncologica Test Report is not a substitute for the Patient's physician's professional judgment. The use of the information provided in the Oncologica Test Report is provided as a tool for the ordering physician's use in determining the appropriate treatment for the Patient. The decision as to what course of treatment and the appropriate use of the information provided by the Oncologica Test Report is solely that of the Patient's physician.

6.6 Oncologica does not warrant or represent or guarantee that the Oncologica Tests will identify an actionable genetic alteration that is linked to anti-cancer targeted therapies. Although the Oncologica Tests are comprehensive, in a proportion of Patients, the Oncologica Test result may not identify any actionable mutations for a patient's cancer. In the event that no actionable alteration in the Sample is identified by the Oncologica Test, then the Patient is still under full obligation to pay the Charges and no refund is available to the Patient and/or Agent.

6.7 The Oncologica Test identifies genomic actionable alterations found in the submitted Sample that are linked to anti-cancer targeted agents. Also note that this test only examines tumour, and not normal tissue from the patient, and therefore cannot distinguish between somatic and germline (i.e., heritable) alterations.

6.8 Subject to Clause 6.8, Oncologica shall not be liable to the Patient whether in contract, tort (including negligence and breach of statutory duty), or otherwise for any:

(a) Error or defect in the Oncologica Test Report as a result of any inaccurate or incomplete information supplied by the Patient;

(b) Loss of data or materials, including the Sample and/or the Report and including any loss arising as a result of the acts or omissions of a courier;

(c) Indirect or consequential loss arising whether or not advised of the possibility of the same.

6.9 Subject to the provisions of this Clause 6, Oncologica's total liability to the Patient in respect of all losses arising under or in connection with the Contract, whether in contract, tort (including negligence and breach of statutory duty), or otherwise, shall in no circumstances exceed the Charges paid for the Test that is the subject of the claim.

6.10 Nothing in the Contract limits or excludes the liability of Oncologica for breach of its obligations under section 12 of the Sale of Goods Act 1979 and/or section 2 of the Supply of Goods and Services Act 1982; death or personal injury resulting from negligence; or fraud or fraudulent misrepresentation.

6.11 If the Patient is a consumer (and not a business), the Patient expressly acknowledges and agrees that the Test is supplied to the Patient's specification and therefore there is no right to cancel the Test following acceptance under Clause 2.2. If the Patient is a consumer, then notwithstanding any other provisions of the Contract, none of the Patient's consumer statutory rights are affected.


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