



[Oncofocus] Patient Test Report

Supplementary Report

Surname		Requesting Clinician	
Forename		Date requested	
DOB		Tumour %	95%
Gender		Tumour %	-
Histology #	Male	(macrodissected)	
Primary site			
Tumour subtype	Brain		
Tissue Type	Glioblastoma Cortex Brain		

Comment: This is a supplementary report to the original which was issued on 28th April 2017. This supplementary report details the testing of the RNA from this sample.

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.

237 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 582 anti-cancer targeted therapies.

The following actionable variants were detected, this confirms the original result, no additional variants were detected in the RNA from this sample.

Variant Summary

Sample Cancer Type: Glioblastoma

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
BRAF p.(V600E) c.1799T>A	<input type="radio"/> (5)	<input type="radio"/> (5)	<input type="radio"/> (5)	<input type="radio"/> (10)	<input checked="" type="radio"/> (24)

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 (PPV) of 92%. Copy number variants; amplifications of CN > 6 with the 5% confidence value of ≥4 after normalization and deletions with 95% CI ≤ 1 are classified as present when the tumour% > 50% with a sensitivity of 80% and PPV 100%. Gene Fusions are reported when occurring in >20 counts and meeting the thresholds of assay specific internal RNA quality control with a sensitivity of 92% and PPV of 99%. Supplementary technical information is available upon request.

ONC17-:

www.oncologica.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.

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

BRAF p.(V600E) c.1799T>A

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
cobimetinib + vemurafenib	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (II)
dabrafenib + trametinib	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (II)
vemurafenib	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (I)
dabrafenib	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
trametinib	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
ipilimumab	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
nivolumab	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
pembrolizumab	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
BRAF inhibitor	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
BRAF inhibitor + MEK inhibitor	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
ipilimumab + nivolumab	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
cetuximab	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
panitumumab	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
sorafenib + chemotherapy	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (II)
AB-024	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I/II)
ASN-003	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I/II)
BAL-3833	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I/II)
cetuximab + vemurafenib + chemotherapy	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I/II)
dabrafenib + navitoclax + trametinib, dabrafenib + trametinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I/II)
LNP3794	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I/II)
NKTR-214	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (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.

ONC17-:

www.oncologica.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.

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

BRAF p.(V600E) c.1799T>A (continued)

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
PLX-8394	×	×	×	×	● (I/II)
abemaciclib + LY3214996 , LY3214996 , LY3214996 + chemotherapy, LY3214996 + midazolam	×	×	×	×	● (I)
BGB-283	×	×	×	×	● (I)
BVD-523	×	×	×	×	● (I)
CB-5083	×	×	×	×	● (I)
crizotinib + vemurafenib, sorafenib + vemurafenib	×	×	×	×	● (I)
dabrafenib + onalespib + trametinib	×	×	×	×	● (I)
dabrafenib, dabrafenib + trametinib	×	×	×	×	● (I)
LTT-462	×	×	×	×	● (I)
LXH254	×	×	×	×	● (I)
RO-5126766	×	×	×	×	● (I)
trametinib + radiation therapy, trametinib + surgical intervention	×	×	×	×	● (I)
vemurafenib + itraconazole, vemurafenib + rifampin	×	×	×	×	● (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.

ONC17-:

www.oncologica.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.

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 2017-01-03. For the most up-to-date information, search www.ema.europa.eu/ema.

BRAF p.(V600E) c.1799T>A

cobimetinib + vemurafenib

Cancer type: Melanoma

Label as of: 2016-07-27

Variant class: BRAF V600 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003960/WC500198563.pdf

dabrafenib + trametinib, trametinib

Cancer type: Melanoma

Label as of: 2016-09-28

Variant class: BRAF V600 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002643/WC500169657.pdf

dabrafenib, dabrafenib + trametinib

Cancer type: Melanoma

Label as of: 2016-06-22

Variant class: BRAF V600 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002604/WC500149671.pdf

vemurafenib

Cancer type: Melanoma

Label as of: 2017-01-16

Variant class: BRAF V600 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002409/WC500124317.pdf

ONC17-:

www.oncologica.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.

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 2017-01-03. For the most up-to-date information, search www.fda.gov.

BRAF p.(V600E) c.1799T>A

cobimetinib + vemurafenib

Cancer type: Melanoma

Label as of: 2016-05-31

Variant class: BRAF V600E mutation

Indications and usage:

COTELLIC™ is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.

Limitation of Use: COTELLIC™ is not indicated for treatment of patients with wild-type BRAF melanoma.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/206192s001lbl.pdf

dabrafenib + trametinib, trametinib

Cancer type: Melanoma

Label as of: 2015-11-20

Variant class: BRAF V600E mutation

Indications and usage:

MEKINIST™ is a kinase inhibitor indicated, as a single agent or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA approved test.

Limitation of use: MEKINIST™ is not indicated for treatment of patients who have received prior BRAF-inhibitor therapy.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/204114s004lbl.pdf

ONC17-:

www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**○ dabrafenib, dabrafenib + trametinib**

Cancer type: Melanoma

Label as of: 2016-06-16

Variant class: BRAF V600E mutation

Indications and usage:

- TAFINLAR® is a kinase inhibitor indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.
- TAFINLAR® is indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.

Limitation of Use: TAFINLAR® is not indicated for treatment of patients with wild-type BRAF melanoma.

Reference:http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/202806s005lbl.pdf**○ vemurafenib**

Cancer type: Melanoma

Label as of: 2016-08-31

Variant class: BRAF V600E mutation

Indications and usage:

ZELBORAF® is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

Limitation of Use: ZELBORAF® is not indicated for treatment of patients with wild-type BRAF melanoma.

Reference:http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/202429s009lbl.pdf

ONC17-:

www.oncologica.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.

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 2016-12-01. For the most up-to-date information, search www.esmo.org.

BRAF p.(V600E) c.1799T>A

BRAF inhibitor

Cancer type: Melanoma

Variant class: BRAF V600 mutation

ESMO Recommendation category: II, B

Population segment (Line of therapy):

- Metastatic (preferred) or primary tumour (First and second line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Cutaneous Melanoma [Ann Oncol (2015) 26 (suppl 5): v126-v132.]

BRAF inhibitor + MEK inhibitor

Cancer type: Melanoma

Variant class: BRAF V600 mutation

ESMO Recommendation category: II, B

Population segment (Line of therapy):

- Metastatic (preferred) or primary tumour (First and second line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Cutaneous Melanoma [Ann Oncol (2015) 26 (suppl 5): v126-v132.]

ipilimumab

Cancer type: Melanoma

Variant class: BRAF V600 mutation

ESMO Recommendation category: II, B

Population segment (Line of therapy):

- Metastatic (preferred) or primary tumour (First and second line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Cutaneous Melanoma [Ann Oncol (2015) 26 (suppl 5): v126-v132.]

ONC17-:

www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued) **nivolumab**

Cancer type: Melanoma

Variant class: BRAF V600 mutation

ESMO Recommendation category: II, B

Population segment (Line of therapy):

- Metastatic (preferred) or primary tumour (First and second line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Cutaneous Melanoma [Ann Oncol (2015) 26 (suppl 5): v126-v132.]

 pembrolizumab

Cancer type: Melanoma

Variant class: BRAF V600 mutation

ESMO Recommendation category: II, B

Population segment (Line of therapy):

- Metastatic (preferred) or primary tumour (First and second line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Cutaneous Melanoma [Ann Oncol (2015) 26 (suppl 5): v126-v132.]

ONC17-:

www.oncologica.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.

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 2016-12-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

BRAF p.(V600E) c.1799T>A

dabrafenib

Cancer type: Non-Small Cell Lung Cancer

Variant class: BRAF V600E mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- NSCLC (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2017]

dabrafenib + trametinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: BRAF V600E mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- NSCLC (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2017]

vemurafenib

Cancer type: Non-Small Cell Lung Cancer

Variant class: BRAF V600E mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- NSCLC (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2017]

ONC17-:

www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued) **cobimetinib + vemurafenib**

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic or unresectable (First line therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 dabrafenib + trametinib

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic or unresectable disease (First-line therapy) (preferred)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 nivolumab

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic or unresectable disease (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 pembrolizumab

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic or unresectable disease (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

ONC17-:

www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued) **cobimetinib + vemurafenib**

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy (preferred)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 dabrafenib

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease, if BRAF/MEK inhibitor combination therapy is contraindicated, BRAF-inhibitor monotherapy with dabrafenib or vemurafenib are recommended options, especially in a population that is not an appropriate candidate for checkpoint immunotherapy (First-line or second-line therapy).
- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy, if not used as first-line and not of the same class (Second-line or Subsequent therapy).

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 dabrafenib + trametinib

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy (preferred)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

ONC17-:

www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued) **ipilimumab**

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy (Second-line or Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 ipilimumab + nivolumab

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease (First-line therapy)
- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy (Second-line or Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 nivolumab

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy (Second-line or Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

ONC17-:

www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued) **pembrolizumab**

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy (Second-line or Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 vemurafenib

Cancer type: Melanoma

Variant class: BRAF V600 mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or unresectable disease, contraindicated to BRAF/MEK inhibitor combination, especially if not appropriate for checkpoint immunotherapy (First-line or Second-line)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 1.2017]

 cetuximab

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Summary:

NCCN Guidelines® do not contain a recommendation regarding BRAF V600 mutations and cetuximab in Colon Cancer, but include the following evidentiary statements:

- "Evidence increasingly suggest that BRAF V600E mutations makes response to panitumumab or cetuximab highly unlikely, as a single agent, or in combination with cytotoxic chemotherapy"

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 1.2017]

BRAF p.(V600E) c.1799T>A (continued)**⊘ cetuximab**

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Summary:

NCCN Guidelines® do not contain a recommendation regarding BRAF V600 mutations and cetuximab in Rectal Cancer, but include the following evidentiary statements:

- "Evidence increasingly suggest that BRAF V600E mutations makes response to panitumumab or cetuximab highly unlikely, as a single agent, or in combination with cytotoxic chemotherapy"

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2017]**⊘ panitumumab**

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Summary:

NCCN Guidelines® do not contain a recommendation regarding BRAF V600 mutations and panitumumab in Colon Cancer, but include the following evidentiary statements:

- "Evidence increasingly suggest that BRAF V600E mutations makes response to panitumumab or cetuximab highly unlikely, as a single agent, or in combination with cytotoxic chemotherapy"

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 1.2017]**⊘ panitumumab**

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Summary:

NCCN Guidelines® do not contain a recommendation regarding BRAF V600 mutations and panitumumab in Rectal Cancer, but include the following evidentiary statements:

- "Evidence increasingly suggest that BRAF V600E mutations makes response to panitumumab or cetuximab highly unlikely, as a single agent, or in combination with cytotoxic chemotherapy"

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2017]

ONC17-:

www.oncologica.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.

Current Global Clinical Trials Information

Global Clinical Trials information is current as of 2016-12-01. 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'.

BRAF p.(V600E) c.1799T>A

NCT02034110

A Phase II, Open-label, Study in Subjects with BRAF V600E-Mutated Rare Cancers with Several Histologies to Investigate the Clinical Efficacy and Safety of the Combination Therapy of Dabrafenib and Trametinib

Cancer type: Glioblastoma

Variant class: BRAF V600E mutation

Other identifiers: 117019, 14-126, 14-C-0131, 2013-0918, BRF117019, CSET 2108, DRKS00007132, EudraCT Number: 2013-001705-87, NCI-14-C-0131, NL46478.031.14, P121120, RECF2277, ROAR, ROAR BRF117019, TrialTroveID-200563

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

Phase: II

Therapy: dabrafenib + trametinib

Locations: Austria, Belgium, Canada, Denmark, France, Germany, Italy, Netherlands, Norway, Republic of Korea, Spain, Sweden, United States

US States: CA, MA, MD, NY, TX

US Contact: US GSK Clinical Trials Call Center [877-379-3718; GSKClinicalSupportHD@gsk.com]

NCT01748149

PNOC-002: Safety, Phase 0, and Pilot Efficacy Study of Vemurafenib, an Oral Inhibitor of BRAFV600E, in Children and Young Adults With Recurrent/Refractory BRAFV600E- or BRAF Ins T Mutant Brain Tumors

Cancer type: Glioblastoma

Variant class: BRAF V600E mutation

Other identifiers: 076373, 092093, 120819, 120819 (PNOC 002), CC#120819, NCI-2014-00387, PNOC 002, TrialTroveID-179131

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

Phase: I

Therapy: vemurafenib

Location: United States

US States: CA, DC, IL, MA, MO, OH, OR, PA, TN, UT, WA

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

ONC17-:

www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**NCT02693535**

Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor**Variant class:** BRAF V600E mutation**Other identifiers:** Pro00014171, TAPUR, TrialTroveID-273941**Population segments:** (N/A), Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line or greater/Refractory/Relapsed, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)**Phase:** II**Therapy:** cobimetinib + vemurafenib**Location:** United States**US States:** IL, MI, NC, PA, SD**US Contact:** Pam Mangat [pam.mangat@asco.org]**NCT02465060**

Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor**Variant class:** BRAF V600E mutation**Other identifiers:** 15-7002, CTSU/EAY131, EAY131, EAY131-A, EAY131-B, EAY131-E, EAY131-F, EAY131-G, EAY131-H, EAY131-I, EAY131-MATCH, EAY131-N, EAY131-P, EAY131-Q, EAY131-R, EAY131-S1, EAY131-S2, EAY131-T, EAY131-U, EAY131-V, EAY131-X, ECOGEAY131-M, MATCH, NCI-2015-00054, NCI-MATCH, TrialTroveID-258747**Population segments:** (N/A), Aggressive, ALK, Classical, EGFR, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV**Phase:** II**Therapy:** dabrafenib + trametinib**Location:** United States**US States:** AK, AL, AR, AZ, CA, CO, CT, DC, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MN, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, NY, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, WA, WI, WV, WY**US Contact:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.**ONC17-:**www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**NCT02091141**

My Pathway: An Open Label Phase IIa Study Evaluating Trastuzumab/Pertuzumab, Erlotinib, Vemurafenib/Cobimetinib, and Vismodegib in Patients Who Have Advanced Solid Tumors With Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents

Cancer type: Unspecified Solid Tumor

Variant class: BRAF activating mutation

Other identifiers: 1403013519, 2014-0459, AAAN9701, J1480, ML28897, ML28897/PRO 02, ML28897PRO/02, My Pathway, NCI-2014-01811, TrialTroveID-205033

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

Exclusion criteria variant class: RAS mutation

Phase: II

Therapy: cobimetinib + vemurafenib

Location: United States

US States: AR, AZ, CA, CO, FL, GA, IL, MD, MN, NC, ND, NY, OH, OK, OR, PA, SD, TN, TX, VA, WA

US Contact: Hoffmann-La Roche, Study Director [888-662-6728; global.roche.genentechtrials@roche.com]

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: RAF mutation

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

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

Phase: II

Therapy: sorafenib + chemotherapy

Location: United States

US State: MO

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

NCT01877811

An Open-Label, Phase 1/1b, Single-Agent Study of RXDX-105 in Patients With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600E mutation

Other identifiers: 15-270, 201307042, C32496/1105, NCI-2013-01795, RXDX-105-01, TrialTroveID-167849, UCI-15-73

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

Phase: I/II

Therapy: AB-024

Location: United States

US States: CA, DC, FL, GA, MA, MI, MO, NY, PA, TX, WA

US Contact: Rupal A. Patel [858-332-0774; rpatel@ignyta.com]

ONC17-:www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**NCT01970956**

Phase I/II Study of Dabrafenib, Trametinib, and Navitoclax in BRAF Mutant Melanoma and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600E mutation

Other identifiers: 091306, 13-424, 2014-0020, 9466, DFCI Protocol ID:13-424, NCI 9466, NCI-2013-02103, TrialTroveID-196241

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

Phase: I/II

Therapies: dabrafenib + navitoclax + trametinib, dabrafenib + trametinib

Locations: Canada, United States

US States: CA, CT, MA, MD, NC, NJ, NY, OH, PA, TX

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

NCT02961283

A Phase I, Open-label, Dose-finding and Cohort Expansion Study of ASN003 in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600 mutation

Other identifiers: ASN003-101, TrialTroveID-290434

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

Phase: I/II

Therapy: ASN-003

Location: United States

US State: TX

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

NCT01787500

A Phase I Trial of Vemurafenib in Combination With Cetuximab and Irinotecan in Patients with BRAF V600 Mutant Advanced Solid Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600 mutation

Other identifiers: 2012-0748, NCI-2013-00541, TrialTroveID-181751

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

Other inclusion criteria: KRAS wild type

Exclusion criteria variant classes: KRAS G12 mutation, KRAS G13 mutation

Phase: I/II

Therapy: cetuximab + vemurafenib + chemotherapy

Location: United States

US State: TX

US Contact: Dr. David S. Hong [713-593-1930]

ONC17-:www.oncologica.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.

BRAF p.(V600E) c.1799T>A (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: BRAF 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

Location: 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: BRAF mutation

Other identifier: TrialTroveID-250171

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

Phase: I/II

Therapy: LNP3794

Location: United Kingdom

NCT02869295

A Phase I/II, Open-Label, Multicenter, Dose Escalation and Dose Expansion Study of NKTR-214 in Subjects with Locally Advanced or Metastatic Solid Tumor Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifiers: 15-214-01, 2015-0573, EudraCT Number: 2016-001134-10, TrialTroveID-258750

Population segments: Adenocarcinoma, First line, HER2 negative, Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: NKTR-214

Location: United States

US States: CT, OR, TX

US Contact: Nektar Recruitment [855-482-8676; StudyInquiry@nektar.com]

ONC17-:www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**NCT02428712**

A Phase I/IIa Study to Assess the Safety, Pharmacokinetics, and Pharmacodynamics of PLX8394 in Patients With Advanced, Unresectable Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifiers: 2015-0158, NCI-2015-00720, PLX120-03, TrialTroveID-256645

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

Phase: I/II

Therapy: PLX-8394

Location: United States

US States: AZ, MI, TX, UT

US Contact: Terry Cho [tcho@plexikon.com]

NCT02097225

Phase I Study of AT13387 in Combination With Dabrafenib and Trametinib in Patients With BRAF-Mutant Melanoma and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600E mutation

Other identifiers: 14-186, 9557, CTEP#9557, NCI 9557, NCI-2014-00615, TrialTroveID-205735

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

Exclusion criteria variant class: RAS mutation

Phase: I

Therapy: dabrafenib + onalespib + trametinib

Location: United States

US State: MA

US Contact: Massachusetts General Hospital Cancer Trials Call Center [877-789-6100]

NCT01767623

An Open Label, Phase I Study to Evaluate the Impact of Severe Hepatic Impairment on the Pharmacokinetics and Safety of Vemurafenib in BRAF V600 mutation Positive Cancer Patients

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600 mutation

Other identifiers: 1803-7, EudraCT Number: 2012-003820-18, G028053, IRAS ID: 120756, PER-052-13, TrialTroveID-152167

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

Phase: I

Therapy: vemurafenib

Locations: Australia, Israel, Turkey

ONC17-:www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**NCT02441465**

A Phase I, Open-Label, Absolute Bioavailability Study of Vemurafenib in Patients With BRAF^{V600} Mutation-Positive Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600 mutation

Other identifiers: EudraCT Number: 2013-004144-34, GO28395, TrialTroveID-257287

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

Phase: I

Therapy: vemurafenib

Location: Hungary

NCT02608034

A Two-Part, Phase I, Open-Label, Multicenter, Two-Period, One-Sequence Study To Investigate The Effect Of Itraconazole And Rifampin On The PK Of Vemurafenib At Steady State

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600 mutation

Other identifiers: GO29475, TrialTroveID-268207

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

Phase: I

Therapies: vemurafenib + itraconazole, vemurafenib + rifampin

Locations: Republic of Korea, United States

US States: KS, TX

US Contact: Study ID Number: GO29475 [888-662-6728; global.roche.genentechtrials@roche.com]

No NCT ID - see other identifier(s)

A Phase Ib, Multi-Center Study to Evaluate the Efficacy of BGB-283 in Patients with Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifier: TrialTroveID-261285

Population segments: (N/A), Line of therapy N/A

Phase: I

Therapy: BGB-283

Locations: Australia, New Zealand

ONC17-:www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**NCT01781429**

Phase I Dose-Escalation, Safety, Pharmacokinetic and Pharmacodynamic Study of BVD-523 in Patients With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifiers: 13-010, 13-254, 2013-0574, AAAP2107, BVD-523-01, NCI-2013-01663, REFMAL 286 IST, TrialTroveID-180584, VICCPHI1375

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

Phase: I

Therapy: BVD-523

Location: United States

US States: CA, CT, FL, MA, MO, NY, TN, TX

US Contact: BioMed Valley Discoveries Inc [816-960-6600; ERK@biomed-valley.com]

NCT01531361

A Phase I Trial of Sorafenib (CRAF, BRAF, KIT, RET, VEGFR, PDGFR Inhibitor) or Crizotinib (MET, ALK, ROS1 Inhibitor) in Combination With Vemurafenib (BRAF Inhibitor) in Patients With Advanced Malignancies

Cancer type: Unspecified Cancer

Variant class: BRAF mutation

Other identifiers: 2011-1183, NCI-2012-00217, TrialTroveID-162168

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

Phase: I

Therapies: crizotinib + vemurafenib, sorafenib + vemurafenib

Location: United States

US State: TX

US Contact: MD Anderson Cancer Center [855-873-4321]

NCT01231594

A Rollover Study to provide Continued Treatment with GSK2118436 to Subjects with BRAF Mutation-Positive Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifiers: 114144, 12-016, 2010-0801, 44629, BRF114144, Eudra CT Number: 2011-000883-83, F14020, HCI 44629, IRAS ID 95276, NCI-2011-02757, OSU-11024, REFMAL 223, TrialTroveID-137250, VICCMEL1209

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

Phase: I

Therapies: dabrafenib, dabrafenib + trametinib

Locations: Australia, Italy, Spain, United Kingdom, United States

US States: AZ, CA, FL, MI, NY, OH, OK, PA, SC, TN, TX, UT, WA

US Contact: US GSK Clinical Call Center [877-379-3718; GSKClinicalSupportHD@gsk.com]

ONC17-:www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**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: BRAF 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

Location: United Kingdom

NCT02015117

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

Cancer type: Unspecified Cancer

Variant class: BRAF mutation

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

Population segments: Adjuvant, CNS mets, Stage IV

Phase: I

Therapies: trametinib + radiation therapy, trametinib + surgical intervention

Location: United States

US States: IL, OH

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

NCT02857270

A Phase I Study of an ERK1/2 Inhibitor (LY3214996) Administered Alone or in Combination With Other Agents in Advanced Cancer

Cancer type: Unspecified Cancer

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 16419, EudraCT Number: 2016-001907-21, I8S-MC-JUAB, TrialTroveID-280743

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

Phase: I

Therapies: abemaciclib + LY3214996, LY3214996, LY3214996 + chemotherapy, LY3214996 + midazolam

Location: United States

US State: TN

US Contact: Eli Lilly and Company [877-285-4559]

ONC17-:www.oncologica.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.

BRAF p.(V600E) c.1799T>A (continued)**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: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

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

Location: United States

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

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

NCT02711345

A Phase I Dose Finding Study of Oral LTT462 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: CLTT462X2101, EudraCT number: 2015-003614-24, NCI-2016-00539, TrialTroveID-275107

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

Phase: I

Therapy: LTT-462

Locations: Germany, Japan, Singapore, Spain, Switzerland, United States

US States: NY, TX

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

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

Locations: Canada, Germany, Japan, Netherlands, Republic of Korea, Spain, Switzerland, United States

US States: NY, TX

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

ONC17-:www.oncologica.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.

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.

BRAF p.(V600E) c.1799T>A

Variant Class	Evidence Items
RAS/RAF/MEK/ERK pathway	4
↳ RAF aberration	0
↳ RAF mutation	1
↳ BRAF mutation	10
↳ BRAF exon 15 mutation	0
↳ BRAF V600 mutation	26
↳ BRAF V600E mutation	18
↳ BRAF activating mutation	1
↳ BRAF V600 mutation	26
↳ BRAF V600E mutation	18

ONC17-:

www.oncologica.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.

Appendix: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency Transcript	Variant Effect	Gene Class	Variant Class
BRAF	p.(V600E)	c.1799T>A	COSM476	33.13% NM_004333.4	missense	Gain of Function	Hotspot

ONC17-:

www.oncologica.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.

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.

ONC17-:

www.oncologica.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.

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.

ONC17-:

www.oncologica.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.

Report Signed by

Report Checked by



Clinical Scientist

Pathologist

BMS (Senior)

BMS

