[Oncofocus] Patient Test Report

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

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.

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	○ (5)	○ (5)	○ (5)	⚠ (10)	● (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.

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

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

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
cobimetinib + vemurafenib	○	○	✖	○	● (II)
dabrafenib + trametinib	○	○	✖	○	● (II)
vemurafenib	○	○	✖	○	● (I)
dabrafenib	○	○	✖	○	✖
trametinib	○	○	✖	✖	✖
ipilimumab	✖	✖	○	○	✖
nivolumab	✖	✖	○	○	✖
pembrolizumab	✖	✖	○	○	✖
BRAF inhibitor	✖	✖	○	✖	✖
BRAF inhibitor + MEK inhibitor	✖	✖	○	✖	✖
ipilimumab + nivolumab	✖	✖	✖	○	✖
cetuximab	✖	✖	✖	⊘	✖
panitumumab	✖	✖	✖	⊘	✖
sorafenib + chemotherapy	✖	✖	✖	✖	● (II)
AB-024	✖	✖	✖	✖	● (I/II)
ASN-003	✖	✖	✖	✖	● (I/II)
BAL-3833	✖	✖	✖	✖	● (I/II)
cetuximab + vemurafenib + chemotherapy	✖	✖	✖	✖	● (I/II)
dabrafenib + navitoclax + trametinib, dabrafenib + trametinib	✖	✖	✖	✖	● (I/II)
LNP3794	✖	✖	✖	✖	● (I/II)
NKTR-214	✖	✖	✖	✖	● (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

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.

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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 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

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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 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

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

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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 2016-12-01. 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.]

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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.]

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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 2016-12-01. 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]

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]

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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]

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]

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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]

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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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]

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.

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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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.

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.rochegenentechtrials@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]

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]

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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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]

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@plexxikon.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, GO28053, 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

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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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.rochegenentechtrials@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

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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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]

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]

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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]

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.

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

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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

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