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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONCOFOCUS® TEST REPORT

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	-		
Surname	-	**Requester**	-
Forename	-	**Contact details**	-
DOB	-	**Date requested**	-
Gender	-		
Histology #	-	**Tumour %**	-
Primary site	Right Colon	**Tumour % (macrodissected)**	95%
Tumour subtype	Adenocarcinoma		
Tissue Type	Right Colon		

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.

Oncofocus currently targets 505 genes covering oncogenes, fusion genes, genes susceptible to copy number variation and tumour suppressors. Actionable genetic variants detected by Oncofocus are currently linked to 770 anti-cancer targeted therapies/therapy combinations.

The following actionable variants were detected:
Please note: Approximately 50% of all colorectal cancers have no mutations detected in exons 2, 3, or 4 of RAS genes KRAS or NRAS. Notably no mutations were identified in hotspot regions in KRAS and NRAS exon 2, 3 or 4.

Within the 'Current Clinical Trials Information' section of this report, starting on page 21, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

Sample Cancer Type: Colorectal Cancer

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
BRAF p.(V600E) c.1799T>A	cetuximab + vemurafenib + chemotherapy panitumumab + vemurafenib + chemotherapy	cobimetinib + vemurafenib[1,2] dabrafenib[1,2] dabrafenib + trametinib[1,2] trametinib[1,2] vemurafenib[1,2] binimetinib + encorafenib[2] nivolumab[2] BRAF inhibitor + MEK inhibitor	23
ERBB2 p.(R678Q) c.2033G>A	Clinical trials and/or off-label	ado-trastuzumab emtansine	13
PIK3CA p.(G1049S) c.3145G>A	Clinical trials and/or off-label	Clinical trials and/or off-label	12
ERBB3 p.(V104M) c.310G>A	Clinical trials and/or off-label	Clinical trials and/or off-label	4

Sources included in relevant therapies: EMA[1], FDA[2], ESMO, NCCN

Hotspot variants with >10% alternate allele reads are classified as 'detected' with an assay sensitivity and positive predictive value(PPV) of 99%. 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 >40 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.

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Tier Criteria Met

Genomic Alteration	Tier Classification for Colorectal Cancer
BRAF p.(V600E) c.1799T>A Tier: IA	IA: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in this cancer type IIC: Biomarker predicts response or resistance to EMA or FDA approved therapies in other cancer types IIC: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in other cancer types IIC: Biomarker is an inclusion criteria for clinical trials
ERBB2 p.(R678Q) c.2033G>A Tier: IIC	IIC: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in other cancer types IIC: Biomarker is an inclusion criteria for clinical trials
PIK3CA p.(G1049S) c.3145G>A Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
ERBB3 p.(V104M) c.310G>A Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials

Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

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	FDA	ESMO	NCCN	Clinical Trials*
cobimetinib + vemurafenib	○	○	✕	○	● (II)
dabrafenib	○	○	✕	○	✕
dabrafenib + trametinib	○	○	✕	○	✕
vemurafenib	○	○	✕	○	✕
trametinib	○	○	✕	✕	✕
binimetinib + encorafenib	✕	○	✕	○	✕
nivolumab	✕	○	✕	✕	✕
BRAF inhibitor + MEK inhibitor	✕	✕	○	✕	✕
cetuximab + vemurafenib + irinotecan	✕	✕	✕	●	✕

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

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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	FDA	ESMO	NCCN	Clinical Trials*
panitumumab + vemurafenib + irinotecan	✖	✖	✖	●	✖
binimetinib + cetuximab + encorafenib, cetuximab + encorafenib	✖	✖	✖	✖	● (III)
cetuximab + chemotherapy	✖	✖	✖	✖	● (III)
BRAF inhibitor + MEK inhibitor + panitumumab, BRAF inhibitor + panitumumab	✖	✖	✖	✖	● (II/III)
bevacizumab + chemotherapy, cetuximab + chemotherapy	✖	✖	✖	✖	● (II)
cobimetinib + vemurafenib, dabrafenib	✖	✖	✖	✖	● (II)
palbociclib	✖	✖	✖	✖	● (II)
sorafenib, sunitinib	✖	✖	✖	✖	● (II)
ASTX029	✖	✖	✖	✖	● (I/II)
cobimetinib	✖	✖	✖	✖	● (I/II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
abemaciclib + LY3214996 , LY3214996 , LY3214996 + chemotherapy, LY3214996 + midazolam	✖	✖	✖	✖	● (I)
adavosertib + chemotherapy	✖	✖	✖	✖	● (I)
camrelizumab + SHR7390	✖	✖	✖	✖	● (I)
cobimetinib + HM-95573	✖	✖	✖	✖	● (I)
dabrafenib + onalespib + trametinib	✖	✖	✖	✖	● (I)
HM-95573	✖	✖	✖	✖	● (I)
KO-947	✖	✖	✖	✖	● (I)
LGK-974	✖	✖	✖	✖	● (I)
LTT-462	✖	✖	✖	✖	● (I)
LXH254 , LXH254 + spartalizumab	✖	✖	✖	✖	● (I)

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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	FDA	ESMO	NCCN	Clinical Trials*
TP-0903	✖	✖	✖	✖	● (I)

ERBB2 p.(R678Q) c.2033G>A

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
ado-trastuzumab emtansine	✖	✖	✖	○	✖
afatinib	✖	✖	✖	✖	● (II)
lapatinib	✖	✖	✖	✖	● (II)
neratinib + trastuzumab	✖	✖	✖	✖	● (II)
pertuzumab + trastuzumab	✖	✖	✖	✖	● (II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
TAS0728	✖	✖	✖	✖	● (I/II)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✖	✖	✖	✖	● (I)
everolimus + trastuzumab + letrozole	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
pyrotinib	✖	✖	✖	✖	● (I)
varlitinib + chemotherapy	✖	✖	✖	✖	● (I)

PIK3CA p.(G1049S) c.3145G>A

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
MEK inhibitor + PIK3/mTOR inhibitor, PIK3/mTOR inhibitor	✖	✖	✖	✖	● (II/III)
capivasertib + olaparib	✖	✖	✖	✖	● (II)
copanlisib	✖	✖	✖	✖	● (II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

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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

PIK3CA p.(G1049S) c.3145G>A (continued)

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
everolimus	✖	✖	✖	✖	● (II)
sirolimus	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
CB-839 + chemotherapy	✖	✖	✖	✖	● (I/II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
GDC-0077	✖	✖	✖	✖	● (I)
gedatolisib + palbociclib	✖	✖	✖	✖	● (I)
LY-3023414 + prexasertib	✖	✖	✖	✖	● (I)
palbociclib + pictilisib, palbociclib + taselisib	✖	✖	✖	✖	● (I)

ERBB3 p.(V104M) c.310G>A

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
afatinib	✖	✖	✖	✖	● (II)
TAS0728	✖	✖	✖	✖	● (I/II)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

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Relevant Therapy Details

Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

EMA information is current as of 2018-10-01. 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:** 2018-08-31 **Variant class:** BRAF V600E mutation

Reference:

https://www.ema.europa.eu/documents/product-information/cotellic-epar-product-information_en.pdf

○ dabrafenib, dabrafenib + trametinib

Cancer type: Melanoma, Non-Small Cell Lung Cancer **Label as of:** 2018-09-11 **Variant class:** BRAF V600E mutation

Reference:

https://www.ema.europa.eu/documents/product-information/tafinlar-epar-product-information_en.pdf

○ trametinib, dabrafenib + trametinib

Cancer type: Melanoma, Non-Small Cell Lung Cancer **Label as of:** 2018-09-07 **Variant class:** BRAF V600E mutation

Reference:

https://www.ema.europa.eu/documents/product-information/mekinist-epar-product-information_en.pdf

○ vemurafenib

Cancer type: Melanoma **Label as of:** 2018-08-23 **Variant class:** BRAF V600 mutation

Reference:

https://www.ema.europa.eu/documents/product-information/zelboraf-epar-product-information_en.pdf

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Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

FDA information is current as of 2018-10-01. For the most up-to-date information, search www.fda.gov.

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

○ binimetinib + encorafenib

Cancer type: Melanoma **Label as of:** 2018-06-27 **Variant class:** BRAF V600E mutation

Indications and usage:
MEKTOVI® is a kinase inhibitor indicated, in combination with encorafenib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210498lbl.pdf

○ binimetinib + encorafenib

Cancer type: Melanoma **Label as of:** 2018-06-27 **Variant class:** BRAF V600E mutation

Indications and usage:

BRAFTOVI™ is a kinase inhibitor indicated, in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210496lbl.pdf

○ cobimetinib + vemurafenib

Cancer type: Melanoma **Label as of:** 2018-01-26 **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.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/206192s002lbl.pdf

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

dabrafenib, dabrafenib + trametinib

Cancer type: Melanoma, Non-Small Cell Lung Cancer, Thyroid Cancer **Label as of:** 2018-05-04 **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.
- the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
- the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
- the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options.

Limitations of Use: TAFINLAR® is not indicated for treatment of patients with wild-type BRAF melanoma, wild-type BRAF NSCLC, or wild-type BRAF ATC.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/202806s010lbl.pdf

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

trametinib, dabrafenib + trametinib

Cancer type: Melanoma, Non-Small Cell Lung Cancer, Thyroid Cancer **Label as of:** 2018-05-04 **Variant class:** BRAF V600E mutation

Indications and usage:

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

MEKINIST® is indicated, 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.
- the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.
- the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
- the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options

Limitations of Use: MEKINIST® is not indicated for treatment of patients with melanoma who have progressed on prior BRAF-inhibitor therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/204114Orig1s009lbl.pdf

vemurafenib

Cancer type: Melanoma **Label as of:** 2017-11-06 **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.
- ZELBORAF® is indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation.

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/202429s016lbl.pdf

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

nivolumab

Cancer type: Melanoma **Label as of:** 2018-08-16 **Variant class:** BRAF V600 mutation

Indications and usage:

OPDIVO® is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of:

- patients with BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent.
- patients with BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent.[a]
- patients with unresectable or metastatic melanoma, in combination with ipilimumab.[a]
- patients with melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting.
- patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO®.
- patients with metastatic small cell lung cancer with progression after platinum-based chemotherapy and at least one other line of therapy.[b]
- patients with advanced renal cell carcinoma who have received prior antiangiogenic therapy.
- patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with ipilimumab.
- adult patients with classical Hodgkin lymphoma that has relapsed or progressed after[b]:
  - autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
  - 3 or more lines of systemic therapy that includes autologous HSCT.
- patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy.
- patients with locally advanced or metastatic urothelial carcinoma who[b]:
  - have disease progression during or following platinum-containing chemotherapy
  - have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as a single agent or in combination with ipilimumab.[b]
- patients with hepatocellular carcinoma who have been previously treated with sorafenib.[b]

[a]This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

[b]This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125554s067lbl.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 | Not recommended | Resistance

ESMO information is current as of 2018-08-16. For the most up-to-date information, search www.esmo.org.

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

BRAF inhibitor + MEK inhibitor

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Stage IV Metastatic Melanoma; BRAF-V600 mutant (First and second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Cutaneous Melanoma [Ann Oncol (2015) 26 (suppl 5): v126-v132. (eUpdate: 19 September 2016; 19 September 2016)]

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Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

NCCN information is current as of 2018-08-16. 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

● cetuximab + vemurafenib + irinotecan

Cancer type: Colon Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Unresectable Metachronus Metastatic Colon Cancer; Previous adjuvant FOLFOX/CAPEOX within past 12 months (Primary therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; If neither cetuximab or panitumumab previously given (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 3.2018]

● cetuximab + vemurafenib + irinotecan

Cancer type: Rectal Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Unresectable Metachronous Metastatic Rectal Cancer; Previous adjuvant FOLFOX/CAPEOX within past 12 months (Primary therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; If neither cetuximab or panitumumab previously given (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 3.2018]

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

● panitumumab + vemurafenib + irinotecan

Cancer type: Colon Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable Metachronus Metastatic Colon Cancer; Previous adjuvant FOLFOX/CAPEOX within past 12 months (Primary therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; If neither cetuximab or panitumumab previously given (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 3.2018]

● panitumumab + vemurafenib + irinotecan

Cancer type: Rectal Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable Metachronous Metastatic Rectal Cancer; Previous adjuvant FOLFOX/CAPEOX within past 12 months (Primary therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; If neither cetuximab or panitumumab previously given (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 3.2018]

○ dabrafenib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; If dabrafenib + trametinib is not tolerated (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line systemic therapy if dabrafenib + trametinib is not tolerated (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 6.2018]

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

dabrafenib + trametinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line systemic therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 6.2018]

dabrafenib + trametinib

Cancer type: Thyroid Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic Anaplastic Carcinoma; Stage IVC; Aggressive therapy (Systemic therapy)

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 1.2018]

vemurafenib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** BRAF V600E mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; If dabrafenib + trametinib is not tolerated (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line systemic therapy if dabrafenib + trametinib is not tolerated (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 6.2018]

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

binimetinib + encorafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Metastatic or Unresectable Melanoma (First-line therapy) (Preferred if clinically needed for early response)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

cobimetinib + vemurafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Metastatic or Unresectable Melanoma (First-line therapy) (Preferred if clinically needed for early response)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

dabrafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Metastatic or Unresectable Melanoma; If BRAF/MEK inhibitor combination therapy is contraindicated, BRAF-inhibitor monotherapy with dabrafenib or vemurafenib are recommended options, especially when checkpoint immunotherapy is not appropriate (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

dabrafenib + trametinib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Metastatic or Unresectable Melanoma (First-line therapy) (Preferred if clinically needed for early response)
- Melanoma; Stage III or Nodal recurrence (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

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

vemurafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Metastatic or Unresectable Melanoma; If BRAF/MEK inhibitor combination therapy is contraindicated, BRAF-inhibitor monotherapy with dabrafenib or vemurafenib are recommended options, especially when checkpoint immunotherapy is not appropriate (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

binimetinib + encorafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic or Unresectable Melanoma; Progression or maximum clinical benefit from BRAF targeted therapy and if not used in first-line therapy or of same drug class (Second-line or subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

cobimetinib + vemurafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic or Unresectable Melanoma; Progression or maximum clinical benefit from BRAF targeted therapy and if not used in first-line therapy or of same drug class (Second-line or subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

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

dabrafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or Unresectable Melanoma; If BRAF/MEK inhibitor combination therapy is contraindicated, BRAF-inhibitor monotherapy with dabrafenib or vemurafenib are recommended options, especially when checkpoint immunotherapy is not appropriate (Second-line or subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

dabrafenib + trametinib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Melanoma; Stage III satellite and/or in-transit recurrence post primary treatment (Second-line, adjuvant, or subsequent therapy)
- Metastatic or Unresectable Melanoma; Progression or maximum clinical benefit from BRAF targeted therapy and if not used in first-line therapy or of same drug class (Second-line or subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

vemurafenib

Cancer type: Melanoma **Variant class:** BRAF V600 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic or Unresectable Melanoma; If BRAF/MEK inhibitor combination therapy is contraindicated, BRAF-inhibitor monotherapy with dabrafenib or vemurafenib are recommended options, especially when checkpoint immunotherapy is not appropriate (Second-line or subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

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

dabrafenib

Cancer type: Thyroid Cancer **Variant class:** BRAF mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Locally Recurrent, Advanced, and/or Metastatic Papillary Carcinoma, Follicular Carcinoma, Hurthle Cell Carcinoma; Not amenable to RAI therapy; Iodine-refractory; Progressive and/or symptomatic disease if clinical trials or other systemic therapies are not available or appropriate (Not specified)

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 1.2018]

vemurafenib

Cancer type: Thyroid Cancer **Variant class:** BRAF mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Locally Recurrent, Advanced, and/or Metastatic Papillary Carcinoma, Follicular Carcinoma, Hurthle Cell Carcinoma; Not amenable to RAI therapy; Iodine-refractory; Progressive and/or symptomatic disease if clinical trials or other systemic therapies are not available or appropriate (Not specified)

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 1.2018]

cetuximab

Cancer type: Colon Cancer **Variant class:** BRAF V600E mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor."

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 3.2018]

cetuximab

Cancer type: Rectal Cancer **Variant class:** BRAF V600E mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor."

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 3.2018]

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

panitumumab

Cancer type: Colon Cancer **Variant class:** BRAF V600E mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor."

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 3.2018]

panitumumab

Cancer type: Rectal Cancer **Variant class:** BRAF V600E mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor."

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 3.2018]

EGFR tyrosine kinase inhibitor

Cancer type: Non-Small Cell Lung Cancer **Variant class:** BRAF V600E mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Sensitizing EGFR TKI therapy is not effective in patients with KRAS mutations, BRAF V600E mutations, ALK gene rearrangements, or ROS1 rearrangements."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 6.2018]

trametinib

Cancer type: Melanoma **Variant class:** BRAF V600E mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Although trametinib is FDA approved for single-agent use to treat patients with unresectable or metastatic melanoma with BRAF V600E mutation, trametinib monotherapy is no longer an NCCN recommended treatment option due to relatively poor efficacy compared with BRAF inhibitor monotherapy and BRAF/MEK inhibitor combination therapy"

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2018]

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ERBB2 p.(R678Q) c.2033G>A

ado-trastuzumab emtansine

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Emerging targeted agents

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 6.2018]

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Current Clinical Trials Information

Clinical Trials information is current as of 2018-09-04. 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

NCT02928224

A Multicenter, Randomized, Open-label, 3-Arm Phase III Study of Encorafenib + Cetuximab Plus or Minus Binimetinib vs. Irinotecan/Cetuximab or Infusional 5-Fluorouracil (5-FU)/Folinic Acid (FA) /Irinotecan (FOLFIRI)/Cetuximab with a Safety Lead-in of Encorafenib + Binimetinib + Cetuximab in Patients with BRAF V600E mutant Metastatic Colorectal Cancer Binimetinib, Encorafenib And Cetuximab Combined to treat BRAF-mutant ColoRectal Cancer (BEACON CRC)

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Other identifiers: 16-1627, 1606017995, 16214, 17-124, 2016-0768, 226949 PAREXEL, 3C-16-5, Array 818-302, ARRAY-818-302, BEACON, BEACON CRC, COH Protocol Number:16214, CT489, EUCTR2015-005805-35-HU, EudraCT Number: 2015-005805-35, F16188, IRAS ID: 208339, J16157, NCI-2016-01543, VICCGI1665

Population segments: Second line, Stage IV, Third line

Phase: III

Therapies: binimetinib + cetuximab + encorafenib, cetuximab + encorafenib

Locations: Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, Czech Republic, Denmark, France, Germany, Hungary, Israel, Italy, Japan, Mexico, Netherlands, Norway, Poland, Republic of Korea, Russian Federation, Spain, Taiwan, Turkey, Ukraine, United Kingdom

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NCT02928224

A Multicenter, Randomized, Open-label, 3-Arm Phase III Study of Encorafenib + Cetuximab Plus or Minus Binimetinib vs. Irinotecan/Cetuximab or Infusional 5-Fluorouracil (5-FU)/Folinic Acid (FA) /Irinotecan (FOLFIRI)/Cetuximab with a Safety Lead-in of Encorafenib + Binimetinib + Cetuximab in Patients with BRAF V600E mutant Metastatic Colorectal Cancer Binimetinib, Encorafenib And Cetuximab Combined to treat BRAF-mutant ColoRectal Cancer (BEACON CRC)

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Other identifiers: 16-1627, 1606017995, 16214, 17-124, 2016-0768, 226949 PAREXEL, 3C-16-5, Array 818-302, ARRAY-818-302, BEACON, BEACON CRC, COH Protocol Number:16214, CT489, EUCTR2015-005805-35-HU, EudraCT Number: 2015-005805-35, F16188, IRAS ID: 208339, J16157, NCI-2016-01543, VICCGI1665

Population segments: Second line, Stage IV, Third line

Other inclusion criteria: KRAS wild type, NRAS wild type

Phase: III

Therapy: cetuximab + chemotherapy

Locations: Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, Czech Republic, Denmark, France, Germany, Hungary, Israel, Italy, Japan, Mexico, Netherlands, Norway, Poland, Republic of Korea, Russian Federation, Spain, Taiwan, Turkey, Ukraine, United Kingdom

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

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

Cancer type: Colorectal Cancer

Variant class: BRAF mutation

Other identifiers: 14893, CR13, CRUK/11/054, EudraCT Number: 2012-005111-12, FOCUS-4, FOCUS4, IRAS ID 119459, ISRCTN90061546, MREC N° 13/SC/0111, UKCRN ID: 14893

Population segments: First line, Stage III, Stage IV

Phase: II/III

Therapies: BRAF inhibitor + MEK inhibitor + panitumumab, BRAF inhibitor + panitumumab

Location: United Kingdom

No NCT ID - see other identifier(s)
Randomised Study To Investigate FOLFOXIRI Plus Cetuximab Or FOLFOXIRI Plus Bevacizumab As First-Line Treatment Of BRAF-Mutated Metastatic Colorectal Cancer (FIRE-4.5)

Cancer type: Colorectal Cancer

Variant class: BRAF V600E mutation

Other identifiers: AIO-KRK-0116, EudraCT Number: 2015-004849-11, FIRE 4.5

Population segments: First line, Stage IV

Phase: II

Therapies: bevacizumab + chemotherapy, cetuximab + chemotherapy

Location: Germany

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

Cancer type: Colorectal Cancer

Variant class: BRAF mutation

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

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, Metastatic, Progesterone receptor positive, Second line, Stage III, Stage IV, Third line, Triple receptor negative

Other inclusion criteria: RB1 positive

Phase: II

Therapy: palbociclib

Location: United States

US State: PA

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

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

NCT02013089
A Pilot Study of Genomic Sequencing Guided Individualized Therapy in Gastrointestinal Cancers

Cancer type: Colorectal Cancer

Variant class: RAF aberration

Other identifiers: GIHSYSU04, GITIC

Population segments: Second line, Stage IV

Phase: II

Therapies: sorafenib, sunitinib

Location: China

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

Cancer type: Colorectal Cancer

Variant class: BRAF aberration

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

Population segments: Adenocarcinoma, EGFR, FGFR, HER2 negative, KRAS, Large Cell, Second line, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Location: United Kingdom

NCT02906059
A Phase Ib Study Combining Irinotecan With AZD1775, a Selective Wee 1 Inhibitor, in RAS (KRAS or NRAS) or BRAF Mutated Metastatic Colorectal Cancer Patients Who Have Progressed on First Line Therapy

Cancer type: Colorectal Cancer

Variant class: BRAF V600 mutation

Other identifiers: NCI-2016-01443, S14-01168

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

Phase: I

Therapy: adavosertib + chemotherapy

Location: United States

US State: NY

US Contact: Dr. Deirdre Cohen [212-731-5656; Deirdre.Cohen@nyumc.org]

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

NCT01351103
A Phase I, Open-label, Dose Escalation Study of Oral LGK974 in Patients With Malignancies Dependent on Wnt Ligands

Cancer type: Colorectal Cancer

Variant class: BRAF mutation

Other identifiers: 000495-33, 2011-0686, 2011-135, CLGK974X2101, EUDRACT Number: 2011-000495-33, J12121, NCI-2011-03693, NL37140.078.11, UMCC 2014.077

Population segments: HER2 negative, Second line, Stage II, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapy: LGK-974

Locations: Netherlands, Spain, United States

US States: MA, MD, MI, TX

US Contact: Novartis Pharmaceuticals [888-669-6682; Novartis.email@novartis.com]

NCT02729298
A Phase Ia / Ib, First-in-human, Open-label, Dose-escalation, Safety, Pharmacokinetic, and Pharmacodynamic Study of Oral TP-0903 Administered Daily for 21 Days to Patients With Advanced Solid Tumors

Cancer type: Colorectal Cancer

Variant class: BRAF mutation

Other identifiers: NCI-2016-01912, TP-0903-101

Population segments: EGFR, Second line, Stage III, Stage IV, Third line

Phase: I

Therapy: TP-0903

Location: United States

US States: AZ, TX

US Contact: Holly Beever [210-365-9014; hbeever@toleropharma.com]

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600E mutation

Other identifiers: NCI-2017-00510, Pro00014171, TAPUR

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, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: cobimetinib + vemurafenib

Location: United States

US States: AL, AZ, CA, FL, GA, IL, MI, NC, ND, NE, OK, OR, PA, SD, TX, UT, VA, WA

US Contact: Pam Mangat [pam.mangat@asco.org]

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

NCT02091141

My Pathway: An Open-Label Phase IIa Study Evaluating Trastuzumab/ Pertuzumab, Erlotinib, Vemurafenib/ Cobimetinib, Vismodegib, Alectinib, and Atezolizumab 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 V600 mutation

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

Population segments: BRCA, EGFR, Fourth line or greater, HER2 positive, Second line, Stage III, Stage IV, Third line

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, MO, NC, ND, NY, OH, OK, OR, PA, SD, TN, TX, VA, WA, WI

US Contact: Reference Study ID Number: ML28897 [888-662-6728; global-roche-genentech-trials@gene.com]

NCT03297606

Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: BRAF V600 mutation

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: cobimetinib + vemurafenib

Location: Canada

NCT02925234

A Dutch National Study on behalf of the Center for Personalized Cancer Treatment (CPCT) to Facilitate Patient Access to Commercially Available, Targeted Anti-cancer Drugs to determine the Potential Efficacy in Treatment of Advanced Cancers with a Known Molecular Profile

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifiers: DRUP, EudraCT Number: 2015-004398-33, M15DRU, NL54757.031.16

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), First line, Follicular lymphoma (FL), Indolent, Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapies: cobimetinib + vemurafenib, dabrafenib

Location: Netherlands

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

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

NCT03520075
A Phase I/II Study of the Safety, Pharmacokinetics, and Activity of ASTX029 in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifier: ASTX029-01

Population segments: Second line, Stage III, Stage IV

Phase: I/II

Therapy: ASTX029

Location: United States

US States: CT, TX, VA

US Contact: Richard J. Morishige [925-560-2882; Richard.Morishige@astx.com]

NCT02639546
A Phase I/II, Multicenter, Open-Label, Dose-Escalation Study of The Safety And Pharmacokinetics of Cobimetinib In Pediatric And Young Adult Patients With Previously Treated Solid Tumors - iMATRIX Cobi

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 15-524, 16-041, 2015-0929, CTRC#15-0005, DRKS00010690, EudraCT Number: 2014-004685-25, GO29665, iMATRIX Cobi, iMATRIXcobi, IRAS ID: 174562, NCI-2016-00541, NL52503.078.16

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

Phase: I/II

Therapy: cobimetinib

Locations: Canada, France, Germany, Israel, Italy, Spain, United Kingdom, United States

US States: AR, AZ, CA, FL, MA, NY, PA, TX

US Contact: Reference Study ID Number: GO29665 [888-662-6728; global-roche-genentech-trials@gene.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

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapy: dabrafenib + onalespib + trametinib

Location: United States

US State: MA

US Contact: Ryan J. Sullivan [617-724-4000; rsullivan7@partners.org]

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

NCT03182673
A Phase I, Open Label, Dose Escalation Study to Evaluate the Safety, Tolerability and Pharmacokinetics of SHR7390 Combined With SHR-1210 in Patients With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifiers: CTR20170611, SHR7390-SHR-1210-I-102-AST

Population segments: First line, Stage III, Stage IV

Phase: I

Therapy: camrelizumab + SHR7390

Location: China

NCT03118817
A Single-arm, Open-label, Multi-center, Phase I Expansion Study Evaluating the Efficacy and Safety of HM95573 Monotherapy in Patients With BRAF, KRAS or NRAS Mutation-positive Solid Cancers

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifier: HM-RAFI-102

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

Phase: I

Therapy: HM-95573

Location: Republic of Korea

NCT03051035
A Phase I First-in-Human Study of KO-947 in Locally Advanced Unresectable or Metastatic, Relapsed and/or Refractory Non-Hematological Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: BRAF mutation

Other identifiers: 16-1101, 17-150, KO-ERK-001

Population segments: KRAS, Second line, Stage III, Stage IV

Phase: I

Therapy: KO-947

Location: United States

US State: PA

US Contact: Kamn Lacroix [617-251-6535; medicalaffairs@kuraoncology.com]

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

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

NCT03284502
A Phase Ib, Open-label, Multicenter, Dose Escalation Study of the Safety, Tolerability, and Pharmacokinetics of Cobimetinib and HM95573 in Patients With Locally Advanced or Metastatic Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: RAF mutation

Other identifier: HM-RAFI-103

Population segments: First line, Second line, Stage III, Stage IV

Phase: I

Therapy: cobimetinib + HM-95573

Location: Republic of Korea

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 Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 16419, EudraCT Number: 2016-001907-21, I8S-MC-JUAB, JUAB, NCI-2017-00039

Population segments: Second line, Stage III, Stage IV

Phase: I

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

Locations: Australia, France, United States

US States: FL, MA, TN, TX

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

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, JapicCTI-163207, NCI-2016-00539, NL57739.031.16

Population segments: First line, KRAS, Second line, Stage III, Stage IV

Phase: I

Therapy: LTT-462

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

US States: NY, TX

US Contact: Novartis Pharmaceuticals [888-669-6682; Novartis.email@novartis.com]

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

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

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: 16-225, 2015-0913, CLXH254X2101, EudraCT Number: 2015-003421-33, NCI-2015-02280, NL55506.078.15, Nov RAFi (CLXH254X2101), REec-2016-2132, SNCTP000002708

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapies: LXH254 , LXH254 + spartalizumab

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

US States: NY, TX

US Contact: Novartis Pharmaceuticals [888-669-6682; Novartis.email@novartis.com]

ERBB2 p.(R678Q) c.2033G>A

NCT01953926

An Open-Label, Phase II Study Of Neratinib In Patients With Solid Tumors With Somatic Human Epidermal Growth Factor Receptor (EGFR, HER2, HER3) Mutations Or EGFR Gene Amplification

Cancer type: Colorectal Cancer

Variant class: ERBB2 mutation

Other identifiers: 13-140, 13-615, 2013-0904, CTA733, EudraCT Number: 2013-002872-42, IRAS ID: 171670, NCI-2014-00495, PUMA-NER-5201, REec-2014-0843, SUMMIT, SUMMIT basket

Population segments: EGFR, Estrogen receptor positive, First line, Fourth line or greater, HER2 negative, HER2 positive, Progesterone receptor positive, Second line, Stage IV, Third line, Triple receptor negative

Other inclusion criteria: Hormone receptor negative

Phase: II

Therapy: neratinib + trastuzumab

Locations: Australia, Belgium, Denmark, France, Israel, Italy, Republic of Korea, Spain, United States

US States: CA, FL, IL, LA, MA, MO, NY, PA, TN, TX, WI

US Contact: Puma Biotechnology Clinical Operations Senior Director [424-248-6500; ClinicalTrials@pumabiotechnology.com]

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ERBB2 p.(R678Q) c.2033G>A (continued)

NCT03457896
A Phase II Study Evaluating the Combination of Neratinib Plus Trastuzumab or Neratinib Plus Cetuximab in Patients With "Quadruple Wild-Type" (KRAS/NRAS/BRAF/PIK3CA Wild-Type) Metastatic Colorectal Cancer Based on HER2 Status: Amplified, Non-Amplified (Wild-Type) or Mutated

Cancer type: Colorectal Cancer

Variant class: ERBB2 mutation

Other identifier: NSABP FC-11

Population segments: Second line, Stage IV

Other inclusion criteria: BRAF wild type, NRAS wild type, PIK3CA wild type, RAS wild type

Phase: II

Therapy: neratinib + trastuzumab

Location: United States

US State: IL

US Contact: Diana Gosik [412-339-5333; diana.gosik@nsabp.org]

NCT03410927
A Phase I/II, Open Label, Multicenter Study to Investigate the Safety, Pharmacokinetics, and Efficacy of TAS0728, an Oral Covalent Binding Inhibitor of HER2, in Subjects With Advanced Solid Tumors With HER2 or HER3 Abnormalities

Cancer type: Colorectal Cancer

Variant class: ERBB2 mutation

Other identifiers: 18116, 2017-0994, EudraCT Number: 2017-004415-39, NCI-2018-00211, REFMAL 555, TO-TAS0728-101

Population segments: Adenocarcinoma, Fourth line or greater, HER2 positive, Large Cell, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: TAS0728

Locations: United Kingdom, United States

US States: NY, TN, TX

US Contact: Dr. Mark Kirshbaum [609-750-5300; MKirschbaum@taihooncology.com]

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

Cancer type: Colorectal Cancer

Variant class: ERBB2 aberration

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

Population segments: Adenocarcinoma, EGFR, FGFR, HER2 negative, KRAS, Large Cell, Second line, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Location: United Kingdom

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

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ERBB2 p.(R678Q) c.2033G>A (continued)

No NCT ID - see other identifier(s)
Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment

Cancer type: Colorectal Cancer

Variant class: ERBB2 mutation

Other identifiers: 5209-CPK-1002, CTR20150792

Population segments: EGFR, HER2 positive, Second line or greater/Refractory/ Relapsed, Stage III, Stage IV

Phase: I

Therapy: pirotinib

Location: China

No NCT ID - see other identifier(s)
Precision 2: an open explorative phase II, open label study of afatinib in the treatment of advanced cancer carrying an EGFR, a HER2 or a HER3 mutation.

Cancer type: Unspecified Cancer

Variant class: ERBB2 mutation

Other identifiers: 1200.264, EudraCT Number: 2016-003411-34, Precision 2

Population segments: HER2 positive, Line of therapy N/A, Stage III, Stage IV

Phase: II

Therapy: afatinib

Location: Belgium

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

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

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

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV

Phase: II

Therapy: lapatinib

Location: France

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ERBB2 p.(R678Q) c.2033G>A (continued)

NCT02925234
A Dutch National Study on behalf of the Center for Personalized Cancer Treatment (CPCT) to Facilitate Patient Access to Commercially Available, Targeted Anti-cancer Drugs to determine the Potential Efficacy in Treatment of Advanced Cancers with a Known Molecular Profile

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

Other identifiers: DRUP, EudraCT Number: 2015-004398-33, M15DRU, NL54757.031.16

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), First line, Follicular lymphoma (FL), Indolent, Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: pertuzumab + trastuzumab

Location: Netherlands

NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 aberration

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: pertuzumab + trastuzumab

Location: Canada

NCT03065387
Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification or HER3/4 Mutation

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

Other identifiers: 2016-0430, NCI-2018-01218

Population segments: HER2 negative, HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapies: everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul [713-563-1930; spihapau@mdanderson.org]

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ERBB2 p.(R678Q) c.2033G>A (continued)

NCT02152943

Combination Treatment With Everolimus, Letrozole and Trastuzumab in Hormone Receptor and HER2/Neu-positive Patients With Advanced Metastatic Breast Cancer and Other Solid Tumors: Evaluating Synergy and Overcoming Resistance

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

Other identifiers: 2014-0119, NCI-2014-01615

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 positive, Maintenance/Consolidation, Progesterone receptor positive, Second line, Stage III, Stage IV, Third line

Other inclusion criteria: ER positive, PR positive

Phase: I

Therapy: everolimus + trastuzumab + letrozole

Location: United States

US State: TX

US Contact: Dr. Filip Janku [713-563-1930]

NCT02500199

A Two-part Phase I, Open Label, Dose Escalation Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Pyrotinib in Patients With HER2-positive Solid Tumors Whose Disease Progressed on Prior HER2 Targeted Therapy

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

Other identifiers: NCI-2017-00491, SHRUS 1001

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

Phase: I

Therapy: pyrotinib

Location: United States

US States: FL, MA, MI, MO, NY, TN

US Contact: Dr. Ewa Matczak [609-423-2155 ext 215; ewa.matczak@hengruitherapeutics.com]

NCT02435927

Phase I Study to Evaluate the Safety and Tolerability of ASLAN001 in Combination with Oxaliplatin and Capecitabine or Oxaliplatin and 5-FU with Leucovorin

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 aberration

Other identifier: ASLAN001-002SG

Population segments: Second line, Stage IV

Exclusion criteria variant class: EGFR T790M mutation

Phase: I

Therapy: varlitinib + chemotherapy

Location: Singapore

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PIK3CA p.(G1049S) c.3145G>A

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

Cancer type: Colorectal Cancer

Variant class: PIK3CA mutation

Other identifiers: 14893, CR13, CRUK/11/054, EudraCT Number: 2012-005111-12, FOCUS-4, FOCUS4, IRAS ID 119459, ISRCTN90061546, MREC N° 13/SC/0111, UKCRN ID: 14893

Population segments: First line, Stage III, Stage IV

Phase: II/III

Therapies: MEK inhibitor + PIK3/mTOR inhibitor, PIK3/mTOR inhibitor

Location: United Kingdom

NCT02861300
Phase I/II Study of CB-839 and Capecitabine in Patients With Advanced Solid Tumors and Fluoropyrimidine Resistant PIK3CA Mutant Colorectal Cancer

Cancer type: Colorectal Cancer

Variant class: PIK3CA mutation

Other identifiers: CASE1216, NCI-2016-01647

Population segments: Second line, Stage III, Stage IV

Phase: I/II

Therapy: CB-839 + chemotherapy

Location: United States

US State: OH

US Contact: Dr. David Bajor [216-286-4414; david.bajor@uhhospitals.org]

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

Cancer type: Colorectal Cancer

Variant class: PIK3CA aberration

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

Population segments: Adenocarcinoma, EGFR, FGFR, HER2 negative, KRAS, Large Cell, Second line, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Location: United Kingdom

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

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PIK3CA p.(G1049S) c.3145G>A (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

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

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV

Phase: II

Therapy: everolimus

Location: France

NCT02688881
Study to Evaluate the Safety and Efficacy of Sirolimus, in Subject With Refractory Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 2016-02-052, KCT0002997, SMC 2016-02-052-001

Population segments: (N/A), Second line

Phase: II

Therapy: sirolimus

Location: Republic of Korea

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA aberration

Other identifiers: 15-7002, CTSU/EAY131, EAY131, EAY131-A, EAY131-B, EAY131-C1, EAY131-C2, EAY131-E, EAY131-F, EAY131-G, EAY131-H, EAY131-I, EAY131-J, EAY131-L, EAY131-M, EAY131-MATCH, EAY131-N, EAY131-P, EAY131-Q, EAY131-R, EAY131-S1, EAY131-S2, EAY131-T, EAY131-U, EAY131-V, EAY131-W, EAY131-X, EAY131-Y, EAY131-Z1A, EAY131-Z1B, EAY131-Z1C, EAY131-Z1D, EAY131-Z1E, EAY131-Z1F, EAY131-Z1G, EAY131-Z1H, EAY131-Z1I, EAY131-Z1J, ECOGEAY131-M, MATCH, NCI-2015-00054, NCI-MATCH

Population segments: (N/A), Aggressive, Classical, Fourth line or greater, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: copanlisib

Locations: Puerto Rico, 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, VT, WA, WI, WV, WY

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

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PIK3CA p.(G1049S) c.3145G>A (continued)

NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA aberration

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: temsirolimus

Location: Canada

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD6738 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 1508016363, 16-314, NCI-2016-00922, OLAPCO, VICCMD1672

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: capivasertib + olaparib

Location: United States

US States: CT, MA, OH, TN

US Contact: Manuel Avedissian [203-737-3669; manuel.avedissian@yale.edu]

NCT03006172
A Phase I, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, and Pharmacokinetics of GDC-0077 as a Single Agent in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Solid Tumors and in Combination With Endocrine and Targeted Therapies in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Hormone-Receptor Positive Breast Cancer

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 16-1556, EudraCT Number: 2016-003022-17, GO39374, NCI-2017-00262

Population segments: Estrogen receptor positive, HER2 negative, Line of therapy N/A, Progesterone receptor positive, Stage III, Stage IV

Phase: I

Therapy: GDC-0077

Locations: Canada, France, Spain, United Kingdom, United States

US States: MA, NY, TN

US Contact: Reference Study ID Number: GO39374 [888-662-6728; global-roche-genentech-trials@gene.com]

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PIK3CA p.(G1049S) c.3145G>A (continued)

NCT03065062
Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 16-499, NCI-2017-00434

Population segments: Second line, Squamous Cell, Stage III, Stage IV

Phase: I

Therapy: gedatolisib + palbociclib

Location: United States

US State: MA

US Contact: Dr. Nicole Chau [617-632-3090]

NCT02124148
A Phase Ib Trial of LY2606368 in Combination With Chemotherapy or Targeted Agents in Advanced and/or Metastatic Tumors

Cancer type: Unspecified Cancer

Variant class: PIK3CA mutation

Other identifiers: 15295, 2014-0193, I4D-MC-JTJF, NCI-2014-01348

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapy: LY-3023414 + prexasertib

Location: United States

US States: FL, OK, TN, TX

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

NCT02389842
PIPA: A Phase Ib Study to Assess the Safety, Tolerability and Efficacy of the PI3K Inhibitors, Taselisib (GDC-0032) or Pictilisib (GDC-0941), in Combination With PAlbociclib, With the Subsequent Addition of Fulvestrant in PIK3CA-mutant Breast Cancers

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: CCR4191, EudraCT Number: 2014-002658-37, IRAS ID:159997, PIPA

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, KRAS, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapies: palbociclib + pictilisib, palbociclib + taselisib

Location: United Kingdom

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ERBB3 p.(V104M) c.310G>A

No NCT ID - see other identifier(s)
Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment

Cancer type: Colorectal Cancer

Variant class: ERBB3 mutation

Other identifiers: 5209-CPK-1002, CTR20150792

Population segments: EGFR, HER2 positive, Second line or greater/Refractory/ Relapsed, Stage III, Stage IV

Phase: I

Therapy: pirotinib

Location: China

No NCT ID - see other identifier(s)
Precision 2: an open explorative phase II, open label study of afatinib in the treatment of advanced cancer carrying an EGFR, a HER2 or a HER3 mutation.

Cancer type: Unspecified Cancer

Variant class: ERBB3 mutation

Other identifiers: 1200.264, EudraCT Number: 2016-003411-34, Precision 2

Population segments: HER2 positive, Line of therapy N/A, Stage III, Stage IV

Phase: II

Therapy: afatinib

Location: Belgium

NCT03410927
A Phase I/II, Open Label, Multicenter Study to Investigate the Safety, Pharmacokinetics, and Efficacy of TAS0728, an Oral Covalent Binding Inhibitor of HER2, in Subjects With Advanced Solid Tumors With HER2 or HER3 Abnormalities

Cancer type: Unspecified Solid Tumor

Variant class: ERBB3 aberration

Other identifiers: 18116, 2017-0994, EudraCT Number: 2017-004415-39, NCI-2018-00211, REFMAL 555, TO-TAS0728-101

Population segments: Adenocarcinoma, Fourth line or greater, HER2 positive, Large Cell, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: TAS0728

Locations: United Kingdom, United States

US States: NY, TN, TX

US Contact: Dr. Mark Kirshbaum [609-750-5300; MKirschbaum@taihooncology.com]

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ERBB3 p.(V104M) c.310G>A (continued)

NCT03065387
Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification or HER3/4 Mutation

Cancer type: Unspecified Solid Tumor

Variant class: ERBB3 mutation

Other identifiers: 2016-0430, NCI-2018-01218

Population segments: HER2 negative, HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapies: everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul [713-563-1930; spihapau@mdanderson.org]

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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	5
↳ RAS/RAF/MEK/ERK mutation	0
↳ RAF mutation	1
↳ BRAF mutation status	0
↳ BRAF mutation	10
↳ BRAF activating mutation	0
↳ BRAF V600 mutation status	0
↳ BRAF V600 mutation	16
↳ BRAF V600E mutation	28
↳ RAF aberration	1
↳ BRAF aberration	1
↳ BRAF mutation status	0
↳ BRAF mutation	10
↳ BRAF activating mutation	0
↳ BRAF V600 mutation status	0
↳ BRAF V600 mutation	16
↳ BRAF V600E mutation	28
↳ RAF mutation	1
↳ BRAF mutation status	0
↳ BRAF mutation	10
↳ BRAF activating mutation	0
↳ BRAF V600 mutation status	0
↳ BRAF V600 mutation	16

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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Evidence Summary by Variant Class (continued)

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

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

Variant Class	Evidence Items
↳ BRAF V600E mutation	28

ERBB2 p.(R678Q) c.2033G>A

Variant Class	Evidence Items
ERBB aberration	0
↳ ERBB2 status	0
↳ ERBB2 aberration	3
↳ ERBB2 mutation status	0
↳ ERBB2 mutation	11
↳ ERBB2 R678Q mutation	0

PIK3CA p.(G1049S) c.3145G>A

Variant Class	Evidence Items
PI3K/AKT/MTOR pathway	1
↳ PIK3CA aberration	3
↳ PIK3CA mutation status	0
↳ PIK3CA mutation	8
↳ PIK3CA exon 20 mutation	0
↳ PIK3CA G1049 mutation	0

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Evidence Summary by Variant Class (continued)

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

ERBB3 p.(V104M) c.310G>A

Variant Class	Evidence Items
ERBB aberration	0
↳ ERBB3 aberration	1
↳ ERBB3 mutation	3

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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Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency	Transcript	Variant Effect	Gene Class	Variant Class
PIK3CA	p.(G1049S)	c.3145G>A	COSM777	31.79%	NM_006218.3	missense	Gain of Function	Hotspot
BRAF	p.(V600E)	c.1799T>A	COSM476	19.78%	NM_004333.4	missense	Gain of Function	Hotspot
ERBB3	p.(V104M)	c.310G>A	COSM172423	17.75%	NM_001982.3	missense	Gain of Function	Hotspot
ERBB2	p.(R678Q)	c.2033G>A	COSM436498	17.08%	NM_004448.3	missense	Gain of Function	Hotspot

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PD-1/PD-L1 TESTING

IMMUNOFOCUS® TEST REPORT

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ONC18			
Surname		**Requester**	
Forename		**Contact details**	
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	95%
Primary site	Colon	**Tumour %**	-
Tumour subtype	Differentiated Adenocarcinoma	**(macrodissected)**	
Tissue Type	Right Colon		

PD-L1 test report

D-L1 IHC assays are used to help identify those patients most likely to benefit from anti-PD-1/PD-L1 directed immunotherapies. Assessment involves the determination of a range of cut-off/threshold values for PD-L1 positive tumour cells and PD-L1 positive immune cells. These cut off values are identified as predictors of response to anti-PD-L1 directed therapies used in the treatment of a range of different cancer types and include pembrolizumab, atezolizumab, avelumab, nivolumab, and durvalumab. The established cut off values for tumour proportion scores (>1%, >25%, >50%) and PD-L1 positive immune cells (10%), which vary according to immunotherapy, tumour type and whether first or second line therapy is to be used.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay quantifies the proportion of tumour cells that express PD-L1 (Tumour Proportion Score) and the area occupied by tumour infiltrating PD-L1 positive immune cells.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay is a Laboratory Developed Test utilising the RUO rabbit monoclonal antibody clone E1L3N (Cell Signalling Technologies) and Leica Bond III instrumentation. The performance of the Immunofocus assay is continually assessed by involvement in recognised External Quality Assessment schemes and returns performance levels commensurate with approved the PD-L1 diagnostic assays. All Immunofocus assay testing is performed within the scope of UKAS/ISO 15189:2012 accreditation. Clone E1L3N is not licensed and approved for use in clinical testing to direct the use of PD-1/PD-L1 therapies. The PD-L1 protein expression levels in tumour cells generated by the Immunofocus PD-L1 assay should therefore be interpreted within the context of these facts.

PD-L1 Result

This MMR deficient tumour shows markedly high expression levels of PD-L1. The majority of tumour cells show strong or moderate intensity immunostaining for PD-L1 with complete patterns of surface membrane expression. The proportion of PD-L1 expressing tumour cells amounts to 85-90% of the total tumour cell population. The tumour is associated with a diffusely distributed PD-L1 expressing immune cell (IC) infiltrate. The PD-L1 expressing tumour infiltrating immune cells (ICs) cover 5-8% of the tumour area occupied by tumour cells, intratumoural and contiguous peritumoural stroma.

Summary; PD-L1 Tumour Proportion Score 85-90%; PD-L1 positive ICs 5-8% of tumour area

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