



JAX Clinical Knowledgebase (JAX-CKB) Tutorial

CKB BOOST™

<https://ckbhome.jax.org>

Getting Started

The Clinical Knowledgebase (CKB)

Powered by The Jackson Laboratory

CKB is a dynamic digital resource for interpreting complex cancer genomic profiles. Join thousands of clinicians and researchers across the globe, saving time and finding valuable information that connects cancer variants to therapies and clinical trials.

This button returns you to the home page .

This button brings you to a clickable display of the genes available in CKB BOOST™.

This button brings you to a list of associated CKB help documents

CKB BOOST™ can be searched on through gene, gene variant, drug class, drug, and tumor type. Additional advanced searches include clinical trial search and evidence search.

Basic Search

- Explore by Gene
- Explore by Variant
- Explore by DrugClass
- Explore by Drug
- Explore by Indication/Tumor Type

Advanced Search

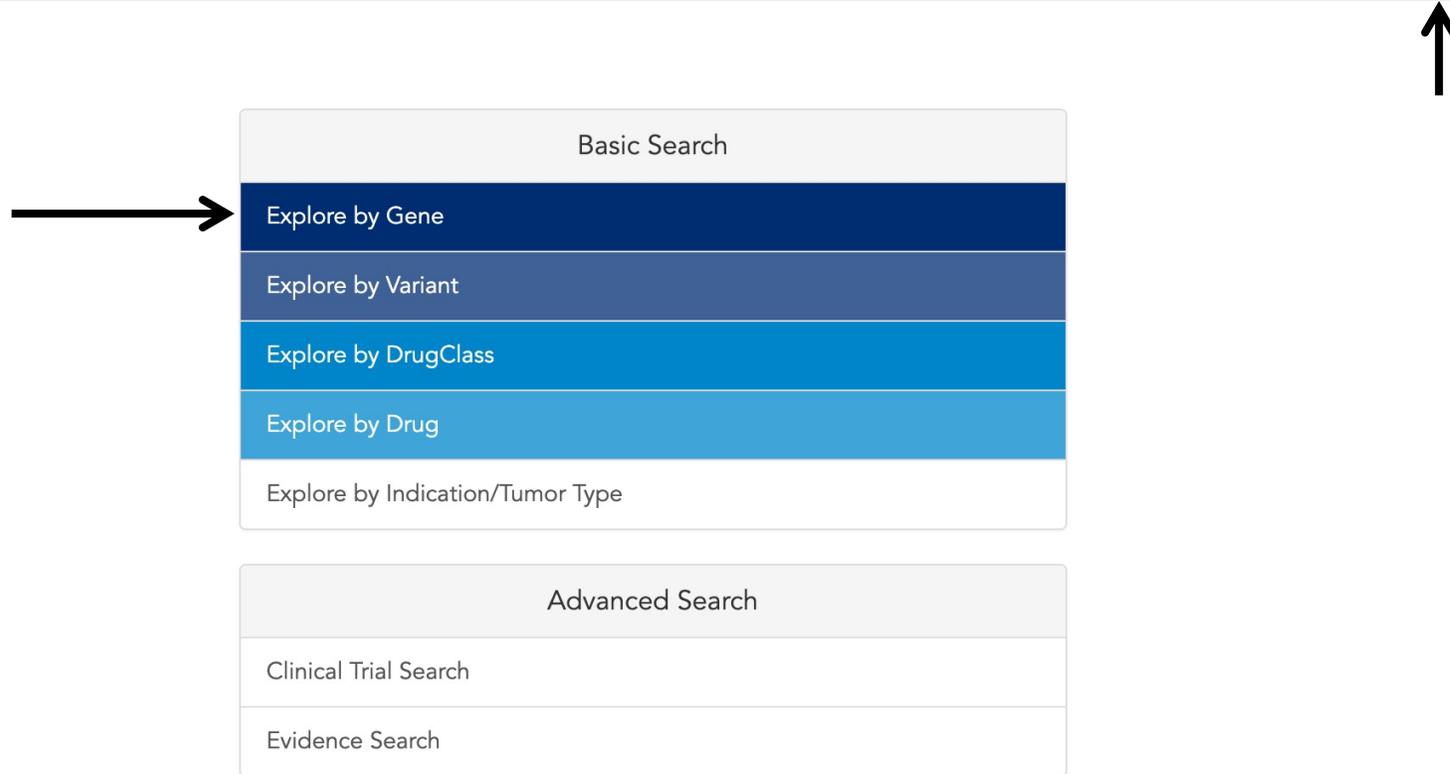
- Clinical Trial Search
- Evidence Search

Request Content ?

News

Apr 9, 2021 - We made some updates to **CKB CORE** with a focus on delivering **high level, thematic** content! To find out more, check out our new quarterly newsletter by clicking [here](#). Have questions or comments? Email us at ckbsupport@jax.org.

Explore By Gene



- Clicking on the “Explore by Gene” button will bring you to a page where you can search for content related to all the genes in CKB.
- Clicking on the “Genes” link in the toolbar will bring you to a clickable list of genes with available content.

Explore By Gene

Find by Gene

- Start typing a gene name to display gene.
- Select **one** gene and click 'Submit' to go to the next page.
- Or search for a gene via the [Gene Grid](#)

Gene Symbol

Start typing to select a gene

BR

[ABR](#) | [MDB](#)

[ACTB](#) | [BRWS1](#) | [PS1TP5BP1](#)

[BRCA1](#) | [BRCAI](#) | [BRCC1](#) | [BROVCA1](#) | [FANCS](#) | [IRIS](#) | [PNCA4](#) | [PPP1R53](#) | [PSCP](#) | [RNF53](#)

[BRAF](#) | [B-raf](#) | [B-RAF1](#) | [BRAF1](#) | [NS7](#) | [RAFB1](#)

[BRCA2](#) | [BRCC2](#) | [BROVCA2](#) | [FACD](#) | [FAD](#) | [FAD1](#) | [FANCD](#) | [FANCD1](#) | [GLM3](#) | [PNCA2](#) | [XRCC11](#)

[BRDT](#) | [BRD6](#) | [CT9](#) | [SPGF21](#)

[ZFP36L1](#) | [Berg36](#) | [BRF1](#) | [cMG1](#) | [ERF-1](#) | [ERF1](#) | [RNF162B](#) | [TIS11B](#)

[CCB4](#) | [CCCKR4](#) | [CD184](#) | [CHST13](#) | [CKB4](#) | [CMKBP4](#) | [HGCN14000](#) | [KIF5](#)

[BRAF](#) | [B-raf](#) | [B-RAF1](#) | [BRAF1](#) | [NS7](#) | [RAFB1](#)

Gene Description:

BRAF, serine/threonine-protein kinase B-raf, is a member of the Raf family of serine/threonine protein kinases, which signals through the MAP kinase pathway to regulate cell proliferation and cell growth (PMID: 24737949, PMID: 29540830). BRAF mutations and fusions have been identified in a variety of cancers, including, colorectal (PMID: 30122982), lung (PMID: 29729495), thyroid (PMID: 12970315), and melanoma (PMID: 24737949), and a number of mutations have also been demonstrated to confer drug resistance (PMID: 27478040).

Typing in the search box will trigger a drop-down list of genes. Genes in CKB are given HGNC approved names, but associated synonyms are also available for searching. **Click** on the desired gene name to select for searching. This will bring you to the “Gene Detail Page” for the selected gene.

Explore By Gene

ckb BOOST News Genes Drug Classes About Terms of Use Help

Gene Detail

Gene Symbol: BRAF
Synonyms: B-raf | B-RAF1 | BRAF1 | NS7 | RAFB1
Gene Description: BRAF, serine/threonine-protein kinase B-raf, is a member of the Raf family of serine/threonine protein kinases, which signals through the MAP kinase pathway to regulate cell proliferation and cell growth (PMID: 24737949, PMID: 29540830). BRAF mutations and fusions have been identified in a variety of cancers, including, colorectal (PMID: 30122982), lung (PMID: 29729495), thyroid (PMID: 12970315), and melanoma (PMID: 24737949), and a number of mutations have also been demonstrated to confer drug resistance (PMID: 27478040).

NCBI Gene ID	Chromosome	Map Location	Canonical Transcript	Gene Role
673	7	7q34	NM_004333	Oncogene (PMID: 30606230)

Variant Impact Variant Protein Effect

Request Content

358 Variants

- gain of function
- gain of function - predicted
- loss of function
- loss of function - predicted
- no effect
- no effect - predicted
- unknown

Explore Visually

Gene Variants 358 Category Variants 32 Molecular Profiles 724 Gene Level Evidence 1660

Filtering and Sorting

Filter rows:

Showing 1 to 358 of 358 entries

Variant	Impact	Protein Effect	Variant Description	Associated with drug Resistance
class 1	unknown	gain of function	BRAF Class 1 variants are BRAF variants that activate BRAF and downstream signaling in a dimer-independent, RAS-independent manner (PMID: 28783719, PMID: 26343582).	
class 2	unknown	gain of function	BRAF Class 2 variants are BRAF variants that activate BRAF and downstream signaling in a dimer-dependent, RAS-independent manner (PMID: 28783719, PMID: 26343582).	

Visuals for Variant Protein Effect and Variant Impact in variants of selected gene.

Link out to PubMed through PMIDs

Link out to NCBI

Text Filtering

Text Filtering and Sorting by Column

- The header of the page contains data relevant to the gene, as well as a link out to the NCBI Gene page (Entrez ID), chromosome and map location, the canonical transcript, and its role in cancer. There are also visuals for types of variant protein effects and variant impact for the selected gene.
- Below, there are 4 tabs related to different areas of content:
 - The 'Gene Variants' tab lists all annotated gene variants associated with the selected gene.
 - The 'Category Variants' tab lists all annotated category variants associated with the selected gene.
 - The 'Molecular Profiles' tab contains all molecular profiles (which contain one or more gene variants) associated with the selected gene.
 - The 'Gene Level' Evidence tab lists all annotated evidence associated with the selected gene.
- All pages also incorporate filtering and sorting capability to enable easy content searching.

Explore By Gene

Gene Variant Tab

Gene Variants 281 Category Variants 32 Molecular Profiles 383 Gene Level Evidence 1031

You can filter on any relevant text here. In this example, we've filtered on 600, which will restrict the display to variants containing "600"

Filtering and Sorting

Filter rows: 600

Showing 1 to 25 of 25 entries (filtered from 281 total entries)

Variant	Impact	Protein Effect	Variant Description	Associated with drug Resistance
L514V	missense	gain of function - predicted	BRAF L514V lies within the protein kinase domain of the Braf protein (UniProt.org). L514V is predicted to lead to a gain of Braf function as indicated by moderate increase of Mek and Erk phosphorylation in culture, enhanced dimerization when expressed in cis with BRAF V600E, and is associated with resistance to Raf inhibitors (PMID: 29880583).	Y
T529I	missense	unknown	BRAF T529I is a gatekeeper mutation that lies within the protein kinase domain of the Braf protein (PMID: 20538618). T529I has been demonstrated to confer resistance to Raf inhibitors in the context of BRAF V600E (PMID: 20538618), but has not been biochemically characterized and therefore, its effect on Braf protein function is unknown (PubMed, Dec 2020).	Y
D594_T599dup	duplication	gain of function	BRAF D594_T599dup (also referred to as T599_V600insDFGLAT) results in the insertion of six amino acids in the protein kinase domain of the Braf protein between amino acids 599 and 600 (UniProt.org). BRAF D594_T599dup results in increased colony formation and downstream Mek and Erk activation in cultured cells (PMID: 17297294).	
G596R	missense	loss of function - predicted	BRAF G596R lies within the protein kinase domain of the Braf protein, within the DFG motif (PMID: 19735675). G596R results in impaired Braf kinase activity and decreased Mek and Erk phosphorylation, including in the presence of BRAF V600E, is not transforming in culture and does not promote tumor formation in mouse models, but results in activation of Erk in the presence of CRAF (PMID: 19735675, PMID: 28783719), however, in another study demonstrates similar cell proliferation and viability levels to wild-type Braf (PMID: 29533785), and is predicted to confer a loss of function to the Braf protein.	
T599A	missense	loss of function	BRAF T599A lies within the protein kinase domain of the Braf protein (UniProt.org). T599A does not result in increased MEK or ERK phosphorylation and does not transactivate CRAF (PMID: 22506009), and demonstrates decreased transformation ability compared to wild-type Braf in cell culture (PMID: 29533785).	

Variants associated with drug resistance will have 'Y' in this column.

The **Gene Variant** tab lists gene variants for the selected gene, their impact on the protein (corresponding to variant type), their effect on the intrinsic activity of the protein, and an annotated description. Links in blue will navigate to outside content. Content can be sorted or filtered. Clicking on the blue "gene variant" buttons will bring you to the Gene Variant Detail Page.

Explore By Gene

Gene Variants 281

Category Variants 32

Molecular Profiles 383

Gene Level Evidence 1031

Category Variants Tab

Filtering and Sorting ⓘ

Filter rows:

Showing 1 to 32 of 32 entries

Variant	Impact	Protein Effect	Variant Description	Associated with drug Resistance
class 1	unknown	gain of function	BRAF Class 1 variants are BRAF variants that activate BRAF and downstream signaling in a dimer-independent, RAS-independent manner (PMID: 28783719, PMID: 26343582).	
class 2	unknown	gain of function	BRAF Class 2 variants are BRAF variants that activate BRAF and downstream signaling in a dimer-dependent, RAS-independent manner (PMID: 28783719, PMID: 26343582).	
class 3	unknown	loss of function	BRAF Class 3 variants are BRAF variants that demonstrate low or no BRAF kinase activity, but activate downstream signaling through CRAF activation, in a dimer-dependent, RAS-dependent manner (PMID: 28783719).	
T241X	missense	unknown	BRAF T241X indicates any Braf missense mutation that results in replacement of the threonine (T) at amino acid 241 by a different amino acid.	
Q257X	missense	unknown	BRAF Q257X indicates any Braf missense mutation that results in replacement of the glutamine (Q) at amino acid 257 by a different amino acid.	
P367X	missense	unknown	BRAF P367X indicates any Braf missense mutation that results in replacement of the proline (P) at amino acid 367 by a different amino acid.	
P403fs	frameshift	loss of function - predicted	BRAF P403fs results in a change in the amino acid sequence of the Braf protein beginning at aa 403 of 766, likely resulting in premature truncation of the functional protein (UniProt.org). Due to the loss of the protein kinase domain (UniProt.org), P403fs is predicted to lead to a loss of Braf protein function.	
R462X	missense	unknown	BRAF R462X indicates any Braf missense mutation that results in replacement of the arginine (R) at amino acid 462 by a different amino acid.	

The **Category Variants** tab displays all category variants associated with the selected gene. Category variants can be classified as functional and/or positional. Functional category variants include act mut and inact mut. Examples of positional variants include exon, codon, and short form frameshifts. Category variants can include member variants and can be used to identify relevant efficacy evidence. For more information about category variants, click [here](#).

Explore By Gene

Gene Variants 281

Category Variants 32

Molecular Profiles 383

Gene Level Evidence 1031

Molecular Profile Tab

Filtering and Sorting ⓘ

Filter rows:

Showing 1 to 383 of 383 entries

Molecular Profile	Protein Effect	Treatment Approaches
BRAF A598_T599insARC	gain of function - predicted	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF A598_T599insV	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF A598V	gain of function - predicted	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF A728V	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF act mut	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF D594_T599dup	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF E586K	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF F247L	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF F468C	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120
BRAF G464E	gain of function	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor LY3009120

The **Molecular Profile** tab displays all molecular profiles associated with the selected gene, which can contain one or more gene variants. If appropriate, any related treatment approaches are listed. Treatment approaches are either Drug Classes or individual Therapies that have been assigned to variants based on evidence from the literature. Clicking on these buttons will bring you to the “Profile Treatment Approach Detail” page.

Explore By Gene

Gene Variants 358

Category Variants 32

Molecular Profiles 724

Gene Level Evidence 1660

Gene Level Evidence Tab

Filtering and Sorting ⓘ

NOTE: AMP/CAP/ASCO evidence levels have been assigned at the efficacy evidence level. The corresponding molecular profile tier has been inferred based on the specific annotation, however the variant and/or molecular profile may have other levels of evidence, providing a higher tier ranking for the therapy/tumor type. Use the filter rows to search for additional evidence and tier ranking.

Filter rows:

Showing 1 to 1,660 of 1,660 entries

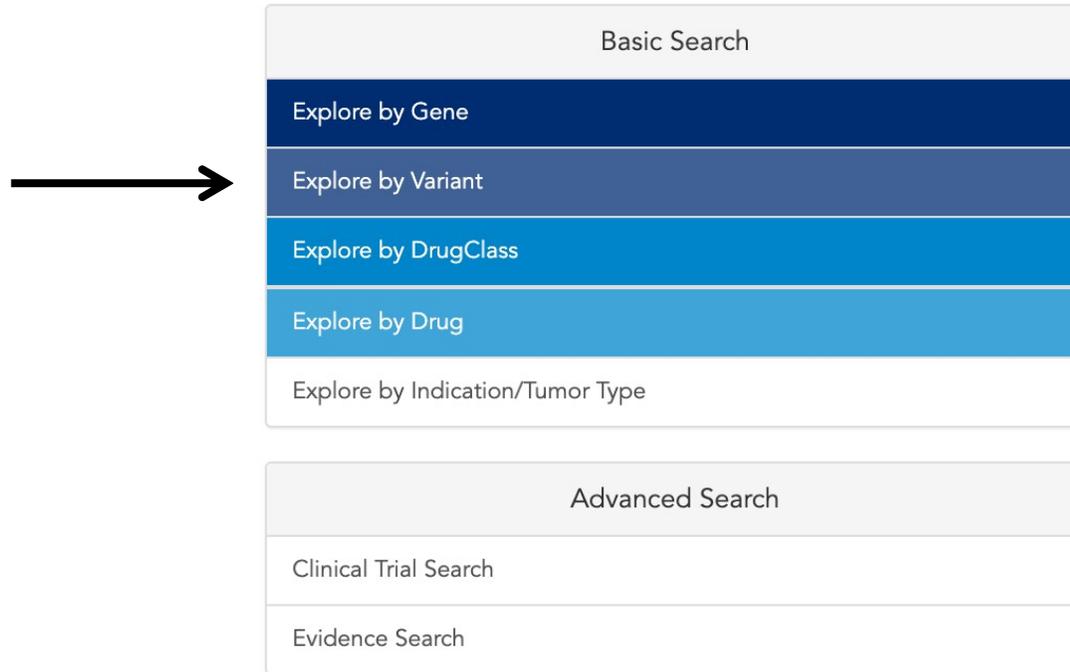
Molecular Profile	Indication/Tumor Type	Response Type	Therapy Name	Approval Status	Evidence Type	Efficacy Evidence	Evidence Level	Inferred Tier
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
BRAF V600E	melanoma	sensitive	Dabrafenib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III clinical trial (BREAK-3) that supported FDA approval, Tafinlar (dabrafenib) improved median progression-free survival compared to Deticene (dacarbazine) (5.1 vs 2.7 months, HR=0.3, p<0.0001) in patients with BRAF V600E positive melanoma (PMID: 22735384; NCT01227889). detail...	A	I
BRAF V600E	melanoma	sensitive	Vemurafenib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III trial (BRIM-3) that supported FDA approval, Zelboraf (vemurafenib), as compared to Deticene (dacarbazine), resulted in an improved overall survival (OS) (13.6 vs 9.7 months, HR=0.81, p=0.03) in patients with BRAF V600E-positive metastatic melanoma, with estimated OS rates of 56%, 30%, 21%, and 17% at 1, 2, 3, and 4 years, respectively (PMID: 28961848, PMID: 21639808; NCT01006980), and BRAF V600E is included on the companion diagnostic (FDA.gov). 28961848 detail... detail... 21639808	A	I

The **Gene Level Evidence** tab displays all annotated evidence associated with gene variants in the selected gene. Links in blue go out to PubMed for the associated references.

There are multiple 'Evidence Types'. The majority are "Actionable", meaning there is an association between a gene variant and therapy. Other evidence types are: "Prognostic" (variant association with disease outcome), "Diagnostic" (variant association with disease diagnosis), "Risk Factor" (germline variant association with risk of disease onset), and "Emerging" (variant as a potential therapeutic target).

The last two columns of the 'Gene Level Evidence' tab includes the evidence level and inferred tier for the evidence annotation based on the AMP/CAP/ASCO guidelines for somatic variant reporting. The corresponding molecular profile is inferred based on the specific annotation but could have a higher inferred tier depending on the evidence.

Explore By Gene Variant



- Clicking on the “Explore by Variant” button will bring you to a page where you can search for content related to a gene variant.

Explore By Gene Variant

Find by Gene Variant

- Start typing a gene variant name to display gene variant.
- Select **one** gene variant and click 'Submit' to go to the next page.

Gene Variant

Start typing to select one or more variants

BRAF V600E

BRAF V600E (gain of function)

BRAF V600E/K (gain of function)

BRAF V600E (gain of function)

Gene Description:

BRAF, serine/threonine-protein kinase B-raf, is a member of the Raf family of serine/threonine protein kinases, which signals through the MAP kinase pathway to regulate cell proliferation and cell growth (PMID: 24737949, PMID: 29540830). BRAF mutations and fusions have been identified in a variety of cancers, including, colorectal (PMID: 30122982), lung (PMID: 29729495), thyroid (PMID: 12970315), and melanoma (PMID: 24737949), and a number of mutations have also been demonstrated to confer drug resistance (PMID: 27478040).

Gene Variant Description:

BRAF V600E (previously reported as V599E) lies within the activation segment of the kinase domain of the Braf protein (PMID: 15035987). V600E confers a gain of function to the Braf protein as demonstrated by increased Braf kinase activity, downstream signaling, and the ability to transform cells in culture (PMID: 15035987, PMID: 29533785).

Typing in the search box will trigger a drop-down list of gene variants. Gene variants in CKB follow HGVS nomenclature. **Click** on the desired gene variant to select for searching. This will bring you to the “Molecular Profile Detail Page” for the selected gene variant.

Explore By Gene Variant

ckb BOOST News Genes Drug Classes About Terms of Use Help

Molecular Profile Detail

Profile Name: BRAF V600E

Gene Variant Detail: BRAF V600E (gain of function)

Relevant Treatment Approaches: BRAF Inhibitor

Gene Variant Description: BRAF V600E (previously reported as V599E) lies within the activation segment of the kinase domain of the Braf protein (PMID: 15035987). V600E confers a gain of function to the Braf protein as demonstrated by increased Braf kinase activity, downstream signaling, and the ability to transform cells in culture (PMID: 15035987, PMID: 29533785).

Variant Level Evidence 323 Complex Molecular Profile Evidence 186 Extended Evidence 128 Gene Level Evidence 1031 Treatment Approach Evidence 145 Variant Associated Clinical Trials 87 Gene Associated Clinical Trials 309

Filtering and Sorting

Filter rows:

Showing 1 to 323 of 323 entries

Molecular Profile	Indication/Tumor Type	Response Type	Relevant Treatment Approaches	Therapy Name	Approval Status	Evidence Type	Efficacy Evidence	References
BRAF V600E	colorectal cancer	sensitive	BRAF Inhibitor	Cetuximab + Encorafenib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III (BEACON CRC) trial that supported FDA approval, Braftovi (encorafenib) and Erbitux (cetuximab) combination treatment (n=113) resulted in improved median overall survival (8.4 vs 5.4 months, HR=0.60, p<0.001), confirmed response rate (20% vs 2%, p<0.001), and median progression-free survival (4.2 vs 1.5 months, HR=0.40, p<0.001) compared to control (n=107) in patients with metastatic colorectal cancer.	detail... 31566309

- To view the gene variant description, hover over the variant button next to Gene Variant Detail in the header.
- Below, there are 7 tabs related to different areas of content:
 - The 'Variant Level Evidence' tab lists all annotated evidence that includes only the gene variant in the molecular profile.
 - The 'Complex Molecular Profile Evidence' tab lists all annotated evidence that includes the gene variant plus one or more other variants in the molecular profile.
 - The 'Extended Evidence' tab lists all annotated evidence that includes the category variant(s) in which the gene variant is a member.
 - The 'Gene Level Evidence' tab lists all annotated evidence associated with the gene.
 - The 'Treatment Approach Evidence' tab lists all the annotated evidence related to the Relevant Treatment Approaches listed in the header under Gene Variant Detail.
 - The 'Variant Associated Clinical Trials' tab lists all the trials that include the gene variant as a variant requirement.
 - The 'Gene Associated Clinical Trials' tab lists all the trials that include a any variant in the associated gene.
- All pages also incorporate filtering and sorting capability to enable easy content searching.

Explore By Gene Variant

Variant Level Evidence 323

Complex Molecular Profile Evidence 186

Extended Evidence 128

Gene Level Evidence 1031

Treatment Approach Evidence 145

Variant Associated Clinical Trials 87

Gene Associated Clinical Trials 309

Variant Associated Clinical Trials

Filtering and Sorting ⓘ

Filter rows:

Showing 1 to 87 of 87 entries

Clinical Trial	Phase	Therapies	Title	Recruitment Status	Covered Countries	Other Countries
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
NCT01089101	Phase Ib/II	Selumetinib	Selumetinib in Treating Young Patients With Recurrent or Refractory Low Grade Glioma	Active, not recruiting		
NCT01659151	Phase II	Aldesleukin Fludarabine Vemurafenib	Vemurafenib With Lymphodepletion Plus Adoptive Cell Transfer and High Dose IL-2 Metastatic Melanoma	Active, not recruiting		
NCT01709292	Phase II	Vemurafenib	Vemurafenib Neoadjuvant Trial in Locally Advanced Thyroid Cancer	Active, not recruiting		
NCT01711632	Phase II	Vemurafenib	BRAF Inhibitor, Vemurafenib, in Patients With Relapsed or Refractory Hairy Cell Leukemia	Active, not recruiting		
NCT01740648	Phase I	Fluorouracil + Trametinib	Trametinib, Fluorouracil, and Radiation Therapy Before Surgery in Treating Patients With Stage II-III Rectal Cancer	Active, not recruiting		
NCT01748149	Phase I	Vemurafenib	Vemurafenib in Children With Recurrent/Refractory BRAF Gene V600E (BRAFFV600E)-Mutant Gliomas	Active, not recruiting		
NCT02034110	Phase II	Dabrafenib + Trametinib	Efficacy and Safety of the Combination Therapy of Dabrafenib and Trametinib in Subjects With BRAF V600E- Mutated Rare Cancers	Active, not recruiting		

The **Variant Associated Clinical Trials** tab displays clinical trials that include the selected gene variant as a variant requirement. NCTID buttons navigate to the 'Clinical Trial Detail Page'. Recruitment status updates daily.

Explore By Gene Variant

Variant Level Evidence **323** Complex Molecular Profile Evidence **186** Extended Evidence **128** Gene Level Evidence **1031** Treatment Approach Evidence **145** Variant Associated Clinical Trials **87**

Gene Associated Clinical Trials **309**

Gene Associated Clinical Trials

Filtering and Sorting ⓘ

Filter rows:

Showing 1 to 309 of 309 entries

Clinical Trial	Phase	Therapies	Title	Recruitment Status	Covered Countries	Other Countries
NCT01089101	Phase Ib/II	Selumetinib	Selumetinib in Treating Young Patients With Recurrent or Refractory Low Grade Glioma	Active, not recruiting		
NCT01306045	Phase II	Erlotinib Lapatinib MK2206 Sunitinib Selumetinib	Molecular Profiling and Targeted Therapy for Advanced Non-Small Cell Lung Cancer, Small Cell Lung Cancer, and Thymic Malignancies	Active, not recruiting		
NCT01436656	Phase I	Encorafenib	A Phase I Study of Oral LGX818 in Adult Patients With Advanced or Metastatic BRAF Mutant Melanoma	Active, not recruiting		
NCT01543698	Phase Ib/II	Binimetinib + Encorafenib Binimetinib + Encorafenib + Ribociclib	A Phase Ib/II Study of LGX818 in Combination With MEK162 in Adult Patients With BRAF Dependent Advanced Solid Tumors	Active, not recruiting		
NCT01657591	Phase I	Vemurafenib + XL888	Study of XL888 With Vemurafenib for Patients With Unresectable BRAF Mutated Stage III/IV Melanoma	Active, not recruiting		
NCT01659151	Phase II	Aldesleukin Fludarabine Vemurafenib	Vemurafenib With Lymphodepletion Plus Adoptive Cell Transfer and High Dose IL-2 Metastatic Melanoma	Active, not recruiting		

The **Gene Associated Clinical Trials** tab displays clinical trials that include any gene variant specific to the gene for the selected gene variant. NCTID buttons navigate to the 'Clinical Trial Detail Page'. Recruitment status updates daily.

Explore By Gene Variant

Molecular Profile Detail

Request Content ?

Profile Name: BRAF V600E

Gene Variant Detail: **BRAF V600E (gain of function)** ← **Gene Variant Button**

Relevant Treatment Approaches: BRAF Inhibitor, MEK inhibitor (Pan), MEK1 Inhibitor, MEK2 Inhibitor, RAF Inhibitor (Pan)

Explore Visually

Variant Level Evidence 323 Complex Molecular Profile Evidence 636 Extended Evidence 128 Gene Level Evidence 1660 Treatment Approach Evidence 145 Variant Associated Clinical Trials 67 Gene Associated Clinical Trials 311

Filtering and Sorting ?

NOTE: AMP/CAP/ASCO evidence levels have been assigned at the efficacy evidence level. The corresponding molecular profile tier has been inferred based on the specific annotation, however the variant and/or molecular profile may have other levels of evidence, providing a higher tier ranking for the therapy/tumor type. Use the filter rows to search for additional evidence and tier ranking.

Filter rows:

Showing 1 to 323 of 323 entries

Molecular Profile	Indication/Tumor Type	Response Type	Relevant Treatment Approaches	Therapy Name	Approval Status	Evidence Type	Efficacy Evidence	Evidence Level	Inferred Tier
BRAF V600E	melanoma	sensitive	BRAF Inhibitor	Dabrafenib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III clinical trial (BREAK-3) that supported FDA approval, Tafinlar (dabrafenib) improved median progression-free survival compared to Deticene (dacarbazine) (5.1 vs 2.7 months, HR=0.3, p<0.0001) in patients with BRAF V600E positive melanoma (PMID: 22735384; NCT01227889). detail... detail...	A	I
BRAF V600E	melanoma	sensitive	MEK inhibitor (Pan) MEK1 Inhibitor MEK2 Inhibitor	Trametinib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III trial (METRIC) that supported FDA approval, Mekinist (trametinib) treatment, as compared to Deticene (dacarbazine) or Taxol (paclitaxel) treatment, resulted in improved progression-free survival of 4.8 months versus 1.5 months and an overall six month survival rate of 81% versus 67% in patients with BRAF V600E/K-positive metastatic melanoma (PMID: 22663011; NCT01245062). 22663011 detail... detail...	A	I

To view the gene variant detail page, click on the gene variant button next to 'Gene Variant Detail' in the top header

Explore By Gene Variant

Gene Variant Detail

[Request Content](#)

Gene **BRAF**

Variant V600E

Impact List missense

Protein Effect gain of function

Gene Variant Descriptions BRAF V600E (previously reported as V599E) lies within the activation segment of the kinase domain of the Braf protein (PMID: 15035987). V600E confers a gain of function to the Braf protein as demonstrated by increased Braf kinase activity, downstream signaling, and the ability to transform cells in culture (PMID: 15035987, PMID: 29533785).

Associated Drug Resistance

Category Variants [BRAF mutant](#) > [BRAF act mut](#) > [BRAF V600E/K](#) > [BRAF V600E](#)

Paths [BRAF mutant](#) > [BRAF V600X](#) > [BRAF V600E/K](#) > [BRAF V600E](#)

[Explore Visually](#)

Variant Reference Transcript [All Transcripts](#)

Filtering and Sorting

Transcript	NM_004333.5
gDNA	chr7:g.140753336A>T
cDNA	c.1799T>A
Protein	p.V600E
Source Database	RefSeq
Genome Build	GRCh38/hg38

Evidence **959** [Extended Evidence](#) **128** [Molecular Profiles](#) **317**

Filtering and Sorting

NOTE: AMP/CAP/ASCO evidence levels have been assigned at the efficacy evidence level. The corresponding molecular profile tier has been inferred based on the specific annotation, however the variant and/or molecular profile may have other levels of evidence, providing a higher tier ranking for the therapy/tumor type. Use the filter rows to search for additional evidence and tier ranking.

Filter rows:

Showing 1 to 959 of 959 entries

Molecular Profile	Indication/Tumor Type	Response Type	Therapy Name	Approval Status	Evidence Type	Efficacy Evidence	Evidence Level	Inferred Tier
BRAF V600E	melanoma	sensitive	Binimetinib + Encorafenib	FDA approved - On Companion	Actionable	In a Phase III (COLUMBUS) trial that supported FDA approval, Braftovi (encorafenib) in combination with Mektovi (binimetinib) resulted in a median overall survival (OS) of 33.6 months, a 1-year OS rate of 77.5%, and a 2-year OS rate of 57.7% in patients with advanced melanoma harboring BRAF V600E/K mutations compared to a median OS of 16.9 months and 1- and 2-year OS rates of 63.1% and 43.2%, respectively, in the Zelboraf (vemurafenib) treated group (PMID: 30219628; NCT01909453). detail... 30219628 detail... detail...	A	I

The header includes the variant description, the category variants in which the specific gene variant is a member, and to the right, the variant reference transcript and a second tab with other relevant transcripts. There are three tabs below the header.

- The 'Evidence' tab lists all the evidence annotations specific to the gene variant selected and includes both single and complex molecular profiles.
- The 'Extended Evidence' tab lists all the evidence annotations specific to the category variant(s) in which the selected gene variant belongs.
- The 'Molecular Profiles' tab lists all the molecular files that include the selected gene variant.

Explore By Drug Class

The image shows a screenshot of the CKB BOOST website interface. At the top, there is a navigation bar with the CKB BOOST logo on the left and links for News, Genes, Drug Classes, About, Terms of Use, and Help on the right. Below the navigation bar, there are two main sections: 'Basic Search' and 'Advanced Search'. The 'Basic Search' section contains six buttons: 'Explore by Gene', 'Explore by Variant', 'Explore by DrugClass', 'Explore by Drug', and 'Explore by Indication/Tumor Type'. The 'Advanced Search' section contains two buttons: 'Clinical Trial Search' and 'Evidence Search'. A horizontal arrow points from the left towards the 'Explore by DrugClass' button. A vertical arrow points from the 'Drug Classes' link in the top navigation bar down to the 'Explore by DrugClass' button.

Clicking on the “Explore by Drug Class” button will bring you to a page where you can search for content based on drugs. Drug classes can be explored through the ‘Drug Class’ grid found on the top header next to ‘Genes’. Drug classes are named based on the drug target.

Explore By Drug Class

Find DrugClass

- Start typing a DrugClass to display DrugClass.
- Select **one** DrugClass and click 'Submit' to go to the next page.

DrugClass

Start typing to select a drugClass

BR

BRAF Inhibitor

BRD2 Inhibitor

BRD3 Inhibitor

BRD4 Inhibitor

TGFBR inhibitor (pan)

TGFBR1 inhibitor

TGFBR2 Antibody

TGFR2 inhibitor

Typing a drug target (i.e. BRAF), will trigger a drop down list. **Click** to select the desired drug class. This will bring you to the “Associated Evidence and Clinical Trials “ page for that drug.

Explore By Drug Class

Drug Class Detail

Request Content

Drug Class BRAF Inhibitor

Drugs 21 Profile Treatment Approaches 10 Associated Evidence 768

Filtering and Sorting

Filter rows:

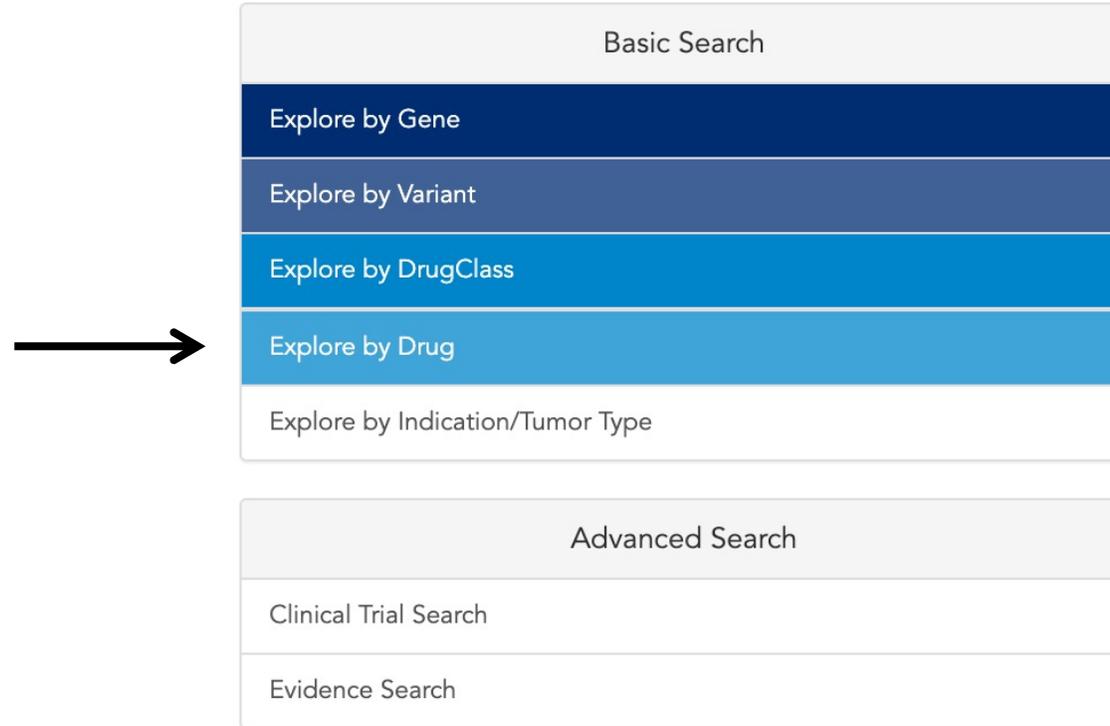
Showing 1 to 21 of 21 entries

Drug Name	Trade Name	Synonyms	Drug Classes	Drug Description
ABM-1310		ABM1310 ABM 1310	BRAF Inhibitor 21	ABM-1310 is a BRAF V600E inhibitor that reduces cell proliferation (NCI Thesaurus).
ASN003		ASN-003 ASN 003	BRAF Inhibitor 21 PIK3CA inhibitor 16 PIK3CG inhibitor 8	ASN003 is a small molecule inhibitor of BRAF, PIK3CA, and PIK3CG, which may result in inhibition of cell proliferation and antitumor activity (J Clin Oncol 35, 2017 (suppl); abstr e14102)).
Belvarafenib		HM95573 GDC-5573	BRAF Inhibitor 21 CRAF Inhibitor 12	Belvarafenib (HM95573) selectively inhibits BRAF and CRAF, resulting in growth inhibition in tumor cells (Cancer Res 2015;75(15 Suppl):Abstract nr 2607).
BGB-283		Lifirafenib	BRAF Inhibitor 21 EGFR Inhibitor (Pan) 47	Lifirafenib (BGB-283) is a dual RAF kinase and EGFR inhibitor, which may lead to decreased tumor cell proliferation and reduced growth of tumors with activation of BRAF and/or EGFR (PMID: 26208524, PMID: 32182156).
BI 882370		XP-102 BI-882370	BRAF Inhibitor 21	BI 882370 is a Raf kinase inhibitor with potent activity against the inactive conformation of Braf and may result in tumor regression (PMID: 26916115).

Typing a drug target (i.e. BRAF), will trigger a drop down list. **Click** to select the desired drug class. This will bring you to the “Drug Class Detail” page for that drug. There are three tabs on this page.

- The ‘Drugs’ tab lists all the drugs that are members of the selected drug class.
- The ‘Profile Treatment Approaches’ tab lists all the molecular profiles that include the selected drug class as a treatment approach.
- The ‘Associated Evidence’ tab lists all the evidence that includes a drug that is a member of that drug class.

Explore By Drug



The image shows a navigation menu with two main sections: 'Basic Search' and 'Advanced Search'. The 'Basic Search' section contains six buttons: 'Explore by Gene', 'Explore by Variant', 'Explore by DrugClass', 'Explore by Drug', and 'Explore by Indication/Tumor Type'. The 'Advanced Search' section contains two buttons: 'Clinical Trial Search' and 'Evidence Search'. A black arrow points to the 'Explore by Drug' button.

Basic Search	
Explore by Gene	
Explore by Variant	
Explore by DrugClass	
Explore by Drug	
Explore by Indication/Tumor Type	

Advanced Search	
Clinical Trial Search	
Evidence Search	

Clicking on the “Explore by Drug” button will bring you to a page where you can search for content based on drugs.

Explore By Drug

Find Evidence and Clinical Trials By Drug

Drug Term

Start typing to select a drug

Vem

Vemurafenib | Zelboraf | PLX4032 | RO5185426

Vemurafenib | Zelboraf | PLX4032 | RO5185426

Drug Description:

Zelboraf (vemurafenib) inhibits BRAF V600E, wild-type BRAF, ARAF, and CRAF (PMID: 20179705), which may result in an inhibition of the MAPK signaling pathway resulting in a reduction of tumor cell proliferation (PMID: 20823850). Zelboraf (vemurafenib) is FDA approved for BRAF V600E-mutant melanoma and for BRAF V600-positive Erdheim-Chester disease (FDA.gov).

Typing a drug term, including trade name or synonym, will trigger a drop down list. **Click** to select the desired drug. This will bring you to the “Associated Evidence and Clinical Trials “ page for that drug.

Explore By Drug

Associated Evidence and Clinical Trials

Drug Name **Vemurafenib**

Trade Name Zelboraf

Synonyms RO5185426/PLX4032

Drug Description Zelboraf (vemurafenib) inhibits BRAF V600E, wild-type BRAF, ARAF, and CRAF (PMID: 20179705), which may result in an inhibition of the MAPK signaling pathway resulting in a reduction of tumor cell proliferation (PMID: 20823850). Zelboraf (vemurafenib) is FDA approved for BRAF V600E-mutant melanoma and for BRAF V600-positive Erdheim-Chester disease (FDA.gov).

DrugClasses **RAF Inhibitor (Pan) 17**

Associated Evidence **316** Clinical Trials **69**

Filtering and Sorting **1**

NOTE: AMP/CAP/ASCO evidence levels have been assigned at the efficacy evidence level. The corresponding molecular profile tier has been inferred based on the specific annotation, however the variant and/or molecular profile may have other levels of evidence, providing a higher tier ranking for the therapy/tumor type. Use the filter rows to search for additional evidence and tier ranking.

Filter rows:

Showing 1 to 316 of 316 entries

Molecular Profile	Indication/Tumor Type	Response Type	Therapy Name	Approval Status	Evidence Type	Efficacy Evidence	Evidence Level	Inferred Tier
BRAF V600E	melanoma	sensitive	Cobimetinib + Vemurafenib	FDA approved - On Companion Diagnostic	Actionable	In a Phase III trial (coBRIM) that supported FDA approval, treatment with the combination of Zelboraf (vemurafenib) and Cotellic (cobimetinib) resulted in an improved progression-free survival of 12.3 months, compared to 7.2 months with Zelboraf (vemurafenib) plus placebo, among patients with BRAF V600-mutated metastatic melanoma, and BRAF V600E and BRAF V600K are on the companion diagnostic (PMID: 27480103; NCT01689519). 27480103 detail... detail...	A	I
BRAF V600E	melanoma	sensitive	Vemurafenib	FDA approved - On Companion	Actionable	In a Phase III trial (BRIM-3) that supported FDA approval, Zelboraf (vemurafenib), as compared to Deticene (dacarbazine), resulted in an improved overall survival (OS) (13.6 vs 9.7 months, HR=0.81, p=0.03) in patients with BRAF V600E-positive metastatic melanoma, with estimated OS rates of 56%, 30%, 21%, and 17% at 1, 2, 3, and 4 years, respectively (PMID: 20823850; PMID: 21439808; NCT01004980). and BRAF V600E is included on the companion diagnostic (FDA.gov) 20823850 21439808 NCT01004980 detail... detail... detail... 21439808	A	I

Below the header are two tabs related to different areas of content:

- The 'Associated Evidence' tab displays all efficacy evidence associated with selected drug, similar to what is displayed with gene.
- The 'Clinical Trials' tab displays all clinical trials associated with the selected drug, alone or in combination therapy.

Explore By Indication

The image shows a screenshot of the CKB BOOST search interface. It features two main sections: 'Basic Search' and 'Advanced Search'. The 'Basic Search' section contains five buttons: 'Explore by Gene', 'Explore by Variant', 'Explore by DrugClass', 'Explore by Drug', and 'Explore by Indication/Tumor Type'. The 'Advanced Search' section contains two buttons: 'Clinical Trial Search' and 'Evidence Search'. A black arrow points to the 'Explore by Indication/Tumor Type' button.

Basic Search	
Explore by Gene	
Explore by Variant	
Explore by DrugClass	
Explore by Drug	
Explore by Indication/Tumor Type	

Advanced Search	
Clinical Trial Search	
Evidence Search	

Clicking on the “Explore by Indication” button will bring you to a page where you can search for content based on disease terms.

Explore By Indication

Find By Indication

- Start typing a disease term to display indication (DO Term).
- Select **one** DO term and click 'Submit' to go to the next page.

Indication

Start typing to select an indication

breast cancer

disease of cellular proliferation > cancer > organ system cancer > thoracic cancer > breast cancer

disease of cellular proliferation > cancer > organ system cancer > thoracic cancer > breast cancer > breast carcinoma

disease of cellular proliferation > cancer > organ system cancer > thoracic cancer > breast cancer > breast carcinoma > bilateral breast cancer

disease of cellular proliferation > cancer > organ system cancer > thoracic cancer > breast cancer > breast carcinoma > bilateral breast cancer > lipid rich breast carcinoma

disease of cellular proliferation > cancer > organ system cancer > thoracic cancer > breast cancer > breast carcinoma > bilateral breast cancer > synchronous bilateral breast carcinoma

disease of cellular proliferation > cancer > organ system cancer > thoracic cancer > breast cancer > breast carcinoma > breast adenocarcinoma

disease of cellular proliferation > cancer > organ system cancer > thoracic cancer > breast cancer > breast carcinoma > breast adenocarcinoma > acinic cell breast carcinoma

Typing in the indication search box will bring up a drop down list of disease terms. Disease terms in CKB are incorporated from the Disease Ontology (<http://disease-ontology.org>), which is a hierarchical disease ontology, composed of parent terms (ex. “breast cancer”), and child terms (ex. “synchronous bilateral breast carcinoma”).

Select a term from the drop down list to begin the search. Results returned will pertain only to the indication searched, and not “child” terms (those beneath the chosen term in the hierarchy).

Explore By Indication

Associated Evidence and Clinical Trials

Request Content ?

Indication/Tumor Type:

Definition: A thoracic cancer that originates in the mammary gland.

Source: [DiseaseOntology.org](https://www.ebi.ac.uk/ontology/diseaseontology.org)

Associated Evidence **1046** Clinical Trials **246**

Filtering and Sorting ⓘ

NOTE: AMP/CAP/ASCO evidence levels have been assigned at the efficacy evidence level. The corresponding molecular profile tier has been inferred based on the specific annotation, however the variant and/or molecular profile may have other levels of evidence, providing a higher tier ranking for the therapy/tumor type. Use the filter rows to search for additional evidence and tier ranking.

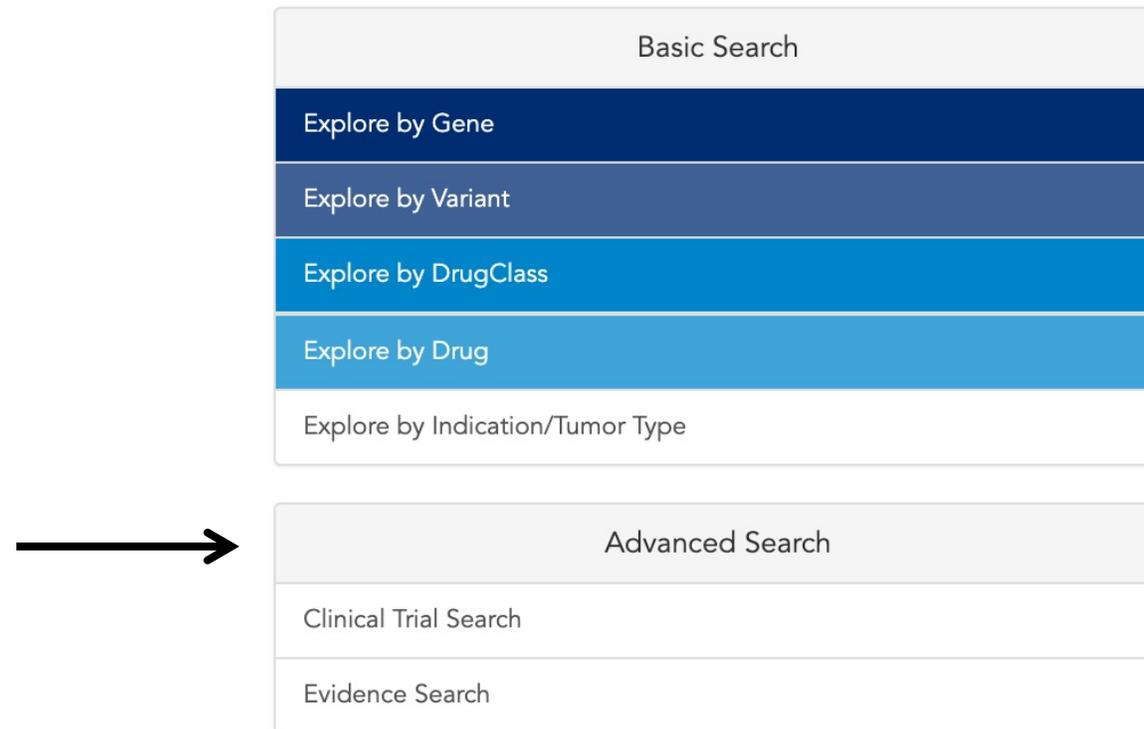
Filter rows:

Showing 1 to 1,046 of 1,046 entries

Molecular Profile	Indication/Tumor Type	Response Type	Therapy Name	Approval Status	Evidence Type	Efficacy Evidence	Evidence Level	Inferred Tier
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
ERBB2 over exp	breast cancer	sensitive	Trastuzumab-anns	FDA approved - On Companion Diagnostic	Actionable	In a Phase I trial that supported FDA approval, the Herceptin (trastuzumab) biosimilar Kanjinti (Trastuzumab-anns) demonstrated structure, function, and pharmacokinetic profile comparable to Herceptin (trastuzumab) (PMID: 28341959), thus supporting the extrapolation of data from the Phase III trial that supported the approval of Herceptin (trastuzumab) in Erbb2 (Her2) overexpressing breast cancer (PMID: 23602601; NCT00567190) for approval of Kanjinti (Trastuzumab-anns) (FDA.gov). 23602601 detail... 28341959 detail... detail...	A	I
BRCA1 inact mut	breast cancer	sensitive	Olaparib	Guideline	Actionable	Lynparza (olaparib) is included in guidelines as systemic treatment for patients with recurrent or metastatic breast cancer harboring BRCA1/2 germline mutations (NCCN.org). detail...	A	I
BRCA1 inact mut	breast cancer	sensitive	Talazoparib	Guideline	Actionable	Talzenna (talazoparib) is included in guidelines as systemic treatment for patients with recurrent or metastatic breast cancer harboring BRCA1/2 germline mutations (NCCN.org). detail...	A	I

There are 2 tabs on the returned results page : ‘Associated Evidence’ and ‘Clinical Trials’, which display results pertaining to the disease term searched, similar to the results for “Explore by Drug”.

Advanced Searching



There are two “Advanced Search” options, which allow the user to search on multiple search parameters simultaneously. The ‘Clinical Trial Search’ returns clinical trials that match the search term, and the ‘Evidence Search’ return matching annotated evidence. Clicking on either of these buttons will bring you to the search page.

Advanced Clinical Trials Search

Advanced Clinical Trial Search

- Select **at least one** input (i.e. Gene Variant, Drug, or Indication/Tumor Type) to retrieve clinical trials that match specified input(s).
- Multiple values can be selected for State.
- Search ONLY supports covered countries (i.e. United States and Canada).
- Click 'Submit' to go to the next page and view list of clinical trials.

Info ⓘ

Gene Variant

EGFR L858R (gain of function) ← Gene Variant Selected

Drug

Start typing to select a drug

Indication/Tumor Type

Start typing to select an indication/tumor type

Include child terms as well as the indication itself based on the Disease Ontology hierarchy

Phase

Start typing to select a clinical trial phase

Country

Start typing to select a country

State (Country is required in order to search by State)

Start typing to select state

Submit

In this example, all other terms are left blank

The Advanced Clinical Trial Search enables the user to search for clinical trials based on 'gene variant', 'drug', 'indication', clinical trial 'phase', 'country', and/or 'state'. A user must select **at least one** attribute from either 'gene variant', 'drug', or 'Indication/Tumor Type' to search on. Selecting only a 'gene variant' will return all clinical trials that match that gene variant, regardless of all other attributes.

Once you have selected the desired search terms, click 'Submit' to begin the search.

Advanced Clinical Trials Search

Advanced Clinical Trial Search Results

Search Parameters

Gene Variant	EGFR L858R (gain of function)
Drug	
Indication/Tumor Type(s)	
Phase	
Countries	
States	
State Synonyms	

Directly Associated Clinical Trials **98** Gene Associated Clinical Trials **444**

Showing 1 to 98 of 98 entries

Click on this button to get more information about the trial

Filtering and Sorting ⓘ

Filter rows:

Clinical Trial	Variant Requirement	Therapies	Phase	Title	Indication/Tumor Type(s)	Recruitment Status	Covered Countries	Other Countries
<input type="button" value="NCT02108964"/>	Yes	<input type="button" value="Nazartinib"/>	Phase Ib/II	A Phase I/II, Multicenter, Open-label Study of EGFRmut-TKI EGF816, Administered Orally in Adult Patients With EGFRmut Solid Malignancies	<input type="button" value="lung non-small cell carcinoma"/>	Active, not recruiting	USA CAN	7
<input type="button" value="NCT02143466"/>	Yes	<input type="button" value="Osimertinib + Savolitinib"/> <input type="button" value="Osimertinib + Selumetinib"/> <input type="button" value="Durvalumab + Osimertinib"/>	Phase I	AZD9291 in Combination With Ascending Doses of Novel Therapeutics	<input type="button" value="lung non-small cell carcinoma"/>	Active, not recruiting	USA CAN	6
<input type="button" value="NCT02296125"/>	Yes	<input type="button" value="Erlotinib"/> <input type="button" value="Osimertinib"/> <input type="button" value="Gefitinib"/>	Phase III	AZD9291 Versus Gefitinib or Erlotinib in Patients With Locally Advanced or Metastatic Non-small Cell Lung Cancer (FLAURA)	<input type="button" value="lung non-small cell carcinoma"/>	Active, not recruiting	USA CAN	28

- The header of the **Advanced Clinical Trials Search Results** page lists the search parameters. Fields left blank in the search will be blank in the header. Clinical trial results will pertain to the searched terms.
- When gene variant is used as a search parameter, the results page will have 2 tabs: “Directly Associated Clinical Trials’ and ‘Gene Associated Clinical Trials’. The ‘Directly Associated Clinical Trials’ tab will display clinical trials with ‘variant requirement’ matching the searched variant. The ‘Gene Associated Clinical Trials’ tab will display all clinical trials with variant requirements related to the Gene of the searched variant. Searches lacking gene variant selection will not have a “Gene Associated Clinical Trials’ tab.
- Clicking the white clinical trial button will bring you to the “Clinical Trial Detail” Page, which contains more detail about the trial, including specifics on variant requirements.

Advanced Clinical Trials Search

Clinical Trial Detail

[Request Content](#)

NCT ID	NCT02108964
Title	A Phase I/II, Multicenter, Open-label Study of EGFRmut-TKI EGf816, Administered Orally in Adult Patients With EGFRmut Solid Malignancies
Recruitment	Active, not recruiting
Gender	both
Phase	Phase Ib/II
Variant Requirements	Yes
Sponsors	Novartis Pharmaceuticals
Indications	lung non-small cell carcinoma
Therapies	Nazartinib
Age Groups:	senior adult
Covered Countries	USA CAN

Variant Requirements **5**[Locations](#) **14**

Filtering and Sorting

Filter rows:

Showing 1 to 5 of 5 entries

Molecular Profile	Requirement Type
EGFR act mut	required
EGFR exon 19 del	partial - required
EGFR L858R	partial - required

For this trial, patients are required to have an EGFR activating mutation, and it could include EGFR exon 19 del or EGFR L858R.

The **Clinical Trial Detail** page lists additional information about the clinical trial, curated from clinicaltrials.gov, including the sponsor and variant requirements. The specific variant requirements are listed in the table. Requirement types can be “required” (variant is required for enrollment), “excluded” (variant is excluded from enrollment), “partial” (variant is required or excluded for a subset of the enrollment population).

The second tab ‘Locations’ lists the locations of the trial, which are imported from clinicaltrials.gov.

Advanced Clinical Trials Search

Advanced Clinical Trial Search

- Select at least one input (i.e. Gene Variant, Drug, or Indication/Tumor Type) to retrieve clinical trials that match specified input(s).
- Multiple values can be selected for State.
- Search **ONLY** supports covered countries (i.e. United States and Canada).
- Click 'Submit' to go to the next page and view list of clinical trials.

Info ⓘ

Gene Variant
EGFR L858R (gain of function) x ▾

Drug
Start typing to select a drug ▾

Indication/Tumor Type
lung cancer x ▾

Include child terms as well as the indication itself based on the Disease Ontology hierarchy

Phase
Start typing to select a clinical trial phase ▾

Country
Start typing to select a country ▾

State (Country is required in order to search by State)
Start typing to select state

Submit

Click on this box to enable searching of child terms to selected disease term

Multiple Attribute Searching

Users can also search using multiple attributes. Typing in each box will trigger a drop-down list of terms from which to select. Results returned will relate to ALL items selected ('AND' searching).

When choosing an indication, users have the option to include child terms (those below the selected term in the hierarchy). To enable this function, click the box below. In this example, all child terms for "lung cancer" will be searched on in addition to the parent term. Hit 'Submit' to begin the search. All results returned will pertain to the combination of terms selected.

Advanced Clinical Trials Search

Advanced Clinical Trial Search Results

Search Parameters

Gene Variant	EGFR L858R (gain of function)
Drug	
Indication/Tumor Type(s)	<input type="text" value="lung cancer"/> <input type="text" value="pulmonary neuroendocrine tumor"/> <input type="text" value="lung mixed small cell and squamous cell carcinoma"/> <input type="text" value="lung meningioma"/> <input type="text" value="lung sarcoma"/> <input type="text" value="lung hilum cancer"/> <input type="text" value="pulmonary blastoma"/> <input type="text" value="epithelial predominant pulmonary blastoma"/> <input type="text" value="pleuropulmonary blastoma"/> <input type="text" value="classic pulmonary blastoma"/> <input type="text" value="adenosquamous lung carcinoma"/> <input type="text" value="Pancoast tumor"/> <input type="text" value="lung superior sulcus carcinoma"/> <input type="text" value="main bronchus cancer"/> <input type="text" value="lung carcinoma"/> <input type="text" value="lung clear cell carcinoma"/> <input type="text" value="lung sarcomatoid carcinoma"/> <input type="text" value="asbestos-related lung carcinoma"/> <input type="text" value="hilar lung carcinoma"/> <input type="text" value="lung non-small cell carcinoma"/> <input type="text" value="lung large cell carcinoma"/> <input type="text" value="pulmonary large cell neuroendocrine carcinoma"/> <input type="text" value="lung combined large cell neuroendocrine carcinoma"/> <input type="text" value="large cell neuroendocrine carcinoma"/> <input type="text" value="lung giant cell carcinoma"/> <input type="text" value="large cell carcinoma with rhabdoid phenotype"/> <input type="text" value="lung occult large cell carcinoma"/> <input type="text" value="lung squamous cell carcinoma"/> <input type="text" value="basaloid lung carcinoma"/> <input type="text" value="lung occult squamous cell carcinoma"/> <input type="text" value="lung non-squamous non-small cell carcinoma"/> <input type="text" value="lung adenocarcinoma"/> <input type="text" value="mucinous lung adenocarcinoma"/> <input type="text" value="signet ring lung adenocarcinoma"/> <input type="text" value="lung acinar adenocarcinoma"/> <input type="text" value="lung mucinous cystadenocarcinoma"/> <input type="text" value="bronchiolo-alveolar adenocarcinoma"/> <input type="text" value="mucinous bronchioloalveolar adenocarcinoma"/> <input type="text" value="mixed mucinous and nonmucinous bronchioloalveolar adenocarcinoma"/> <input type="text" value="nonmucinous bronchioloalveolar adenocarcinoma"/> <input type="text" value="lung papillary adenocarcinoma"/> <input type="text" value="lung occult adenocarcinoma"/> <input type="text" value="solid adenocarcinoma with mucin production"/> <input type="text" value="lung mucoepidermoid carcinoma"/> <input type="text" value="lung small cell carcinoma"/> <input type="text" value="lung oat cell carcinoma"/> <input type="text" value="lung occult small cell carcinoma"/> <input type="text" value="lung combined type small cell carcinoma"/> <input type="text" value="lung combined type small cell adenocarcinoma"/> <input type="text" value="lung adenoid cystic carcinoma"/> <input type="text" value="lung lymphoma"/>
Phase	
Countries	
States	
State Synonyms	

When the “include child terms” button is selected, the header of the results page will list the selected indication as well as all child terms included in the search.

In this example, ‘gene variant’ and ‘indication’ were used as search parameters. Other fields were left blank. Results returned will pertain to the gene variant selected **AND** one of the listed indication terms.

Advanced Evidence Search

Advanced Evidence Search

- Select at least one input to retrieve evidence that match input selections.
- Click 'Submit' to go to the next page and view list of evidences.

Molecular Profile

Drug

Indication/Tumor Type

Include child terms as well as the indication itself based on the Disease Ontology hierarchy

Response Type

Evidence Type

The Advanced Evidence Search operates in a similar way to the Advanced Clinical Trial Search and enables the user to search for annotated *evidence* related to 'molecular profile', 'drug', 'indication', and/or clinical trial 'phase'. A user can select **one or more** of these attributes to search on.

Once you have selected the desired search terms, click 'Submit' to begin the search. Results returned will pertain to **all** attributes selected.

Advanced Evidence Search

Request Content ?

Advanced Evidence Search Results

Search Parameters

Molecular Profile: PIK3CA H1047R

Drug:

Indication/Tumor Type(s):

Response Type: sensitive

Evidence Type:

Associated Evidences 44

Filtering and Sorting ?

NOTE: AMP/CAP/ASCO evidence levels have been assigned at the efficacy evidence level. The corresponding molecular profile tier has been inferred based on the specific annotation, however the variant and/or molecular profile may have other levels of evidence, providing a higher tier ranking for the therapy/tumor type. Use the filter rows to search for additional evidence and tier ranking.

Filter rows:

Showing 1 to 44 of 44 entries

Molecular Profile	Indication/Tumor Type	Response Type	Therapy Name	Approval Status	Evidence Type	Efficacy Evidence	Evidence Level	Inferred Tier
PIK3CA H1047R	breast cancer	sensitive	Taselisib	Phase I	Actionable	In a Phase I trial, four patients with breast cancer harboring PIK3CA H1047R demonstrated a confirmed partial response when treated with Taselisib (GDC-0032) (PMID: 28331003).	C	II
PIK3CA H1047R	ovarian cancer	sensitive	CH5132799	Phase I	Actionable	In a Phase I trial, CH5132799 demonstrated safety and preliminary efficacy in patients with advanced solid tumors, including a partial response in a patient with ovarian cancer harboring PIK3CA H1047R (PMID: 25231405).	C	II
PIK3CA H1047R	colorectal cancer	sensitive	Cetuximab	Case Reports/Case Series	Actionable	In a retrospective analysis, Erbitux (cetuximab) combined with radiation therapy resulted in stable disease for 6 months in a colorectal carcinoma patient harboring a PIK3CA H1047R mutation (PMID: 25714871).	D	II

The **Advanced Evidence Search Results** page lists all evidence that matches **all** search terms. In this example, evidence annotations that have both the response type: “sensitive” **and** contains the molecular profile: “PIK3CA H1047R” are returned.