

## BRAF Inhibitors

BRAF Inhibitors are chemotherapeutic agents that target the mutated BRAF proto-oncogene in several cancers. The BRAF proto-oncogene is a serine/threonine kinase. A valine-to-glutamic acid mutation in the 600th codon position of this protein is a common mutation (V600E). BRAF inhibitors can be used to treat melanoma, non-Hodgkin lymphoma, papillary thyroid cancer, and hairy cell leukemia. Examples of these drugs are dabrafenib and vemurafenib.



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### Characteristics

#### BRAF Proto-oncogene

##### B-Raft Propeller On-switch

The BRAF proto-oncogene works by sending signals inside cells responsible for cell growth. It can become an oncogene from mutations or an increase in expression.

#### Serine/Threonine Kinase

##### S-ring/Throw-ninja Kite-ace

The BRAF gene encodes a protein that is known as serine/threonine-protein kinase. This protein is a kinase enzyme that phosphorylates the -OH groups of serine or threonine (which have similar side-chains). It mediates signal transduction from Ras to MEK in the MAPK/ERK signaling pathway resulting in cell division, proliferation, and differentiation.

#### V600E Mutation

##### V-600-sax-E Mutant

The most frequent mutation of BRAF is a valine to glutamic acid substitution at codon 600 (V600E). This mutation has been found in more than 60% of melanomas, and 7-8% of other cancers.

### Indications

#### Melanoma

##### Melon-gnome

Melanoma is the 5<sup>th</sup> most common cancer among men and 6<sup>th</sup> among women. About half of all melanomas have BRAF mutations. Advanced melanoma with a mutation in BRAF has a three-fold increased risk of death compared with melanoma without BRAF mutations.

#### Non-Hodgkin Lymphoma

##### Nun-hog-king with Lime-foam

Changes of Ras-RAF kinase pathway by BRAF mutation may contribute to non-Hodgkin lymphoma carcinogenesis. BRAF inhibitors can be used for this disease.

## Papillary Thyroid Carcinoma

### Paper Thigh-droid Car-gnome

BRAF mutations are found in around 45-50% of all papillary thyroid cancers. Higher recurrence rates, extrathyroidal extension, lymph node metastases, and worse survival are associated with this mutation. BRAF<sup>V600E</sup>-positive advanced RAI-refractory thyroid cancer can be treated with vemurafenib. Dabrafenib is used for BRAF<sup>V600E</sup> mutated metastatic papillary thyroid carcinoma.

## Hairy Cell Leukemia

### Leukemia's Hairy-friend

The BRAF<sup>V600E</sup> mutation is seen in 90% to 100% of hairy cell leukemia (HCL) patients. This mutation is a potential therapeutic target, especially for HCL patients who do not respond well to initial therapy with purine analogs.

## Drugs

### Dabrafenib

#### Dab-raft

Dabrafenib is often co-administered with MEK inhibitors (eg, trametinib) which are used after surgery in patients with stage III melanoma.

### Vemurafenib

#### Van-raft

Vemurafenib (brand name Zelboraf) is used to treat metastatic melanoma with BRAF<sup>V600E</sup> mutation as detected by an FDA-approved test or melanoma that cannot be treated with resection. This medication is not indicated for wild-type BRAF melanoma.