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 5th most common cancer among men and 6th 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^{V600E}-positive advanced RAI-refractory thyroid cancer can be treated with vemurafenib. Dabrafenib is used for BRAF^{V600E} mutated metastatic papillary thyroid carcinoma.

Hairy Cell Leukemia

Leukemia's Hairy-friend

The BRAF^{V600E} 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^{V600E} 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.

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