

## New Targeted Therapies for Melanoma: BRAF

When you are diagnosed with melanoma your oncologist may bring up the term BRAF with you. If you qualify, there may be opportunities to participate in clinical trials with BRAF targeted therapies which have been shown to extend progression-free survival by tumor reduction. Sometimes these drugs are given in combination with other drugs, or alone. One of these BRAF therapies, Vemurafenib will most likely receive FDA approval soon.

In order for these therapies to work most effectively, you need first to determine if your tumor tissue is positive for the BRAF mutation. As demonstrated in laboratory studies, the most common alteration in the *BRAF* gene leads to the V600E mutation and that is what the testing will seek to determine. Currently, testing takes place at most university based pathology labs or through the clinical trial pre-testing program but there may soon be an approved test for those centers without the testing available.

- BRAF is not an easy concept to explain. The BRAF gene makes a protein called B-RAF which is involved in sending signals on pathways in cells that contribute to cell growth. It is found in normal cellular growth activity. When it is overactive, it can lead to excessive cell growth and cancer. BRAF is the most prominent protein researchers have looked at among others involved in the cell signaling pathway.

A gene may become mutated (changed) in many types of cancer. In melanoma, the BRAF gene is commonly mutated which causes a change in the B-RAF protein. A mutated BRAF accelerates tumor cell growth and this change can increase the growth and spread of cancer cells. Therefore these BRAF drugs target the cancer- causing mutation in melanoma. About 50% of melanoma patients have this mutation. Interestingly enough, this BRAF mutation is also seen in benign moles. BRAF mutations are largely restricted to melanoma that arise from sun

exposed skin, and rarely from those types of melanoma, acral, ocular, or mucosal, whose origin is not clearly known yet.

These new BRAF targeted therapies are administered as oral capsules. They are intended to inhibit the BRAF protein from potential tumor growth and activity. A BRAF inhibitor selectively binds to and inhibits the activity of BRAF, which in turn may inhibit the proliferation of tumor cells which contain a mutated BRAF gene. Some refer to these therapies simply as anti-BRAF. Side-effects of the drug include rash, gastro-intestinal disturbance, and fatigue.

These therapies are moving quickly towards approval by the Food and Drug Administration which means they may be prescribed by an oncologist in the near future. Also on the horizon is current research exploring combinations with other drugs that may provide longer, durable responses to increase overall survival time.