My Cancer Genome News: GenomOncology Partnership

The Vanderbilt-Ingram Cancer Center and My Cancer Genome have announced an agreement with GenomOncology, a technology company developing clinical tools to analyze genomic cancer data. GenomOncology will hold the exclusive license to My Cancer Genome content, with non-commercial use of the My Cancer Genome website and mobile apps continuing to be open to the public. As part of the partnership, the groups will develop a decision support tool based on My Cancer Genome data.

Additional information about My Cancer Genome’s collaboration with GenomOncology can be found in the Vanderbilt Reporter: Agreement sets stage for enhanced My Cancer Genome.

Content Update Highlight: Case reports in BRAF-mutated melanoma other than V600E and implications for targeted therapies

In a recent case report, Bahadoran et al., describe a patient with metastatic melanoma harboring a BRAF c.1790T>G L597R mutation, located in the activating kinase domain of BRAF. The patient was treated with the BRAF inhibitor vemurafenib (Zelboraf) and experienced an objective response lasting four months. Similarly, in several reports with implications for targeted therapeutics, a patient with metastatic melanoma whose tumor harbored a BRAF L597S mutation responded to the MEK inhibitor TAK-733 and a patient with metastatic melanoma whose tumor harbored a BRAF L597V mutation responded to the MEK inhibitor trametinib (Mekinist). Vemurafenib, TAK-733, and trametinib all target tyrosine kinases in the RAS/RAF/MEK/ERK pathway, which may be activated by BRAF mutations in the kinase domain.

Vemurafenib, trametinib, and dabrafenib (Tafinlar) are FDA-approved agents for use in patients with metastatic melanoma harboring the V600E mutation, which occurs in 50% of metastatic melanoma, as detected by an FDA-approved BRAF...
V600 mutation test. An additional 10% of metastatic melanoma patients may harbor other BRAF mutations and may benefit from targeted therapeutics such as these agents. The following My Cancer Genome pages have been recently updated with the data from these case reports: BRAF L597V, L597S, L597Q and L597R mutations in melanoma.

**Content Update Highlight: Accelerated FDA approval for Mekinist and Tafinlar in metastatic melanoma harboring a BRAF V600E or V600K mutation**

In January 2014, the FDA granted accelerated approval for the combination of the MEK inhibitor trametinib (Mekinist) and the BRAF inhibitor dabrafenib (Tafinlar) for metastatic melanoma with a BRAF V600E or V600K mutation, based on a phase I/II study of this combination therapy. In the randomized phase II portion of the study, 162 patients were randomized to receive combination therapy of trametinib plus dabrafenib and 85 patients received dabrafenib monotherapy. Patients treated with combination therapy demonstrated a median progression-free survival of 9.4 months and a 76% response rate, compared with 5.8 months and 56% for the control group treated with dabrafenib alone. The primary safety endpoint, the incidence of cutaneous squamous-cell carcinoma, was reported to be 7% with the combination therapy compared with 19% with dabrafenib monotherapy, although the difference was not significant. Patients treated with combination therapy experienced a higher rate of pyrexia than the patients receiving dabrafenib alone. The regimen of trametinib with dabrafenib was approved on an accelerated basis based on the reported response rate, and is concurrently being evaluated in a phase III trial. An updated list of FDA-approved oncology targeted agents and their indications can be found on the Overview of Targeted Therapeutics page.

**Article of Interest Highlight**

**Crizotinib in advanced chemoresistant anaplastic lymphoma kinase-positive lymphoma patients**


Study Type: Prospective compassionate-use named-patient protocol with single-agent crizotinib in ALK+ non-Hodgkin lymphoma (NHL) patients. Compassionate use was carried out under the indication from NCT00932893, building on an initial observation of rapid efficacy in two patients.

Eligibility: Refractory or relapsed ALK+ NHL after at least one prior line of chemotherapy.

Study Treatment: Crizotinib 250 mg twice daily until disease progression.
**Results:** 11 patients were treated. Overall response rate = 90.9% (10 of 11 patients); 2-yr overall survival rate = 72.7%; 2-yr progression free survival rate = 63.7% (latest follow up October 2013).

**Resistance mutations:** Peripheral blood samples from two ALCL patients at pre-treatment and at relapse were tested for mutations in the kinase domain of NPM/ALK. ALK Q1064R was identified in one patient's sample at relapse, and this mutation was not present in the pre-treatment sample. ALK I117N + M1328I was identified in a second patient.