CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120505

Project Title:
Clinical and molecular characterization of combined BRAF and MEK inhibitor treatment in patients with metastatic melanoma resistant to BRAF inhibitor alone

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Patients with advanced melanoma survive on average for < 1 year. Currently available therapies for advanced melanoma are largely ineffective and have many side effects. The development of more effective therapies, and the ability to identify the optimal treatment for each patient, is critical to improving outcomes in this disease. It is now known that approximately 50% of melanomas have an activating mutation in the BRAF gene. Recently, new targeted therapies that inhibit the mutant BRAF have shown a 50-80% rate of tumor size reduction in melanoma patients. However, the overwhelming majority of the responding patients develop resistance to the inhibitors in less than a year. Scientists have found that many of the tumors become resistant to the BRAF inhibitors by finding a way to reactivate the same survival pathway that the BRAF inhibitors initially shut down. In this case, treating the cells with 2 different inhibitors against the same pathway can overcome resistance. However, there is evidence some tumors have resistance that is due to the activation of other survival pathways. These tumors will likely be resistant to treatment combinations that only inhibit one pathway. We are conducting a clinical trial which will test these hypotheses by treating patients who have developed resistance to a BRAF inhibitor with the combination of the BRAF inhibitor and a MEK inhibitor that targets the same pathway. We will determine how safe and effective this treatment is. We will also analyze tumor samples from patients to determine if the activation of other pathways, either before or after they start treatment, correlates with resistance to this therapy. These studies will help determine which patients are most likely to benefit from this treatment. The data will also identify rational treatment strategies for patients in whom this combination is not effective. These studies will lead to more effective, personalized treatments for patients with advanced melanoma.