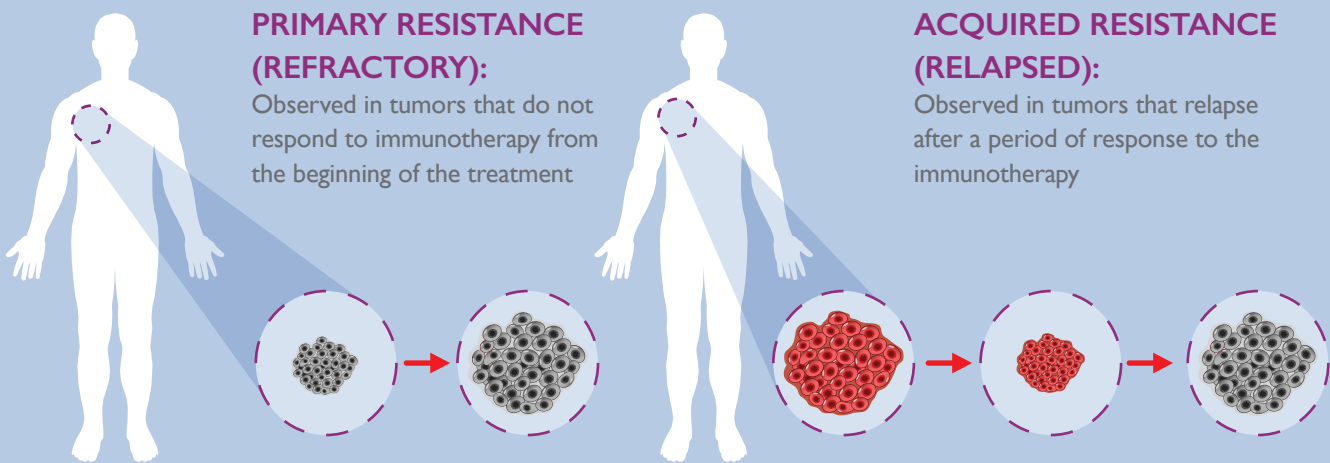


Understanding I-O Resistance

The immune system is extremely complex, and can play a powerful role in cancer. Immuno-Oncology (I-O) investigates innovative approaches that aim to harness the body's natural response to fight cancer. Immunotherapy drugs are designed to target the body's natural immune system to help fight cancer.

Some tumors do not respond to immunotherapies:



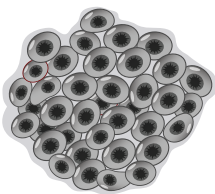
With more and more patients being treated with immunotherapies, there is an increasing number of patients who have begun to experience acquired resistance.

Understanding Mechanisms of Resistance

Immunotherapy resistance is an emerging issue, and there are several approaches being studied to uncover more information on these mechanisms of resistance.

NON-T CELL-INFLAMED TUMOR

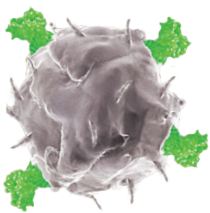
Preliminary research shows that I-O resistance can manifest due to a tumor being non-T cell-inflamed (aka “cold”) in primary resistance, or changes in a T cell-inflamed (aka “hot”) tumor that make it non-responsive and potentially lead to acquired resistance.



“Cold tumors” are not accompanied with an immune response, leaving the tumor unresponsive to immunotherapy

T CELL EXHAUSTION

Cancer cells prevent destruction by the immune system by functionally silencing effector T cells in a process called T cell exhaustion.



From the therapeutic point of view, it is essential to recognize the pathways and molecular signatures governing the T cell exhaustion, to restore the antitumor immunity and overcome I-O resistance in some patients.

Research in Immunotherapy Resistance

The identification of mechanisms of resistance is a key question in immunotherapy resistance that will inform appropriate treatment options for patients.



BASKET TRIALS

are used to evaluate the effect of a drug in a type of patient with T cell-inflamed tumors, in order to identify the patient population most responsive to the immunotherapy



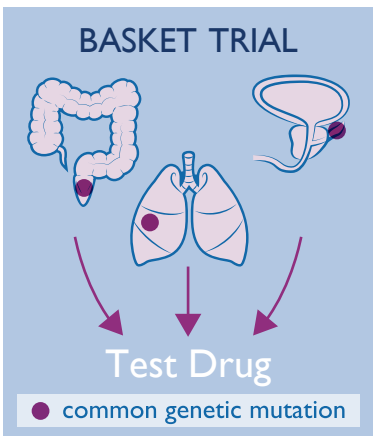
COMBINATION THERAPIES

are being studied by utilizing immunotherapy drugs with known activity, different mechanisms of action and minimally overlapping toxicities



PREDICTIVE BIOMARKERS

are being identified to guide potentially personalized strategies with the goal of overcoming I-O resistance



Bristol-Myers Squibb is actively studying predictive biomarkers with the hopes of informing rational treatment combinations for I-O experienced patients who did not respond to or progressed on treatment.