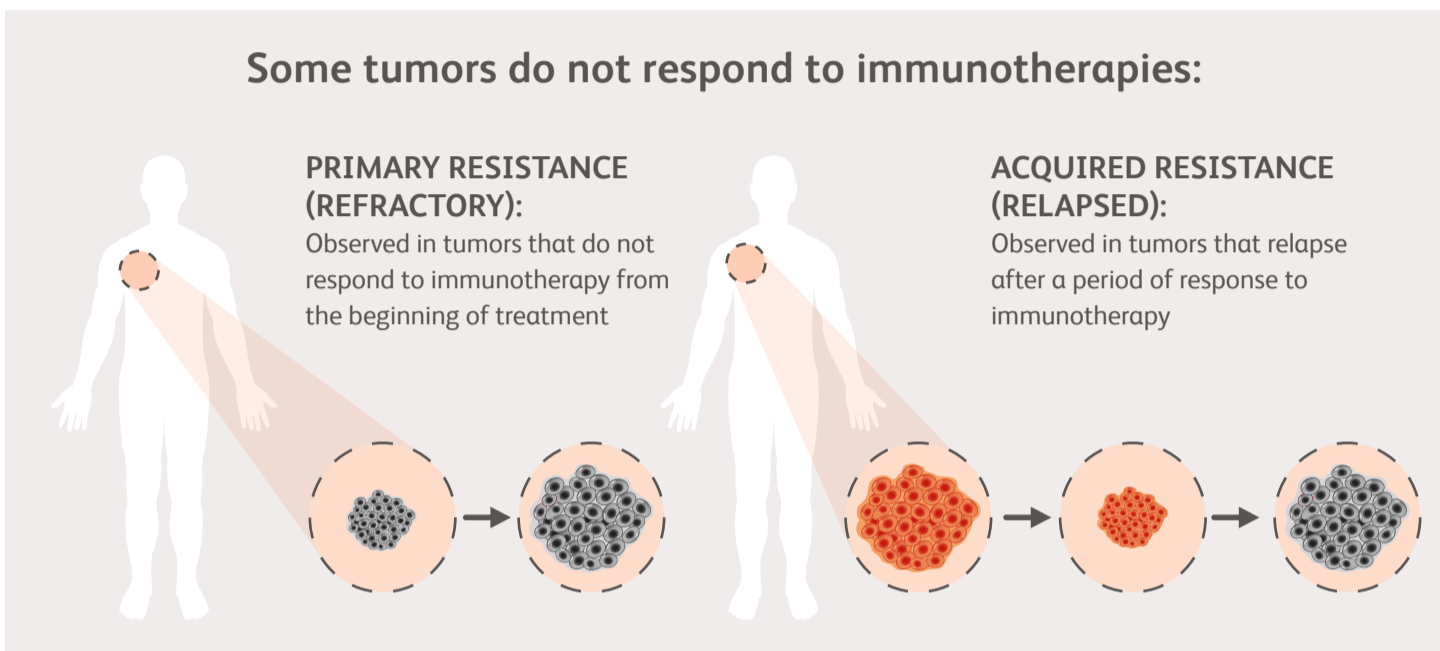


Understanding I-O Resistance

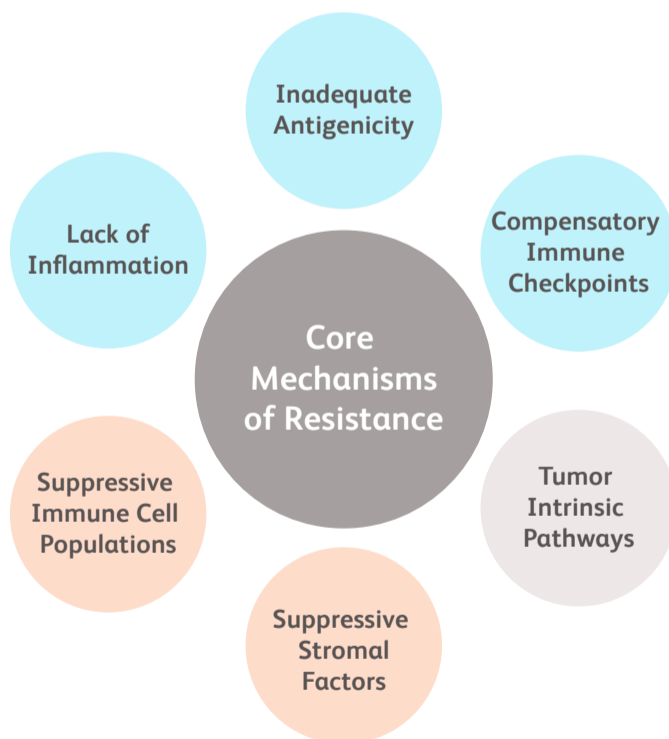
The immune system is extremely complex and can play a powerful role in cancer. Immuno-Oncology (I-O) investigates innovative approaches that aim to harness the body's natural response to fight cancer with checkpoint inhibitors, a type of immunotherapy drug. While checkpoint inhibitors have changed survival expectations for some patients, not all patients respond to them and some stop responding over time.



Understanding Mechanisms of Resistance

Researchers at Bristol Myers Squibb are pursuing a holistic approach to tackle I-O resistance that encompasses interplay between the immune, tumor and stromal compartments.

- **Foundational mechanisms** under investigation include lack of inflammation, insufficient antigenicity and compensatory immune checkpoints, which research has shown to be drivers of response and resistance.
- **Emerging areas of study** include suppressive immune cell types and suppressive stromal factors, which implicate the role of the tumor microenvironment in resistance.
- Through **tumor intrinsic pathways**, researchers are exploring how to exploit tumor vulnerabilities that lead to I-O resistance (such as through targeted protein degradation) and interrogate oncogenic pathways that mediate immune evasion.



Research in I-O Resistance

The identification of mechanisms of resistance is a key question in immunotherapy resistance that will inform appropriate treatment options for patients. Researchers at Bristol Myers Squibb are actively committed to advancing research into the mechanisms of I-O resistance and are utilizing basket trials, combination therapies and predictive biomarkers to inform potentially personalized strategies with the goal of overcoming I-O resistance.

