

SUCCESS IN FIGHTING THE TOUGHEST CANCERS DEMANDS INNOVATION

Over the last half-century, cancer survival rates have increased. But for the toughest cancers today, successful treatment remains elusive. The toughest cancers have seen minimal therapeutic advances, limited improvement in prognosis, and pose the most difficult challenges for patients and clinicians.¹ Researchers at Amgen are invested in gaining a better understanding of the underlying characteristics of tumor cells that historically have been difficult to treat. These efforts have inspired new thinking in our research labs to address the lack of successful treatment options for some of these cancers.

THERAPEUTIC CHALLENGES AND NEW OPPORTUNITIES

The toughest cancers are commonly characterized as being refractory and resistant, rapidly progressing, diagnosed in advanced stages, invasive and metastatic, limited in therapeutic options, and heterogeneous with multiple subtypes.¹⁻⁷ These cancers present many barriers to treatment and are the focus of the most robust and exciting research today.

CANCER TYPE	CHALLENGES/BARRIERS	THERAPEUTIC OPPORTUNITY
Refractory and resistant¹	<ul style="list-style-type: none"> Intrinsically unresponsive to therapy Acquired resistance 	<ul style="list-style-type: none"> Identifying mechanisms or mutations of resistance Mutations include: KRAS, BRAF, MDR1
Rapidly progressing^{1,8,9}	<ul style="list-style-type: none"> Rapid growth Adaptive therapy Infiltrative nature 	<ul style="list-style-type: none"> Identifying targets for molecular therapy Research into microRNA and cancer stem cells
Commonly diagnosed in advanced stages⁴	<ul style="list-style-type: none"> Regional/distant metastasis Can seem to suddenly appear 	<ul style="list-style-type: none"> Increased screening Detection in earlier stages More effective therapies at advanced stages of disease
Invasive and metastatic⁶	<ul style="list-style-type: none"> Spread from primary tumor to regional and distant organs 	<ul style="list-style-type: none"> Improve understanding of metastatic process at cellular and molecular level Interrupting interactions of metastatic cells and host homeostatic mechanisms
Limited lines of therapy¹⁻⁷	<ul style="list-style-type: none"> Cancers have escaped effectiveness of surgery or radiation therapy 	<ul style="list-style-type: none"> Discovering new signaling pathways using microarray testing for intervention
Heterogeneity with multiple subtypes⁶	<ul style="list-style-type: none"> Tumors with subpopulation of cancer cells that are drug resistant and highly metastatic Cancer cells differ from primary tumor cells in terms of treatment and prognosis 	<ul style="list-style-type: none"> Development of innovative strategies to control these subtypes Stimulating human immune system to destroy cancer cells

Attempts to treat these advanced and difficult cancers can often exceed the capabilities of traditional cornerstones of cancer therapy. Conventional therapeutic options such as surgery, hormonal and radiation therapy, and chemotherapy have the most impact during early stages of the disease or in tumors highly unresponsive to drug therapy. Once cancer cells adapt and mutate in late stages of the disease, traditional treatment options lack effectiveness and patients experience relapse and require re-treatment.

LOOKING FORWARD TO THE FUTURE

As the toughest cancers adapt and evolve, our approach in turn must be innovative and agile in the fight against cancer. Amgen continues to take on some of the toughest cancers, and this effort requires a greater understanding of the pathophysiology of cancer cells and the identification of new targets and signaling pathways so that novel oncologic therapies may be developed.

Our researchers are investigating a number of targeted agents to take on the toughest cancers.

The last two decades have seen remarkable progress, with scientific breakthroughs in genetics, molecular biology, and biotechnology. These advances have led to the emergence of biologic therapies and immunotherapies, which have now become important components of cancer therapy.¹⁰ More recently, a greater appreciation of the human immune system has inspired the development of therapies that use the body's immune response. In fact, immuno-oncology may herald the beginning of an era that holds great promise for the long-term control of many cancer types.

Look for more in this series at AmgenOncology.com as we continue to take on the toughest cancers.

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