

IN EVERY ISSUE

## Message from the Editor

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*Have targeted therapies lived up to our expectations?*

We all have a curious habit of marveling briefly at new technology when it dazzles at center stage, only to take it for granted when it becomes a routine part of life. Whether it's an automobile, cell phone, or CT scanner, we only tend to notice when it breaks down or fails to perform up to standards.

We are now a little more than a decade out from the debut of molecularly targeted therapies for cancer. Has some of the luster worn off? In this issue's cover story, ["Targeted Therapy: Hope or Hype?"](#) you will see there's no simple answer to that question.

On one hand, we have seen small stepwise improvements in therapy that have translated into added longevity and higher cure rates in some cases. On the other hand, we are encountering new side effects and the development of resistance to therapy, frustratingly similar to what has been seen with chemotherapy. However, the majority of new drugs in testing for cancer are targeted therapies that have been rationally designed to attack a specific feature of cancer. And they're safer, with far fewer patients being admitted for treatment side effects compared with one or two decades ago.

While chemotherapy may injure normal tissue more readily, it also deals cancer cells a more lethal blow since it goes directly after the process of cell division—the main abnormality of cancer, but also a necessary process for normal tissue. Although targeted therapy is more nuanced and more selective for cancer cells than chemotherapy, in most cases, the best results are obtained when the two are combined.

But we're learning there's no perfect magic bullet. Many of the pathways we thought were unique to cancer actually turn out to be important for normal cells as well. In nature, many interrelationships are obscure and complex, and such is the case with targeted therapy, where its effects, good and bad, can be hidden. As I write this, a warning letter from the Food and Drug Administration was made public about newly uncovered side effects—holes in the intestine or stomach,

blistering skin, and eye ulcers—of Tarceva (erlotinib), a drug approved five years ago for lung cancer and, shortly thereafter, for pancreatic cancer.

Are we becoming disillusioned with targeted therapies? Not quite yet. The biotech industry has more drugs in the pipeline than ever before and the investment community is still supporting more drug innovation and development. Another generation of targeted drugs is addressing cellular pathways that were not even known a few years ago. One of the “newer” targets is mTOR (mammalian target of rapamycin), a central component of several pathways that mediate cell growth and angiogenesis. As outlined in [“Reining In Renal Cancer.”](#) mTOR inhibitors are now approved for advanced kidney cancer and are in clinical trials for other cancers.

There are reasons for optimism about targeted drugs despite their sobering limitations. New tools are being rolled out to characterize tumors and define which treatment will work best, and the number of patients in clinical trials and centers offering these trials has grown, meaning less time needed to test and approve drugs.

The revolution of targeted agents is not quite over. There’s still much we need to learn about how to decipher the inner workings of cancer, and how to safely use these agents earlier in the course of treatment, when they may be more effective. At the dawn of a new era in health care policy, targeted therapy for cancer will remain at center stage.