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OPINION | COMMENTARY

Every Cancer Patient Is One in a Billion

The disease's endless variety is reminiscent of Tolstoy's observation about unhappy families.

By Robert Nagourney
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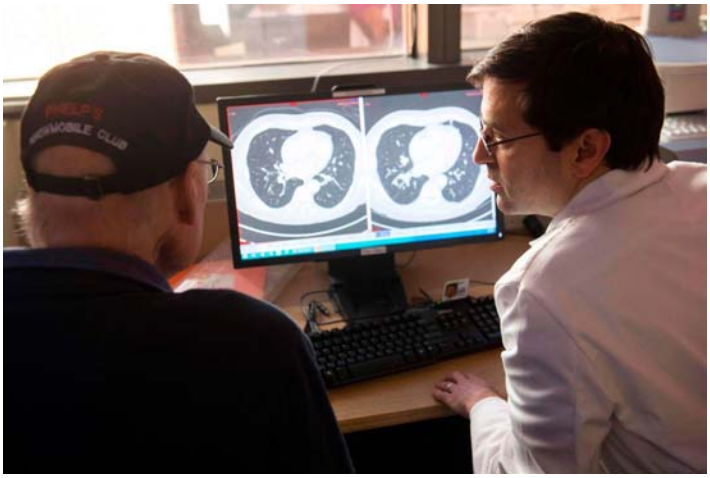

A doctor and patient compare scans of tumors in Bethesda, Md., Feb. 8, 2018. PHOTO: SAUL LOEB/AGENCE FRANCE-PRESSE/GETTY IMAGES

Cancer physicians for more than a century have followed the simple dictum that more is better—more surgery, more radiation, more chemotherapy and, most recently, more immunotherapy. But how much is enough? Do we escalate doses to the point of lethality, as those engaged in bone-marrow transplantation are forced to do regularly? Is this struggle to eliminate every patient's cancer achievable or even warranted?

These questions have taken on a new urgency because oncology has lost sight of a basic principle: Every patient is a uniquely complex person with different medical needs requiring different treatments.

Every oncologist has patients who simply "live" with their cancers. After I told one patient with advanced lung cancer that she was unlikely to respond to conventional

therapy, she declined intervention and proceeded to outlive all of her "treated" counterparts by several years. I describe her to my medical students as "my best response I never treated."

We now know that cancer is a disease of altered cell survival, not excessive proliferation. That is, cancer doesn't grow too much, it dies too little. Applying cell kinetics, we can trace a newly diagnosed colon cancer back to its first cell. This reveals that a cancer that has spread to the liver by the time it's diagnosed may have its origins some 30 years earlier yet remain undetectable with current diagnostic techniques for well over two decades. The same holds true for pancreatic, lung and other tumors. By the time many patients are diagnosed, they have unknowingly lived more of their lives with cancer than without.

Cancer cells are normal cells that distort physiologic stress responses to succeed under conditions of deprivation. Drawing on genetic elements, either mutated or normal, they configure a new biology: the cancer phenotype. Since there are some 1,000 cancer-related genes and each cancer requires up to three distinct gene alterations to succeed, every cancer patient is literally one in a billion. It's reminiscent of Tolstoy's observation: "All happy families resemble one another, each unhappy family is unhappy in its own way."

Despite the manifest complexity of cancer biology, modern oncologists are being asked by insurers, hospital systems and regulatory agencies to reduce therapy options to an ever-shrinking number of guideline-based treatments. This one-size-fits-all approach —attempting to apply population statistics to individual patients—is rapidly proving to be one-size-fits-almost-none.

The physician's role is to discern what makes each patient unique, but few take the time to find out. While gene profiling offers hope, cancer has proved much more complex than the sum of its genes. The study of human tumors at the tissue level suggests that it may be possible to reverse-engineer the process by moving away from top-down genomic analyses toward bottom-up cellular studies. The Physical Sciences Oncology Network is applying physical principles to cancer medicine to explore the dynamics of human tumors in three dimensions. One concept is that in select patients less may be more, since responses can be prolonged using intermittent dosing.

Cancer-cell defenses can now be examined in the laboratory by using drugs, gene-targeted agents and inhibitors of cellular metabolism to probe human tumor biology. We can ask: What cell survival process is your cancer using? More important: Can it be targeted therapeutically? If the answer is yes, and a drug or combination is identified,

the patient would likely respond favorably—twice as likely in fact. But if the answer is no, treatments would be more likely to cause suffering without benefit.

The laboratory process by gauging cancer-cell response to injury, regardless of mechanism, can provide simple answers for the most complex questions. This provides the opportunity for drug-resistant patients to explore experimental therapies upfront, while drug-sensitive patients can seek solutions closer to home.

A newly diagnosed patient with lung cancer and metastases to the brain once arrived in my office and told me that her first oncologist was so pessimistic that she was told to "get my affairs in order." Her studies revealed a simple two-drug combination that provided a remission that has now lasted more than 10 years. When we met shortly after her diagnosis to discuss the recommended treatment, she blurted out, "You mean I'm not going to die?"

"No" I said, "you're not sick. You just have cancer."

Dr. Nagourney is an oncologist and associate clinical professor at the University of California Irvine School of Medicine. He is the author of "Outliving Cancer."

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