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Editorial

EDITORIAL

Talking the Talk About Tumor Genomic Testing

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Cancer drug development continues at a rapid pace fueled largely by new scientific insight, persistent unmet medical need, and the perceived value of precision medicine as an essential strategy in cancer care. Just from 2018 to the time of this writing, the US Food and Drug Administration (FDA) approved more than 70 new cancer drugs or indications, not including biosimilars (1). Many of these approvals require use of a companion biomarker test to identify the patient population most likely to benefit from the treatment, and more than 30 such tests have now been cleared or approved by the FDA (2). In 2017, the FDA also approved the first next-generation sequencing-based test that can detect hundreds of genetic mutations in any solid tumor type. The Centers for Medicare and Medicaid Services simultaneously approved coverage for the test (3). Although some new molecularly targeted drugs have transformed the treatment of some cancers, particularly when used in a biomarker-selected population, many still produce only small incremental improvements in patient outcomes, fueling discussion about the hype vs hope of precision medicine and calling for a reassessment of the standards of evidence required to demonstrate the benefit of precision cancer therapies (4).

The prices of cancer drugs at market entry now typically exceed $10 000 per month (5), and the financial burden faced by many patients continues to escalate as insurance companies shift more costs directly to them in the form of higher premiums, co-payments, and deductibles. Indeed, the term "financial toxicity" has been coined to reflect the impact that the high cost of cancer care has on personal bankruptcy, stress level, physical symptoms, quality of life, adherence to treatment, and mortality (6–8).

These disturbing trends have led to the development of several frameworks that aim to assess the value of new cancer treatments rather than just the cost, recognizing that even a costly treatment could be considered high value if it delivers superior outcomes. Each model attempts to describe the magnitude of clinical benefit delivered by an intervention, its impact on the disease and the patient, and, in some cases, relate these to its cost. The American Society of Clinical Oncology, European Society of Medical Oncology, Institute for Comparative Effectiveness Research, and the National Comprehensive Cancer Network have all developed such value frameworks to facilitate an overall assessment of the incremental health benefits delivered by a new treatment (9–13). However, the extent to which any of these frameworks is useful to guide decision making is hard to determine, perhaps because the perceived value of an intervention often depends on the lens through which it is viewed (14). For many patients, value is defined primarily by health outcomes, that is, cure of disease, longevity, relief of symptoms, resumption of usual daily activities, improvement in quality of life, and achievement of personal goals. To make informed choices about their care, patients need information not just about the costs of care but about the relationship between the costs they will incur and the benefits they will receive for different treatment options.

The extent to which oncologists engage in such discussions with patients is the focus of an article by Yabroff et al. in this issue of the Journal (15). These authors present information drawn from the 2017 National Survey of Precision Medicine in Cancer Treatment, a nationally representative survey of medical oncologists sponsored by the National Cancer Institute, National Human Genomic Research Institute, and the American Cancer Society that collected information on oncologists' sociodemographic and practice characteristics and use of genomic tests. Of the 1220 oncologists who reported discussing genomic testing with patients within the last 12 months, 50% reported often discussing the costs of genomic testing and related treatments, 26.3% reported sometimes, and 23.7% reported rarely or never having such discussions. Oncologists who treated only patients with solid tumors, had formal training in genomic testing, used next-generation sequencing tests in the past 12 months, or worked in practices with electronic medical record alerts for genomic test recommendations were most likely to report discussing the cost of genomic tests and related treatments with their patients. The authors point out that such

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discussions are a necessary first step but not sufficient to ensure that patients and their families can make fully informed decisions about treatment options. The reason for this, of course, is that, like for drugs, the value of a tumor biomarker test depends heavily on its context of use and impact on clinical outcomes, not just on its cost. Dinan and colleagues recently proposed a framework for value-based assessment of tumor biomarker tests that can be applied in many clinical contexts including assessment of cancer risk, early detection, differential diagnosis, prognosis, prediction, and monitoring of disease status (16). In any context, the value of the test depends on its impact on clinical decision making and patient outcome, that is, its clinical utility. Some tests may result in savings that far exceed the cost of the test by reducing the use of unnecessary or ineffective therapies, either by indicating that the patient does not need further therapy or that the therapy being considered is unlikely to work. The use of the 21-gene recurrence score to identify patients with early-stage breast cancer who can safely forgo adjuvant chemotherapy is a prime example (17,18). In other contexts, the value of the tumor biomarker test is to help select the strategy most likely to benefit the patient, such as molecularly targeted treatment rather than cytotoxic chemotherapy in patients with non-small cell lung cancer (19). Tests that detect emergence of resistant disease that can be effectively treated by switching to an alternative therapy (20) or that detect potentially curable oligometastases may also deliver high value to patients by improving the chances of long-term disease control. Of course, a tumor biomarker test that has low clinical utility can also deliver little benefit and drive up the costs of care. Indeed, arguments have been made that next-generation sequencing tests used to identify treatment options for patients with advanced cancer represent one such example because many recent studies demonstrate little clinical benefit for such patients treated using this strategy (21,22).

Yabroff et al. (15) acknowledge many of the challenges faced by oncologists in discussing the costs of genomic testing and related treatments with patients, including limited time, lack of training materials and discussion guides, and little price transparency for cancer tests and treatments. But the biggest challenge may be explaining to a patient the nuances of context of use and clinical utility that define the true value of a tumor biomarker test. Patients need to know not just what the test will cost but how it will inform their care, affect their options and outcomes, and whether, in the long run, it might even guide them to better treatments and/or lower their overall costs of care. Further research on how best to convey these complex issues in the course of a clinical encounter is desperately needed before we can effectively "talk the talk" about tumor genomic testing.

Notes

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