Economics and the New Generation of Targeted Therapies for Non–Small Cell Lung Cancer

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Lung cancer is probably the most substantial cancer problem faced by public and private health-care systems in the developed world, in terms of its human impact on lives lost and morbidity burden and in terms of its budget impact on those health-care systems. New treatments for lung cancer are thus an opportunity and a threat to every system that simultaneously seeks to improve the health of its members or citizens and to work within ever-tightening budget constraints. Most health-care payers outside the United States manage this tension between the needs for fiscal responsibility while improving health by using cost-effectiveness analyses to guide coverage and reimbursement for new treatments.

Erlotinib, a tyrosine kinase inhibitor, is an excellent example of the many challenges posed to health systems by modern targeted therapies in cancer. First, erlotinib has unequivocally been shown to be effective—albeit modestly so—for progression after platinum-based first-line chemotherapy for patients with non–small cell lung cancer. Because the tumors of almost all of these patients will eventually progress, erlotinib could in theory be seen as an extension of the general pharmacological management of lung cancer, with incremental impact on the overall budget for managing these patients. Should systems then expect (and support) erlotinib as part of the overall management? Second, emerging pharmacogenomic information indicates that we might be able to preselect patients for erlotinib therapy, which would allow systems to limit the budget impact and to improve outcomes for patients who receive the drug. Although the clinical data on the predictive value of testing for epidermal growth factor receptor (EGFR), which has tyrosine kinase activity, or of differential response by phenotype are incomplete, do the economic data compel us to modify our current approach to selecting patients for treatment?

The economic analysis of the National Cancer Institute of Canada Clinical Trials Group's BR.21 trial by Bradbury et al. (1) provides important new information to address these questions. First, they examined clinical information, resource use, and survival data for all 731 patients who participated in the study and found overall that the incremental cost-effectiveness of adding erlotinib was $95,000 per life-year gained, a marginal level of cost-effectiveness in their estimation. Second, the use of genomic data, specifically EGFR gene copy number, to preselect patients for erlotinib appears to greatly improve its cost-effectiveness. What should health systems, clinicians, and patients do with these data? As the authors note, many national health systems outside the United States have restrictions on erlotinib treatment because of earlier model–derived estimates of its cost-effectiveness. These trial-based results, although perhaps having greater internal validity, are unlikely to change those policies. The reason is that the confidence intervals around each point estimate are extremely wide, ranging from high value or even cost saving to extremely poor value. The high degree of uncertainty surrounding the estimate is an unfortunate limitation of cost-effectiveness studies conducted alongside clinical trials: The sample sizes are often insufficient to test economic hypotheses. Thus, as with clinical studies with confidence intervals that cross 1, it would be difficult for decision makers to make new policies, given the imprecision of these estimates.

In the United States, decisions are not made explicitly on the basis of cost-effectiveness, and erlotinib is in widespread use. In the United States, sales of erlotinib totalled $457 million in 2008 (Annual report to shareholders, 2008. Genentech, http://www.gene.com/gene/ir/financials/annual-reports/2008/2008annualreport.pdf). Is $95,000 per life-year gained poor value in the United States? In other words, are we wasting money by treating patients with erlotinib? Although the authors cite the threshold of $50,000 per life-year gained as evidence of poor cost-effectiveness, this number is suspect in its origin and is almost certainly too low by today's standards as a threshold for estimating acceptable vs poor treatment value (2,3). Although it is far less cost-effective than many things we do in medicine, erlotinib's cost-effectiveness as a second-line therapy is within the range of many commonly used cancer therapies and is well below the implied thresholds that have been derived from surveys of US oncologists (4).

It is thus possible that cost-effectiveness studies such as this one will lead to divergent treatment of non–small lung cancer in the United States compared with other developed countries. Outside the United States, health systems will likely refine their policies toward erlotinib as evidence emerges about predictive biomarkers. Given the cost of these biomarker tests (the authors did not include cost in their estimates of the various EGFR subgroup analyses) and the fact that biomarker assays are generally not standardized, studies would be quite helpful that evaluate the cost-effectiveness of phenotypic-guided (eg, preferential use in women with adenocarcinoma who are nonsmokers) vs biomarker-guided therapy with erlotinib and/or other EGFR tyrosine kinase inhibitor therapies. Given the prevalence of lung cancer, differential survival outcomes for patients, and the potential budget impact of guided therapy, the economic value of future studies in this area is likely to be quite high.

In the United States, it is unclear whether selective use of erlotinib that is based on phenotypic or genomic information would be acceptable to clinicians or patients. Because public and private
health insurers are unlikely to restrict access to erlotinib on the basis of EGFR test results, it would seem to be illogical that they would be willing to pay for such testing. Thus, the role of predictive testing in this country is unclear. The possible exception is if future studies that use these tests find complete or near-complete lack of benefit for specific subgroups of patients.

Erlotinib is one of several new therapies for non–small cell lung cancer that offers modest survival benefits at high cost. The unwillingness of public and private health systems and providers in the United States to consider costs in decisions about access to these products presents a clear signal to drug manufacturers. It also presents the rest of the world with a need for information that identifies patients for whom the amount of benefit of therapies such as erlotinib can support a value argument for their use.

References

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