Effectiveness and Cost Effectiveness of Bevacizumab in Metastatic Colorectal Cancer

TO THE EDITOR: In the comment by Saltz1 concerning the cost-effectiveness study on bevacizumab in metastatic colorectal cancer (MCRC) by Goldstein et al.,2 two points deserve additional scrutiny. First, Goldstein et al2 employed the pivotal trial on bevacizumab in MCRC as the source of effectiveness data for the estimation of the incremental benefit of the drug, and correctly posed the question of whether the data from a single trial could be suitable. In 2014, we published a meta-regression analysis on treatments for MCRC in which all randomized trials conducted between 2000 and 2012 were included (data were from 52 randomized trials with 130 study arms).3 The improvement in overall survival over this time interval was estimated to be 3.9 months per patient. By using meta-regression, we tried to parcel out the magnitude of the benefit directly related to bevacizumab (as opposed to the benefit related to other factors, such as favorable time trends or type of chemotherapy), and we estimated a value of 1.66 months per patient attributable to bevacizumab (data were from 17 patient arms treated with bevacizumab and 113 patient arms treated without bevacizumab). Interestingly, our estimate of incremental benefit, which was based on a series of numerous randomized trials, was nearly identical to the value determined by Goldstein et al2 from the pivotal trial (1.68 months per patient).

Second, the need to identify practical procedures that can lead to drug price reductions is, of course, a priority in this field. From this point of view, the Italian experience carried out by our National Medicines Agency (ie, AIFA)4 is interesting, because the agency has chosen to keep the drug prices of anticancer agents close to the prices of these agents in other European countries to avoid international parallel exports driven by price differences. At the same time, the agency has settled with the manufacturers a series of payment-by-results agreements that refund drug costs for all occurrences of clinical failure (ie, paybacks). These paybacks, which are quantified according to the nationwide success rates observed with these drugs in the Italian hospitals, have led to the creation of national registries that include all treated patients. For bevacizumab, the national registry was set up in June 2008 and has since enrolled a total of 9,678 patients treated for MCRC plus 8,720 patients treated for other clinical indications of the drug (information up to date as of March 8, 2015). When the same drug is approved for two or more clinical indications, one advantage of this approach is that the cost-effectiveness ratio is tailored to the benefit expected for each individual indication; this allows us to keep the same nominal price for the different indications of a given drug and, at the same time, to increase the amount of refunded money for the indications when a small benefit is expected.4

Despite some practical problems that hampered the management of these registries, paybacks are now an important component of our pharmaceutical sustainability. In an Italian study on the cost effectiveness of newly marketed anticancer agents5 (from 2010 to 2013), the incremental cost-effectiveness ratios (ICERs) were more favorable in Italy (including adjustments for paybacks when applicable) than those reported in the United States for the same agents.6 With bevacizumab, the drug cost estimate employed by Goldstein et al2 was $64.62 per 10 mg; in Italy, the cost of bevacizumab in our National Health System (without paybacks) is approximately €30.6 per 10 mg (or $33.05 if €1 = $1.08) but can be reduced by up to 29% if paybacks are included. Thus, our drug cost is approximately three-fold less than that in the United States. Consequently, our ICER tends to be three-fold more favorable than in the United States; conversely, our ICER remains unfavorable (approximately $140,000 per life-year gained in first-line treatment), but much less unfavorable than the ICER in the United States (approximately $408,000 per life-year gained2).

In conclusion, different countries are currently facing the same problems represented by high-cost, oncologic, targeted therapies. Although solutions to this problem differ among countries because of the differences in the organization of their health care systems and in the drug prices, one critical issue clearly emerges when the ICER of specific treatments goes beyond the threshold of acceptability. Because these negative outliers are not necessarily the same across different countries, regulatory agencies and health care payers will have the duty, more now than in the past, to systematically monitor the ICER of anticancer treatments and to devise corrective interventions for treatments characterized by unfavorable pharmacoeconomic profiles.

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AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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1. Saltz LB: Can money really be no object when cancer care is the subject? J Clin Oncol 33:1093-1094, 2015

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