Cost-Minimization Analysis of the Treatment of Patients With Metastatic Colorectal Cancer in Greece

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ABSTRACT

Background: In 2008, colorectal cancer was the fourth most common cause of cancer-related death worldwide. Monotherapy with monoclonal antibodies directed against the epidermal growth factor receptor, such as cetuximab and panitumumab, has recently been introduced in the management of metastatic colorectal cancer (mCRC) patients.

Objective: The aim of this study was to conduct a cost-minimization analysis comparing panitumumab with cetuximab in the treatment of patients with epidermal growth factor receptor–expressing mCRC with nonmutated (wild-type) Kirsten rat sarcoma viral oncogene homolog in Greece. The perspective of analysis was that of payers (Social Security Sickness Fund) and the country's National Health Service (NHS).

Methods: The model was designed to contain probabilistic parameters to account for uncertainty and variation in these parameters. All resources consumed in local hospitals in the management of patients in each case were evaluated. Two analyses were performed: 1 evaluating cost per milligram and another evaluating cost per vial.

Results: From a payer perspective, the mean 20-week total cost per patient for panitumumab and cetuximab was: (1) per-milligram analysis: €16,349 and €18,242, respectively; and (2) per-vial analysis: €18,808 and €19,701. From the NHS perspective, the mean total costs per patient were slightly higher; however, the use of panitumumab was associated with a 17.7% and 12.4% cost reduction in per-milligram and per-vial analysis, respectively. The results of probabilistic models confirmed those of the deterministic analyses.

Conclusion: In the Greek NHS and Social Security Sickness Fund setting, panitumumab monotherapy potentially constitutes a cost-saving option (versus cetuximab monotherapy) in the management of patients with mCRC and no mutation of Kirsten rat sarcoma viral oncogene homolog. (*Clin Ther*. 2012; 34:2132–2142) © 2012 Elsevier HS Journals, Inc. All rights reserved.

Key words: antiepidermal growth factor receptors, colon and rectum patients, cost-minimization analysis, monoclonal antibodies.

INTRODUCTION

In 2008, according to figures from the International Agency for Research on Cancer, colorectal cancer (CRC) was the third most commonly diagnosed cancer worldwide (9.7%) and the fourth leading cause of cancer-related mortality, accounting for 610,000 deaths (8.1% among all cancer deaths).[1,2] In the same year in Europe, CRC was the most common type of malignancy (13.6% of the total) and the second leading cause of cancer-related deaths (12.4%). In Greece, incidence rates have been estimated at 15.4 and 11.15 per 100,000 men and women, respectively, and the age-standardized mortality rate was estimated, in 2008, at 9.1 and 6.1 per 100,000 men and women.[2,3]

The choice of treatment depends on the stage of the cancer. Surgery remains the definitive treatment for localized CRC, offering the only chance of cure, whereas chemotherapy and/or radiotherapy may be used as adjuvant interventions depending on the loca-

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tion of the patient's staging tumor and other medical factors. Nonetheless, the disease may be diagnosed at a late stage or patients originally treated with surgery may eventually develop metastatic disease, for which palliative systemic chemotherapy is recommended.[4] There is evidence from many studies and systematic reviews that chemotherapy for metastatic CRC (mCRC) can alleviate symptoms and prolong survival.[5,6] Conventional chemotherapy used to treat mCRC include intravenous drugs such as oxaliplatin, irinotecan, and 5-fluorouracil (5-FU; usually given with intravenous leucovorin) and the 5-FU prodrug capecitabine. These drugs work by interfering with the ability of the rapidly growing cancer cells to divide or reproduce.

In addition to chemotherapy, 3 other agents are available for the treatment of mCRC. To date, 2 types of monoclonal antibodies have been approved by the US Food and Drug Administration and the European Medicines Agency for clinical use in the first- and second-line management of mCRC: the anti–vascular endothelial growth factor (VEGF) receptor antibody bevacizumab and the anti– epidermal growth factor receptor (EGFR) antibodies cetuximab and panitumumab.[7] Clinical trials have shown that these regimens improve the overall survival and progression-free survival of patients with mCRC.[7–12]

These antibodies inhibit specific proteins that are important for the growth and/or survival of colon cancer cells. Because targeted chemotherapy does not directly interfere with rapidly dividing cells, they do not have the usual adverse effects of conventional chemotherapy. Bevacizumab binds to a protein called VEGF. Bevacizumab is generally given in combination with other drugs, such as oxaliplatin or irinotecan. Cetuximab and panitumumab target a different protein, the EGFR, which is found in ~80% of CRC. Cetuximab is a chimeric antibody whereas panitumumab is a fully human antibody designed to act against EGFR. Both cetuximab and panitumumab are indicated for use in patients in whom the tumor does not possess the Kirsten rat sarcoma viral oncogene homolog gene mutation; it has been shown that neither agent is effective in patients whose tumor has the Kirsten rat sarcoma viral oncogene homolog mutation. Administration of these 2 antibodies is dependent on each country's authorities; however, in Greece, cetuximab can be given either as monotherapy or in combination with chemotherapy, while panitumumab was available as a monotherapy until November 2011.*

Several combination chemotherapy regimens may be considered for the initial treatment (first-line) of mCRC. Each of these regimens consists of 2 or 3 drugs, used together in a specific way: oxaliplatin plus 5-FU and leucovorin, irinotecan plus 5-FU and leucovorin, oxaliplatin plus capecitabine, or irinotecan plus capecitabine. In Greece, as elsewhere, adding bevacizumab to these 4 regimens is often an available therapy option.* When, despite initial treatment with chemotherapy, CRC tumor continues to grow or when it begins to progress after an initial response to chemotherapy, patients have to be managed with second- or third-line chemotherapy, as long as the patient is well enough to tolerate additional therapy.[7,13] The choice of subsequent treatment typically depends on what was administered originally. Because bevacizumab, which targets VEGF, is often administered during first-line therapy, cetuximab and panitumumab, which target EGFR, are often considered in second- and third-line therapy.[7,9,14,15] Several studies have established the role of panitumumab and cetuximab in the management of patients with nonmutated (wild-type) Kirsten rat sarcoma viral oncogene homolog mCRC, after failure of first-line therapies containing fluoropyrimidine, oxaliplatin, and irinotecan regimens.[7–9,16,17]

The related literature and published studies indicate that the 2 regimens may be comparable in terms of efficacy.[8,9] However, differences in the unit drug price of the 2 alternatives, their model of administration, premedication, and monitoring requirements still exist, in which case their resource utilization and consequently their total treatment cost may differ substantially. For instance, panitumumab is more costly compared with cetuximab when their unit drug cost is considered. Conversely, the treatment schedule contains 2 visits per month for panitumumab but 4 visits per month for cetuximab; thus, total costs for these 2 drugs are different. In light of these factors, it may be important to examine which treatment is superior from an economic point of view for hospitals and payers.

Therefore, the aim of the current study was to conduct an economic evaluation comparing, from varying perspectives, panitumumab with cetuximab in the

*National Formulary, National Organization for Medicines, http://www.eof.gr.