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Survey and analysis of the costs of metastatic colorectal cancer treatment in Slovenia

Jakub Rutkowski[1], Mateusz Haldas[1], Kinga Jedynasty[2], Janja Ocvirk[3]

[1]HTA Consulting Krakow, Poland [2]Amgen GmbH, Head Office for Central & Eastern Europe [3]Institute of Oncology Lubljana

INTRODUCTION

- Colorectal cancer (CRC) is the fourth most common malignant tumour in the world. Worldwide, one million new cases are reported every year, and in 2007 CRC was the cause of death of 319,000 men and 284,000 women globally [1]. According to the Cancer registry of Republic of Slovenia and World Health Organization (WHO), the standardised mortality ratio in Slovenia is currently 20.3 per 100,000 people [2, 3].
- This study was designed to assess the cost of first-, second, third- and fourth-line treatment in patients with metastatic CRC (mCRC) in Slovenia in 2008 (as part of a multinational study in Central Europe) and to examine current practice in Slovenia, especially the utilization of monoclonal antibodies and to investigate the possibility of introducing new biological therapies in current practice.

OBJECTIVES

Primary objectives:

- describe the chemotherapy regimens used
- estimate the costs of the chemotherapy regimens, supportive care and medical procedures.

Secondary objectives:

- estimate additional costs related to chemotherapy (additional medications and services),
- estimate the proportion of patients treated with particular chemotherapy regimens,
- estimate the proportion of patients who refused chemotherapy,
- describe the factors affecting treatment choices made by oncologists.

METHODS

- This was expert opinion based study (based on the review of medical data). The data were collected by oncologist from oncology centre in Slovenia providing access to medical records of approximately 800 patients treated in 2008.
- Access to CEDAR was granted to the investigators. All connections were encrypted. Data on chemotherapy regimens used in clinical practice in the treatment of mCRC were collected and automatically validated by the application. Data on chemotherapy regimens used in clinical trials were excluded from the study.
- Direct medical costs from a public payer perspective were calculated from information provided by an oncologist on unit costs of medicines and services. Costs of chemotherapeutic drugs, administration of chemotherapy and hospitalisation, and additional medicines and services (related to application of chemotherapy and monitoring) were included in calculating the total cost of each regimen. Costs of treatment of adverse events were not estimated in this study.

CONCLUSION

- Most commonly used regimens were based on capecitabine, irinotecan (XELIRI) and bevacizumab or capecitabine, irinotecan (XELOX) and bevacizumab. All patients received regimens with monoclonal antibody in the first line. Less than 50% of patients was treated with the third line of chemotherapy.
- The average regimen cost was the highest in first-line therapy and decreased in the following lines. Costs of additional medications and services appeared to have minimal impact on the overall cost of therapy, irrespective of the treatment line.
- Ultimately, our study has shown that the use of targeted anti-cancer agents is associated with substantially high costs, however many studies have shown that they are also associated with survival gains, safety and reduction in adverse events.

REFERENCES

1. American Cancer Society. Global Cancer Facts and Figures 2007. http://www.cancer.org/acs/groups/content/@nho/documents/document/globalfactsandfigures-2007rev2p.pdf (6.9.2010).
2. Cancer Registry of RS. http://www.onko-i.si/eng/dejavnosti/epidemiologija_in_register_raka/registri_raka/register_raka_rs/index.html (21.9.2010).
3. http://www.who.int/entity/healthinfo/statistics/bodgbddeathdalyestimates.xls (6.9.2010).

RESULTS

Most commonly used regimens

- In first-line therapy, the highest percentage of patients (40%) was treated with regimens based on capecitabine, irinotecan and one of the monoclonal antibodies – bevacizumab or cetuximab (XELIRI + cetuximab, XELIRI + bevacizumab). 35% of patients received irinotecan, 5-FU, calcium folinate and monoclonal antibodies (regimens FOLFIRI + bevacizumab and FOLFIRI + cetuximab).
- In second line, nearly 39% was treated with capecitabine, oxaliplatin and monoclonal antibodies (XELOX + bevacizumab and XELOX + cetuximab). A similar percentage of patients in the third and fourth line was treated with FOLFIRI, FOLFOX, XELIRI, XELOX and one of the monoclonal antibodies (cetuximab or bevacizumab).
- Monoclonal antibodies were used in all regimens in the first, third and fourth line. Only 17% in the second line did not receive monoclonal antibodies.
- The most popular regimens administrated in the first, second, third or fourth line of treatment was XELIRI + bevacizumab (39% of patients) and XELOX + bevacizumab (34%).
- Approximately 10% of patients refused chemotherapy.

Figure 1. Most commonly used regimens in each line

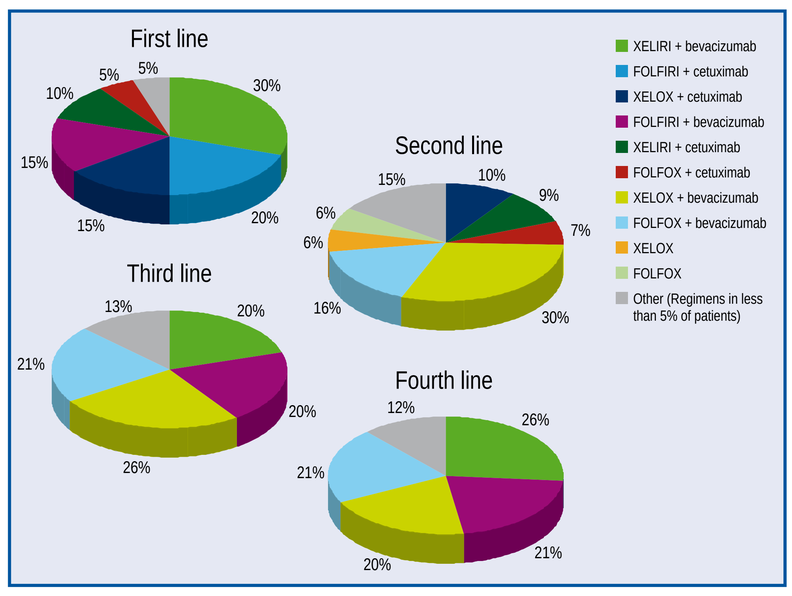

Table 1. Chemotherapy regimens used in the treatment of mCRC in Slovenia

Regimen	Medications
FOLFIRI + bevacizumab	irinotecan (1 dose x180 mg/m2 per cycle), 5-FU (1x400 mg/m2), calcium folinate (1x200 mg/m2), bevacizumab (1x5 mg/m2), 5-FU (1x2400 mg/m2)
FOLFIRI + cetuximab	cetuximab (2x250 mg/m2), irinotecan (1x180 mg/m2), calcium folinate (1x200 mg/m2), 5-FU (1x400 mg/m2), 5-FU (1x2400 mg/m2)
FOLFOX	oxaliplatin (1x100 mg/m2), calcium folinate (1x200 mg/m2), 5-FU (1x400 mg/m2), 5-FU (1x2400 mg/m2)
FOLFOX + bevacizumab	oxaliplatin (1x100 mg/m2), calcium folinate (1x200 mg/m2), 5-FU (1x400 mg/m2), bevacizumab (1x5 mg/m2), 5-FU (1x2400 mg/m2)
FOLFOX + cetuximab	cetuximab (2x250 mg/m2), calcium folinate (1x200 mg/m2), 5-FU (1x400 mg/m2), 5-FU (1x2400 mg/m2), oxaliplatin (1x100 mg/m2)
XELIRI	capecitabine (28x1000 mg/m2), irinotecan (1x250 mg/m2)
XELIRI + bevacizumab	capecitabine (28x1000 mg/m2), irinotecan (1x250 mg/m2), bevacizumab (1x7.5 mg/m2)
XELIRI + cetuximab	capecitabine (28x1000 mg/m2), irinotecan (1x250 mg/m2), cetuximab (3x250 mg/m2)
XELOX	capecitabine (28x1000 mg/m2), oxaliplatin (1x130 mg/m2)
XELOX + bevacizumab	capecitabine (28x1000 mg/m2), oxaliplatin (1x130 mg/m2), bevacizumab (1x7,5 mg/m2)
XELOX + cetuximab	capecitabine (28x1000 mg/m2), oxaliplatin (1x130 mg/m2), cetuximab (3x250 mg/m2)

Paths of treatment

- Most commonly used paths of chemotherapy with two lines are presented in Table 2.
- The percentages of patients receiving chemotherapy after the first line are presented in Figure 2.

Costs of treatment

- The mean cost of each regimen in each line of therapy is summarised in Figures 3–6.
- Overall, first-line therapy was most expensive, followed by second, third and then fourth line.
- Factors influencing the selection of chemotherapy by oncologists included: previous therapies, course of the disease, the patient's performance status, adverse events after previous chemotherapies, age of patient and concomitant diseases.

Table 2. Most common paths of treatment

First line	Second line	% of patients
XELIRI + bevacizumab	XELOX + bevacizumab	21%
FOLFIRI + bevacizumab	FOLFOX + bevacizumab	8%
XELIRI + bevacizumab	FOLFOX + bevacizumab	5%
FOLFIRI + bevacizumab	XELOX + bevacizumab	4%
FOLFIRI + cetuximab	XELOX + cetuximab	4%

Figure 2. Patients receiving chemotherapy after the first line

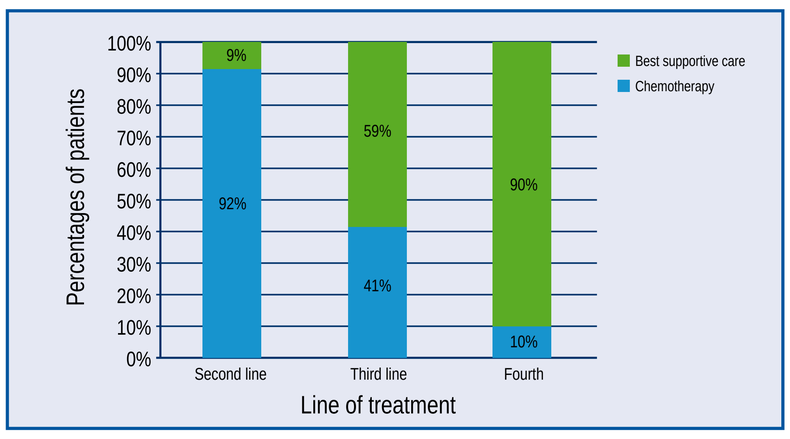

Figure 3. Total cost of regimens per patient in first-line therapy

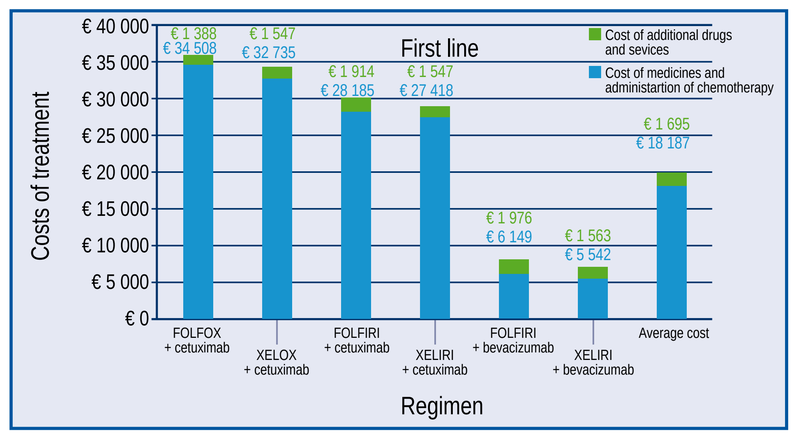

Figure 4. Total cost of regimens per patient in second-line therapy

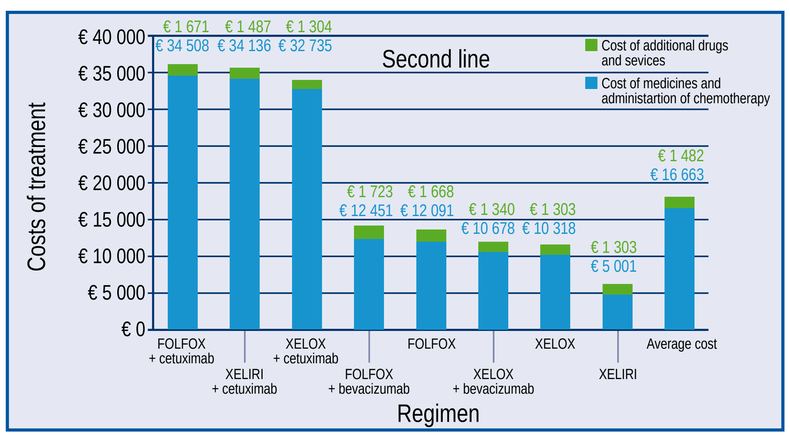

Figure 5. Total cost of regimens per patient in third-line therapy

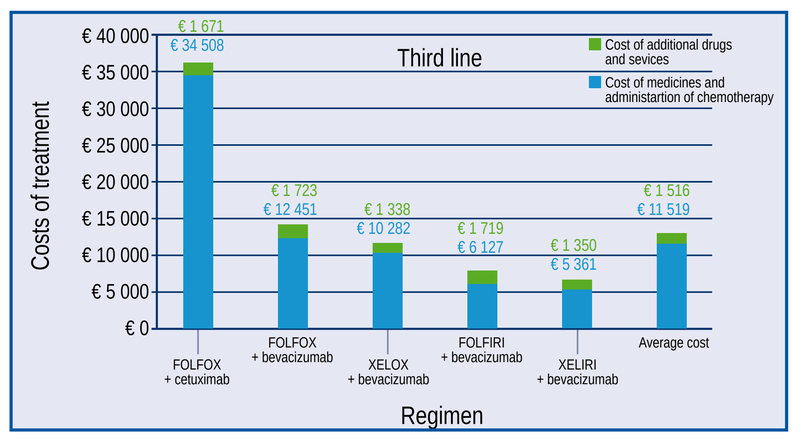

Figure 6. Total cost of regimens per patient in fourth-line therapy