

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

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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 World Health Organization (WHO), the standardised mortality ratio in Serbia is currently 16.7 per 100,000 people [2].
- This study was designed to assess the cost of first-, second, third- and fourth-line treatment in patients with metastatic CRC (mCRC) in Serbia (as part of a multinational study in Central Europe) and to examine current practice in Serbia, 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 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 choice made by oncologists.

METHODS

- This was an expert opinion-based study (based on the review of medical data). The data were collected by oncologists from four oncology centers in Serbia providing access to medical records of approximately 1,760 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 FOLFOX 4 A or FOLFIRI B. The vast majority of patients received chemotherapy in first, second and third line.
- Monoclonal antibodies were used rarely in Serbia. Bevacizumab was the most commonly used monoclonal antibody, primarily in the first-line therapy.
- The average regimen cost in third- and fourth-line therapy was higher than in first and second line. Costs of additional medications and services appeared to have minimal impact on the overall cost of therapy, irrespective of the treatment line.
- Regimens based on monoclonal antibodies incurred the highest costs. The average cost of these regimens was almost five times more expensive than the average cost of regimens without monoclonal antibodies.
- 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

- 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).
- <http://www.who.int/entity/healthinfo/statistics/bodgbdddeathalyestimates.xls> (6.9.2010).

RESULTS

Most commonly used regimens

- In first-line therapy, more than 40% of patients were treated with a calcium folinate and 5-FU regimen (Mayo clinic; Figure 1). A similar percentage of patients received regimens based on oxaliplatin, calcium folinate and 5-FU (FOLFOX 4) in the first-line setting. In approximately 16% of patients, bevacizumab (Avastin®; Roche) was used in combination with these medications.
- In second line, the majority of patients (51%) were treated with FOLFOX 4. A significant percentage of patients (almost 28%) received irinotecan, calcium folinate and 5-FU (FOLFIRI).
- In third line, more than 57% of patients received regimens based on FOLFIRI.
- The vast majority of patients in the fourth line received FOLFIRI and cetuximab (Erbix®; Merck Serono).
- The most popular regimens administered in the first, second or third line of treatment were FOLFOX 4 A (70% of patients) and FOLFIRI (50%).
- More than 2% of patients refused chemotherapy.

Figure 1. Most commonly used regimens in each line

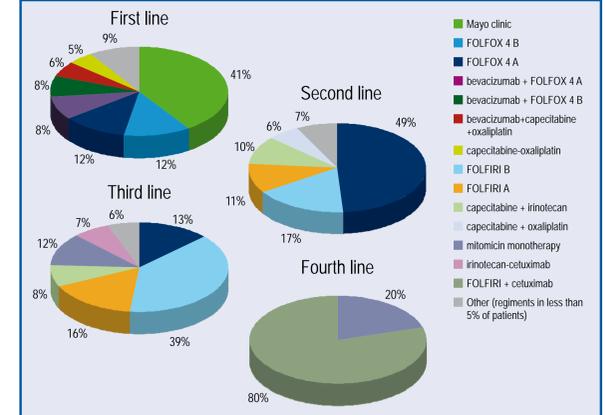


Table 1. Chemotherapy regimens used in the treatment of mCRC in Serbia

Regimen	Medications
bevacizumab + capecitabine + oxaliplatin	capecitabine (28 doses x2000 mg/m2 per cycle), oxaliplatin (1x130 mg/m2), bevacizumab (1x7.5 mg/kg)
bevacizumab + FOLFOX 4 A	bevacizumab (1x5 mg/kg), folinic acid (2x200 mg/m2), oxaliplatin (1x85 mg/m2), 5-FU (2x400 mg/m2), 5-FU (2x600 mg/m2)
bevacizumab + FOLFOX 4 B	bevacizumab (1x5 mg/kg), folinic acid (2x30 mg/m2), oxaliplatin (1x85 mg/m2), 5-FU (2x400 mg/m2), 5-FU (2x600 mg/m2)
capecitabine + irinotecan	irinotecan (1x180 mg/m2), capecitabine (28x1000 mg/m2)
capecitabine + oxaliplatin	oxaliplatin (1x130 mg/m2), capecitabine (28x1000 mg/m2)
capecitabine	capecitabine (28x1250 mg/m2)
capecitabine-oxaliplatin	oxaliplatin (1x100 mg/m2), capecitabine (28x1000 mg/m2)
FOLFIRI A	irinotecan (1x180 mg/m2), folinic acid (1x400 mg/m2), 5-FU (1x400 mg/m2), 5-FU (1x2400 mg/m2)
FOLFIRI B	irinotecan (1x180 mg/m2), folinic acid (2x30 mg/m2), 5-FU (2x400 mg/m2), 5-FU (2x600 mg/m2)
FOLFIRI + cetuximab	5-FU (2x400 mg/m2), 5-FU (2x600 mg/m2), folinic acid (2x200 mg/m2), irinotecan (1x180 mg/m2), cetuximab (1x400 mg/m2)
FOLFOX 4 A	folinic acid (2x200 mg/m2), oxaliplatin (1x85 mg/m2), 5-FU (2x400 mg/m2), 5-FU (2x600 mg/m2)
FOLFOX 4 B	folinic acid (2x30 mg/m2), oxaliplatin (1x85 mg/m2), 5-FU (2x400 mg/m2), 5-FU (2x600 mg/m2)
irinotecan-cetuximab	irinotecan (1x180 mg/m2), cetuximab (1x500 mg/m2)
Mayo clinic	folinic acid (5x20 mg/m2), 5-FU (5x425 mg/m2)
mitomycin monotherapy	mitomycin (1x10 mg/m2)

Paths of treatment

- Most commonly used paths of chemotherapy are presented in Table 2.
- The percentages of patients receiving chemotherapy after the first line are presented in Figure 2.
- The remaining patients received best supportive care.

Costs of treatment

- The mean cost of each regimen in each line of therapy is summarised in Figures 3–6.
- Overall, fourth-line therapy was the most expensive, followed by third, first and then second line. Biologic drug-containing regimens were always the most expensive in each line of therapy.
- 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 patients and concomitant diseases.

Table 2. Most common paths of chemotherapy (followed in ≥ 5% of patients)

First line	Second line	Third line	Fourth line	% of patients
FOLFOX 4 B	FOLFIRI B	mitomycin monotherapy	-	9%
Mayo clinic	FOLFOX 4 A	FOLFIRI A	-	9%
Mayo clinic	FOLFOX 4 A	FOLFIRI B	-	7%
FOLFOX 4 A	FOLFIRI A	-	-	6%
Mayo clinic	FOLFOX 4 A	-	-	5%
bevacizumab + FOLFOX 4 B	FOLFIRI B	mitomycin monotherapy	-	5%

Figure 2. Patients receiving chemotherapy after the first line

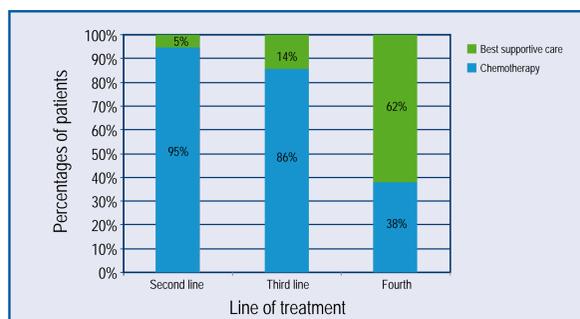


Figure 3. Total cost of regimens per patient in first-line therapy

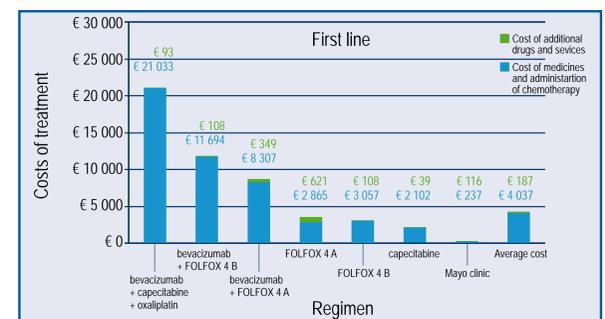


Figure 4. Total cost of regimens per patient in second-line therapy

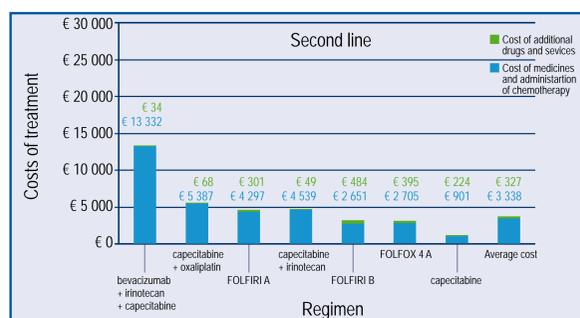


Figure 5. Total cost of regimens per patient in third-line therapy

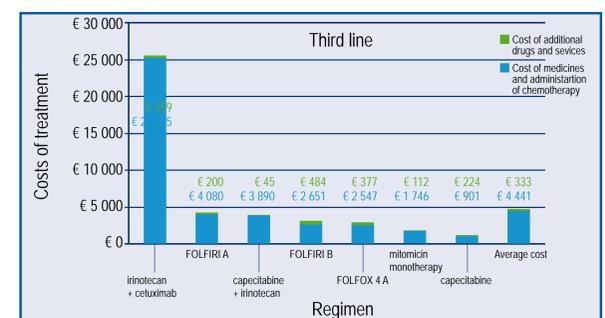


Figure 6. Total cost of regimens per patient in fourth-line therapy

