

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

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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 Bulgaria is currently 17.2 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 Bulgaria (as part of a multinational study in Central Europe) and to examine current practice in Bulgaria, 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 an expert opinion based study (based on the review of medical data). The data were collected by oncologists from 4 oncology centres in Bulgaria providing access to medical records of approximately 1,220 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 oxaliplatin, calcium folinate and 5-FU (FOLFOX 4, FOLFOX 6) or irinotecan, calcium folinate and 5-FU (FOLFIRI).
- Monoclonal antibodies were used rarely in Bulgaria. Less than 50% of patients was treated with the third line of chemotherapy.
- The average regimen cost in first-line therapy was the highest in comparison with costs in other lines. 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 60% higher than the average cost of regimens without monoclonal antibodies, however the most expensive regimens (FOLFOX 4, FOLFIRI) did not contain biologic drugs.
- 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/bodgbddeathalyestimates.xls> (6.9.2010).

RESULTS

Most commonly used regimens

- In first-line therapy, the vast majority of patients (over 70%) was treated with regimens based on oxaliplatin, calcium folinate and 5-FU (FOLFOX 4 and FOLFOX 6). Nearly 20% received regimen based on irinotecan, calcium folinate and 5-FU (FOLFIRI).
- The FOLFIRI regimen was the most used in the second line (almost 75% of patients). 11% of patients treated with FOLFIRI were receiving additionally bevacizumab. Regimens based on oxaliplatin, calcium folinate and 5-FU were used less often (18% of patients).
- Starting with the third line the most commonly used regimen was capecitabine (more than 55% and 59% of patients in the third and fourth lines respectively).
- The regimens administered most often in first, second or third line therapy were FOLFOX 4 (62%), FOLFIRI (64% of patients) and capecitabine (55%)
- 4% of patients refused chemotherapy.

Figure 1. Most commonly used regimens in each line of therapy

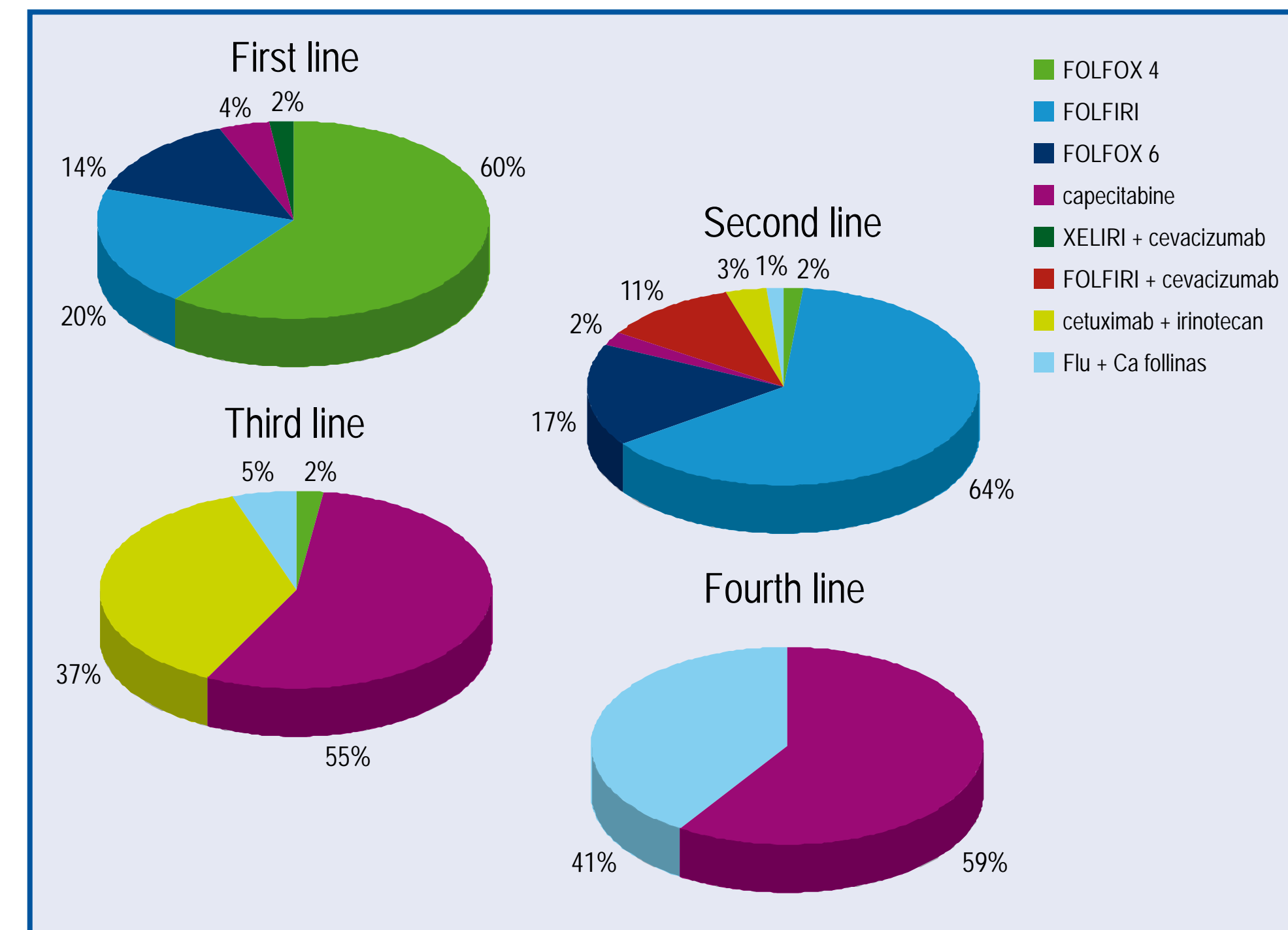


Table 1. Chemotherapy regimens used in the treatment of mCRC in Bulgaria

Regimen	Medications
Flu + Ca follinas	5-FU (2 doses x425 mg/m2 per cycle), calcium folinate (2x200 mg/m2)
FOLFOX 4	oxaliplatin (1x85 mg/m2), calcium folinate (2x200 mg/m2), 5-FU (2x2000 mg/m2)
capecitabine	capecitabine (14x2500 mg/m2)
FOLFOX 6	oxaliplatin (1x100 mg/m2), calcium folinate (1x400 mg/m2), 5-FU (1x400 mg/m2), 5-FU (1x2400 mg/m2)
FOLFIRI	irinotecan (1x180 mg/m2), calcium folinate (2x200 mg/m2), 5-FU (1x400 mg/m2), 5-FU (1x600 mg/m2)
FOLFIRI + bevacizumab	irinotecan (1x180 mg/m2), calcium folinate (2x200 mg/m2), 5-FU (1x400 mg/m2), 5-FU (1x600 mg/m2), bevacizumab (1x5 mg/kg)
XELIRI + bevacizumab	irinotecan (1x250 mg/m2), capecitabine (14x2000 mg/m2), bevacizumab (1x7.5 mg/kg)
cetuximab + irinotecan	irinotecan (1x250 mg/m2), cetuximab (1x250 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, first-line therapy was the most expensive, followed by third, second and fourth line therapies. 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 patient, availability of drugs in the catalogue of the Health Fund, data from clinical research 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	FOLFIRI	-	-	18%
FOLFOX 4	FOLFIRI	cetuximab + irinotecan	-	15%
FOLFOX 4	-	-	-	13%
FOLFOX 4	FOLFIRI	capecitabine	-	13%
FOLFIRI	FOLFOX 6	-	-	5%

Figure 2. Patients receiving chemotherapy after the first line

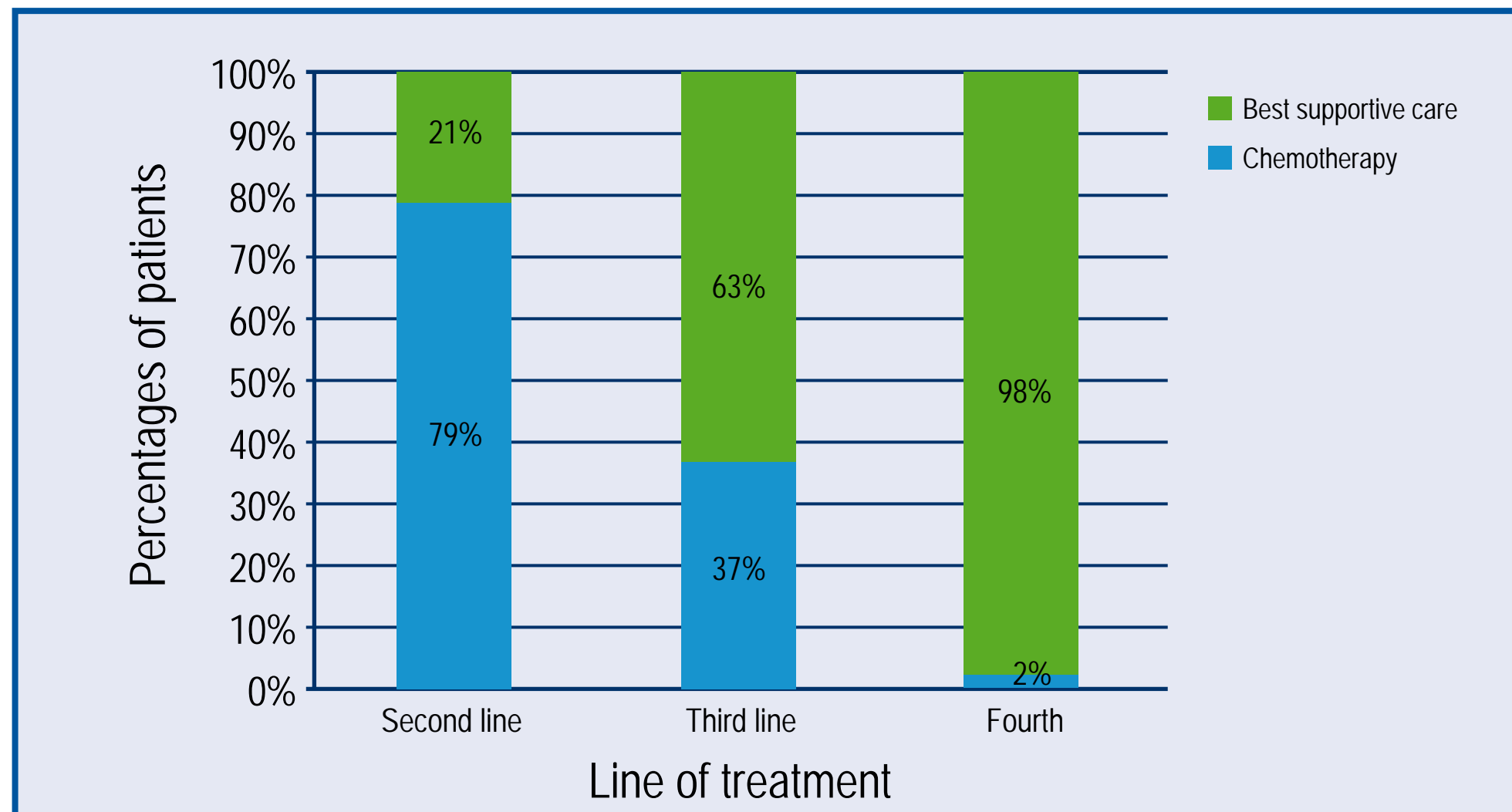


Figure 3. Total cost of regimens per patient in first-line therapy

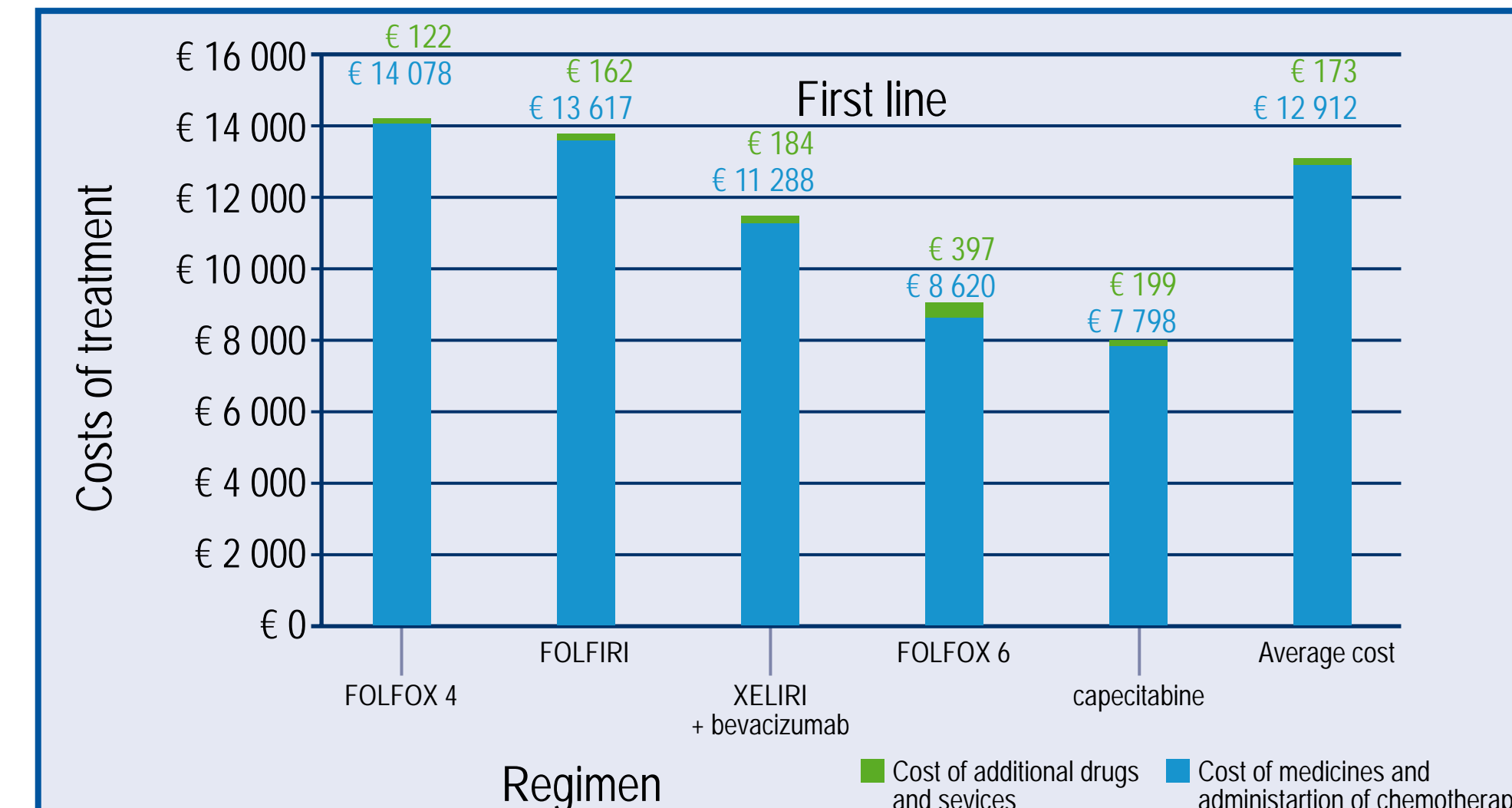


Figure 4. Total cost of regimens per patient in second-line therapy

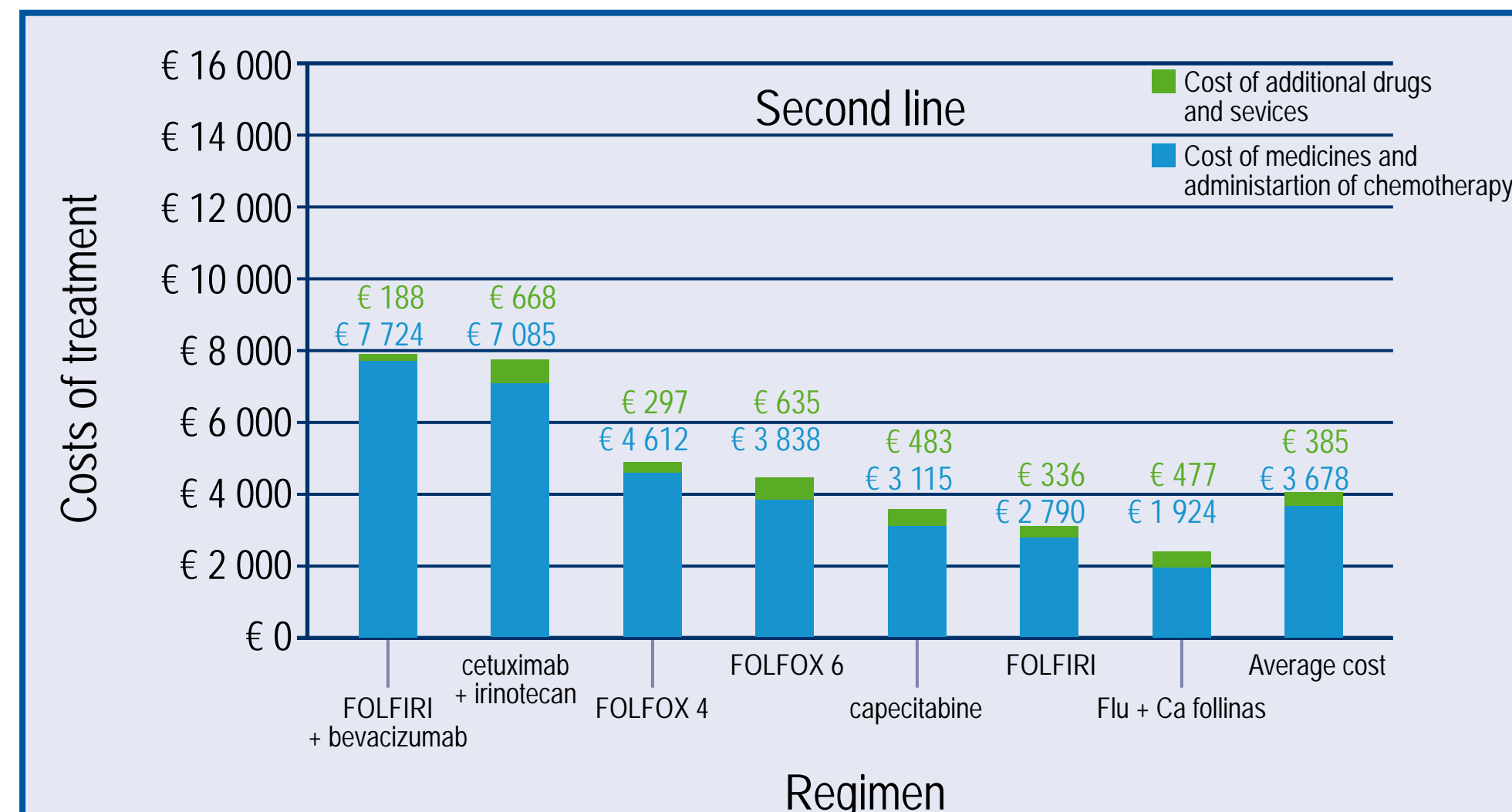


Figure 5. Total cost of regimens per patient in third-line therapy

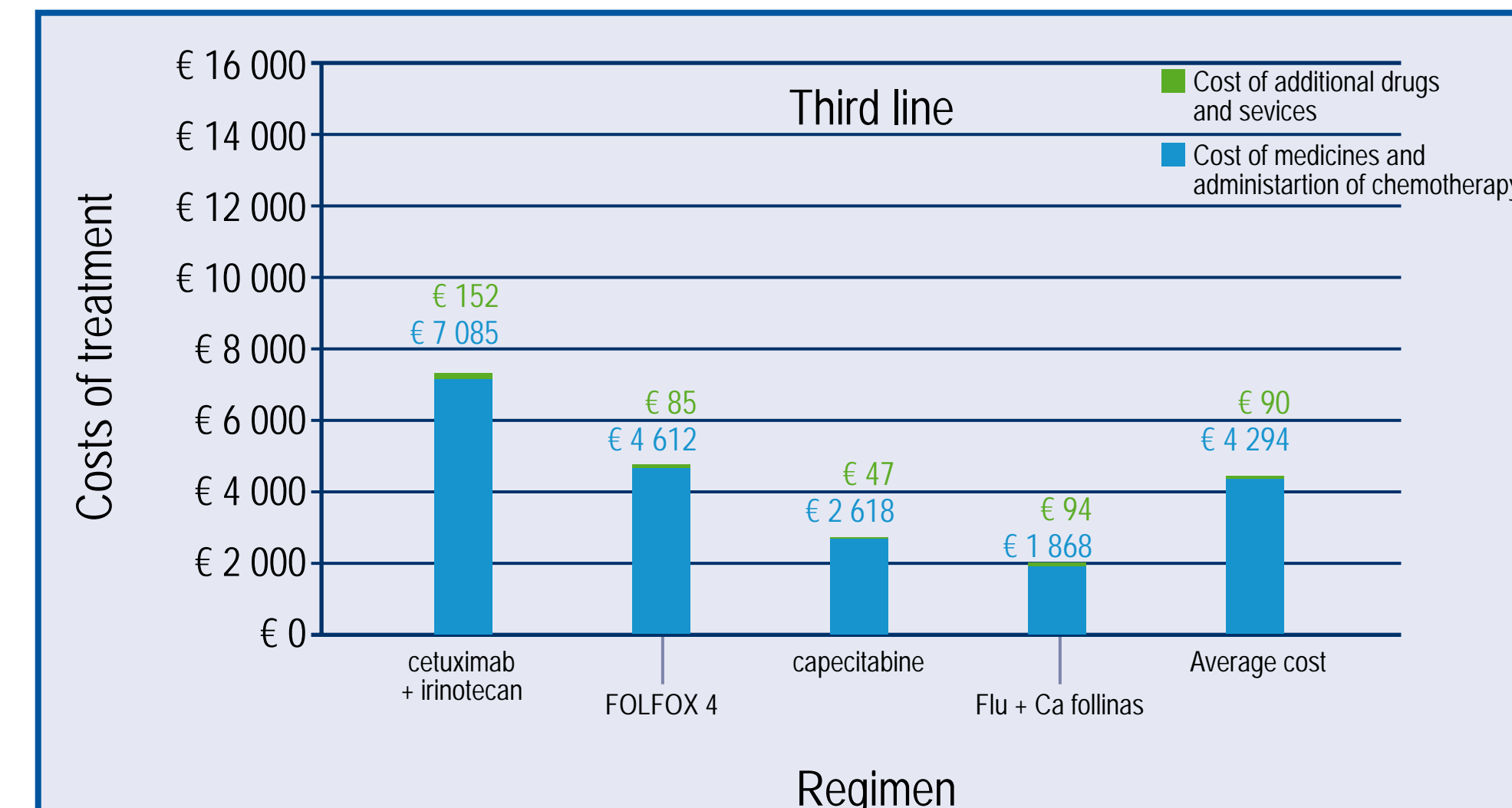


Figure 6. Total cost of regimens per patient in fourth-line therapy

