RBFHSS
Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde

Original Paper

Open Access

Cost minimization analysis of two chemotherapy regimens in the treatment of colorectal cancer in a public reimbursement hospital in Brazil

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Submitted: 06-12-2020 Resubmitted: 28-03-2021 Accepted: 01-04-2021

Peer review: Gustavo Baldin Tiguman and Mário Jorge Sobreira

Abstract

Objective: To conduct a pharmacoeconomic evaluation between XELOX and mFOLFOX6 in the adjuvant and metastatic treatment of colorectal cancer from the perspective of a public reimbursement hospital. **Methods:** The cost minimization analysis was conducted for patients who started treatment in 2013 and 2014. The micro-costing technique was used to verify expenditures on drugs, materials, laboratory and imaging tests, ambulatory and daily hospitalization, human and administrative resources and determine the individual cost of each alternative, per patient. To evaluate the robustness of the economic analysis, multivariate sensitivity analysis was performed in six different scenarios. **Results:** There was a mean cost for XELOX of USD 4,637.14 for adjuvant treatment and of USD 3,831.48 for palliative treatment, and a cost for mFOLFOX6 of USD 5,474.89 for the adjuvant treatment and of USD 4,432.95 for the palliative treatment. The sensitivity analysis maintained the dominance of XELOX. Material and drug costs accounted for approximately 85% of the total cost of XELOX; for mFOLFOX6, this cost was around 36%. On the other hand, the cost of hospitalization and placement of a catheter occurred exclusively for mFOLFOX6, which also presented a higher cost with human resources. **Conclusion:** From the perspective of the hospital, XELOX proved to be the least costly alternative for the treatment of colorectal cancer.

Keywords: colorectal neoplasms; antineoplastic agents; capecitabine; fluorouracil; leucovorin; costs and cost analysis.

Análise de custo minimização de dois esquemas quimioterápicos utilizados no tratamento do câncer colorretal em um hospital de ressarcimento público no Brasil

Resumo

Objetivo: Conduzir uma avaliação farmacoeconômica entre XELOX e mFOLFOX6 no tratamento adjuvante e metastático do câncer colorretal, na perspectiva de um hospital ressarcimento público. **Métodos:** A análise de custo minimização foi conduzida para pacientes que iniciaram o tratamento nos anos de 2013 e 2014. Técnica de microcusteio foi utilizada para verificar gastos com medicamentos, materiais, exames laboratoriais e de imagem, atendimento ambulatorial e diária de internação, recursos humanos e administrativos e determinar o custo individual de cada alternativa, por paciente. Para avaliar a robustez da análise econômica, foi realizada análise de sensibilidade multivariada em seis diferentes cenários. **Resultados:** Custo médio para XELOX foi de USD$ 4.637,14 na adjuvância e USD$ 3.831,48 para tratamento paliativo, e um custo para mFOLFOX6 de USD$ 5.474,89 na adjuvância e USD$ 4.432,95 no tratamento paliativo. A análise de sensibilidade manteve a dominância de XELOX. Os custos de materiais e medicamentos representaram cerca de 85% do custo total de XELOX; para mFOLFOX6 esse custo foi em torno de 36%. Já os custos com internação e colocação de cateter ocorreram exclusivamente para mFOLFOX6, que também apresentou maior custo com recursos humanos. **Conclusão:** Da perspectiva do hospital, XELOX mostrou-se a alternativa menos custosa no tratamento do câncer colorretal.

Palavras-chave: neoplasias colorretais; antineoplásicos; capecitabina; fluoruracila; leucovorina; custos e análise de custo.

Introduction

According to the WHO Global Cancer Observatory (GLOBOCAN), colorectal cancer (CRC) is the third most common cancer type in the world and the second in terms of mortality. It represents 10% of all cases, second only to breast (11.7%) and lung (11.4%) cancer.[1]

In Brazil, excluding non-melanoma skin cancer, CRC is the second most frequent, both in men and women. It accounts for approximately 40,000 new cases and around 20,000 deaths annually.[2] In addition to potential years of life lost, cancer has major impacts on the patient's quality of life and on family routine, as well as on individual and collective expenditures. A study that

analyzed the hospitalization rate of patients with CRC in Brazil between 1996 and 2008, in the Unified Health System (*Sistema Único de Saúde*, SUS), as well as the economic impact, verified that hospital admissions increased 173% from 1996 to 2008, and the total charges increased from USD 16.5 million to USD 33.5 million.[3]

Much of the health care expenses are related to chemotherapy. Since the 1960s, the fluorouracil compound (5FU) has been used in the treatment of CRC. Later it started to be administered with the leucovorin (LV) biochemical modulator and was associated with other compounds. The addition of irinotecan to 5FU/LV results in the FOLFIRI protocol. While the addition of oxaliplatin in different schemes sets up the FOLFOX 4, FOLFOX 6, mFOLFOX6, and FLOX protocols; mFOLFOX6 being a modification widely employed in Brazil. In the XELOX protocol, oxaliplatin is associated with capecitabine, a fluoropyrimidine that replaces fluorouracil.[4]

Comparisons between XELOX and FOLFOX were performed in studies such as the meta-analysis by Arkenau *et al* (2008)[5] for patients with stage IV CRC, by Schmoll *et al* (2014)[6] for stage III CRC, and by Guo *et al* (2016)[7] for metastatic CRC. Rothenberg *et al* (2008)[8] showed that XELOX is not inferior to FOLFOX4 as a second-line treatment for metastatic CRC. Cassidy *et al* (2008)[9] also showed the non-inferiority of XELOX in comparison to FOLFOX in the first line of metastatic CRC. In 2015, a randomized control trial (RCT) showed that XELOX and mFOLFOX6 are equally effective as adjuvants in stage II and III CRC[10], the only direct comparison clinical trial found for the adjuvant treatment.

To date, few economic assessments comparing XELOX and FOLFOX in CRC in Brazil have been reported; the papers by Caponero *et al* (2008)[11] and Ungari *et al* (2015) were identified.[12] Thus, this study aimed to conduct a pharmacoeconomic assessment between XELOX and mFOLFOX6 in the adjuvant and metastatic treatments of colorectal cancer from the perspective of a public reimbursement hospital and is noteworthy for being a cost minimization analysis using the micro-costing method and for including an assessment of the adjuvant treatment of colorectal cancer.

Methods

The study consisted in a pharmacoeconomic assessment of the cost-minimization type to compare the costs of the XELOX and mFOLFOX6 protocols. The study was conducted from the perspective of a teaching hospital, run by a philanthropic foundation, reference for 49 cities in the mountainous region of Rio Grande do Sul, which serves SUS patients, totaling a population of over one million inhabitants.

The cost-minimization method is the most adequate, since the literature indicated that the effectiveness of the treatment regimens is equivalent.[5,6,8-10]

The variables collected for the study population (clinical and sociodemographic characteristics) were extracted from the institution's electronic records. The following inclusion criteria were adopted: patient aged 18 years or older; diagnosed with malignant colon neoplasm and/or rectosigmoid and/or rectal junction by the International Classification of Diseases (ICD) codes C10- C18, C19 or C20, respectively; with a procedure from the High Complexity Procedure Authorization (*Autorização de Procedimento de Alta Complexidade*, APAC) table for mFOLFOX6 and/or XELOX; and who started treatment between January 1st, 2013 and December 31st, 2014. The exclusion criteria were the following: not having information in the computerized or physical record; and having started treatment at another institution.

The study was analyzed and approved by the Research Ethics Committee of the *Universidade de Caxias do Sul* Foundation under opinion number 1,774,890 on October 14th, 2016.

Cost identification and quantification

Using the micro-costing approach, where each cost component is estimated together with its cost unit[16], information on the consumption of health goods and services was collected retrospectively in consumption reports and electronic medical records, using the Tasy – Philips Healthcare system, to identify direct medical and non-medical costs. Micro-costing is a more accurate method for estimating hospital costs. To this end, analysis is carried out via hospital records of patients to determine the specific services used and, thus, assign the real cost to each of them.[15,16]

Considering that the number of treatment cycles is different between the protocols, a cost comparison was made over the treatment days, as recommended by Hirschfeld (2009).[17]

Data analysis had a descriptive character of the costs, expressed in dollars (USD), considering the purchasing power parity (PPP) of the year 2014 for Brazil[18], converted on January 10th, 2021.

The costs were computed during the time horizon corresponding to the duration of treatment, from the first medical consultation (when treatment was defined) until the end (end of treatment, disease progression or death), plus one month (return time for follow-up). As the costs came from different years, the official inflation index, the National Consumer Price Index (*Índice Nacional de Preços ao Consumidor*, IPCA), was used to make the monetary update of the values for the year 2013, the base date being 12/2014. No discount adjustment was applied, as the treatment time was less than one year.

The values of care in the Oncology Outpatient Clinic and the daily rate for Oncology Hospitalization were calculated based on administrative records on the number of care appointments and hospitalizations performed in the outpatient clinic and in the hospitalization sector, resulting from the reports of the management system. In addition to this, this information was used to apportion expenses for consumption of items in common use. The electronic medical records provided information on the use of supplies, medications and services for each patient included in the study throughout their treatment.

To determine the direct medical personnel cost, Nurses, Physicians and Pharmacists were interviewed regarding the mean time in minutes spent on patient care. The amount of the remuneration per minute was obtained from the administrative records of the human resources sector, and the hourly wage plus labor charges was computed. Also in the measurement of e direct medical costs, the cost was assessed with a nursing technician, assigning a mean cost per patient, according to the sector where the patient was treated. To determine the direct non-medical costs with the Nurse Manager, Secretary, and Sanitizers, the number of professionals, the workload, and the wage/hour plus charges were obtained. Subsequently, the number of professionals in each sector was multiplied by the workload, by the hourly work value. The result was divided either

by the number of care appointments or by its mean, number of hospitalizations or hospitalization rate, to then compose the cost of the day or care appointment.

Statistical analysis and sensitivity analysis

The descriptive statistical analysis of the data was performed in the STATA/SE program, version 12.0. To assess the robustness of the economic analysis, multivariate sensitivity analysis was performed. The plausible variation ranges built the scenarios: 1 – mean costs and mean quantity used; 2 – minimum costs and minimum quantity used; 3 – maximum costs and maximum quantity used; 4 – purchasing costs for the Federal Government and mean quantity used; and scenarios 5 and 6 – variation of 20% increase and reduction of the mean costs.

In scenario 4, for the costs of the Federal Government, via the Ministry of Health with materials and medicines, the data were collected from the database of the Integrated System of General Services (*Sistema Integrado de Serviços Gerais*, SIASG), through access to the Health Price Bank (*Banco de Preços em Saúde*, BPS), locating the last purchase made for the state of Rio Grande do Sul, in 2016.

To verify the robustness of the results regarding the remuneration of the human resources, the sensitivity analysis used amounts paid in other health institutions. Thus, we used data from the Transparency Portal of the Caxias do Sul City Hall, referring to the December 2016 salaries, to identify the amounts paid per hour worked of public servants with 5 years of service time, for each professional category.

The study underwent reporting quality assessment, by one of the authors, using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) from the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force[19], a tool that contains 24 items to be verified. The total score was obtained by assigning a point for each "yes" answer and zero for all other answers. The score obtained was 18 for the 24 items evaluated.

Results

Ninety-eight patients with CRC were identified, where 59 presented APAC for treatment. Of these, 42 met the inclusion criteria, but five patients did not have follow-up records. Thus, the study population was 37 patients: 6 in the XELOX group and 31 in the mFOLFOX6 group, Table 1.

Direct medical cost categories identified: medications (chemotherapy and pre-chemotherapy), materials (preparation and administration of medications), personnel (pharmaceutical assistance, Nursing care and nursing technician; medical consultation and assessment), laboratory tests (previous examinations at each cycle), imaging exams (exams during treatment), catheter (cost and placement by the vascular doctor). The direct non-medical costs were identified in nine categories: water and sewage; electrical energy; nutrition; maintenance and conservation; cleaning and hygiene materials; Personal Protective Equipment (PPE) (outpatient and inpatient consumption); personnel (Nurse Manager, Nursing Technician, Secretary, Sanitizer at the Oncology Outpatient Clinic and Sanitizer at the Oncology Hospital); laundry (supplies and human resources to wash 1 kg of clothes); medical and statistical filing service (*Serviço de Arquivamento Médico e Estatístico*, SAME).

Table 1. Sociodemographic and clinical characteristics of the population under study (n=37) in number of patients (N) and percentage (%) according to the treatment protocol.

Information	FOLFOX6 N = 31	XELOX N = 6
	n (%)	n (%)
Sociodemographic		
Age at diagnosis (years old)		
<30	2 (6.45)	-
31-50	6 (19.35)	1 (16.67)
51-70	21 (67.75)	3 (50.00)
71-90	2 (6.45)	2 (33.33)
Male gender[1]	17 (54.84)	4 (66.67)
Clinical data		
Comorbidities[1]	23 (74.20)	3 (50.00)
Smoking		
Yes	6 (19.35)	1 (16.67)
No	14 (45.16)	2 (33.33)
Former smoker	9 (29.04)	3 (50.00)
Stranger	2 (6.45)	-
Alcoholism		
Yes	3 (9.68)	-
No	21 (67.75)	2 (33.33)
Former drinker	5 (16.12)	4 (66.67)
Stranger	2 (6.45)	-
Concomitant medications		
0-2	23 (74.19)	5 (83.33)
3-5	7 (22.58)	1 (16.67)
> 6	1 (3.23)	-
Diagnosis		
Colonic Neoplasm (C18)	21 (67.74)	5 (83.33)
Rectal neoplasm (C20)	10 (32.25)	1 (16.67)
Morphological type: adenocarcinoma	31 (100.00)	6 (100.00)
Topography		
Cecum	-	-
Sigmoid colon	8 (25.80)	5 (83.33)
Ascending colon	10 (32.25)	-
Descending colon	2 (6.45)	-
Transverse colon	1 (3.23)	-
Upper rectum	3 (9.70)	1 (16.67)
Mid rectum	2 (6.45)	-
Lower rectum	5 (16.12)	-
Staging		
I	-	1 (16.67)
II	2 (6.45)	-
III	12 (38.70)	2 (33.33)
IV	17 (54.84)	3 (50.00)
Performance Status		
0	17 (54.84)	2 (33.33)
1	14 (45.16)	4 (66.67)
Surgical treatment[1]	19 (61.29)	2 (33.33)
Previous chemotherapy treatment[1]	4 (12.90)	1 (16.67)
Alive at the end of the treatment[1]	18 (58.06)	2 (33.33)

[1] Dichotomous variable for which the result of only one category was presented.

Table 2. Cost of outpatient care and inpatient daily rate (USD) for the years 2013 and 2014.

Cost Elements	Outpatient Care		Daily Inpatient Care Cost	
	2013	2014	2013	2014
General expenses	**Annual cost (USD)**		**Annual cost (USD)**	
Water and sewage, electricity, maintenance and conservation, cleaning and hygiene materials.	18,192.61	19,316.11	35,246.46	44,931.34
Number of care appointments/hospitalizations	7,317.15	7,007.17	442.36	440.15
Cost per care appointment/hospitalization	1.37	1.52	43.95	56.30
Human Resources	**Daily cost (USD)**		**Daily cost (USD)**	
Nurse Manager, Secretary, Sanitizer.	7.59	7.50	11.13	13.70
Other costs	Daily cost (USD)		Daily cost (USD)	
Nutrition, PPE[1], SAME[2]	2.62	2.63	-	-
Laundry (0.5 kg of linen) and SAME	-	-	0.78	0.83
Total	11.59	11.65	55.86	70.85
Monetary restatement by the IPCA[3] (6.40%)	0.75	-	3.57	-
Final cost per care appointment (USD)	12.33	11.65	59.44	70.85

[1]PPE: Personal Protective Equipment. [2]SAME: Serviço de Armazenamento e Estatística. [3]IPCA: Índice Nacional de Preços ao Consumidor. [4]USD: United States Dollars.

Table 3. Mean time in minutes (min) and mean cost in American dollars (USD) for mFOLFOX6 and XELOX for hospitalization and day and/or day of outpatient care.

Protocol		Pharmacist		Nurse		Physician	
		Time (min)	Cost (USD)	Time (min)	Cost (USD)	Time (min)	Cost (USD)
mFOLFOX6	1st hospitalization day	80	17.08	40	8.14	30	35.03
	Subsequent hospitalization days	50/hospitalization	10.67	20/day	4.07	15/day	17.51
	1st day of outpatient care	80	17.07	75	15.27	30	35.03
	Subsequent days of outpatient care	50	10.67	55	11.18	15	17.51
XELOX	1st day of outpatient care	70	14.94	70	14.24	30	35.03
	Subsequent days of outpatient care	35	7.46	50	10.17	15	17.52

Table 2 presents the cost elements by cost minimization analysis that constitute the cost of outpatient care and inpatient daily rate. The outpatient and daily inpatient care costs in 2013 were USD 12.33 and USD 59.44, respectively; and, in 2014, they were USD 11.65 and USD 70.85, respectively. Afterwards, the frequencies of care appointments and hospitalizations for each patient were considered to obtain the final cost of each therapeutic protocol.

The analysis of the personnel cost was performed by recording the mean time spent by each professional, valued according to the mean value of the hours worked in the years 2013 and 2014. It is verified that the costs of medical activities were higher, although the pharmacist and nurse spent more time in the activities, Table 3. The nurse is the professional who spent the most time in caring for the treated patients, in both protocols.

In the group treated with mFOLFOX6, 28 of the 31 patients were hospitalized for some chemotherapy cycle. The mean length of stay was 3.31 days, with a minimum of 3 and a maximum of 5 days. In addition, 20 of the 31 patients underwent some outpatient cycle. While in the XELOX group, there were no hospitalizations because the treatment cycles are performed on an outpatient basis.

The mean numbers of cycles performed in the adjuvant treatment with mFOLFOX6 and XELOX were 9.26 and 5.67 cycles; and, for the palliative treatment it was 7.87 and 4.67 cycles, respectively.

Then, the mean cost for each therapeutic protocol was obtained. The cost of the adjuvant treatment with mFOLFOX6 was USD 5,474.89, while that for XELOX was USD 4,637.14, with the mean cost per cycle being USD 591.24 and USD 817.84, respectively. In palliative treatment, the mean cost with mFOLFOX6 and XELOX was USD 4,432.95 and USD 3,831.48, respectively. The cost of each treatment cycle with mFOLFOX6 was USD 563.27 and with XELOX, it was USD 820.45.

Thus, supposing that there were no complications that would cause treatment interruption, in the XELOX protocol, the complete adjuvant treatment (8 cycles) would cost USD 6,542.70 and the palliative, USD 6,563.56. In the mFOLFOX6 protocol, the complete treatment (12 cycles) would cost a mean of USD 7,094.90 in the adjuvant and USD 6,759.27 for the palliative treatment.

Figure 1 shows the proportion of the cost components of each treatment. The component that added the most cost to XELOX was the cost of materials and medications, corresponding to 84%-85% of its cost, while for mFOLFOX6 it corresponds to 35%-37%. In the mFOLFOX6 regime, the personnel component (human resources) represented 24%-26% of the cost versus 5%-6% for XELOX, showing the weight that the activities of the professionals linked to assistance have in the final expense.

The results of the sensitivity analysis can be seen in Table 4. In the six scenarios built for the mean cost with each treatment (using the mean of the cycles verified in the study population), XELOX was a less expensive option than mFOLFOX6. The same was observed for all six scenarios assuming complete treatment by the patients.

Figure 1. Proportion (%) of each component of the costs with mFOLFOX6 and with XELOX in the palliative and adjuvant treatments.

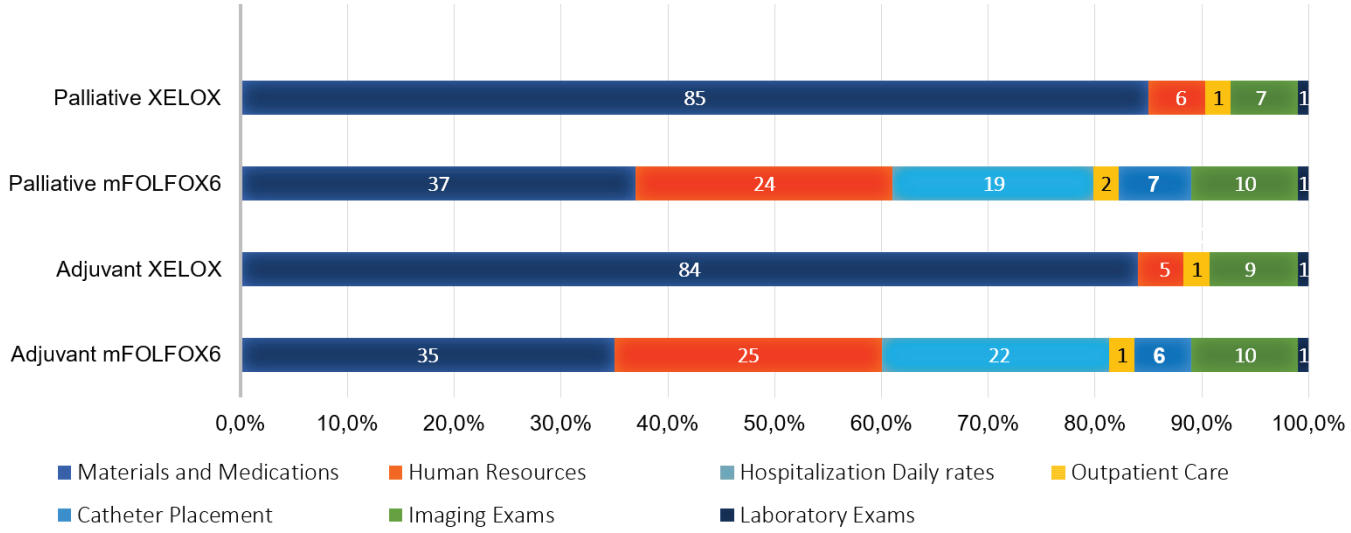

Table 4. Sensitivity analysis of the mean cost with XELOX (5.17 cycles) and mFOLFOX6 (8.55 cycles) and of the full cost with XELOX (8 cycles) and mFOLFOX6 (12 cycles).

Mean cost of the treatment (USD)			Full cost of the treatment (USD)		
Scenario	**XELOX**	**mFOLFOX6**	**Scenario**	**XELOX**	**mFOLFOX6**
1	3,946.15	6,977.77	1	6,106.22	8,001.64
2	2,804.52	4,314.22	2	4,339.68	4,819.57
3	5,231.88	11,140.66	3	8,095.76	12,944.89
4	2,517.63	8,459.06	4	3,895.74	9,872.54
5	3,106.82	5,582.21	5	4,807.44	6,401.31
6	4,670.08	8,517.39	6	7,226.44	9,813.73

Scenario 1- Mean population cost of the study; Scenario 2- Minimum population cost of the study; Scenario 3- Maximum population cost of the study; Scenario 4- Federal Government cost; Scenario 5- 20% reduction in the mean cost; Scenario 6- 20% increase in the mean cost; USD- American dollars.

Discussion

The cost minimization analysis resulted in a mean cost of USD 5,474.89 per patient in the adjuvant scenario and of USD 4,432.95 in the metastatic setting for mFOLFOX6, and USD 4,637.14 per patient treated in the adjuvant scenario and USD 3,831.48 in metastatic for XELOX. The difference in adjuvant and palliative treatment between the protocols was USD 837.75 and USD 601.48, respectively, in favor of mFOLFOX6.

Assuming that the 31 patients treated with mFOLFOX6 would have been treated with XELOX, the hospital would have saved USD 12,566.33 in the adjuvant treatment and USD 9,623.65 in the palliative modality, generating total savings of USD 22,189.98.

Hospitalization was the third component to add more cost to mFOLFOX6, constituting 19%-23% of the total cost. The costs of hospitalization and catheter placement occurred exclusively for mFOLFOX6; and for the other components, the mean cost per patient was higher for mFOLFOX6 than for XELOX.

The impact of each component on the regimens is similar to that shown in other pharmacoeconomic studies, where medications make up the main cost of the XELOX protocol, and care personnel costs are the main cost of mFOLFOX6[20-23]. The human resource costs with XELOX are evidently lower, up to four times lower than the costs with mFOLFOX6, a feature also observed in other studies[20,22-26], especially due to the reduction in time with protocol preparation and administration and with hospitalizations.

The XELOX protocol presented a higher cost per cycle than mFOLFOX6, for both scenarios; however, it is necessary to emphasize that the number of cycles required is 8 for XELOX and 12 for mFOLFOX6. Thus, when all the resources and the number of cycles are considered, XELOX becomes a dominant alternative, as it is less expensive.

It is important to compare the cost of the treatment cycle observed for the alternatives with the reimbursement made by the government. For stage III colon adenocarcinoma and advanced colon and rectal adenocarcinoma, the SUS pays hospitals a total of USD 1,226.70 per month regardless of the protocol adopted. Thus, XELOX (USD 817.84 and USD 820.45 per cycle) and mFOLOX6 (USD 591.24 and USD 563.27 per cycle) are options that fit the reimbursement amount since the treatment cycles take place every 21 days for XELOX and every 14 days for mFOLFOX6. For the treatment of stage III rectal adenocarcinoma, the APAC value is USD 235.80, without the possibility of covering the treatment with any of the alternatives. However, our costs are underestimated, since not all the costs involved could be estimated.

In the sensitivity analysis, XELOX remained at a lower cost for all scenarios, even when using current data from the Federal Government and the transfers defined by the SUS.

Although a microcurrency technique was used, not all costs could be verified as not all the administrative reports contained all the necessary information. In addition to that, it was not possible to estimate the indirect non-medical costs because these data were not available. However, the costs estimated by the micro-costing technique provide accurate information on the real costs of patients treated in a high-complexity public hospital, a reference in Oncology in the region.

Another limitation of the study is its small sample size. This is explained by the fact that protocols with intravenous rather than oral chemotherapy are more frequently prescribed in the hospital, a trend that can possibly be explained by the high cost of the oral antineoplastic medications themselves.

Conclusion

From the perspective of the hospital, XELOX presented a lower cost when compared to mFOLFOX6 in the adjuvant and palliative treatment of CRC. Despite the limitations, the estimates obtained are satisfactorily reliable and can assist in decision-making for the definition of treatment protocols for metastatic and adjuvant treatment of colorectal cancer in the country.

Funding sources

This research did not receive funding for its conduction.

Collaborators

SCB: conception of the project, data collection, data analysis and interpretation, and writing of the article. MRG: data analysis and interpretation, writing of the article and relevant critical review of the intellectual content. IH: conception of the project, data analysis and interpretation, writing of the article and relevant critical review of the intellectual content. The authors approve the final version of the manuscript and are responsible for all the information presented in the paper, ensuring the accuracy and integrity of any of its parts.

Acknowledgments

To the *Universidade de Caxias do Sul* Foundation and the Caixas do Sol General Hospital (*Hospital Geral de Caxias do Sul*, HGCS), which allowed us to conduct this research. To physicians Dr. André Reiriz, Dr. Rita Costamila and Dr. Janaína Brollo, for opening the doors of the High-Complexity Unit in Oncology (*Unidade de Alta Complexidade em Oncologia*, UNACON) of the HGCS to us. To Prof. Dr. Diego Gnatta and to Prof. Dr. Giácomo Balbinotto, for their encouragement and valuable teachings.

Conflicts of interest statement

The authors declare that there are no conflicts of interest regarding this article.

References

1. Sung H, Ferlay J, Siegel RL, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021.DOI: 10.3322/caac.21660.
2. Instituto Nacional do Câncer (INCA). Estimativa 2020: incidência de câncer no Brasil. Rio de Janeiro: INCA; 2019.
3. Torres US, Almeida US, Netinho JG. Increasing hospital admission rates and economic burden for colorectal cancer in Brazil, 1996-2008. Rev Panam Salud Publica. 2010;28(4):244-8. 10.1590/s1020-49892010001000002
4. Boscato SC, Heineck I, Godoy MR. Análise farmacoeconômica de XELOX em comparação à mFOLFOX6 no tratamento do câncer colorretal na perspectiva de um hospital universitário no sul do Brasil. Dissertação (Mestrado em Assistência Farmacêutica) – Programa de pós graduação em Assistência Farmacêutica, Universidade Federal do Rio Grande do Sul. Porto Alegre, 2017.
5. Arkenau HT, Arnold D, Cassidy J, *et al.* Efficacy of oxaliplatin plus capecitabine or infusional fluorouracil/leucovorin in patients with metastatic colorectal cancer: a pooled analysis of randomized trials. J Clin Oncol. 2008;20;26(36):5910-7. DOI: 10.1200/JCO.2008.16.7759.
6. Schmoll HJ, Twelves C, Sun W, *et al*. Effect of adjuvant capecitabine or fluorouracil, with or without oxaliplatin, on survival outcomes in stage III colon cancer and the effect of oxaliplatin on post-relapse survival: a pooled analysis of individual patient data from four randomised controlled trials. Lancet Oncol. 2014;15(13):1481-92. DOI: 10.1016/S1470-2045(14)70486-3.
7. Guo Y, Xiong BH, Zhang T, *et al*. XELOX vs. FOLFOX in metastatic colorectal cancer: An updated meta-analysis. Cancer Invest. 2016;34(2):94-104. DOI: 10.3109/07357907.2015.1104689.
8. Rothenberg ML, Cox JV, Butts C, *et al.* Capecitabine plus oxaliplatin (XELOX) versus s-fluorouracil/folinic acid plus oxaliplatin (FOLFOX-4) as second-line therapy in metastatic colorectal cancer: a randomized phase III noninferiority study. Ann Oncol. 2008;19(10):1720-6. DOI: 10.1093/annonc/mdn370.
9. Cassidy J, Clarke S, Díaz-Rubio E, *et al*. A randomized phase III study of capecitabine plus oxaliplatin (XELOX) versus fluorouracil/folinic acid plus oxaliplatin (FOLFOX4) as first line therapy for metastatic colorectal cancer. J Clin Oncol. 2008;26(12):2006-12. DOI: 10.1200/JCO.2007.14.9898.
10. Pectasides D, Karavasilis V, Papaxoinis G, *et al.* Randomized phase III clinical trial comparing the combination of capecitabine and oxaliplatin (CAPOX) with the combination of 5-fluorouracil, leucovorin and oxaliplatin (modified FOLFOX6) as adjuvant therapy in patients with operated high-risk stage II or stage III colorectal cancer. BMC Cancer. 2015;10; 15:384. DOI: 10.1186/s12885-015-1406-7.
11. Caponero R, Ribeiro RA, Santos E, *et al.* Medical resource use and cost of different first-line treatments for metastatic colorectal cancer in Brazil. J Med Econ. 2008;11(2):311-25. DOI: 10.3111/13696990802160817.
12. Ungari AQ, Pereira LRL, Perdoná GSC, *et al*. Cost evaluation of metastatic colorectal cancer treatment in the Brazilian Public Healthcare System. J Integr Oncol. 2015;4(2):1-5. DOI: : 10.4172/2329-6771.1000136.
13. Husereau D, Drummond M, Petrou S, *et al.* Consolidated Health Economic Evaluation Reporting Standards (CHEERS) - explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. Value Health. 2013;16(2):231-250.
14. Álvarez JS. Evaluación económica de medicamentos y tecnologias sanitarias: Principios, métodos y aplicaciones en política sanitária. Madrid: Springer; 2012.
15. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Ciência e Tecnologia. Diretrizes metodológicas: Estudos de avaliação econômica de tecnologias em saúde. Brasília: Ministério da Saúde; 2014.
16. Rascati K.L. Introdução à farmacoeconomia. Porto Alegre: Artmed; 2010.
17. Tan SS. Microcosting in Economic Evaluations: Issues of accuracy, feasibility, consistency and generalizability. Rotterdam: Erasmus Universiteit Rotterdam; 2009.

18. Organização para a Cooperação e Desenvolvimento Econômico (OECD) 2021, Purchasing power parities (PPP) (indicator). doi: 10.1787/1290ee5a-en. Available in: https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm#indicator-chart. Accessed on: January 10, 2021.

19. Hirschfeld H. Engenharia Econômica e Analise de Custos. Edição 7. São Paulo: Atlas; 2009.

20. Tse VC, Ng WT, Lee V, *et al.* Cost-analysis of XELOX and FOLFOX4 for treatment of colorectal cancer to assist decision-making on reimbursement. BMC Cancer. 2011;11:288. DOI: 10.1186/1471-2407-11-288

21. Van Gils CW, de Groot S, Redekop WK, *et al*. Real-world cost-effectiveness of oxaliplatin in stage III colon cancer: a synthesis of clinical trial and daily practice evidence. Pharmacoeconomics. 2013;31(8):703-18. DOI: 10.1007/s40273-013-0061-6.

22. Ho MY, Chang AY, Ruan JY, *et al.* Population-based Cost Minimization analysis of CAPOX versus modified FOLFOX6 in the adjuvant treatment of stage III colon cancer. Clin Colorectal Cancer. 2016;15(2):158-63. DOI: 10.1016/j.clcc.2015.09.004

23. Ducreux M, Bennouna J, Hebbar M, *et al.* Capecitabine plus oxaliplatin (XELOX) versus 5-fluorouracil/leucovorin plus oxaliplatin (FOLFOX-6) as first-line treatment for metastatic colorectal cancer. Int J Cancer. 2011;1;128(3):682-90. DOI: 10.1002/ijc.25369

24. Aitini E, Rossi A, Morselli P, *et al.* Economic comparison of capecitabine plus oxaliplatin and 5-fluorouracil plus oxaliplatin in the adjuvant treatment of colon cancer. Cancer Manag Res. 2012;4:99–103. DOI: 10.2147/CMAR.S29267.

25. Wen F, Yao K, Du ZD, *et al.* Cost-effectiveness analysis of colon cancer treatments from MOSAIC and No. 16968 trials. World J Gastroenterol. 2014;21;20(47):17976–84. : 10.3748/wjg.v20.i47.17976.

26. Tran G, Hack SP, Kerr A, *et al.* Pharmaco-economic analysis of direct medical costs of metastatic colorectal cancer therapy with XELOX or modified FOLFOX-6 regimens: implications for health-care utilization in Australia. Asia Pac J Clin Oncol. 2013;9(3):239-48. DOI: 10.1111/ajco.12044.