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Chemotherapy for advanced colorectal patients: daily practice results may not reflect the outcomes of prospective clinical trials

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Introduction. Colorectal cancer is the second cause of cancer deaths worldwide. The development of new drugs in recent years has improved the outcomes, but it is not clear whether this progress also includes patients managed in daily clinical practice. Treatment outcomes in patients with advanced colorectal cancer treated in Poland outside of clinical trials are scare.

Methods. We analyzed the results of first-line chemotherapy in 165 patients with advanced colorectal cancer treated between May 2010 and December 2013 in two institutions.

Results. The mean patient age was 61 ± 8.7 years; 105 patients received irinotecan-based regimens (CLF1 or XELIRI), 41 oxaliplatin-based regimens (FOLFOX4 or XELOX) and 19 patients received single-agent 5-fluorouracil. A partial response was achieved in 48 patients (29%), stable disease in 71 (43%) and 46 patients (28%) progressed during treatment. Median survival in the entre group was 14 months. Respective average response rate and median overall survival in recent clinical trials were 39% and 17 months, respectively. Compared to single agent treatment, multi-drug chemotherapy was associated with increased general toxicity ($p = 0.039$), in particular with higher occurrence of diarrhea ($p = 0.003$) and peripheral neuropathy ($p < 0.001$). There was no apparent impact of chemotherapy on overall quality of life.

Conclusions. Treatment results of advanced colorectal cancer in daily practice may be worse than those obtained in prospective clinical trials. The use of palliative chemotherapy has no noticeable impact on quality of life.

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Key words: colorectal cancer, chemotherapy, treatment outcomes

Introduction

Colorectal cancer is the third most common malignancy in the world and the second most common cause of cancer mortality, with 1.3 million new cases and 700,000 deaths recorded annually [1]. According to the National Cancer Registry in Poland, around 16,200 cases of colorectal cancer are diagnosed per year [2]. Despite certain progress in early diagnosis and therapy during past decades, approximately 50% of patients still die within 5 years of diagnosis [3]. Patients with multi-organ metastases who are not candidates for surgery have a particularly poor prognosis [4, 5].

Within the past decade the median survival of metastatic colorectal cancer patients treated within clinical trials has increased from 12 to over 20 months [6, 7]. Such improvements have been achieved by virtue of introduction new therapeutic options, such as long-term infusion of 5-fluorouracil (5-FU) with leucovorin (LV) biomodulation instead of short term 5-FU infusions [8], or by the use of new cytotoxics, such as irinotecan or oxaliplatin [9]. A better understanding of the biology of colorectal cancer has also led to the development of molecular targeted drugs including the anti-angiogenic monoclonal antibody bevacizumab and the anti-EGFR (epidermal growth factor receptor) monoclonal antibodies cetuximab and panitumumab.

However, patients selected for prospective clinical trials are typically in good general condition, with no significant

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comorbidities and with unaffected organ functions. In contrast, patients managed routinely are usually older, with worse general health and with more comorbidities. Thus, it is important to learn whether patient outcomes achieved in clinical studies apply to a daily clinical practice. Apart from standard treatment outcomes, such as overall survival and disease-free survival, an important endpoint for new therapeutic strategies is treatment toxicity and the impact of treatment on patient's quality of life. Whereas toxicity is routinely assessed within the context of clinical trials, the quality of life is evaluated less frequently. In Poland, the data on the outcomes of palliative chemotherapy in patients with advanced colorectal cancer are scare. This study, by assessing the efficacy of palliative chemotherapy in a large group of patients treated in daily clinical practice, aims at filling this gap.

Materials and methods

The study group included 165 patients with metastatic colorectal cancer (ICD10 C18 to C20), who from May 2010 to December 2013, received palliative chemotherapy at the Specialist Hospital in Wejherowo and the Regional Oncology Centre in Gdansk, Poland. Included were patients with a primary or secondary spread of cancer, ineligible for resection of metastatic lesions. Clinical data were obtained from source patient documentation. In total, 171 patient records were analysed, 6 of which were excluded due to incomplete documentation. The individual patient data were coded to secure complete anonymity.

The clinical database contained the following information; age, gender, education, cigarette status, alcohol consumption, family history of cancer, height, weight, severity of pain, diagnosis according to the ICD-10 classification, and the administered treatment. Those currently smoking were defined as having smoked at least one cigarette per day during the previous 12 months. Ex-smokers were defined as those not having smoked for the previous 12 months, whilst non-smokers were those who had never compulsively smoked. A positive cancer family history was based on the anamnesis and was defined as the presence of colorectal cancer in relatives of the first and/or second degree. Weight and height were measured for all patients at baseline. The treatment response was assessed retrospectively using the RECIST 1.1 criteria, based on subsequent computed tomography (CT), and was performed centrally by an experienced radiologist, independently of local assessments.

Treatment toxicity was assessed during the first day of planned chemotherapy cycle, irrespective of the schedule, using the World Health Organization (WHO) classification for adverse drug reactions. Haematological toxicity was based on laboratory testing results on the day of chemotherapy. Other adverse side effects were analysed from patient medical records.

The quality of life was assessed using the Polish language version of the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire [10]. Patients completed questionnaires within the last week prior to starting chemotherapy, and in the first week after its completion.

Results were analysed with basic descriptive statistics. The Student's t-test was used to assess the significance of differences between two variables, whilst ANOVA was used for comparisons including more than two variables. Logistic regression was used to assess the relationship between the applied treatment regimen and response (stratified by age, gender, family history, alcohol consumption and cigarette smoking). A p-value below 0.05 was considered statistically significant. Additionally, the regression and correlation analyses were performed. Sufficient sample size was determined and no external validation was performed.

The association between individual factors and patient survival was evaluated using Cox Proportional Hazard Regression together with the Likelihood Ratio Test. Treatment toxicity and quality of life for particular treatment regimens were evaluated using logistic regression after adjusting for age, gender, family history, alcohol consumption and cigarette smoking. Statistical calculations were performed using Microsoft Excel version 2003 and PQStat programme, version 1.4. The study was approved by the directors of both participating centres and by the Bioethics Committee at the Regional Medical Chamber in Gdansk.

Results

Patient ages ranged between 41 to 84 years (mean 61 ± ± 8.7 years), 53% of patients were women and 62% presented with primary metastatic cancer (Table I). Colon and rectal cancers included 82% and 18% of patients, respectively. Of the 165 subjects, 98 (59%) had earlier received postoperative chemotherapy, including 79 (81%) who were administered oxaliplatin.

Irinotecan chemotherapy (CLF1 or XELIRI) was given to 105 patients, 41 received the FOLFOX4 or XELOX regimen, whilst the remaining 19 received single-agent 5-fluorouracil (5FU) with leucovorin biomodulation. Treatment regimens were unrelated to gender ($p = 0.087$), place of residence ($p = 0.21$), smoking habit ($p = 0.49$) and to primary or secondary tumour dissemination ($p = 0.85$). Single agent 5FU chemotherapy was more often administered to patients aged over 70 years ($p < 0.001$). Likewise, the oral route of drug administrating was more frequently used in patients aged over 70 years and to those from rural areas ($p < 0.001$ and < 0.024 respectively). Single drug chemotherapy was more commonly used in patients with poorer performance status ($p < 0.001$). There were no correlations between age and the performance status ($p = 0.33$).

A partial response was achieved in 48 patients (29%), in 71 (43%) the tumour was stable and 46 patients (28%) developed progression. In the parametric multivariate analysis treatment response was not associated with performance status (p = 0.93), age (p = 0.65), type of chemotherapy (p = 0.53), education (p = 0.92), gender (p = 0.37), primary versus secondary dissemination (p = 0.96), cigarette smoking (p = 0.55) and place of residence (p = 0.38).

Of the 165 subjects, 17 remained alive at the time of the analysis. The median survival for the entire group was 14 months. Multivariate analysis showed that survival was significantly affected by the performance status and response to treatment. There was also a trend towards a shorter survival in patients treated with single-agent 5FU and for elderly patients (Table II). There was no difference between the groups administered oxaliplatin and irinotecan (p = 0.74).

The most common adverse reactions were haematological toxicity including neutropenia, thrombocytopenia and anaemia, along with peripheral neuropathy, vomiting and diarrhoea (Table III); less frequent were infection, alopecia, weakness and constipation. Overall toxicity was not associated with performance status (p = 0.22), gender (p = 0.35), education (p = 0.13), place of residence (p = 0.56), family history (p = 0,41), cigarette smoking (p = 0.27), primary or secondary tumour dissemination (p = 0.85), diabetes (p = 0.11), hypertension (p = 0.36) and treatment response (p = 0.79). General toxicity, however, depended on the type of chemotherapy (single-agent 5FU versus multi-drug regimens; p = 0.039) and age (below versus above 65 years; p = 0.006). Specific toxicity differences induced diarrhoea (p = 0.003) and peripheral neuropathy (p < 0.001). Overall toxicity was not related to the chemotherapy regimen (irinotecan versus oxaliplatin; p = 0.88). The occurrence of peripheral neuropathy was higher in patients with diabetes (p = 0.039). Diarrhoea was more frequent in patients receiving irinotecan-based regimens, whereas peripheral neuropathy occurred more often in patients receiving oxaliplatin.

The average number of chemotherapy cycles for all patients was 6 (range, 2 to 11 cycles) and was not related to treatment regimen (p = 0.67). There were no toxicity-related deaths, however due to toxicity 306 (15.1%) chemotherapy cycles had to be postponed. Serious adverse events (WHO grade 3 and 4 WHO) occurred in 89 patients (54%). The most common causes for deferrals were neutropenia (73%; including 2.3% of febrile neutropenia), diarrhoea (8.5%), anaemia (6.5%), thrombocytopenia (4.9%) and neuropathy (4.9%). Dose reduction was applied in 9 patients (5.4%), 6 of whom had peripheral neuropathy and 3 febrile neutropenia. In 3 patients (1.8%) treatment was discontinued due to neuropathy. The severity of pain before and after treatment did not differ significantly (p = 0.34) and was unrelated to treatment response (p = 0.09).

Table I. Patient clinical features

Characteristic	Numbers
Performance/fitness status	
0	79 (48%)
1	60 (36%)
2	26 (16%)
Localisation	
Rectum	30 (18%)
Colon	135 (82%)
Age (years))	
41–50	10 (6%)
51–60	82 (50%)
61–70	46 (28%)
71–84	27 (16%)
Gender	
Women	88 (53%)
Men	77 (47%)
Family history of cancer	
Yes	15 (9%)
No	150 (91%)
Place of residence	
Urban	97 (59%)
Rural	68 (41%)
Smoking cigarettes	
Yes	73 (44%)
No	92 (56%)
Education	
Below secondary level	48 (29%)
Secondary	72 (44%)
Higher	45 (27%)
Cancer dissemination	
Primary	102 (62%)
Secondary	63 (38%)
Chemotherapy regimen	
CLF1/XELIRI	105 (64%)
FOLFOX/XELOX	41 (25%)
LF/capecitabine	19 (11%)

Since the quality of life assessment was introduced in January 2013 only 49 patients were assessed; the average age of those was 61 ± 7.9 years. The quality of life was not associated with age, gender, place of residence and treatment response. The small size of this group, however, precluded a meaningful analysis of the quality of life according to chemotherapy regimens. The only two changes that occurred during chemotherapy included increase in diarrhoea and pain relief (Table IV).

Second-line chemotherapy was administered in 148 patients (90%) and was abandoned in another 16 due to poor

Table II. Overall survival according to demographics and clinical factors (multivariate analysis)

Variable	Risk factor (95% CI)	p
ECOG performance status	1.44 (1.11–1.88)	**0.006**
Chemotherapy regimen	0.72 (0.51–1.02)	0.067
Age	0.97 (0.94–1.00)	0.059
Education	1.07 (0.83–1.38)	0.593
Gender	0.98 (0.67–1.44)	0.933
Place of residence	1.01 (0.68–1.52)	0.94
Treatment centre	1.03 (0.73–1.53)	0.97
Cigarette smoking	0.71 (0.48–1.05)	0.08
Treatment response	0.44 (0.34–0.57)	**< 0.001**

performance status and or patient refusal (Table V). Second-line chemotherapy was rarely used in patients who had received first-line single-agent 5FU. Patients who received irinotecan as first-line chemotherapy were subsequently administered oxaliplatin with the optional addition of bevacizumab, whereas those treated with first-line oxaliplatin most frequently received irinotecan in the second-line.

Median survival of patients who received only one chemotherapy line was shorter compared with those treated with subsequent chemotherapy lines (10.5 versus 14.1 months; $p < 0.01$). Patients receiving first-line irinotecan and oxaliplatin as second-line chemotherapy showed similar survival times compared to those with the opposite sequence (median 13.8 versus 13.6 months, $p = 0.31$). The median survival of patients who additionally received second-line bevacizumab was 14.1 months, and did not differ from that following exclusive chemotherapy ($p = 0.73$). The *RAS*-family gene mutation was evaluated in 93 patients (56%), and was absent in 45 (48%). Third-line treatment was administered in 39 patients and included monoclonal anti-EGFR antibodies: cetuximab or panitumumab.

Discussion

In this series, the median survival was 14 months and response rate was 29%. These outcomes seem to be lower compared to those reported in recent prospective clinical trials (average median survival of 16.9 months, mean response rate 39%, Table VI). As expected, survival was longer in patients administered two or more lines of therapy compared to those administered only one-line therapy, likely due to differences in clinical characteristics between these groups. Indeed, the second-line chemotherapy was generally not considered in patients with a poor performance status or rapid progression. The retrospective nature of this study, however, does not allow for assessment of the survival impact of second-line chemotherapy.

Inferior study outcomes compared to those in clinical trials should be treated with caution since our assumptions were based on comparisons between retrospective series of patients. Our series included consecutive groups of patients from two institutions, with no formal selection such as performance status, disease comorbidity or other factors typically considered in clinical trials. There were 27 subjects aged over 70 years, including 4 that were over 80 years, the group with higher occurrence of chronic comorbidities. In addition, standard regimens used in this series (irinotecan, oxaliplatin, single-agent 5-FU) might have been less effective than those used in clinical trials. Further, even though only 17 patients had censored survival data, the retrospec-

Table III. Treatment toxicity; significant differences marked in bold

Toxicity	Indicator	Grade 3 and 4 toxicities			
		CLF1/XELIRI	FOLFOX/XELOX	5FU	P
Vomiting	Number of episodes/applications (%)	88/1074 (8.2%	29/386 (7.5%)	13/191 (6.8%)	0.072
	Average toxicity WHO (95% CI)	0.62 (0.48–0.77)	0.56 (0.44–0.69)	0.59 (0.46–0.72)	
Diarrhoea	Number of episodes/applications (%)	125/1074 (11.6%)	35/386 (9.1%)	14/191 (7.3%)	**0.003**
	Average toxicity WHO (95% CI)	1.31 (1.13–1.49)	0.60 (0.51–0.71)	0.70 (0.56–0.85)	
	Number of episodes/applications (%)	48/1074 (4.5)	15/386 (3.7)	9/191 (4.7)	0.94
	Average toxicity WHO (95% CI)	0.20 (0.11–0.30)	0.18 (0.11–0.25)	0.20 (0.1–0.31)	
Anaemia	Number of episodes/applications (%)	76/1074 (7.1%)	25/386 (6.5%)	9/191 (4.7%)	0.12
	Average toxicity WHO (95% CI)	0.53 (0.43–0.63)	0.52 (0.43–0.62)	0.5 (0.37–0.63)	
Thrombocytopenia	Number of episodes/applications (%)	46/1074 (4.3%)	14/386 (3.6%)	5/191 (2.6%)	0.19
	Average toxicity WHO (95% CI)	0.44 (0.33–0.54)	0.43 (0.35–0.51)	0.37 (0.26–0.48)	
Neutropenia	Number of episodes/applications (%)	333/1074 (31%)	112/386 (29%)	50/191 (26%)	0.79
	Average toxicity WHO (95% CI)	1.22 (0.99–1.4)	1.22 (1.08–1.36)	1.17 (0.98–1.37)	
Peripheral neuropathy	Number of episodes/applications (%)	31/1074 (2.9%)	37/386 (9.6%)	0/191 (0%)	**< 0.001**
	Average toxicity WHO (95% CI)	0.23 (0.12–0.31)	0.65 (0.53–0.75)	0	

95% CI — confidence interwal 95%

Table IV. Patient quality of life (EORTC QLQ C-30) before and after treatment; significant differences marked in bold

	Average before treatment (standard deviation)	Average after treatment (standard deviation	
General quality of life/ health status	65 (18.5)	66 (17.4)	0.78
Physical fitness	78 (16.7)	80 (14.9)	0.43
Role	87 (19.9)	87 (18.2)	0.73
Emotional functions	76 (12.6)	78 (10.8)	0.67
Cognitive functions	94 (11.3)	92 (13.3)	0.82
Societal functions	85 (24.9)	85 (22.8)	0.76
Symptoms			
Fatigue	21 (22.8)	26 (19.6)	0.08
Nausea / vomiting	5.5 (12.7)	7.0 (11.2)	0.15
Pain	21 (19.4)	17 (18.3)	**0.03**
Dyspnoea	8.2 (11.2)	10 (12.2)	0.67
Insomnia	36 (29.0)	37 (28.0)	0.89
Appetite loss	9.0 (19.0)	11 (18.3)	0.73
Constipation	7.5 (13.5)	6.3 (14.3)	0.81
Diarrhea	6.5 (8.2)	15 (22.4)	**< 0.001**
Financial problems	38 (28.0)	39 (26.7)	0.62

Table V. Second and third line treatment regimens according to first-line chemotherapy

First-line (N)	Second-line (N)	Third-line(N)
CLF1/XELIRI	FOLFOX4/XELOX	Cetuximab/panitumumab
	FOLFOX4+ bevacizumab	Cetuximab/panitumumab
	Not used	Not applicable
FOLFOX4/XELOX	CLF1/XELIRI	Cetuximab/panitumumab
	LF3	Not used
	Not used	Not applicable
LF3	XELOX	Not used
	CLF1	Not used
	Not used	Not applicable

tive nature of the study did not allow for considering such factors as comorbidities or previous surgery. The lower remission rates might have also been due to a relatively long interval (average 3.8 weeks) between initial CT evaluation and chemotherapy commencement, usually not allowed in clinical trials.

Regardless of the different characteristics of patients managed in routine practice and in clinical trials, it is important to consider the representativeness of a given patient sample in relation to the general population of colorectal cancer patients. A large majority of colorectal cancer cases (94%) in Poland occur in persons aged over 50 years and in 75% of those aged over 60 years; with the men/women ratio of 1.5–2 [2]. Most of the patients in this series were aged 51–70 years (mean 61 years) and more than a half were women. This structure may reasonably reflect the actual demographics of advanced colorectal cancer patients in Poland.

In 1.8% of cases in this series treatment had to be discontinued due to toxicity, whilst 5.5% needed reduced doses of chemotherapy. Serious adverse events (WHO grade 3 and 4) occurred in 89 patients (54%), and 23 patients developed at least two serious side effects. Such results do not significantly differ from those reported in large clinical trials [6, 8, 9, 11–15]. Nevertheless, our toxicity data may have been underestimated due to several reasons. Firstly, our study showed that some symptoms, such as lethargy and fatigue were relatively rare, likely due to their omissions in medical records. The patient's mental status was an overall deemed satisfactory, without depressed mood or any sleep disorders. Information on the adverse side effects were nonetheless incomplete because of the retrospective nature of our study, resulting in inevitably inferior data collection compared with the on-line recording required in clinical trials. This discrepancy, however, did not include analytically measurable

Table VI. Outcomes of palliative treatment for colorectal cancer patients in phase III trials since 1998, excluding trials using targeted therapies (detailed data and references available from authors)

Author	Year	Primary endpoint	Median survival (months)	Response rate (RR)	Number of patients
Kohne	1998	RR	19.6	44%	236
Bandealy	1998	RR	12.0	13%	182
Borner	1998	OS	12.4	22%	309
Glimelius	1998	RR, Toxicity	BD	27%	203
Cocconi	1998	RR, OS, TTP	12.3	19%	495
Aranda	1998	RR	12.0	30%	306
Colucci	1999	RR and OS	12.0	24%	204
Hausmaninger	1999	RR, OS and TTP	12.6	36%	249
Giacchetti	2000	RR	19.9	53%	200
Douillard	2000	RR	17.4	49%	387
de Gramont	2000	PFS	16.2	51%	420
Saltz	2000	PFS	14.8	39%	683
Sobrero	2000	RR	14.8	32%	214
Hoff	2001	RR	13.3	25%	605
O'Dwyer	2001	Toxicity	14.8	16%	1120
Van Cutsem	2001	RR	13.2	19%	602
Blanke	2002	TTP	16.8	26%	382
Punt	2002	PFS	13.4	29%	365
Schilsky	2002	OS	14.5	12%	981
Comella	2002	OS	14.8	36%	234
Douillard	2002	OS	13.4	15%	816
Kohne	2003	OS	13.7	17%	497
Tournigand	2004	PFS	21.5	56%	220
Goldberg	2004	TTP	19.5	31%	795
Comella	2005	RR	18.9	44%	274
Colucci	2005	RR	15.0	34%	360
Kohne	2005	PFS	20.1	62%	430
Tournigand	2006	PFS	21.2	59%	620
Hospers	2006	RR	13.8	34%	302
Souglakos	2006	OS	21.5	43%	285
Giacchetti	2006	OS	19.6	42%	564
Falcone	2007	RR	22.6	60%	244
Diaz-Rubio	2007	TTP	20.8	46%	348
Porschen	2007	PFS	18.8	54%	474
Seymour	2007	OS	15.4	BD	2135
Glimelius	2008	PFS	19.0	49%	567
Cassidy	2008	PFS	19.8	48%	2034
Gamelin	2008	RR	22.0	34%	208
Aranda	2008	RR	21.6	57%	346
Cunningham	2008	OS	15.9	54%	725
Chibaudel	2009	PFS	23.8	60%	210
Madi	2012	OS	15.4	BD	2397
Qvortrup	2010	Toxicity	17.6	56%	141
Labianca	2011	OS	18.0	42%	337
Mean			16.9	39%	

OS — Overall survival; PFS — Progression free survival; TTP — Time to progression; RR — Response ratio; BD — No data

parameters, such as peripheral blood cell counts. Indeed, proportions of patients with neutropenic fever and grade 3 and 4 peripheral neuropathy was slightly higher compared to the literature data [11–15]. It should also be noted that some patients were managed by their general practitioners and other physicians and such symptoms might have not been captured in the analysed records.

Only 9 patients (5.5%) needed hospitalisation during treatment, in all cases due to anaemia requiring blood transfusion. Such results indicate that palliative chemotherapy in advanced colorectal cancer patients may usually be carried out safely on an outpatient basis. Notably, at both participating institutions patients treated with irinotecan routinely received atropine, and those peripheral neuropathy — a symptomatic treatment. Most patients also received secondary prophylaxis with granulocyte-colony stimulating factors, thereby reducing the risk of neutropenia. The severity of neuropathy was higher in patients with diabetes, but this relationship should be considered with caution, as only a small group of patients had been diagnosed with this comorbidity. Similarly to other studies, the toxicity was higher in patients administered multidrug regimens, compared to single-agent 5FU. The study results seem to indicate that chemotherapy toxicity in clinical practice may be actually be higher than that recorded in clinical trials.

The chemotherapy used in our study had no apparent impact on the overall quality of life, and neither was there association between treatment response and the quality of life. Indeed, we have previously demonstrated that systemic palliative chemotherapy has relatively modest influence on the quality of life in patients with advanced malignancies [16, 17]. An important symptom affecting quality of life was treatment-related diarrhoea. The pain relief observed during treatment requires cautious interpretation. Firstly, there was generally no connection between pain relief and treatment response, and secondly, effective pain management might have masked its actual intensity. Our study did not evaluate how depression or mood disorders affect general health. Earlier studies demonstrated that the quality of life is significantly worse in colorectal cancer patients with high levels of anxiety and depression [18]. This therefore indicates the need for considering the impact of other factors other than treatment on quality of life in cancer patients administered palliative chemotherapy.

Our study provides data on treatment pattern in metastatic colorectal cancer patients managed in daily clinical practice in Poland. Applied methods generally followed current therapeutic guidelines, with individualised decisions wherever necessary. Most patients received first-line chemotherapy regimens containing newer generation drugs — irinotecan (64%) or oxaliplatin (25%). Single-agent 5-FU chemotherapy was mostly used in elderly or fragile patients. The reason for more frequent use of irinotecan-based regimens was probably mainly due to the previous exposure to oxaliplatin as a part of postoperative chemotherapy. Another important factor were the regulations for the use of bevacizumab in Poland, including its reimbursement only in second-line treatment in combination with oxaliplatin. Despite this, most patients managed with first-line irinotecan did not receive bevacizumab in the second line, likely due its limited availability or failure to meet the required inclusion criteria. Monoclonal anti-EGFR antibodies are reimbursed in Poland for patients undergoing third-line treatment for wild-type *RAS* mutation cancers, and the majority of patients meeting this criterion actually received this medication.

Conclusions

The study illustrates the current practice and efficacy of palliative chemotherapy in Polish patients with advanced colorectal cancer. Our results suggest that the outcomes of routine treatment in this population may be inferior than those reported in clinical trials, typically including carefully selected groups of patients. This conclusion, however, should be drawn cautiously due to the retrospective nature of our study. Nevertheless, this data indicates the need for cautions extrapolation of the results from clinical trials into daily clinical practice.

Conflicts of interest: The authors declare no conflicts of interest

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