

■ Research Article

## Reevaluating regorafenib: Do we need the full dose?

### *Regorafenibi yeniden değerlendirmek: Tam doza ihtiyacımız var mı?*

 Beliz Bahar Karaoglan<sup>1\*</sup>,  Erman Akkus<sup>1</sup>,  Mehmet Kayaalp<sup>1</sup>,  Buse Arslan Ozcobanlar<sup>1</sup>,  
 Gungor Utkan<sup>1</sup>

<sup>1</sup>Department of Medical Oncology, Faculty of Medicine, Ankara University, Ankara, Türkiye

#### Abstract

**Aim:** Regorafenib is a standard treatment for metastatic colorectal cancer (mCRC), typically administered at a dose of 160 mg/day. This study evaluates the efficacy and tolerability of lower doses of regorafenib compared to the standard dose.

**Material and Methods:** A total of 58 mCRC patients were divided into two groups: low-dose ( $\leq 120$  mg/day) and high-dose ( $> 120$  mg/day). We assessed disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and adverse events (AEs). Dose modifications and treatment discontinuations were recorded.

**Results:** 58 patients with a median age of 57 years were included. Regorafenib was administered as a median fourth-line treatment, with 34 patients in the low-dose group and 24 in the high-dose group. Disease control rates were 37.9%, with no significant difference between low-dose and high-dose groups (35.3% vs. 41.7%,  $P=0.625$ ). Median PFS was similar between the groups [3.3 months (95% CI: 2.2-4.3) vs. 4.1 months (95% CI: 2.3-5.8),  $P=0.695$ ]. OS was also comparable across groups [7.8 months (95% CI: 5.8-9.7) vs. 10.3 months (95% CI: 5.1-15.5),  $P=0.213$ ]. AEs were reported in 89.6% of patients, with a significantly higher rate of dose reductions or discontinuations in the high-dose group (41.7% vs. 11.8%,  $P=0.013$ ).

**Conclusion:** Lower doses of regorafenib ( $\leq 120$  mg/day) provide comparable efficacy and similar disease control rates to the standard dose. The high-dose regimen is associated with greater tolerability issues, suggesting that lower doses may be a viable alternative for better patient management.

**Keywords:** colorectal cancer; dose response relationship; drug tolerance

Corresponding Author\*: Beliz Bahar Karaoglan, M.D. Department of Medical Oncology, Faculty of Medicine, Ankara University, Ankara, Türkiye.

E-mail: bbaharulas@gmail.com Phone: +90 533 170 86 74

Orcid: 0000-0002-5021-7588

Doi: 10.18663/tjcl.1874059

Received: 28.01.2026 accepted: 31.01.2026 Publication date: 28.03.2026

## Öz

**Amaç:** Regorafenib, metastatik kolorektal kanser (mKRK) için standart bir tedavi olup genellikle 160 mg/gün dozunda uygulanmaktadır. Bu çalışma, regorafenibin düşük dozlarının etkinliğini ve yan etkilerini standart dozla karşılaştırmayı amaçlamaktadır.

**Gereç ve Yöntemler:** Toplam 58 mKRK hastası, düşük doz ( $\leq 120$  mg/gün) ve yüksek doz ( $> 120$  mg/gün) olmak üzere iki gruba ayrılmıştır. Hastalık kontrol oranı (DCR), progresyonsuz sağkalım (PFS), genel sağkalım (OS) ve yan etkiler (AEs) değerlendirilmiştir.

**Bulgular:** Çalışmaya 58 hasta dahil edilmiş olup medyan yaş 57'dir. Regorafenib, medyan dördüncü basamak tedavi şeklinde uygulanmış; düşük doz grubunda 34, yüksek doz grubunda ise 24 hasta yer almıştır. Tüm kohortta hastalık kontrol oranı %37,9 olup gruplar arasında anlamlı bir fark saptanmamıştır (%35,3'e karşı %41,7,  $P=0.625$ ). Medyan PFS [3,3 ay (95% CI: 2,2-4,3) ve 4,1 ay (95% CI: 2,3-5,8),  $P=0.695$ ] ve OS [7,8 ay (95% CI: 5,8-9,7) ve 10,3 ay (95% CI: 5,1-15,5),  $P=0.213$ ] gruplar arasında benzer bulunmuştur. Yan etkiler tüm kohortta %89,6 oranında görülmüştür ve yüksek doz grubunda doz azaltımı veya tedavi kesilme oranı belirgin olarak daha yüksek bulunmuştur (%41,7'ye karşı %11,8,  $P=0.013$ ).

**Sonuçlar:** Daha düşük dozlarda ( $\leq 120$  mg/gün) uygulanan regorafenib, standart doz ile benzer etkinlik ve hastalık kontrol oranları sağlamaktadır. Standart doz regorafenib daha zor tolere edilmektedir. Bu sonuçlar, düşük doz uygulamasının daha iyi tedavi tolerasyonu ile, standart doza alternatif olabileceğini göstermektedir.

**Anahtar Kelimeler:** kolorektal kanser, doz yanıt ilişkisi, ilaç toleransı

## Introduction

Regorafenib is a multikinase inhibitor which has been approved for the treatment of metastatic colorectal cancer (mCRC). CORRECT trial demonstrated a significant survival benefit of regorafenib treatment in mCRC patients who had progressed on standard treatments [1]. The CONCUR study later confirmed these findings in Asian patients[2]. Regorafenib has been used as a  $\geq 3$ rd line therapy and beyond in mCRC patients, with a recommended dose of 160 mg/day (3 weeks on/1 week off).

However, regorafenib's adverse event (AE) profile, including hand-foot syndrome, fatigue, decreased appetite, diarrhea, and hypertension, has limited its use in clinical practice, often necessitating dose reductions or treatment discontinuation. These AEs typically emerge early in therapy but tend to decrease over time without cumulative toxicity [1,2]. The ReDOS and CORRELATE studies demonstrated that starting regorafenib at a lower dose improves tolerability without compromising efficacy [3,4]. As a result, guidelines now include a dose-escalation regimen as an alternative, where treatment begins at 80 mg/day and is gradually increased to the recommended dose at weekly intervals, based on patient tolerability [5].

Despite the use of dose-escalation strategies in current practice, it is often observed that regorafenib cannot be escalated to the target dose due to side effects and tolerance

challenges. This raises concerns among oncologists about whether patients are receiving adequate treatment. However, there are a few studies investigating the efficacy of regorafenib at lower target doses, which could potentially address this concern. The aim of this study is to evaluate the efficacy and safety of lower regorafenib doses in patients with mCRC receiving regorafenib treatment.

## Material and Methods

### Patient Cohorts and Regorafenib Dosing

Clinicopathological data of mCRC patients treated at Ankara University Faculty of Medicine between January 2010 and May 2022 were retrospectively collected. Eligible patients were mCRC patients with histologically confirmed diagnosis and had progressed on standard therapies, as defined by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 [6]. Regorafenib was orally administered once daily after meals on days 1-21.

Variables included demographics, stage at diagnosis, previous therapy details, and prior local therapies or metastasectomy. RAS and BRAF mutational status, as well as MSI status, were also assessed.

Patients were categorized based on their daily regorafenib dose intensity:  $> 120$  mg/day (high-dose=HD group) and  $\leq 120$  mg/day (low-dose=LD group). HD group included patients who started on 120 mg/day and escalated to 160 mg/day,

those who initiated treatment at 160 mg/day and maintained that dose, and those who started at 160 mg/day but later reduced to a minimum of 120 mg/day. LD group comprised patients who began at 120 mg/day and either continued at that dose or reduced to 80 mg/day, as well as those who started at 80 mg/day and either remained at that dose or tolerated up to a maximum of 120 mg/day.

For patients with dose escalation of regorafenib, those who reached the escalated dose within less than 14 days were included in the escalated dose group. Conversely, patients who could not escalate to the planned dose within 14 days or longer due to low tolerance were evaluated in their current dose group. Changes in dose and their timing during treatment were recorded, and the daily dose intensity was calculated for each patient throughout the treatment period.

### Outcomes

The primary endpoint was progression-free survival (PFS), defined as the time between the initiation of regorafenib and end of the therapy or death, whichever comes first.

Secondary endpoints are overall survival (OS), defined as the time between starting of regorafenib to the last visit or death, whichever comes first; disease control rate (DCR), defined as partial response to regorafenib treatment or stable disease; and treatment related AEs.

This study was approved by the Ankara University clinical research ethics committee (approval no: İ01- 103-25, date: 17.02.2025) and followed the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from participants.

### Statistical Analysis

Descriptive statistics were presented as mean  $\pm$  standard deviation or median (min-max), whichever appropriate. Nominal variables were reported as frequency and percentage. Group comparisons were performed using t-test, Mann-Whitney U, chi-square, or Fisher's exact test, whichever was appropriate. Survival outcomes were evaluated using Kaplan-Meier analysis and p-value of  $<0.05$  was considered statistically significant. SPSS version 25 was used for statistical analyses.

## Results

### Baseline Characteristics

Fifty-eight patients with a median age of 57 years (IQR: 36-80) were included. Forty patients (69%) had de novo metastatic disease; 43 patients (75%) were diagnosed with colon cancer, and 15 patients (25%) with rectal cancer. RAS and BRAF mutation

assessments were available for all patients, whereas MSI status was unknown for 9 patients. Sixty percent of the patients had RAS mutant CRC. Three patients (5%) with MSI-H mCRC could not receive immunotherapy due to unavailability (Table 1).

In the entire cohort, regorafenib was administered as a median fourth-line treatment (IQR: 3-5). The median time from diagnosis to the start of regorafenib was 25.6 months (IQR: 9.1-140.6). Prior to regorafenib, 44 patients (75%) had received anti-VEGF, and 22 patients (37%) had received anti-EGFR treatment. Additionally, 19 patients (32%) had a history of metastasectomy (for liver or lung metastases), and 16 patients (27%) had received local treatments other than surgery for liver metastases (Table 2).

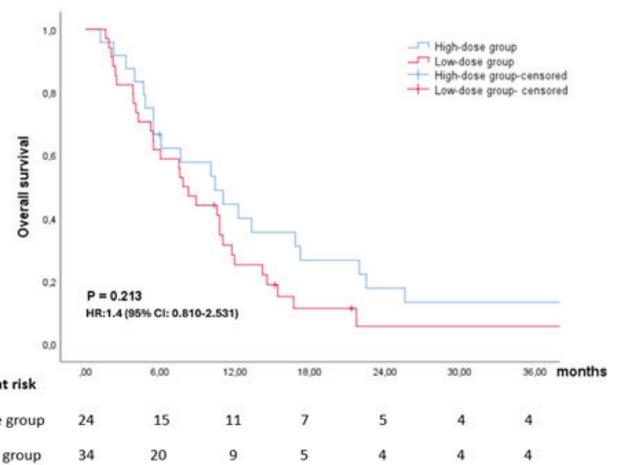
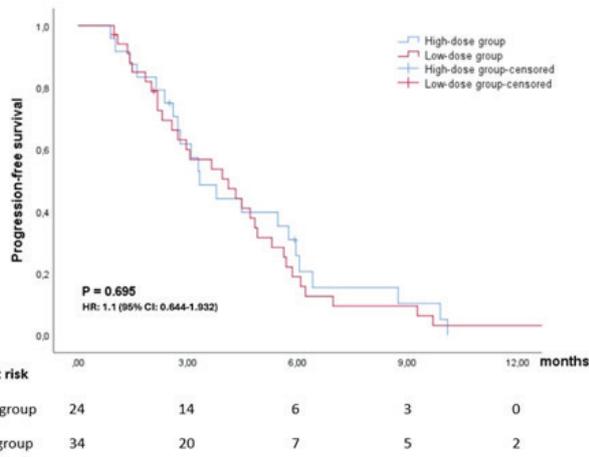
### Regorafenib Efficacy, Adverse Events, and Survival Outcomes

A total of 34 patients were assessed in the LD group and 24 in the HD group. In the LD group, 12 patients started treatment with 80 mg/day of regorafenib, of whom 3 could tolerate up to a maximum of 120 mg/day. The remaining 22 patients began treatment at 120 mg/day but could not escalate to a higher dose due to limited tolerability.

The median regorafenib dose intensity in the LD group was 120 mg/day (IQR: 80-120), with a median duration of 74 days (IQR: 19-758) until the first dose change. In the HD group, 3 out of 24 patients initiated treatment at 80 mg/day and 6 at 120 mg/day, with all reaching the target dose of 160 mg/day in subsequent cycles. Among the 15 patients who began treatment at 160 mg/day, 4 had their dose reduced to 120 mg/day due to side effects. The median regorafenib dose intensity in the HD group was 154 mg/day (IQR: 126-160), and the median time to the first dose revision was 39 days (IQR: 21-209).

All patients' responses to treatment were assessed radiologically. Disease control was achieved with regorafenib in 22 patients (37.9%) in the entire cohort. Partial responses to regorafenib were observed in 3 patients (8.8%) in the LD group and 4 patients (16.7%) in the HD group. The DCRs were similar between the groups (35.3% vs. 41.7%,  $P=0.625$ ).

After a median duration of 3.2 months (IQR: 0.72-24.9) on regorafenib treatment, PFS was 3.7 months (95% CI: 2.5-4.9). PFS was similar between the HD and LD groups [3.3 months (95% CI: 2.2-4.3) vs. 4.1 months (95% CI: 2.3-5.8),  $P=0.695$ ] (Figure 1). OS was 8.8 months (95% CI: 5.7-11.9) in the entire cohort and was also comparable between the groups [7.8 months (95% CI: 5.8-9.7) vs. 10.3 months (95% CI: 5.1-15.5),  $P=0.213$ ] (Figure 2).



**Figure 1.** Progression-free survival according to the dose pattern of regorafenib.

**Figure 2.** Overall survival according to the dose pattern of regorafenib.

**Table 1.** Baseline characteristics of patients.

Characteristic	Low-dose group n=34	High-dose group n= 24	P
<b>Age, year, median (IQR)</b>	61 (36-80)	55 (42-74)	0.420
<b>Gender, n (%)</b>			0.786
Male	21 (61.8)	16 (66.7)	
Female	13 (38.2)	8 (33.3)	
<b>Tumor location, n (%)</b>			0.342
Right sided	18 (52.9)	9 (37.5)	
Left-sided	8 (23.5)	8 (33.3)	
Rectal	8 (23.5)	7 (29.2)	
<b>Stage at diagnosis</b>			0.796
Non-metastatic	11 (32.4)	7 (29.3)	
Metastatic	23 (67.6)	17 (70.8)	
<b>MSI status, n (%)</b>			0.842
MSS	28 (93.3)	18 (94.7)	
MSI-H	2 (6.7)	1 (5.3)	
<b>RAS mutation, n (%)</b>	20 (58.8)	15 (62.5)	0.778
<b>BRAF mutation, n (%)</b>	3 (8.8)	0 (0)	0.260
<b>Plasma CEA level</b>			0.149
≤5 ng/mL, n (%)	1 (2.9)	4 (16.7)	
>5 ng/mL, n (%)	33 (97.1)	20 (83.3)	
<b>Site of metastasis, n (%)</b>			
Liver	19 (55.9)	15 (62.5)	0.787
Lung	7 (20.6)	5 (20.8)	0.982
Lymph node(s)	7 (20.6)	4 (16.7)	0.708
Bone(s)	10 (29.4)	7 (29.2)	0.984

Abbrev.: CEA: carcinoembryonic antigen, MSI: microsatellite instability, MSI-H: microsatellite instability high

**Table 2.** Treatment characteristics of patients.

Characteristic	Low-dose group n=34	High-dose group n= 24	P
<b>Resection of primary tumor, n (%)</b>	26 (76.5)	20 (83.3)	0.744
<b>Number of previous lines</b>			0.790
3 line	15 (44.1)	12 (50)	
>3 lines	19 (55.9)	12 (50)	
<b>Prior targeted therapies, n (%)</b>			
Anti-VEGF monoclonal antibody	25 (73.5)	19 (79.2)	0.759
Anti-EGFR monoclonal antibody	14 (41.2)	8 (33.3)	0.593
<b>Best response to regorafenib, n (%)</b>			
Partial response	3 (8.8)	4 (16.7)	
Stable disease	9 (26.5)	6 (25)	
Progressive disease	22 (64.7)	14 (58.3)	
<b>LT for liver metastases, n (%)</b>	10 (29.4)	6 (25)	0.773
<b>Prior metastasectomy, n (%)</b>	11 (32.4)	8 (33.3)	0.938

Abbrev.: anti-EGFR: anti epidermal growth factor receptor monoclonal antibody, anti-VEGFR: anti vascular endothelial growth factor, LT: local therapy

**Table 3.** Adverse events by regorafenib dose pattern.

	Low-dose group n=34	High-dose group n= 24	P
<b>PPES, n (%)</b>			0.451
Grade 1-2	8 (23.5)	8 (33.3)	
Grade 3	1 (2.9)	1 (4.2)	
<b>Fatigue, n (%)</b>			0.343
Grade 1-2	19 (55.9)	12 (50)	
Grade 3	3 (8.8)	1 (4.2)	
<b>Diarrhea, n (%)</b>			0.196
Grade 1-2	9 (26.5)	3 (12.5)	
Grade 3	0 (0)	0 (0)	
<b>Decreased appetite, n (%)</b>			0.854
Grade 1-2	15 (44.1)	10 (41.7)	
Grade 3	0 (0)	0 (0)	
<b>Hypertension, n (%)</b>			0.524
Grade 1-2	3 (8.8)	1 (4.2)	
Grade 3	0 (0)	1 (4.2)	
<b>Anemia, n (%)</b>			0.888
Grade 1-2	3 (8.8)	4 (16.7)	
Grade 3	2 (5.9)	1 (4.2)	
<b>Elevated transaminase, n (%)</b>			0.982
Grade 1-2	7 (20.6)	5 (20.8)	
Grade 3	0 (0)	0 (0)	

Abbrev.: PPES: palmar-plantar erythrodysesthesia syndrome

Fifty-two patients (89.6%) experienced at least one grade of AEs related to regorafenib. The most common side effects were fatigue (60.3%), anorexia (43.1%), palmar-plantar erythrodysesthesia syndrome (PPES) (31%), and elevated transaminases (20.7%). No grade 4 AE was observed. During the treatment period, 14 patients (24.1%) had their dose

reduced or treatment discontinued due to tolerability issues or AEs. The proportion was significantly higher in the HD group (41.7% vs. 11.8%,  $P=0.013$ ). In the HD group, PPES and anemia were reported more frequently, but AEs were similar between groups (Table 3).

## Discussion

We concluded that regorafenib doses of 120 mg or lower had similar efficacy and DCR, with a less frequent PPES and anemia, compared to the recommended dose of 160 mg/day.

The patients included in this study were typical mCRC patients, progressing after multiple lines of therapy, with characteristics similar to those in previous studies. Our patients were slightly younger than those in earlier trials. The proportions of patients with RAS mutations (60%) and BRAF mutations (5%) were also consistent with prior studies. Additionally, the percentage of patients who had received targeted therapies before regorafenib and the fact that more than half of our cohort used regorafenib as a 4th-line or later therapy were comparable to those reported in previous studies [1-4,7,8].

Phase 1 and 2 studies conducted prior to approval of regorafenib, indicated that active metabolite levels increased up to 120 mg, with no significant rise at higher doses [9,10]. Initially approved at 160 mg/day for 21 of 28 days, an alternative dosing regimen starting at 80 mg/day and escalating to 160 mg/day was later introduced due to tolerability concerns, with similar efficacy [3]. Despite this, many patients in our clinical practice have been unable to tolerate the target dose.

As one of the few studies investigating the efficacy of regorafenib at lower doses, we retrospectively evaluated doses of 120 mg/day or less, which we hypothesized would be better tolerated without compromising efficacy. Our results showed similar PFS, OS, or AEs between the groups. The PFS in our cohort was similar to previous studies [1-4]. Notably, the DCR in our patients was comparable to that observed in the RESET trial, where nearly all patients tolerated 120 mg/day of regorafenib, and similar to the DCR reported in the CORRECT trial [1,7]. However, the overall DCR was lower at 38%, compared to the 41-74% reported in earlier trials, regardless of dose intensity [14].

The lower DCR observed in our study did not negatively impact PFS or OS, which can be explained by several factors. First, it may be attributed to the lack of standardized response evaluation times in our patient cohort. Additionally, regorafenib may provide clinical benefits through alternative mechanisms, such as modulation of the tumor microenvironment, which might not directly translate into higher response rates but still slow disease progression. Furthermore, the better tolerability of lower doses may not lead to a significant increase in DCR but could extend the duration of response, thereby supporting prolonged disease control and survival. Importantly, although no statistically

significant difference in OS was observed between dose groups, this finding should be interpreted with caution, as the relatively small sample size may have limited the statistical power to detect clinically meaningful survival differences. Taken together, these observations suggest that, particularly in heavily pretreated metastatic colorectal cancer populations, survival outcomes are not always directly linked to response rates.

In our study, the proportion of patients who had their regorafenib dose reduced or treatment discontinued due to adverse events (AEs) or tolerability issues was 24%, which is comparable to the CORRECT trial, where one in five participants required a dose reduction [1]. In contrast, the CONSIGN study found that up to 49% of participants needed a dose reduction and 9% discontinued treatment due to AEs, leading to 60% of participants needing some form of treatment modification [11]. Additionally, a multicenter retrospective study reported regorafenib modification rate of 79.0%, due to AEs or intolerance. This study also found that there was no significant effect of dose escalation strategy [12].

Recent research has investigated numerous factors influencing the efficacy of regorafenib. Studies have demonstrated that regorafenib remains effective regardless of factors such as age, sex, tumor location (right vs. left colon or rectum), RAS or BRAF mutation status, previous treatments, and whether the primary tumor has been resected [1,2,4]. However, a recent study advocating for dose adjustment based on body weight found that lower regorafenib doses can achieve similar antitumor efficacy in patients with lower body weight [13]. While our study lacked data on patients' body mass index, it suggests that lower regorafenib doses may be sufficient for patients with low body weight, although further research is needed in this area. Additionally, polypharmacy has been shown to have a prognostic effect on OS in patients receiving regorafenib, as it can alter the drug's pharmacokinetics and pharmacodynamics [14].

## Limitations of the Study

This study has certain limitations, including its retrospective design, relatively small sample size, and heterogeneity within the dose groups. These factors may have influenced the observed outcomes. Nevertheless, the results reflect real-world clinical practice and provide relevant insights into the use of lower-dose regorafenib in heavily pretreated mCRC patients.

In conclusion, this retrospective analysis suggests that regorafenib doses of 120 mg/day or lower are associated with comparable efficacy and disease control rates to the standard dose. Lower doses were also associated with improved

tolerability, which may facilitate longer treatment exposure in clinical practice. These findings support the consideration of lower-dose regorafenib as a feasible option in real-world settings, while highlighting the need for prospective studies to confirm these observations.

### Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

### Funding

The authors received no financial support for the research and/or authorship of this article.

### Ethics approval

This study was approved by the Ankara University clinical research ethics committee (approval no: İ01- 103-25, date: 17.02.2025)

### Authors' contributions

Conceptualization: B.B.K., G.U.; Methodology: B.B.K., E.A.; Data curation: B.B.K., E.A., M.K., B.A.Ö.; Formal analysis: B.B.K., M.K., B.A.Ö.; Investigation: B.B.K., E.A., M.K., B.A.Ö.; Writing – original draft: B.B.K., E.A., M.K.; Writing – review & editing: G.U.; Supervision: G.U. All authors read and approved the final manuscript.

### References

1. Grothey A, Van Cutsem E, Sobrero A, Siena S, Falcone A, Ychou M et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet* 2013; 381: 303-12.
2. Li J, Qin S, Xu R, Yau TC, Ma B, Pan H et al. Regorafenib plus best supportive care versus placebo plus best supportive care in Asian patients with previously treated metastatic colorectal cancer (CONCUR): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2015; 16: 619-29.
3. Bekaii-Saab TS, Ou FS, Ahn DH, Boland PM, Ciombor KK, Heying EN et al. Regorafenib dose-optimisation in patients with refractory metastatic colorectal cancer (ReDOS): a randomised, multicentre, open-label, phase 2 study. *Lancet Oncol* 2019; 20: 1070-82.
4. Ducreux M, Petersen LN, Öhler L, Bergamo F, Metges JP, de Groot JW et al. Safety and effectiveness of regorafenib in patients with metastatic colorectal cancer in routine clinical practice in the prospective, observational CORRELATE study. *Eur J Cancer* 2019; 123: 146-54.
5. Adam M, Chang GJ, Chen YJ. NCCN Guidelines Version 5.2024 Colon Cancer. Available from: <https://www.nccn.org>
6. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 2009; 45: 228-47.
7. Suzuki T, Sukawa Y, Imamura CK, Masuishi T, Satake H, Kumekawa Y et al. A Phase II Study of Regorafenib With a Lower Starting Dose in Patients With Metastatic Colorectal Cancer: Exposure-Toxicity Analysis of Unbound Regorafenib and Its Active Metabolites (RESET Trial). *Clin Colorectal Cancer* 2020; 19: 13-21.
8. López Muñoz AM, González Flores E, Carral Maseda A, Pimentel Cáceres P, Afonso Gómez R, López López C et al. Real-world dosing patterns of regorafenib for patients with metastatic colorectal cancer in Spain: the RE-SEARCH study. *Clin Transl Oncol* 2025; 27: 1176-84.
9. Mross K, Frost A, Steinbild S, Hedbom S, Büchert M, Fasol U et al. A phase I dose-escalation study of regorafenib (BAY 73-4506), an inhibitor of oncogenic, angiogenic, and stromal kinases, in patients with advanced solid tumors. *Clin Cancer Res* 2012; 18: 2658-67.
10. Strumberg D, Scheulen ME, Schultheis B, Richly H, Frost A, Büchert M et al. Regorafenib (BAY 73-4506) in advanced colorectal cancer: a phase I study. *Br J Cancer* 2012; 106: 1722-7.
11. Van Cutsem E, Martinelli E, Cascinu S, Sobrero A, Banzi M, Seitz JF et al. Regorafenib for Patients with Metastatic Colorectal Cancer Who Progressed After Standard Therapy: Results of the Large, Single-Arm, Open-Label Phase IIIb CONSIGN Study. *Oncologist* 2019; 24: 185-92.
12. Goktas Aydin S, Kavak EE, Topcu A, Bayramgil A, Akgul F, Kahraman S et al. Prognostic factors for regorafenib treatment in patients with refractory metastatic colorectal cancer: A real-life retrospective multi-center study. *Biomol Biomed* 2023; 23: 1089-95.
13. Nakashima M, Li K, Chen Q, de Silva S, Li H, Kawakami K et al. Appropriate dose of regorafenib based on body weight of colorectal cancer patients: a retrospective cohort study. *BMC Cancer* 2023; 23: 1268.
14. Yekedüz E, Aktaş EG, Köksoy EB, Doğan N, Ürün Y, Utkan G. The prognostic role of polypharmacy in metastatic colorectal cancer patients treated with regorafenib. *Future Oncol* 2022; 18: 1067-76.

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