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Research Article

Survival outcomes according to adjuvant chemotherapy duration and oxaliplatin use in patients aged 70 years and older with stage II–III colon cancer

Evre II–III kolon kanserli 70 yaş ve üzeri hastalarda adjuvan kemoterapi süresi ve oksaliplatin kullanımına göre sağkalım sonuçları

Omer Acar [1*], Emine Turkmen[2], Mustafa Sahbazlar[2], Ferhat Ekinci[2], Atike Pinar Erdogan[2]

[1]Department of Medical Oncology, Mardin Training and Research Hospital, Mardin, Türkiye
[2]Department of Medical Oncology, Manisa Celal Bayar University, Manisa, Türkiye

Abstract

Aim: The optimal balance between treatment duration and regimen selection in older patients with stage II–III colon cancer remains uncertain in real-world practice. This study aimed to evaluate survival outcomes according to adjuvant chemotherapy duration and oxaliplatin use in older patients with stage II–III colon cancer.

Material and Methods: This retrospective cohort study included patients aged ≥70 years with stage II–III colon adenocarcinoma who underwent curative-intent surgery and received adjuvant chemotherapy between 2015 and 2023. Patients were grouped according to adjuvant chemotherapy regimen (oxaliplatin-based vs non-oxaliplatin) and treatment duration. Overall survival (OS) and disease-free survival (DFS) were analyzed using the Kaplan–Meier method. Factors associated with survival outcomes were evaluated using Cox proportional hazards regression, and multivariable logistic regression analyses were additionally performed for all-cause mortality and recurrence.

Results: A total of 65 patients were included, of whom 35 received oxaliplatin-based regimens. Patients treated with oxaliplatin were younger and more frequently had stage III disease. In multivariable analysis, age >75 years (OR 3.45, 95% CI 1.16–10.21; p = 0.026) and adjuvant chemotherapy duration <6 months (OR 3.80, 95% CI 1.32–10.91; p = 0.013) were independently associated with increased all-cause mortality. Oxaliplatin use was not independently associated with overall survival (OR 1.36, 95% CI 0.45–4.11; p = 0.584) or recurrence risk. Kaplan–Meier analyses demonstrated significantly improved overall survival among patients who completed a full 6-month course of adjuvant chemotherapy, whereas no significant differences in overall or disease-free survival were observed according to oxaliplatin use.

Conclusion: In older patients with stage II–III colon cancer, completion of the planned duration of adjuvant chemotherapy appeared more impactful than regimen intensification with oxaliplatin in this real-world cohort. These findings highlight the importance of treatment continuity in routine clinical practice, particularly among older patients with limited tolerance to treatment.

Keywords: colon cancer, adjuvant chemotherapy, oxaliplatin, survival, older patients

Corresponding Author*: Omer Acar, MD. Department of Medical Oncology, Mardin Training and Research Hospital, 47100, Mardin, Turkey.
E-mail: dracaromer@gmail.com Phone: +90 501910909
Orcid: 0000-0003-4408-1976
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Öz

Amaç: Evre II–III kolon kanseri olan yaşlı hastalarda adjuvan kemoterapi süresi ve rejim seçimi arasındaki optimal denge, gerçek dünya pratiğinde halen net değildir. Bu çalışmada, evre II–III kolon kanseri olan yaşlı hastalarda adjuvan kemoterapi süresi ve oksaliplatin kullanımına göre sağkalım sonuçlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif kohort çalışması, 2015 ile 2023 yılları arasında küratif amaçlı cerrahi geçiren ve adjuvan kemoterapi alan, evre II-III kolon adenokarsinomlu ve 70 yaş ve üzeri hastaları içermiştir. Hastalar, adjuvan kemoterapi rejimine (oksaliplatin bazlı ve oksaliplatin içermeyen) ve tedavi süresine göre gruplandırılmıştır. Genel sağkalım (OS) ve hastalıksız sağkalım (DFS), Kaplan–Meier yöntemi ile analiz edilmiştir. Tüm nedenlere bağlı mortalite ve nüks ile ilişkili faktörler, çok değişkenli lojistik regresyon analizi kullanılarak değerlendirilmiştir.

Bulgular: Toplam 65 hasta çalışmaya dâhil edilmiş olup, bunların 35'i oksaliplatin bazlı rejimler almıştır. Oksaliplatin ile tedavi edilen hastalar daha genç olup, evre III hastalık daha sık görülmüştür. Çok değişkenli analizde, >75 yaş (OR 3,45; %95 GA 1,16–10,21; p = 0,026) ve adjuvan kemoterapi süresinin <6 ay olması (OR 3,80; %95 GA 1,32–10,91; p = 0,013) tüm nedenlere bağlı mortalite ile bağımsız olarak ilişkili bulunmuştur. Oksaliplatin kullanımı, genel sağkalım (OR 1,36; %95 GA 0,45–4,11; p = 0,584) veya nüks riski ile bağımsız olarak ilişkili değildir. Kaplan–Meier analizleri, adjuvan kemoterapinin tam 6 ay tamamlandığı hastalarda genel sağkalımın anlamlı olarak daha iyi olduğunu göstermiş; buna karşın oksaliplatin kullanımına göre genel sağkalım veya hastalıksız sağkalım açısından anlamlı bir fark saptanmamıştır.

Sonuç: Evre II–III kolon kanseri olan yaşlı hastalarda, adjuvan kemoterapinin 6 ay süreyle tamamlanması, floropirimidin bazlı rejimlere oksaliplatin eklenmesine kıyasla sağkalım ile daha güçlü bir ilişki göstermektedir. Bu bulgular, rutin klinik uygulamada, özellikle tedavi toleransı sınırlı olan yaşlı hastalarda, tedavi süresi ve sürekliliğinin rejim yoğunluğundan daha belirleyici olabileceğini düşündürmektedir.

Anahtar Kelimeler: kolon kanseri, adjuvan kemoterapi, oksaliplatin, sağkalım, yaşlı hastalar

Introduction

Colon cancer remains a leading cause of cancer-related morbidity and mortality worldwide, and a substantial proportion of patients are diagnosed with stage II or III disease amenable to curative surgery. In this setting, adjuvant chemotherapy has been shown to reduce recurrence risk and improve survival, particularly in patients with node-positive disease. Fluoropyrimidine-based regimens constitute the backbone of adjuvant treatment, while the addition of oxaliplatin has been associated with further improvements in disease-free survival in selected patient groups [1].

Oxaliplatin-based doublet regimens such as FOLFOX and CAPEOX are widely used in stage III and high-risk stage II colon cancer; however, cumulative neurotoxicity remains a clinically relevant limitation, often leading to dose reductions or early treatment discontinuation. This concern has prompted extensive investigation into whether shorter durations of oxaliplatin exposure can maintain efficacy while reducing treatment-related toxicity [2,3].

The International Duration Evaluation of Adjuvant Therapy (IDEA) collaboration and subsequent randomized trials demonstrated that treatment duration may be safely reduced in certain subgroups, particularly in patients with low-risk stage III disease treated with CAPEOX, whereas patients with high-risk stage III disease appear to derive greater disease-free survival benefit from a full 6-month course of FOLFOX. These findings have influenced contemporary clinical guidelines, which now recommend risk-adapted treatment duration rather than a uniform approach [3,4].

Recently, a comprehensive meta-analysis by Kuang et al. synthesizing data from randomized controlled trials further clarified the interaction between disease risk, chemotherapy regimen, and treatment duration. This analysis showed that a 6-month FOLFOX regimen provided superior disease-free survival only in patients with high-risk stage III colon cancer, whereas extending oxaliplatin duration did not improve overall survival in other stage II–III subgroups. Importantly, shorter regimens were associated with significantly higher treatment completion rates and markedly lower rates of grade ≥2 peripheral neuropathy [5].

Despite these advances, most evidence guiding treatment duration and regimen selection is derived from clinical trial populations that may not fully reflect real-world patients, particularly older adults and those with comorbid conditions.

Observational studies in elderly cohorts have suggested that the survival advantage of adding oxaliplatin may be attenuated with increasing age, while toxicity risk remains substantial. Consequently, the optimal balance between efficacy and tolerability in routine clinical practice remains an area of ongoing uncertainty [4,6].

In light of these considerations, real-world analyses that account for pathological risk factors, treatment duration, and patient characteristics are needed to better define the role of oxaliplatin-based adjuvant chemotherapy. Therefore, this study aimed to evaluate survival outcomes in patients with stage II–III colon cancer treated with oxaliplatin-containing versus non-oxaliplatin regimens, with particular emphasis on treatment duration and clinically relevant risk stratification using adjusted survival analyses.

Material and Methods

This retrospective single-center cohort study included patients aged 70 years and older who underwent curative-intent surgery for colon cancer and subsequently received adjuvant chemotherapy between 2015 and 2023. The study was conducted using the institutional oncology database and electronic medical records of the Department of Medical Oncology, Manisa Celal Bayar University Faculty of Medicine, a tertiary referral center in Turkey. Eligible patients had pathologically confirmed stage II or III colon adenocarcinoma and received at least one cycle of adjuvant chemotherapy. Patients with rectal cancer, metastatic disease at diagnosis, synchronous or metachronous malignancies, prior systemic chemotherapy or radiotherapy before colon cancer diagnosis, or incomplete clinical or follow-up data were excluded. Patients with stage II–III disease who did not receive adjuvant chemotherapy due to comorbid conditions, frailty, or other clinical considerations were also excluded. Due to the retrospective design, standardized frailty assessments and formal ECOG performance status documentation were not consistently available; therefore, treatment allocation was not randomized, and adjuvant chemotherapy regimens oxaliplatin-based (FOLFOX, CAPEOX/XELOX) or non-oxaliplatin (capecitabine or 5-fluorouracil) were selected at the discretion of the treating medical oncologist based on routine clinical practice, patient characteristics, pathological risk factors, and treatment tolerability. A total of 65 patients met the inclusion criteria and were included in the final analysis.

Clinical, pathological, and treatment-related data were extracted from hospital medical records. Collected variables included age at diagnosis, sex, body mass index (BMI), tumor localization (right vs left colon), histopathological subtype, tumor differentiation, presence of lymphovascular invasion (LVI) and perineural invasion (PNI), lymph node status, number of dissected lymph nodes, surgical margin status, disease stage, comorbidities, smoking status, family history of colon cancer, molecular characteristics (KRAS, NRAS, BRAF, and MSI status), adjuvant chemotherapy regimen, treatment duration, and number of chemotherapy cycles.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Manisa Celal Bayar University Faculty of Medicine Health Sciences Ethics Committee (approval date: 05 June 2024, decision number: 2024/486). Because the study was retrospective, informed consent was waived.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows. Descriptive statistics were presented as numbers and percentages for categorical variables and as means ± standard deviations or medians (minimum–maximum) for continuous variables, as appropriate. Comparisons between treatment groups were conducted using the Chi-square test for categorical variables. Since continuous variables did not follow a normal distribution, the Mann–Whitney U test was used for group comparisons.

OS was defined as the time from the date of curative-intent surgery to death from any cause or last follow-up. Disease-free survival (DFS) was defined as the time from surgery to the first documented recurrence or death from any cause, whichever occurred first. OS and DFS were estimated using the Kaplan–Meier method, and survival curves were compared using the log-rank test.

Factors associated with survival outcomes were evaluated using Cox proportional hazards regression analysis, and results were reported as hazard ratios (HRs) with 95% confidence intervals (CIs). In addition, multivariable logistic regression analyses were performed to identify factors associated with all-cause mortality and first recurrence. Age was dichotomized at 75 years for multivariable analyses to evaluate the impact of advanced age within the older patient population. A two-sided p-value <0.05 was considered statistically significant.

Results

A total of 65 patients with stage II–III colon cancer who received adjuvant chemotherapy were included in the analysis. Of these, 35 patients received oxaliplatin-based regimens, while 30 received non-oxaliplatin chemotherapy. Baseline clinical and pathological characteristics according to oxaliplatin use are presented in table 1.

Table 1. Clinical, pathological, and treatment characteristics according to oxaliplatin use.

		Oxaliplatin (n =35)	Non-oxaliplatin (n = 30)	p
Adjuvant Chemotherapy	5-FU		3 (10.0)	
	Capecitabine		27 (90.0)	
	XELOX	29 (82.9)		
	FOLFOX	6 (17.1)		
Sex	Female	13 (37.1)	14 (46.7)	0.461
	Male	22 (62.9)	16 (53.3)	
Age at diagnosis (years)		73 (70–81)	76 (70–82)	0.010
BMI (kg/m^2)		25.33 ± 3.82	24.33 ± 4.36	0.211
Tumor location	Right colon	17 (48.6)	16 (53.3)	0.805
	Left colon	18 (51.4)	14 (46.7)	
Histopathology	Adenocarcinoma	34 (97.1)	28 (93.3)	0.591
	Mucinous	1 (2.9)	2 (6.7)	
Differentiation	Well	11 (32.4)	10 (33.3)	0.840
	Moderate	22 (64.7)	18 (60.0)	
	Poor	1 (2.9)	2 (6.7)	
Comorbidities	No	4 (11.4)	5 (16.7)	0.722
	Yes	31 (88.6)	25 (83.3)	
Emergency surgery	No	31 (88.6)	22 (73.3)	0.199
	Yes	4 (11.4)	8 (26.7)	
LVI	No	15 (45.5)	19 (65.5)	0.132
	Yes	18 (54.5)	10 (34.5)	
PNI	No	18 (54.5)	19 (65.5)	0.443
	Yes	15 (45.5)	10 (34.5)	
N stage	N0	10 (30.3)	18 (60.0)	0.056
	N1 (1–3)	16 (48.5)	9 (30.0)	
	N2a (4–6)	4 (12.1)	3 (10.0)	
	N2b (≥7)	3 (9.1)	0 (0.0)	
Lymph node dissection	<12 LN	6 (18.2)	7 (23.3)	0.758
	≥12 LN	27 (81.8)	23 (76.7)	
Surgical margin	Negative	32 (97.0)	29 (96.7)	1.000
	Positive	1 (3.0)	1 (3.3)	
Stage	Stage II	6 (17.6)	16 (53.3)	0.004
	Stage III	28 (82.4)	14 (46.7)	
KRAS	Mutant	5 (55.6)	1 (33.3)	1.000
	Wild-type	4 (44.4)	2 (66.7)	
NRAS	Mutant	1 (16.7)	0 (0.0)	1.000
	Wild-type	5 (83.3)	1 (100.0)	
BRAF	Mutant	1 (16.7)	0 (0.0)	1.000
	Wild-type	5 (83.3)	1 (100.0)	
MSI status	MSS	18 (94.7)	13 (92.9)	1.000
	MSI-H	1 (5.3)	1 (7.1)	
Smoking Status	Never	17 (48.6)	13 (43.3)	0.290
	Former	13 (37.1)	8 (26.7)	
	Current	5 (14.3)	9 (30.0)	
Adjuvant chemotherapy completion	<3 months	5 (14.3)	8 (26.7)	0.447
	3–6 months	18 (51.4)	12 (40.0)	
	6 months	12 (34.3)	10 (33.3)	

Data are presented as n (%) or median (minimum–maximum). Percentages were calculated within each treatment group. LVI: lymphovascular invasion; PNI: perineural invasion; MSI: microsatellite instability.

Patients treated with oxaliplatin were younger than those in the non-oxaliplatin group (median age 73 vs 76 years, p = 0.010) and were more likely to have stage III disease (82.4% vs 46.7%, p = 0.004). Other demographic, pathological, molecular, and treatment-related variables were comparable between groups.

In multivariable logistic regression analysis for all-cause mortality (Table 2), age >75 years (OR 3.45, 95% CI 1.16–10.21; p = 0.026) and adjuvant chemotherapy duration of less than 6 months (OR 3.80, 95% CI 1.32–10.91; p = 0.013) were independently associated with increased mortality. Oxaliplatin use was not independently associated with all-cause mortality.

In the multivariable analysis for recurrence (Table 3), none of the evaluated variables, including oxaliplatin use and chemotherapy duration, were significantly associated with recurrence risk.

Kaplan–Meier survival analysis demonstrated significantly improved overall survival among patients who completed a full 6-month course of adjuvant chemotherapy compared with those who received shorter durations (Figure 1). Patients completing 6 months of therapy had a significantly lower risk of death (HR 0.22, 95% CI 0.07–0.70; p = 0.010).

When stratified by oxaliplatin use, overall survival differed significantly only among patients who completed 6 months of adjuvant chemotherapy, with longer survival observed in the oxaliplatin group (log-rank p = 0.023). In contrast, no statistically significant difference in overall survival was observed according to oxaliplatin use among patients who received adjuvant chemotherapy for less than 6 months (log-rank p = 0.699) (Figure 1).

In multivariable analyses, disease stage—including comparisons between low-risk (T3N1) and high-risk (T4 and/or N2) stage III disease—was not independently associated with all-cause mortality or recurrence (Tables 2,3).

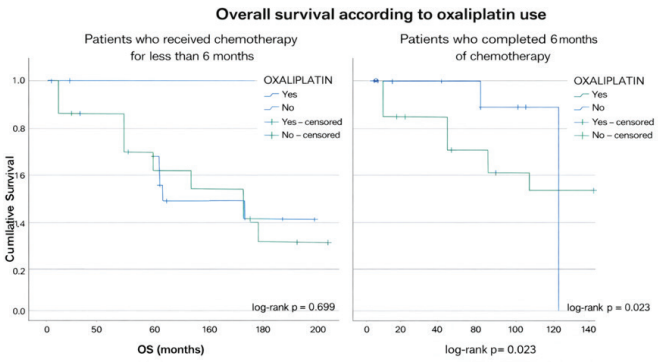

Figure 1. Kaplan–Meier overall survival curves by oxaliplatin use. stratified by adjuvant chemotherapy duration.

In patients who completed 6 months of adjuvant chemotherapy. overall survival differed significantly by oxaliplatin use (log-rank p = 0.023). In this subgroup. the median overall survival was 149 months in the oxaliplatin group and 59 months in the non-oxaliplatin group (95% CI: 22.4–95.6). In contrast. among patients who received chemotherapy for less than 6 months. no statistically significant difference in overall survival was observed between patients treated with and without oxaliplatin (log-rank p = 0.699).

Table 2. Multivariable logistic regression analysis for all-cause mortality.

Variable	Comparison (Category vs Reference)	OR	95% CI	p
Age	>75 vs ≤75	3.445	1.162–10.213	0.026
PNI	Present vs Absent	2.232	0.584–8.533	0.241
LVI	Present vs Absent	1.125	0.305–4.152	0.859
lymph node dissection	<12 LNs vs ≥12 LNs	1.526	0.550–4.234	0.417
Tumor location	Right colon vs Left colon	1.322	0.461–3.788	0.604
Differentiation	Ref: Well differentiated	—	—	0.124
	Moderate vs Well	2.724	0.810–9.166	0.105
	Poor vs Well	5.416	0.839–34.947	0.076
Adjuvant chemotherapy duration	<6 months vs 6 months	3.800	1.324–10.908	0.013
Oxaliplatin use	No vs Yes	1.362	0.452–4.106	0.584
Stage	Ref: high-risk stage 3	—	—	0.445
	Stage 2 vs high-risk stage 3	0.506	0.158–1.628	0.254
	Low-risk vs high-risk stage 3	1.335	0.397–4.494	0.641

OR: odds ratio; CI: confidence interval; LVI: lymphovascular invasion; PNI: perineural invasion.

Table 3. Multivariable logistic regression analysis for first recurrence (local or distant).				
Variable	Comparison (Category vs Reference)	OR	95% CI	p
Age	>75 vs ≤75	1.715	0.476–6.176	0.409
PNI	Present vs Absent	1.671	0.276–10.129	0.576
LVI	Present vs Absent	0.970	0.156–6.018	0.974
lymph node dissection	<12 LNs vs ≥12 LNs	1.599	0.406–6.307	0.502
Tumor location	Right colon vs Left colon	1.699	0.494–5.848	0.401
Differentiation	Ref: Well differentiated	—	—	0.470
	Moderate vs Well	1.079	0.281–4.142	0.911
	Poor vs Well	4.731	0.390–57.369	0.222
Adjuvant chemotherapy duration	<6 months vs 6 months	1.579	0.446–5.583	0.479
Oxaliplatin	No vs Yes	0.404	0.090–1.813	0.237
Stage	Ref: high-risk stage 3	—	—	0.237
	Stage 2 vs high-risk stage 3	0.432	0.086–2.169	0.308
	Low-risk vs high-risk stage 3	0.195	0.022–1.722	0.141
OR: odds ratio; CI: confidence interval; LVI: lymphovascular invasion; PNI: perineural invasion.				

Discussion

In this retrospective cohort of 65 patients with stage II–III colon cancer treated with adjuvant chemotherapy, we observed three main findings. First, oxaliplatin use was not independently associated with overall or disease-free survival, despite a clear imbalance in baseline stage distribution (more stage III disease in the oxaliplatin group). Second, age >75 years and adjuvant chemotherapy duration of less than 6 months were independently associated with increased all-cause mortality. Third, none of the assessed clinicopathologic or treatment-related variables including oxaliplatin exposure and chemotherapy duration were significantly associated with the risk of first recurrence.

The optimal duration of oxaliplatin-based adjuvant chemotherapy has been extensively investigated in randomized trials and meta-analyses. The IDEA collaboration demonstrated that treatment duration should be individualized by regimen and risk profile, with 3 months of CAPOX acceptable for selected low-risk patients, while high-risk stage III disease may derive greater benefit from a 6-month course, particularly with FOLFOX [7,8]. Results from the ACHIEVE trial and subsequent pooled analyses confirmed that shorter durations substantially reduce cumulative neurotoxicity with minimal compromise of survival outcomes in appropriate subgroups [2,6].

In this study, the duration of adjuvant chemotherapy, rather than regimen intensification with oxaliplatin, appeared to be the key determinant of survival outcomes in this cohort. Importantly, this finding should not be interpreted as evidence of oxaliplatin inefficacy, but rather as a reflection of the clinical importance of treatment continuity and tolerability in older patients treated in routine practice. Completing a full 6-month course of adjuvant treatment was independently associated with improved survival, whereas incorporating oxaliplatin into combination regimens such as FOLFOX or CAPEOX did not confer additional survival benefit. These findings suggest that, in real-world clinical practice, maintaining treatment continuity and achieving adequate treatment duration may be more critical than intensifying therapy by adding oxaliplatin, particularly in older or comorbid patients with limited treatment tolerance [9].

No variables were independently associated with recurrence risk in multivariable analysis. This may be explained by limited sample size, heterogeneous disease stages, and a relatively low number of recurrence events. Although established pathological risk factors such as lymphovascular invasion, perineural invasion, and inadequate lymph node dissection are known to influence recurrence risk, their prognostic impact may be difficult to demonstrate in small retrospective cohorts after adjustment [10-14]. Accordingly, the recurrence analysis should be interpreted as exploratory rather than definitive.

Emerging evidence supports integrating circulating tumor DNA (ctDNA) for risk stratification and personalizing adjuvant therapy in colon cancer. Recent randomized trials and meta-analyses have shown that ctDNA positivity after surgery is strongly associated with recurrence and may guide escalation or de-escalation strategies without compromising oncologic outcomes. Although ctDNA data were not available in our study, these approaches represent an important future direction for optimizing adjuvant treatment decisions [15-17].

Limitations of the study

This study has several limitations inherent to its retrospective design, including selection bias in regimen assignment, residual confounding particularly in older patients with multiple comorbidities and a limited sample size. In addition, the specific reasons for early discontinuation of adjuvant chemotherapy among patients who received less than 6 months of treatment could not be systematically identified, as detailed documentation distinguishing treatment-related toxicity, patient preference, early disease progression or recurrence, and logistical or access-related factors was not consistently available in medical records. Furthermore, all-cause mortality was used in the logistic regression analyses, which may have been influenced by competing non-cancer deaths, especially in patients older than 75 years. Despite these limitations, our findings provide pragmatic real-world signals suggesting that completion of planned adjuvant therapy may be more impactful than regimen intensification in this selected older cohort, while the incremental survival benefit of oxaliplatin may be attenuated in patients with limited treatment tolerance. Larger prospective, multicenter studies incorporating treatment-related toxicity, dose intensity, competing-risk analyses, and molecular risk stratification are warranted to better define individualized adjuvant treatment strategies in routine clinical practice.

In conclusion, this real-world retrospective cohort study suggests that, among older patients with stage II–III colon cancer, completion of the planned duration of adjuvant chemotherapy may be more strongly associated with survival outcomes than regimen intensification within this selected population. Importantly, these findings should not be interpreted as evidence of oxaliplatin inefficacy; rather, they highlight the potential clinical relevance of treatment continuity and tolerability in routine practice, particularly in older and comorbid patients. Accordingly, prioritizing completion of planned adjuvant therapy may represent a pragmatic approach in selected individuals. Larger, prospective, multicenter studies that incorporate treatment-related toxicity, dose intensity, and molecular risk stratification are warranted to further clarify the optimal role of oxaliplatin-based adjuvant therapy in this population.

Declaration of conflicting interests

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Ethics approval

The study was approved by the Manisa Celal Bayar University Faculty of Medicine Health Sciences Ethics Committee (approval date: 05 June 2024, decision number: 2024/486).

Authors' contribution

Ö.A., E.T., and A.P.E. contributed to the conception and design of the study. M.Ş. and F.E. organized the database. All authors wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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