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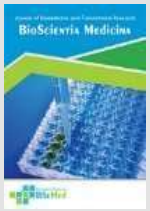

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FOLFOX vs. FOLFIRI in Colorectal Adenocarcinoma: A Retrospective Study of Treatment Patterns, Side Effects, and Treatment Response

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A B S T R A C T

Background: Colorectal adenocarcinoma (CRC) is a prevalent malignancy with a high recurrence rate, necessitating multimodal treatment strategies. Chemotherapy regimens like FOLFOX (folinic acid, fluorouracil, oxaliplatin) and FOLFIRI (folinic acid, fluorouracil, irinotecan) are crucial components of this approach. This study aimed to analyze treatment patterns, side effects, and treatment response of FOLFOX and FOLFIRI in a real-world cohort of CRC patients. **Methods:** A retrospective observational study was conducted on CRC patients who received FOLFOX or FOLFIRI between January 2020 and December 2023. Data on demographics, disease stage, chemotherapy regimen, side effects, comorbidities, and treatment response were collected from electronic medical records. **Results:** A total of 146 patients were included. The majority were male (57.5%) with a mean of age 58.4 years. Most tumors were located in the rectum and sigmoid (75.3%), with over 50% of patients presenting with stage IV disease. FOLFIRI was the most common regimen (45.9%), followed by FOLFOX (36.3%). Common side effects included nausea, vomiting, decreased appetite, and hair loss. Hypertension was the most prevalent comorbidity. A total of 79.5% of patients were alive after chemotherapy. **Conclusion:** This study provides insights into the real-world treatment patterns and outcomes of FOLFOX and FOLFIRI in CRC patients. The choice of regimen appears to be influenced by factors such as disease stage and patient characteristics. Further research is needed to compare the efficacy and safety of these regimens and identify optimal treatment strategies for specific patient subgroups.

1. Introduction

Colorectal adenocarcinoma (CRC) is a significant global health concern, representing a leading cause of cancer-related morbidity and mortality worldwide. It is the third most commonly diagnosed cancer and the second leading cause of cancer death, accounting for a substantial portion of the global cancer burden. The incidence of CRC varies geographically, with higher rates observed in developed countries and an increasing trend in developing nations, likely attributed to lifestyle and dietary factors. Despite advancements in screening and treatment modalities, CRC continues to pose a significant challenge to healthcare systems, underscoring the need for continued research and optimization of therapeutic strategies. The clinical presentation of CRC can range from asymptomatic to overt symptoms such as rectal bleeding, changes in bowel habits, abdominal pain, and weight loss. The disease typically arises from adenomatous polyps, which undergo malignant transformation over time. The prognosis of CRC is largely dependent on the stage at diagnosis, with early-stage disease having a favorable outcome compared to advanced or metastatic disease. The mainstay of treatment for localized CRC is surgical resection, which aims to remove the primary tumor

and any involved lymph nodes. However, the risk of recurrence remains a concern, particularly in patients with locally advanced or metastatic disease.[1-4]

For patients with locally advanced or metastatic CRC (mCRC), multimodal therapy combining surgery, chemotherapy, and radiotherapy is the preferred approach. Chemotherapy plays a crucial role in both the adjuvant and palliative settings for CRC. In the adjuvant setting, chemotherapy is administered after surgery to eradicate micrometastatic disease and improve overall survival (OS). It aims to target any residual cancer cells that may have spread beyond the primary tumor site, reducing the risk of recurrence and improving long-term outcomes. In the palliative setting, chemotherapy is used to control tumor growth, alleviate symptoms, and prolong survival in patients with unresectable or metastatic disease. The goal is to provide symptomatic relief and improve quality of life, even if a cure is not achievable. Several chemotherapy regimens have been established for CRC, with FOLFOX (folinic acid, fluorouracil, and oxaliplatin) and FOLFIRI (folinic acid, fluorouracil, and irinotecan) being two of the most commonly used regimens. These regimens have been extensively studied in clinical trials and have demonstrated significant efficacy in improving OS and progression-free survival (PFS) in patients with mCRC. They are considered the backbone of chemotherapy treatment for mCRC, and their selection is often guided by factors such as disease stage, patient characteristics, and comorbidities.[5-7]

FOLFOX and FOLFIRI are combination chemotherapy regimens that work by interfering with the growth and division of cancer cells. Folinic acid enhances the activity of fluorouracil, a pyrimidine analog that disrupts DNA synthesis and repair. Oxaliplatin, a platinum-based compound, forms DNA adducts that inhibit DNA replication and transcription. Irinotecan, a topoisomerase I inhibitor, prevents DNA unwinding and replication. These agents, in combination, exert synergistic cytotoxic effects on cancer cells, leading to tumor regression and disease control. While clinical trials have provided valuable evidence on the efficacy and safety of FOLFOX and FOLFIRI, there is limited real-world data on their comparative effectiveness and safety in a broader patient population. Most clinical trials have strict inclusion and exclusion criteria, which may not reflect the heterogeneity of CRC patients encountered in routine clinical practice. Real-world studies are essential to understand the treatment patterns, side effects, and treatment response of FOLFOX and FOLFIRI in a more diverse and representative patient population, including those with comorbidities and other factors that may influence treatment outcomes.[8-10] This retrospective study aimed to analyze the treatment patterns, side effects, and treatment response of FOLFOX and FOLFIRI in a cohort of CRC patients treated at our institution.

2. Methods

This research employed a retrospective observational study design, conducted within a tertiary care hospital setting. The study population encompassed patients diagnosed with colorectal adenocarcinoma who had undergone at least one cycle of either FOLFOX or FOLFIRI chemotherapy during the study period spanning from January 2020 to December 2023. To maintain data integrity and ensure the reliability of the analysis, patients with incomplete medical records or missing information pertinent to the chemotherapy regimen and treatment response were excluded from the study cohort.

Data utilized in this study were meticulously collected from electronic medical records (EMRs), ensuring a comprehensive and standardized approach. EMRs provide a rich source of patient-specific information, allowing for a detailed retrospective analysis of treatment patterns, side effects, and treatment responses. The following data points were systematically extracted from the EMRs; Demographics: Age, gender, education level, and employment status were documented to characterize the study population's baseline characteristics. These factors may influence treatment decisions and outcomes, providing valuable insights into the real-

world application of FOLFOX and FOLFIRI regimens; Disease Characteristics: Tumor location, tumor stage (as per the American Joint Committee on Cancer [AJCC] TNM staging system), and histologic subtype were recorded. These disease-specific factors play a crucial role in determining the appropriate treatment strategy and provide context for evaluating treatment response; Treatment Details: Chemotherapy regimen (FOLFOX or FOLFIRI), number of cycles received, and dose modifications were meticulously documented. This information elucidates the treatment patterns and provides insights into the clinical decision-making process regarding dose adjustments based on individual patient needs and tolerances; Side Effects: Hematologic toxicities (neutropenia, anemia, thrombocytopenia), gastrointestinal toxicities (nausea, vomiting, diarrhea), and neurotoxicity were systematically recorded. Monitoring and documenting side effects is essential for assessing the safety and tolerability of chemotherapy regimens, guiding supportive care measures, and ensuring patient well-being; Comorbidities: The presence of other medical conditions, such as hypertension, diabetes mellitus, chronic kidney disease, and heart disease, was documented. Comorbidities can influence treatment decisions, increase the risk of complications, and affect overall survival, necessitating careful consideration in the context of chemotherapy treatment; Treatment Response: Treatment response was rigorously assessed using the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, a standardized and widely accepted framework for evaluating tumor response to treatment. RECIST criteria provide objective measures of tumor size changes, allowing for consistent classification of treatment responses into categories such as complete response, partial response, stable disease, and progressive disease.

The data collected were subjected to rigorous statistical analysis to derive meaningful insights and characterize the study findings. Descriptive statistics were employed to summarize patient characteristics, treatment patterns, and outcomes, providing a comprehensive overview of the study cohort and the observed trends. Categorical variables were presented as frequencies and percentages, enabling a clear understanding of the distribution of these variables within the study population. Continuous variables were presented as means and standard deviations, providing measures of central tendency and variability. To explore the relationship between patient characteristics and treatment outcomes, appropriate statistical tests were employed. These tests aimed to identify potential associations between demographic factors, disease characteristics, and treatment responses, shedding light on factors that may influence the effectiveness of FOLFOX and FOLFIRI regimens. The statistical analyses were conducted using SPSS software version 27, a robust statistical package widely used in healthcare research.

3. Results

Table 1 provides a detailed breakdown of the characteristics of the 146 colorectal adenocarcinoma patients participating in the study. The average age of the participants was 58.4 years, suggesting the study population primarily consisted of older adults. This aligns with the general trend of colorectal cancer being more common in older age groups. A slightly higher proportion of males (57.5%) than females (42.5%) were included. This is somewhat consistent with epidemiological data that shows a slightly higher incidence of colorectal cancer in men. The majority of participants had attained a high school education or below (71.2%). This might indicate a potential link between lower education levels and colorectal cancer risk, which could be explored in further research. Most participants were employed (47.9%), followed by those who were retired (34.2%). This information provides context about the participants' socioeconomic status and lifestyle, which could influence treatment choices and outcomes. The most frequent tumor locations were the rectum and sigmoid colon (75.3%). This is consistent with the known distribution of colorectal cancer, where tumors are more commonly found in the distal colon and rectum.

Over half of the patients (50.7%) presented with stage IV disease, indicating advanced or metastatic cancer. This highlights the severity of the disease in the study population and the need for effective systemic therapies like FOLFOX and FOLFIRI. The majority of tumors were T3 or T4 (73.3%), indicating larger tumor sizes and potentially more advanced disease. This further emphasizes the need for aggressive treatment strategies in this patient population. FOLFIRI was the most commonly used regimen (45.9%), followed by FOLFOX (36.3%). The reasons for this preference could be multifaceted, including physician preference, patient characteristics, and treatment center protocols. The most frequently reported side effects were nausea, vomiting, decreased appetite, and hair loss. These are common side effects associated with both FOLFOX and FOLFIRI regimens and underscore the importance of supportive care measures to manage these toxicities. Hypertension was the most prevalent comorbidity (31.5%), followed by diabetes mellitus (17.8%). The presence of comorbidities can influence treatment decisions and potentially increase the risk of complications, highlighting the need for careful patient selection and monitoring. A significant proportion of patients (79.5%) were alive after chemotherapy, suggesting that these regimens provide a survival benefit in this population. However, further analysis is needed to determine the long-term survival outcomes and factors associated with survival.

Table 2 delves into the treatment patterns observed within the study cohort, specifically examining the relationship between various patient and disease characteristics and the chosen chemotherapy regimen (FOLFOX, FOLFIRI, or a combination of both). A slightly higher proportion of males received FOLFOX (67.9%) compared to FOLFIRI (46.3%). This could suggest a potential preference for FOLFOX in male patients, although the reasons for this are not clear from the table alone. Conversely, FOLFIRI was more common in females (53.7%) than FOLFOX (32.1%). This might indicate that FOLFIRI is better tolerated or perceived as more suitable for female patients, but further investigation is needed to confirm this. For tumors located in the sigmoid/rectosigmoid colon, FOLFOX was slightly more common (47.2%) than FOLFIRI (37.3%). This could be due to factors such as tumor biology or location-specific treatment preferences. In contrast, FOLFIRI was more frequently used for rectal tumors (34.3%) compared to FOLFOX (30.2%). This might reflect differences in treatment approaches based on tumor location. For stage II tumors, FOLFIRI was considerably more prevalent (68.4%) than FOLFOX (26.3%). This could suggest that FOLFIRI is preferred for earlier-stage disease, possibly due to its perceived tolerability or efficacy in this setting. In stage IV disease, FOLFOX was more common (49.3%) than FOLFIRI (30.4%). This might indicate that FOLFOX is considered more effective or suitable for advanced or metastatic disease. Patients with a history of biopsy were more likely to receive FOLFIRI (91%) compared to those without a biopsy (75.5% for FOLFOX). This could be related to factors such as tumor characteristics or the timing of chemotherapy in relation to surgery. Similarly, patients who had undergone a laparotomy were more likely to receive FOLFIRI (44.8%) than those who had not (55.2% for FOLFOX). This might reflect differences in treatment approaches based on surgical history. Patients who had undergone a colonoscopy were more likely to receive FOLFIRI (22.4%) compared to those who had not (20.8% for FOLFOX). This could be due to factors such as the timing of chemotherapy in relation to diagnostic procedures. Patients who had undergone tumor resection were more likely to receive FOLFIRI (31.3%) compared to those who had not (17% for FOLFOX). This might reflect differences in treatment strategies based on the extent of surgical intervention.

Table 1. Participants characteristics.

Variable	Frequency (n)	Percentage (%)
Age (years), Mean±SD	58.4 ± 11.3	-
Gender		
Male	84	57.5
Female	62	42.5
Education level		
Elementary School	5	3.4
Junior High School	6	4.1
Senior High School	13	8.9
Vocational School	2	8.9
Bechelor	16	11
Not schooled	1	0.7
Occupation		
Housewife	8	5.5
Retired	7	4.9
Unemployed	6	4.1
Housewife	4	2.7
Trader/entrepreneur	4	2.8
Farmer	3	2.1
Laborer	2	1.4
Teacher	2	1.4
Motorcycle taxi driver	1	0.7
Doctor	1	0.7
Domestic worker	1	0.7
Tour guide	1	0.7
Tumor location		
Rectosigmoid/sigmoid	57	39
Rectum	53	36.3
Colon	33	22.6
Caecum	3	2.1
Tumor size		
T4	64	43.8
T3	69	47.3
T2	12	8.2
T1	1	0.7
Stage		
I	5	3.4
II	19	13.0
IIIA	2	1.4
IIIB	24	16.4
IIIC	17	11.6
IV	79	54.1
Surgical history		
Post-laparotomy	69	47.3
Post-resection	39	26.8
None	33	22.6
Post-colonoscopy	32	21.9
Post-biopsy	21	14.4
Chemotherapy regimen		
FOLFIRI	67	45.9
FOLFOX	53	36.3
FOLFOX & FOLFIRI	26	17.8
Side effects		
Nausea and vomiting	14	9.8
Hair loss	2	1.4
Decreased appetite	5	3.4
None	49	33.6
Diagnosis		
NOS adenocarcinoma	125	85.6
Mucinous adenocarcinoma	17	11.6
Signet ring adenocarcinoma	4	2.7
Mortality		
Alive	116	79.5
Deceased	30	20.5
Comorbidity		
CKD, AKI, & Nephrolithiasis	8	5.5
Hypertension	11	7.5
Diabetes mellitus	6	4.1
Heart disease	2	1.4
Liver disease	1	0.7
None	61	41.8

Table 2. Treatment patterns.

Variable	FOLFOX	FOLFIRI	FOLFOX & FOLFIRI	Total
Gender				
Male	36 (67.9%)	31 (46.3%)	17 (65.4%)	84 (57.5%)
Female	17 (32.1%)	36 (53.7%)	9 (34.6%)	62 (42.5%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
Tumor location				
Sigmoid/Rectosigmoid	25 (47.2%)	25 (37.3%)	7 (26.9%)	57 (39.0%)
Rectum	16 (30.2%)	23 (34.3%)	14 (53.8%)	53 (36.4%)
Colon	10 (18.9%)	18 (26.9%)	5 (19.3%)	33 (22.6%)
Caecum	2 (3.7%)	1 (1.5%)	0	3 (2.0%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
Stage				
I	0	3 (60%)	2 (40%)	5 (3.4%)
II	5 (26.3%)	13 (68.4%)	1 (5.2%)	19 (13.1%)
IIIA	0	2 (100%)	0	2 (1.4%)
IIIB	6 (25%)	14 (58.3%)	4 (16.7%)	24 (16.4%)
IIIC	3 (17.6%)	11 (64.7%)	3 (17.6%)	17 (11.6%)
IV	39 (49.3%)	24 (30.4%)	16 (20.2%)	79 (54.1%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
Surgical history				
No biopsy	40 (75.5%)	61 (91.0%)	24 (92.3%)	125 (85.6%)
Biopsy	13 (24.5%)	6 (9.0%)	2 (7.7%)	21 (14.4%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
No laparotomy	29 (54.7%)	37 (55.2%)	11 (42.3%)	77 (52.7%)
Laparotomy	24 (15.3%)	30 (44.8%)	15 (57.7%)	69 (47.3%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
No colonoscopy	42 (79.2%)	52 (77.6%)	20 (76.9%)	114 (78.1%)
Colonoscopy	11 (20.8%)	15 (22.4%)	6 (23.1%)	32 (21.9%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
No resection	44 (83.0%)	46 (68.7%)	17 (65.4%)	107 (73.3%)
Resection	9 (17.0%)	21 (31.3%)	9 (34.6%)	39 (26.7%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)

Table 3 provides a clear picture of the side effects experienced by patients receiving FOLFOX and FOLFIRI chemotherapy regimens. Both FOLFOX and FOLFIRI showed a high percentage of patients without nausea and vomiting (92.5% and 89.6%, respectively). This suggests that these regimens are generally well-tolerated in terms of nausea and vomiting, especially with modern antiemetic medications. A small percentage of patients experienced nausea and vomiting (7.5% for FOLFOX and 10.4% for FOLFIRI). This highlights the importance of proactively managing these side effects with appropriate antiemetic therapy to maintain patient comfort and quality of life. Hair loss was a rare side effect with both FOLFOX and FOLFIRI (1.9% and 1.5%, respectively). This is reassuring for patients, as hair loss can be a distressing side effect of chemotherapy. The very low incidence of hair loss might be attributed to the specific drugs used in these regimens or the dosages administered. The majority of patients maintained their appetite on both FOLFOX and FOLFIRI (94.3% and 97%, respectively). This is crucial for patients undergoing chemotherapy, as adequate nutrition is essential for maintaining strength and overall health. A small percentage of patients experienced appetite loss (5.7% for FOLFOX and 3% for FOLFIRI). This emphasizes the need for nutritional counseling and support for patients who experience this side effect to prevent malnutrition and its associated complications.

Table 3. Side effects.

Variable	FOLFOX	FOLFIRI	FOLFOX & FOLFIRI	Total
No Nausea and Vomiting	49 (92.5%)	60 (89.6%)	23 (88.5%)	132 (90.4%)
Nausea and Vomiting	4 (7.5%)	7 (10.4%)	3 (11.5%)	14 (9.6%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
No Hair Loss	52 (98.1%)	66 (98.5%)	26 (100.0%)	144 (98.6%)
Hair Loss	1 (1.9%)	1 (1.5%)	0	2 (1.4%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)
No Appetite Loss	50 (94.3%)	65 (97.0%)	26 (100.0%)	141 (96.6%)
Appetite Loss	3 (5.7%)	2 (3.0%)	0	5 (3.4%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)

Table 4 presents the treatment responses observed in the study cohort following treatment with FOLFOX and FOLFIRI, categorized using the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Both FOLFOX and FOLFIRI demonstrated similar overall response rates (combining Complete Response [CR] and Partial Response [PR]). This suggests that both regimens have comparable efficacy in inducing tumor shrinkage. FOLFIRI had a slightly higher overall response rate (46.3%) compared to FOLFOX (43.4%). However, this difference is not substantial and may not be clinically significant. CR rates were low for both FOLFOX (9.4%) and FOLFIRI (9.0%). This is not unexpected, as achieving complete tumor eradication is challenging in advanced colorectal cancer. The combination of FOLFOX and FOLFIRI did not appear to significantly improve CR rates (11.5%). FOLFIRI showed a slightly higher PR rate (37.3%) compared to FOLFOX (34.0%). This might indicate a slightly better ability of FOLFIRI to induce tumor shrinkage, although further analysis is needed to confirm this. Both FOLFOX and FOLFIRI had similar rates of stable disease (45.3% and 43.3%, respectively). This suggests that both regimens are capable of controlling disease progression in a significant proportion of patients. Progressive disease rates were low for both FOLFOX (11.3%) and FOLFIRI (10.4%). This indicates that both regimens are generally effective in preventing disease progression.

Table 4. Treatment response.

Variable	FOLFOX	FOLFIRI	FOLFOX & FOLFIRI	Total
Complete Response (CR)	5 (9.4%)	6 (9.0%)	3 (11.5%)	14 (9.6%)
Partial Response (PR)	18 (34.0%)	25 (37.3%)	7 (26.9%)	50 (34.2%)
Stable Disease (SD)	24 (45.3%)	29 (43.3%)	13 (50.0%)	66 (45.2%)
Progressive Disease (PD)	6 (11.3%)	7 (10.4%)	3 (11.5%)	16 (10.9%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)

Table 5 presents the survival status of patients who received FOLFOX and FOLFIRI, providing insights into the overall survival outcomes associated with these treatments. The majority of patients were alive after receiving either FOLFOX (75.5%) or FOLFIRI (83.6%). This indicates that both regimens offer a significant survival benefit for colorectal cancer patients. FOLFIRI appears to be associated with a slightly higher survival rate compared to FOLFOX. This difference may warrant further investigation to determine if it's

clinically significant. A smaller proportion of patients who received FOLFIRI died (16.4%) compared to those who received FOLFOX (24.5%). This further supports the observation that FOLFIRI might be associated with better survival outcomes. The group receiving both FOLFOX and FOLFIRI had a survival rate (76.9%) closer to that of the FOLFIRI-only group. This suggests that the sequential or combined use of these regimens might offer a survival advantage similar to FOLFIRI alone.

Table 5. Survival rate.

Variable	FOLFOX	FOLFIRI	FOLFOX & FOLFIRI	Total
Alive	40 (75.5%)	56 (83.6%)	20 (76.9%)	116 (79.5%)
Deceased	13 (24.5%)	11 (16.4%)	6 (23.1%)	30 (20.5%)
Total	53 (36.3%)	67 (45.9%)	26 (17.8%)	146 (100.0%)

4. Discussion

Our analysis revealed that FOLFIRI was the most commonly used regimen (45.9%), followed by FOLFOX (36.3%). This observation contrasts with some previous studies that reported a higher prevalence of FOLFOX usage. This discrepancy could be attributed to several factors, including evolving treatment paradigms, physician preferences, institutional protocols, and patient-specific considerations. The choice between FOLFOX and FOLFIRI is often guided by factors such as disease stage, tumor location, patient comorbidities, and performance status. In our study, we observed some trends in treatment selection based on these factors. For instance, FOLFIRI was more frequently used in patients with stage II disease, while FOLFOX was more common in those with stage IV disease. This might reflect a preference for FOLFIRI in earlier-stage disease due to its perceived tolerability, while FOLFOX might be favored in advanced disease due to its potential for greater efficacy. Furthermore, we observed differences in treatment selection based on tumor location. FOLFIRI was more commonly used for rectal tumors, while FOLFOX was more prevalent for tumors located in the sigmoid/rectosigmoid colon. This could be attributed to variations in tumor biology or location-specific treatment approaches. The landscape of colorectal cancer treatment is dynamic and constantly evolving, with new research and clinical trials continuously shaping treatment recommendations and guidelines. Over time, the perceived efficacy and safety profiles of FOLFOX and FOLFIRI may have shifted, leading to changes in their relative usage patterns. New clinical trial data may demonstrate the superiority of one regimen over the other in specific patient populations or disease stages. For example, recent trials might suggest that FOLFIRI is more effective in patients with microsatellite instability-high (MSI-H) tumors, while FOLFOX might be preferred for those with RAS wild-type tumors. The introduction of novel therapeutic agents, such as targeted therapies and immunotherapies, has expanded the treatment options for colorectal cancer. These agents may be used in combination with FOLFOX or FOLFIRI, or they may replace these regimens altogether in certain situations. This evolving treatment landscape can influence the choice between FOLFOX and FOLFIRI, as physicians consider the optimal sequencing and combination of therapies. Treatment strategies for colorectal cancer are constantly being refined, with a growing emphasis on personalized medicine and precision oncology. This involves tailoring treatment decisions based on individual patient characteristics, tumor biology, and molecular profiling. As our understanding of the molecular underpinnings of colorectal cancer deepens, treatment selection may become increasingly individualized, leading to variations in the usage patterns of FOLFOX and

FOLFIRI. Individual physicians may have different preferences for FOLFOX or FOLFIRI based on their clinical experience, familiarity with the regimens, and perceived risk-benefit profiles for specific patient populations. This can lead to variations in treatment patterns across different healthcare settings. Physicians may develop preferences for certain regimens based on their own clinical experience and observations. For example, a physician who has observed favorable outcomes with FOLFIRI in their practice might be more inclined to prescribe this regimen for their patients. The complexity of chemotherapy regimens, including dosing schedules, administration protocols, and side effect management, can influence physician preferences. Physicians might be more comfortable prescribing regimens they are more familiar with, leading to variations in treatment patterns. Physicians carefully weigh the potential benefits of a treatment against its potential risks and side effects. This risk-benefit assessment can vary based on individual patient characteristics and disease stage. For instance, a physician might favor FOLFIRI in older patients or those with comorbidities due to its perceived lower risk of neurotoxicity compared to FOLFOX. Institutional protocols and guidelines can also influence treatment selection, promoting the use of one regimen over the other based on local expertise and resource availability. Many healthcare institutions develop standardized treatment protocols or guidelines to ensure consistency and quality of care. These protocols may recommend specific chemotherapy regimens for different disease stages or patient populations, leading to variations in treatment patterns across different institutions. The availability of resources, such as specialized chemotherapy administration facilities, pharmacy support, and supportive care services, can also influence treatment selection. Institutions with limited resources might favor regimens that are easier to administer or have lower resource requirements. The choice between FOLFOX and FOLFIRI should always be individualized based on patient-specific factors. These factors include the patient's overall health status, comorbidities, performance status, and preferences. Patients with significant comorbidities, such as cardiovascular disease, renal dysfunction, or liver disease, might require modifications in chemotherapy dosing or selection. For example, patients with pre-existing neuropathy might be considered for FOLFIRI to avoid the potential neurotoxic effects of oxaliplatin, a component of FOLFOX. Similarly, patients with renal dysfunction might be better suited for FOLFOX, as irinotecan, a component of FOLFIRI, is primarily excreted by the kidneys. The patient's performance status, which reflects their overall functional ability and well-being, can influence treatment decisions. Patients with poor performance status might not tolerate the intensive nature of FOLFOX or FOLFIRI and might require alternative treatment approaches. It is essential to involve patients in the treatment decision-making process, ensuring their preferences and values are considered. Shared decision-making, where patients and physicians collaboratively weigh the risks and benefits of different treatment options, can lead to greater patient satisfaction and adherence to treatment. The specific molecular subtype of colorectal cancer can also influence treatment selection. For instance, tumors with certain genetic mutations may be more or less sensitive to the cytotoxic effects of FOLFOX or FOLFIRI. Tumors with high microsatellite instability (MSI-H) are often associated with a better prognosis and may respond differently to chemotherapy compared to microsatellite stable (MSS) tumors. Some studies suggest that FOLFIRI might be more effective in MSI-H tumors, while FOLFOX might be preferred for MSS tumors. RAS mutations are common in colorectal cancer and can affect the response to targeted therapies. The presence or absence of RAS mutations might influence the choice between FOLFOX and FOLFIRI, especially when considering the use of targeted therapies in combination with chemotherapy. BRAF mutations are associated with a poorer prognosis in colorectal cancer. The presence of a BRAF mutation might influence treatment selection, as these tumors may be

less responsive to standard chemotherapy regimens. As our understanding of the molecular underpinnings of colorectal cancer grows, treatment decisions may become increasingly personalized based on the tumor's genetic profile. The patient's prior treatment history, including previous chemotherapy regimens and responses, can also factor into the decision-making process. If a patient has previously received and progressed on FOLFOX, FOLFIRI might be considered the next line of therapy, and vice versa. This sequential approach aims to maximize the benefits of chemotherapy while minimizing the risk of cumulative toxicity. The patient's response to prior chemotherapy can also inform treatment selection. If a patient experienced a good response to a particular regimen, it might be considered again in the future, either as a re-challenge or in combination with other therapies. It is essential to involve patients in the treatment decision-making process, ensuring their preferences and values are considered. Shared decision-making, where patients and physicians collaboratively weigh the risks and benefits of different treatment options, can lead to greater patient satisfaction and adherence to treatment. Patients should be fully informed about the potential benefits, risks, and side effects of both FOLFOX and FOLFIRI. This information should be presented in a clear and understandable manner, allowing patients to make informed decisions about their care. Patients' values and preferences regarding treatment goals, quality of life, and potential side effects should be taken into account. Some patients might prioritize maximizing treatment efficacy, even if it means accepting a higher risk of side effects, while others might prioritize minimizing side effects and maintaining quality of life. The ideal approach involves a collaborative discussion between the patient and physician, where both parties contribute to the decision-making process. This shared decision-making approach fosters trust, enhances patient autonomy, and promotes adherence to treatment.[11-14]

Both FOLFOX and FOLFIRI are associated with a range of side effects, which can impact patient quality of life and treatment adherence. In our study, the most common side effects were nausea, vomiting, decreased appetite, and hair loss. These findings are consistent with previous reports on the safety profiles of these regimens. The incidence of nausea and vomiting was relatively low in our study, likely due to the use of effective antiemetic medications. However, it is crucial to proactively manage these side effects to ensure patient comfort and adherence to treatment. Hair loss was a rare side effect in our cohort, affecting only a small percentage of patients. This is reassuring for patients, as hair loss can be a distressing side effect of chemotherapy. Appetite loss was also relatively uncommon in our study. Maintaining adequate nutrition is essential for patients undergoing chemotherapy, and strategies to manage appetite loss should be implemented when necessary. Nausea and vomiting are common side effects of chemotherapy, often triggered by the stimulation of the chemoreceptor trigger zone (CTZ) in the brain. Both FOLFOX and FOLFIRI can cause nausea and vomiting, although the incidence varies depending on the specific drugs used, their dosages, and the use of antiemetic medications. Effective antiemetic medications, such as 5-HT3 receptor antagonists (e.g., ondansetron, granisetron), neurokinin-1 receptor antagonists (e.g., aprepitant), and corticosteroids (e.g., dexamethasone), have significantly reduced the incidence and severity of chemotherapy-induced nausea and vomiting (CINV). Proactive management of CINV is crucial to ensure patient comfort and adherence to treatment. This involves administering antiemetic medications before, during, and after chemotherapy, as well as providing non-pharmacological interventions, such as relaxation techniques and dietary modifications. Hair loss is a common side effect of many chemotherapy drugs, including those used in FOLFOX and FOLFIRI. It occurs due to the drugs' effects on rapidly dividing cells, including hair follicle cells. The specific drugs used in FOLFOX and FOLFIRI, their dosages, and the duration of treatment can influence the likelihood and severity of hair loss. Hair loss can be a distressing side

effect for many patients, affecting their self-esteem and body image. Providing emotional support and counseling can help patients cope with this side effect. Appetite loss is another common side effect of chemotherapy, often caused by a combination of factors, including nausea, fatigue, taste changes, and the effects of the drugs on the digestive system. Maintaining adequate nutrition is essential for patients undergoing chemotherapy, as malnutrition can lead to weakness, fatigue, and impaired immune function. Nutritional counseling and support, including dietary modifications and the use of appetite stimulants, can help patients manage appetite loss and maintain their nutritional status. FOLFOX and FOLFIRI can cause hematologic toxicities, such as neutropenia (low white blood cell count), anemia (low red blood cell count), and thrombocytopenia (low platelet count). These toxicities can increase the risk of infections, bleeding, and fatigue. In addition to nausea and vomiting, FOLFOX and FOLFIRI can cause other gastrointestinal side effects, such as diarrhea, constipation, and mucositis (inflammation of the mucous membranes lining the digestive tract). Oxaliplatin, a component of FOLFOX, can cause neurotoxicity, characterized by numbness, tingling, and pain in the hands and feet. This side effect can be dose-limiting and may persist even after treatment discontinuation. Fatigue is a common side effect of chemotherapy, often described as a persistent sense of tiredness and lack of energy. Some patients may experience skin reactions, such as rash, itching, or dryness. The management of side effects is a crucial aspect of cancer care, aiming to minimize the impact of treatment on patients' quality of life and ensure they can complete their planned course of therapy. Supportive care measures, such as antiemetic medications, pain management, nutritional support, and psychological counseling, can help alleviate side effects and improve patient well-being. In some cases, dose modifications or treatment delays might be necessary to manage severe or persistent side effects. Educating patients about potential side effects and their management is essential for empowering them to actively participate in their care and report any concerns promptly.[15-17]

Both FOLFOX and FOLFIRI demonstrated comparable efficacy in our study, with similar overall response rates and disease control rates. FOLFIRI showed a slightly higher partial response rate, but this difference may not be clinically significant. The low complete response rates observed in our study highlight the challenges in achieving complete tumor eradication in advanced colorectal cancer. However, the high rates of stable disease indicate that both regimens are capable of controlling disease progression in a significant proportion of patients. It is important to note that treatment response can be influenced by various factors, including disease stage, tumor biology, and patient-specific factors. Further research is needed to identify predictive biomarkers that can guide treatment selection and optimize patient outcomes. The ORR is a commonly used metric to assess the efficacy of cancer treatments. It combines the complete response (CR) and partial response (PR) rates, reflecting the proportion of patients who experience tumor shrinkage following treatment. In our study, FOLFOX and FOLFIRI demonstrated similar ORRs, suggesting comparable efficacy in inducing tumor regression. CR is defined as the disappearance of all target lesions, indicating complete tumor eradication. Achieving CR is a significant milestone in cancer treatment, often associated with improved long-term outcomes. However, CR rates are typically low in advanced colorectal cancer, as observed in our study. PR is defined as a decrease in the size of target lesions by a certain threshold, indicating a substantial reduction in tumor burden. PR can also be a meaningful outcome, as it can lead to symptom improvement and prolonged survival. The DCR is another metric used to assess treatment efficacy. It combines the CR, PR, and stable disease (SD) rates, reflecting the proportion of patients who experience either tumor shrinkage or disease stabilization following treatment. In our study, FOLFOX and FOLFIRI demonstrated similar DCRs, suggesting comparable efficacy in controlling disease

progression. SD is defined as a lack of significant change in the size of target lesions, indicating that the disease is not progressing. SD can be a valuable outcome, as it can provide symptom control and prevent further tumor growth. Patients with earlier-stage disease are generally more likely to respond to treatment compared to those with advanced or metastatic disease. The specific molecular subtype of colorectal cancer can influence treatment response. For instance, tumors with certain genetic mutations may be more or less sensitive to the cytotoxic effects of FOLFOX or FOLFIRI. Patient-specific factors, such as age, performance status, comorbidities, and nutritional status, can also influence treatment response. Identifying predictive biomarkers that can accurately predict treatment response is a crucial goal in oncology. These biomarkers can help guide treatment selection and optimize patient outcomes. Molecular profiling of tumors can identify specific genetic mutations or alterations that may predict response to FOLFOX or FOLFIRI. For example, tumors with RAS mutations are often less responsive to EGFR-targeted therapies, which may be used in combination with chemotherapy. Immunohistochemical markers, such as mismatch repair (MMR) proteins and PD-L1 expression, can also provide insights into tumor biology and potential treatment response. The duration of treatment can also influence treatment response. Longer treatment durations may lead to deeper responses, but they also increase the risk of cumulative toxicity. The sequencing of FOLFOX and FOLFIRI, either sequentially or in combination, may also impact treatment response. The accurate assessment of treatment response is crucial for guiding clinical decision-making. This involves using standardized criteria, such as RECIST v1.1, and performing regular imaging studies to monitor tumor response.[18-20]

5. Conclusion

Our findings reveal a dynamic landscape influenced by factors such as disease stage, tumor location, patient characteristics, and physician preferences. Both FOLFOX and FOLFIRI regimens demonstrate comparable efficacy in terms of overall response rates and disease control, with FOLFIRI showing a slightly higher partial response rate. However, this difference may not be clinically significant, and the choice between the two regimens should be individualized based on patient-specific factors. The side effect profiles of both regimens are generally manageable, with nausea, vomiting, decreased appetite, and hair loss being the most commonly reported side effects. Proactive management of these side effects is essential to ensure patient comfort and adherence to treatment. It is important to note that our study has certain limitations inherent to its retrospective observational design. Further research, including prospective clinical trials and real-world studies with larger sample sizes, is needed to validate our findings and establish definitive conclusions about the comparative effectiveness and safety of FOLFOX and FOLFIRI in various patient subgroups. As the treatment landscape for colorectal adenocarcinoma continues to evolve, with the emergence of novel therapeutic agents and the growing emphasis on personalized medicine, it is crucial to maintain a patient-centered approach. Shared decision-making, where patients and physicians collaboratively weigh the risks and benefits of different treatment options, should be prioritized to ensure that treatment decisions align with individual patient needs, preferences, and treatment goals.

6. References

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