Comparative efficacy of 5flourouracil/calcium leucovorine versus 5flourouracil/calcium leucovorine plus oxaliplatin in the adjuvant treatment of colonic carcinoma in Kashmir

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Abstract

**Aim:** This prospective, randomized comparative study conducted in Kashmir evaluated the clinical profile of colonic carcinoma and the efficacy, side effects and survival advantage of adjuvant treatment with 5FU/CLV versus FOLFOX7.

**Materials and Methods:** Between 2007 and 2009, the clinical profiles of 50 patients enrolled and randomized equally into Arm A receiving 5FU/CLV alone (Mayo Clinic Regimen) and Arm B receiving the FOLFOX7 regimen (including oxaliplatin) were evaluated. **Results:** Majority of the patients were in the 5th and 6th decade of life (males 70% versus females 30%), and most were from urban dwellings. Consumption of red meat, obesity and physical inactivity were common risk factors. A family history of colonic carcinoma was reported in 12% of the patients. Event-free and disease-free survival for the two arms were: Arm A – 12.8 ± 5 months and 14.2 ± 6 months; Arm B – 13.0 ± 6.7 months and 13.1 ± 6 months, respectively. Treatment-related morbidity was significant in Arm B whereas general well being and surrogate laboratory markers including a hemogram, favored Arm A. **Conclusion:** The clinical profile, risk factors and familial predisposition of Kashmiri colonic carcinoma patients matches that of colon cancer patients elsewhere. There was no added survival advantage by adding oxaliplatin to 5FU and CLV. Although the interim results showed that the Mayo Clinic Regimen has a better total survival advantage compared with the FOLFOX7 regimen, the results were not statistically significant. The Mayo Clinic Regimen was better than the FOLFOX7 regimen in terms of the toxicity profile. However, this finding needs to be studied further. The main idea of conducting this study was to reveal that there is no added advantage of adding oxaliplatin to 5FU and CLV, thereby (a) reducing the toxicity (b) and lowering cost of therapy.

**Key words:** Colonic carcinoma, disease-free survival, event-free survival, FOLFOX7, Mayo clinic regimen

Introduction

Colorectal cancer is the third most common cancer in men (663,000 cases, 10.0% of the total cancer cases) and the second in women (570,000 cases, 9.4% of the total), with a worldwide yearly estimate of more than 1.23 million cases. About 608,000 deaths from colorectal cancer are estimated worldwide, accounting for 8% of all cancer deaths, making it the fourth most common cause of death from cancer.[1] Generally, the incidence and mortality rates of colorectal cancer are higher in the developed Western nations.[1‑5] However, the incidence and mortality rates have been higher in economically disadvantaged countries as well,[6,7] which may be related to consumption of a high-fat and high red-meat diet, lack of physical activity.[6‑12] Familial factors are important contributors to the risk of sporadic colorectal cancer, depending on the involvement of first-degree and/or second-degree relatives and the age of onset of the cancer.[13,14]

Population-based studies strongly support inverse associations between the use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) and the incidence of colorectal cancer and adenomas.[15‑18] Symptoms associated with colorectal cancer include lower gastrointestinal (GI) bleeding, change in bowel habits, abdominal pain, weight loss, change in appetite, weakness, and, in particular, obstructive symptoms, which are alarming.[19]

Laboratory values may reflect iron-deficiency anemia, electrolyte derangements, and liver function abnormalities. Carcinoembryonic antigen (CEA) levels may be elevated, reduced to normal as a result of surgery.[20]

Evaluation should include complete clinical history, family history, physical examination, and laboratory tests, colonoscopy, and pan-body computed tomography (CT) scan,[21] the latter, if metastatic disease is suspected after the primary diagnosis is made.

New noninvasive techniques such as CT-colonography (referred to as virtual colonoscopy)[22‑29] and magnetic resonance (MR)-colonography,[30‑32] are investigational but are receiving attention in clinical studies and may provide...
initial data demonstrating efficacy.

The postoperative treatment of patients with stage II colon cancer is somewhat controversial. To date, no large randomized study has shown benefit from adjuvant chemotherapy for this rather heterogeneous group of patients. The American Society of Clinical Oncology (ASCO) currently suggests a course of 5-fluoururacil (5-FU)-based adjuvant chemotherapy for stage II patients with at least one poor prognostic indicator including insufficient lymph node sampling (<12 nodes resected with the specimen), T4 lesions, poorly differentiated histology, or bowel perforation. The addition of oxaliplatin to the 5-FU/leucovorin regimen (FOLFOX) has been shown to improve disease-free survival rates (disease-free survival rate was 78% versus 73% with 5-FU/leucovorin alone). Irinotecan (Camptosar) has been investigated as an addition to 5-FU–based therapy in the adjuvant setting, based on its benefit against metastatic disease. The treatment of stage IV patients depends on the location and extent of the metastases. These new agents, showing efficacy in treating metastatic disease, are now being studied in the adjuvant setting.

**Materials and Methods**

A total of 50 patients were enrolled after obtaining informed consent from them and randomized into two groups in this randomized prospective and comparative study conducted between October 2007 and October 2009, irrespective of age, sex, dwelling, stage of disease and PS. The study was approved by the ethical committee that looks into the ethical aspects of the human experimentation.

After initial evaluation, the eligibility criteria were as follows:

- Histologically proven colonic adenocarcinoma
- Patients treated surgically with curative intent. (Resection of all tumors with negative margins of resection, with lymph node dissection of minimum of 20 nodes)
- Classification of resected cancer of colon as stage-II ($T_2N_0M_0$) through stage-III ($T_3N_0M_0$)$^{[33]}$
- Performance status of 0-2 (ECOG)
- Adequate functioning of major organs indicated by a normal hemogram, normal liver function test (LFT), kidney function test (KFT)
- Registration within 1 month after surgery and treatment beginning within 7 working days after registration.

After fulfilling the above criteria and taking the proper consent from the patients, the patients were randomly allocated to two groups; Arm A and Arm B, irrespective of age, sex, stage of disease and PS in near equal proportions.

Arm A received conventional 5-FU and calcium leucovorine (CLV) regimen. The 5-FU/CLV was developed by North Central Cancer Treatment Group (Mayo Clinic) Chemotherapy Regimen was as follows:

Arm A received the Mayo Clinic Regimen: Leucovorine 20 mg/m² via intravenous (IV) infusion for 30 minutes on Days 1 through 5 followed by 5FU 425 mg/m² by rapid IV injection, once daily for 5 consecutive days for two 4-week cycles and then every 5 weeks thereafter. Total numbers of cycles were 6.

Arm B received the FOLFOX7 Regimen: Oxaliplatin 130 mg/m² as a 3 hour IV infusion and leucovorine 400 mg/m² as a 2 hour IV infusion on Day 1, followed by 5FU 2400 mg/m² as a 48-hour IV infusion on Days 1 and 2.$^{[34]}$ The total numbers of cycles were 6, each cycle was repeated every 14 days.

After receiving chemotherapy, patients were evaluated for chemotherapy-related morbidity and adverse effects. After completion of treatment, patients were asked to document complete remission. The assessment included: Hemogram, KFT, LFT, chest X-Ray, electrocardiogram (ECG), ultrasonography (USG) of the abdomen/pelvis, colonoscopy and CEA levels.

Both the groups were followed up for disease-free, event-free and overall survival time. Follow-up was monthly for the first 6 months, every 2 months for the next 6 months and then at 3 monthly intervals for the next year. Each visit included – medical history, physical examination, complete blood count, KFT, LFT, chest X-Ray, ECG, 3 monthly CEA levels, CT liver and colonoscopy. The site and date of recurrence, relapse and date of death (if applicable) were recorded.

**The patients who were excluded from the study were those with**

- Age more than 70 years
- Performance status score $\geq$3
- Patients with markedly deranged KFT, LFT
- Patients with comorbid conditions
- Patients who had distant metastasis i.e., M1 disease.

**Results**

This prospective comparative study was conducted in the Department of Medical Oncology, SKIMS. The Mayo Group received 5-FU and CLV whereas the FOLFOX7 Group received 5-FU + CLV + oxaliplatin [Tables 1-7].

The colonic biopsy revealed well-differentiated adenocarcinoma in patients of both Mayo (56.5%) and FOLFOX7 (50.0%) Groups. Histopathology of surgical specimens also corroborated the colonoscopic findings with 60% in the Mayo Group and 52% in the FOLFOX7 Group having well-differentiated adenocarcinoma.

Both the groups received 6 cycles of chemotherapy. The Mayo Group received 4 weekly cycles and the FOLFOX7 Group received fortnightly cycles.

In the immediate post-treatment period, the majority of the patients had PS score of 1 and 2. None of the patients had pallor or signs of neuropathy. At 6-12 months of follow-up, 1 patient each had icterus, abdominal distension and Lung Mets in the form of pleural effusion in the FOLFOX7 Group. At 12-18 months of follow-up only 1 patient in
Adjuvant therapy for colonic carcinoma in Kashmir

Shaiq, et al.: Adjuvant therapy for colonic carcinoma in Kashmir

oxaliplatin, Number of subjects

Flourouracil/calcium leucovorine, Flourouracil/calcium leucovorine plus oxaliplatin, Number of subjects

Chief complaints Mayo group FOLFOX7 group P value

| Complaint                  | 5n   | 5%  | 25n | 25% |
|----------------------------|------|-----|-----|-----|
| Pain abdomen               |      |     |     |     |
| Post-treatment             | 23   | 92.0| 23  | 92.0| 1.000|
| Yes                       | 2    | 8.0 | 2   | 8.0 |       |
| 6-12 months                | 25   | 100.0| 23  | 95.8| 0.307|
| Yes                       | 0    | 0.0 | 1   | 4.2 |       |
| 12-18 months               | 15   | 100.0| 11  | 91.7| 0.264|
| Yes                       | 0    | 0.0 | 1   | 8.3 |       |
| 18-24 months               | 0    | 0.0 | 0   | 0.0 | 1.000|

Abdominal distension

| Complaint                  | Mayo group | FOLFOX7 group |
|----------------------------|------------|---------------|
| Post-treatment             | 25 100.0   | 25 100.0      | 1.000|
| 6-12 months                | 25 100.0   | 23 95.8       | 0.307|
| Yes                       | 0 0.0      | 1 4.2         |       |
| 12-18 months               | 15 100.0   | 12 100.0      | 1.000|
| Yes                       | 0 0.0      | 1 8.3         |       |
| 18-24 months               | 0 0.0      | 0 0.0         | 1.000|

Constipation

| Complaint                  | Mayo group | FOLFOX7 group |
|----------------------------|------------|---------------|
| Post-treatment             | 24 96.0    | 25 100.0      | 0.317|
| Yes                       | 1 4.0      | 0 0.0         |       |
| 6-12 months                | 25 100.0   | 24 100.0      | 1.000|
| 12-18 months               | 15 100.0   | 12 100.0      | 1.000|
| 18-24 months               | 0 0.0      | 0 0.0         | 1.000|

Bleeding PR/Hematochezia

| Complaint                  | Mayo group | FOLFOX7 group |
|----------------------------|------------|---------------|
| Post-treatment             | 24 96.0    | 25 100.0      | 0.317|
| Yes                       | 1 4.0      | 0 0.0         |       |
| 6-12 months                | 25 100.0   | 24 100.0      | 1.000|
| 12-18 months               | 15 100.0   | 12 100.0      | 1.000|
| 18-24 months               | 0 0.0      | 0 0.0         | 1.000|

Symptomatic anemia

| Complaint                  | Mayo group | FOLFOX7 group |
|----------------------------|------------|---------------|
| Post-treatment             | 25 100.0   | 25 100.0      | 1.000|
| 6-12 months                | 25 100.0   | 24 100.0      | 1.000|
| 12-18 months               | 15 100.0   | 12 100.0      | 1.000|
| 18-24 months               | 0 0.0      | 0 0.0         | 1.000|

Altered bowel habits

| Complaint                  | Mayo group | FOLFOX7 group |
|----------------------------|------------|---------------|
| Post-treatment             | 25 100.0   | 25 100.0      | 1.000|
| 6-12 months                | 25 100.0   | 24 100.0      | 1.000|
| 12-18 months               | 15 100.0   | 12 100.0      | 1.000|
| 18-24 months               | 0 0.0      | 0 0.0         | 1.000|

Vomiting/Obstruction

| Complaint                  | Mayo group | FOLFOX7 group |
|----------------------------|------------|---------------|
| Post-treatment             | 25 100.0   | 25 100.0      | 1.000|
| 6-12 months                | 25 100.0   | 24 100.0      | 1.000|
| 12-18 months               | 15 100.0   | 12 100.0      | 1.000|
| 18-24 months               | 0 0.0      | 0 0.0         | 1.000|

Jaundice

| Complaint                  | Mayo group | FOLFOX7 group |
|----------------------------|------------|---------------|
| Post-treatment             | 0 0.0      | 0 0.0         | 1.000|
| 6-12 months                | 0 0.0      | 2 8.3         | 0.149|
| 12-18 months               | 0 0.0      | 0 0.0         | 1.000|
| 18-24 months               | 0 0.0      | 0 0.0         | 1.000|

Table 1: Symptomatology in follow-up patients

Table 2a: Age distribution of the studied subjects

| Age (in yrs) | Mayo group | FOLFOX7 group | Total | P value |
|--------------|------------|---------------|-------|---------|
| <30          | 2 8.0      | 2 8.0         | 4 8.0 | 0.977(NS)|
| 31 to 40     | 4 16.0     | 5 20.0        | 9 18.0|         |
| 41 to 50     | 6 24.0     | 6 24.0        | 12 24.0|         |
| 51 to 60     | 9 36.0     | 7 28.0        | 16 32.0|         |
| 61 to 70     | 4 16.0     | 5 20.0        | 9 18.0|         |
| Total        | 25 100.0   | 25 100.0      | 50 100.0|         |
| Mean±SD      | 50.3±11.5  | 50.4±12.2     | (28,70)|         |
|              |            |               | (25,70)|         |

Table 2b: Sex distribution of the studied subjects

| Gender | Mayo group | FOLFOX7 group | Total | P value |
|--------|------------|---------------|-------|---------|
| Male   | 18 72.0    | 17 68.0       | 35 70.0| 0.76(NS)|
| Female | 7 28.0     | 8 32.0        | 15 30.0|         |

FOLFOX7 Group had recurrence with abdominal lump and at 18-24 months of follow-up 1 patient had recurrence with PS score of IV. This patient had a PS of 2 at the onset of study (fulfilling the inclusion criteria) but post-treatment his PS decreased to IV [Table 1].

Discussion

The present study was carried out against the backdrop of very high incidence of colorectal cancers in the Kashmir valley. The objective was to evaluate the clinical profile of colonic carcinoma and the treatment effectiveness and outcome of two different adjuvant chemotherapy regimens.

The majority of the patients in the study were in the 5th and 6th decade of their life whereas 10% were in the age group of ≤30 years. This is similar to the colon cancer demographics observed in other parts of the world [Table 2a].

About 70% of the patients in this study were males. A literature survey revealed that the incidence of colon cancer is almost equal in males and females. Our results are contrary to this observation [Table 2b].

The clinical features of the patients were almost consistent with the global scenario and world literature [Tables 3a,b, 4].

Before the start of adjuvant chemotherapy, the mean CEA level in the Mayo Group was 3.1 ng/ml and was 2.4 ng/ml in the FOLFOX7 group, the levels showed a downward trend at the end of therapy. These findings were consistent with the international literature.

After a standard randomization procedure, the two groups were given adjuvant chemotherapy. One group received the Mayo Clinic regimen and the other received the FOLFOX7 regimen. All the 25 patients in each group received 6 cycles of chemotherapy. Most of the patients (92%) in each group were in stage IIA (T3N0M0).
Table 3a: Clinical profile of the studied subjects

| Presenting symptom          | Mayo group |           | Folfox7 group |           | Total |           | P value |
|-----------------------------|------------|-----------|---------------|-----------|-------|-----------|---------|
|                             | n  | %      | n  | %      | n  | %      |         |
| Pain abdomen                 | 18 | 72.0   | 17 | 68.0   | 35 | 70.0   | 0.760   |
| Abdominal distension        | 3  | 12.0   | 5  | 20.0   | 8  | 16.0   | 0.445   |
| Abdominal mass              | 3  | 12.0   | 3  | 12.0   | 6  | 12.0   | 1.000   |
| Constipation                 | 12 | 48.0   | 12 | 48.0   | 24 | 48.0   | 1.000   |
| Bleeding PR/Hematochezia    | 6  | 24.0   | 11 | 44.0   | 17 | 34.0   | 0.139   |
| Symptomatic anemia          | 12 | 48.0   | 13 | 52.0   | 25 | 50.0   | 0.779   |
| Altered bowel habits        | 4  | 16.0   | 3  | 12.0   | 7  | 14.0   | 0.687   |
| Vomiting/Obstruction        | 3  | 12.0   | 3  | 12.0   | 6  | 12.0   | 1.000   |
| Duration of symptom (month) | 4.6±1.1 (0.24) | 3.4±0.6 (0.12) | 4.0±0.6 (0.24) | 0.837 |

Table 3b: Clinical profile of the studied subjects

| Examination                  | Mayo group |           | Folfox7 group |           | Total |           | P value |
|------------------------------|------------|-----------|---------------|-----------|-------|-----------|---------|
|                             | n  | %      | n  | %      | n  | %      |         |
| Performance status           |    |        |    |        |    |        |         |
| I                            | 13 | 52.0   | 7  | 28.0   | 20 | 40.0   | 0.086   |
| II                           | 12 | 48.0   | 18 | 72.0   | 30 | 60.0   |         |
| Pallor                       | 18 | 72.0   | 18 | 72.0   | 36 | 72.0   | 1.000   |
| LAP                          | 0  | 0.0    | 0  | 0.0    | 0  | 0.0    |         |
| Abdominal distension        | 3  | 12.0   | 5  | 20.0   | 8  | 16.0   | 0.445   |
| Abdominal mass              | 3  | 12.0   | 3  | 12.0   | 6  | 12.0   | 1.000   |
| Other (Pigmentation)        | 0  | 0.0    | 0  | 0.0    | 0  | 0.0    | 1.000   |

Table 4: Diagnostic profile of the studied subjects (cont’d.)

| Colonicoscopic/Surgical diagnosis | Mayo group |           | Folfox7 group |           | Total |           | P value |
|-----------------------------------|------------|-----------|---------------|-----------|-------|-----------|---------|
|                                  | n  | %      | N  | %      | n  | %      |         |
| Colonoscopic findings            |    |        |    |        |    |        |         |
| Ulceroinfiltrative growth        | 8  | 32.0   | 5  | 20.0   | 13 | 26.0   | 0.333   |
| Colonic stricture/Stenosis       | 2  | 8.0    | 6  | 24.0   | 8  | 16.0   | 0.123   |
| Polypoid mass                    | 4  | 16.0   | 8  | 32.0   | 12 | 24.0   | 0.185   |
| Circumferential growth           | 3  | 12.0   | 4  | 16.0   | 7  | 14.0   | 0.684   |
| Colonic Polyps                   | 2  | 8.0    | 5  | 20.0   | 7  | 14.0   | 0.221   |
| Proliferative growth             | 4  | 16.0   | 2  | 8.0    | 6  | 12.0   | 0.384   |
| Synchronous lesions              | 1  | 4.0    | 0  | 0.0    | 1  | 2.0    | 1.000   |
| Not available                    | 2  | 8.0    | 5  | 20.0   | 7  | 14.0   | 0.221   |
| Site of lesion                   |    |        |    |        |    |        |         |
| Left                             | 12 | 52.2   | 8  | 40.0   | 20 | 46.5   | 0.811   |
| Right                            | 6  | 26.1   | 10 | 50.0   | 16 | 37.2   |         |
| Caeocal                          | 5  | 21.7   | 2  | 10.0   | 7  | 16.3   |         |
| Transverse                      | 0  | 0.00   | 0  | 0.00   | 0  | 0.00   |         |

The common toxicities observed in the Mayo group were in the GI system, in the form of nausea (grade 1 to 2) in 100% and diarrhea (grade 1 to 2) in 32% of the patients. None of the patients had cytopenia or febrile neutropenia or any grade of sensory neuropathy. While toxicities observed in FOLFOX7 group were sensory neuropathy (grade 1 to 2) in 68% and cytopenia (grade 1 to 2) in 16%. There was no chemotherapy related mortality reported.

Andre et al. in their study of semimonthly versus monthly regimens of 5-FU and CLV administered for 24-36 weeks as adjuvant therapy in Stage 2 and Stage 3 colon cancer results of randomized studies, observed the most common toxicities to be grade 3 to 4 neutropenia, diarrhea and mucositis. The toxicities were statistically significantly lower in the LVFU2 group (monthly) with all toxicities P < 0.001.[36] The observed effects were similar to the results of our study, although the percentage of neutropenia was lower in our study.

Andre et al. in their study of adjuvant treatment of colon cancer with oxaliplatin, 5-FU and CLV observed the incidence of febrile neutropenia as 1.8%, that of gastrointestinal adverse effects as low, and the incidence of grade-3 sensory neuropathy as 12.4% during treatment, decreasing to 1.1% at 1 year of follow-up. Six patients died during treatment.[37] The side-effect profile of patients in the FOLFOX7 group was lesser compared with the above quoted reference, and there were no chemotherapy-related deaths.
In another study conducted by Patel K et al., overall, 20% of patients experienced any ≥3 grade toxicity, most commonly diarrhea (14%). [34] Our study showed similar toxicity with 5FU and CLV alone chemotherapy regimen.

In the study conducted by Christophe Tournigand et al. (OPTIMOX1), grade 3 sensory neuropathy was observed in 13.3% of patients in the FOLFOX7 regimen [Table 5]. [38] Our study demonstrated grade 1 to 2 sensory reversible neuropathy in 68% of patients.

The mean follow-up of patients in the Mayo group was 14.2 ± 6.0 months and 13.1 ± 6.5 months in the FOLFOX7 group [Tables 6a-c]. The mean event-free survival of patients in the Mayo group was 12.8 ± 5.9 months and 13.0 ± 6.7 months in FOLFOX7 group.

At the conclusion of the study all 25 patients in the Mayo group were alive whereas in the FOLFOX7 group only 22 patients survived and 3 patients died during follow-up due to recurrence of disease, metastasis and liver failure (Hepatitis B related).

In the IMPACT study which compared 5FU/CLV in an adjuvant setting of colonic carcinoma with surgery alone in stage 2 and 3 concluded that overall survival for all stages combined was improved for this chemotherapy compared with surgery alone (83% vs. 78%, P = 0.003). [39]
The MOSAIC study compared a 2-weekly infusion of 5FU/LV/OX (the FOLFOX regimen) with infusional 5FU/LV alone (LV5FU2) as adjuvant treatments for 2,248 stage II (40%) and III (60%) colon cancer patients. Final results showed that 3-year disease-free survival (all stages) was improved with the addition of OX compared with 5FU/LV alone (78.2% vs. 72.9%; \( P = 0.002 \)), with a 23% reduction in recurrence.\(^{[36]}\) A subgroup analysis did not reveal a statistically significant improvement in disease-free survival for the stage II patients (HR 0.8, 95% CI 0.56 = 1.15).

Christophe Tournigand \textit{et al.} (OPTIMOX1), found that the median progression-free survival and total survival times were 8.7 and 21.2 months, respectively, in the patients treated with FOLFOX7.\(^{[34]}\) Our study showed less total survival with FOLFOX7, but the event-free survival was higher, probably related to shorter follow-up.

In the present study we did not found any survival advantage by adding oxaliplatin to 5FU and CLV in the adjuvant treatment of colonic carcinoma. At 24 months of follow-up with a mean follow-up of 14.2 ± 6.0 in Mayo group the overall survival was 100% as compared to FOLFOX7 group with a mean follow-up of 13.1 ± 6.5 the overall survival was 84% only \( (P = 0.039) \) [Table 7, Figure 1].

Our study also demonstrated lower total recurrence (0%) with the Mayo regimen compared with the FOLFOX7 regimen (4%), though the difference was not statistically significant \( (P = 0.317) \).

Further studies with longer follow-up duration are needed to reach a definite conclusion based on the results above.

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**Table 6b: Follow-up complaints**

| Chief complaints       | Mayo group |       | Folfox7 group |       | \( P \) value |
|------------------------|------------|-------|---------------|-------|-------------|
|                        | \( n\)     | %     | \( n\)        | %     |             |
| Symptomatic anemia     |            |       |               |       |             |
| Post-treatment         |            |       |               |       |             |
| No                     | 25         | 100.0 | 25            | 100.0 | 1.000       |
| 6-12 months            |            |       |               |       |             |
| No                     | 25         | 100.0 | 24            | 100.0 | 1.000       |
| 12-18 months           |            |       |               |       |             |
| No                     | 15         | 100.0 | 12            | 100.0 | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| Altered bowel habits   |            |       |               |       |             |
| Post-treatment         |            |       |               |       |             |
| No                     | 25         | 100.0 | 25            | 100.0 | 1.000       |
| 6-12 months            |            |       |               |       |             |
| No                     | 25         | 100.0 | 24            | 100.0 | 1.000       |
| 12-18 months           |            |       |               |       |             |
| No                     | 15         | 100.0 | 12            | 100.0 | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| Vomiting/Obstruction   |            |       |               |       |             |
| 6-12 months            |            |       |               |       |             |
| No                     | 25         | 100.0 | 24            | 100.0 | 1.000       |
| 12-18 months           |            |       |               |       |             |
| No                     | 15         | 100.0 | 12            | 100.0 | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| Jaundice               |            |       |               |       |             |
| Post-treatment         |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 6-12 months            |            |       |               |       |             |
| Yes                    | 0          | 0.0   | 2             | 8.3   | 0.149       |
| 12-18 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |

**Table 6c: Follow-up complaints**

| Chief complaints       | Mayo group |       | Folfox7 group |       | \( P \) value |
|------------------------|------------|-------|---------------|-------|-------------|
|                        | \( n\)     | %     | \( n\)        | %     |             |
| Diarrhea               |            |       |               |       |             |
| Post-treatment         |            |       |               |       |             |
| Yes                    | 9          | 36    | 1             | 4.0   | 0.005       |
| 6-12 months            |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 12-18 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| Symptoms of peripheral neuropathy |            |       |               |       |             |
| Post-treatment         |            |       |               |       |             |
| Yes                    | 0          | 0.0   | 25            | 100.0 | 0.000       |
| 6-12 months            |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 12-18 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| Seizures               |            |       |               |       |             |
| Post-treatment         |            |       |               |       |             |
| Yes                    | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 6-12 months            |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 12-18 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| Cough/Hemoptysis/ Breathlessness |            |       |               |       |             |
| Post-treatment         |            |       |               |       |             |
| Yes                    | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 6-12 months            |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 12-18 months           |            |       |               |       |             |
| Yes                    | 0          | 0.0   | 0             | 0.0   | 1.000       |
| 18-24 months           |            |       |               |       |             |
| No                     | 0          | 0.0   | 0             | 0.0   | 1.000       |

South Asian Journal of Cancer • April-June 2013 • Volume 2 • Issue 2
patients and short follow-up of the present study warrants further studies with a longer follow-up and patient selection.

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Table 7: Survival data at end of study

| Variable | Mayo group | FOLFOX7 group | P value |
|----------|------------|--------------|---------|
|          | Min¹ | Max¹ | Mean | SD | Min | Max | Mean | SD |       |
| Total survival | 6   | 24  | 14.2 | 6.0 | 0.0 | 24  | 13.1 | 6.8 | 0.599 |
| Event-free survival | 4   | 24  | 12.8 | 5.9 | 0.0 | 24  | 13.0 | 6.7 | 0.808 |
| Total duration of follow-up | 6   | 24  | 14.2 | 6.0 | 0.0 | 24  | 13.1 | 6.8 | 0.599 |

¹Flourouracil/Calcium leucovorin, ²Flourouracil/Calcium leucovorin plus Oxaliplatin, ³Minimum, ⁴Maximum, SD=Standard deviation

To summarize:
- The clinical features, risk factors, familial predisposition and presenting symptoms of patients in this study are similar to patients in other parts of the world.
- There is no added survival advantage by adding oxaliplatin to 5FU and CLV in the adjuvant treatment of colon carcinoma.
- Hematological and neurological toxicities were more common in the oxaliplatin-based regimen.
- GI toxicity is more common in the Mayo clinic regimen.
- Colonic carcinoma is a common malignancy in our population and has shown an increasing trend in younger patients.

Although the interim results showed that the Mayo clinic regimen was better in terms of the total survival advantage compared to the FOLFOX7 regimen, the results were not statistically significant. Keeping in view the toxicity profile of the FOLFOX7 regimen, the Mayo clinic regimen was found to be superior to FOLFOX in the adjuvant setting in treating colon carcinoma.

However, the small sample size, predominantly stage II

Figure 1: The mean duration of symptoms was 4.6 ± 1.1 months in the Mayo Group and 3.4 ± 0.6 months in the FOLFOX7 Group.
Shaiq, et al.: Adjuvant therapy for colonic carcinoma in Kashmir

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