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Immediate Adjuvant Chemotherapy in Non-Metastatic Colon Cancer: Phase I Trial Evaluating a Novel Treatment Protocol

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Abstract

Delays in adjuvant chemotherapy result in decreased survival in colon cancer. Our proposed protocol based on immediate adjuvant chemotherapy starting at the time of surgical resection was found to be safe and feasible with no adverse effects on surgical morbidity or quality of life.

Background: The optimal timing of adjuvant chemotherapy (AC) in non-metastatic colon cancer is poorly defined. Delays in AC result in decreased survival. Effective cytotoxic treatments should be considered during the perioperative phase of care. The immediate adjuvant chemotherapy (IAC) concept intends to capitalize on the therapeutic benefits that can be achieved in the perioperative period. We aim to demonstrate that IAC is safe and tolerable. **Patient and Methods:** Microsatellite stable invasive adenocarcinomas were treated with intravenous Leucovorin 20 mg/m2 and single dose of 5-Flurouracil 400mg/m2 at the time of surgery. High-risk stage II and stage III received the first dose of standard AC at 14 days after surgery. Serial measurements of blood-based biomarkers were measured. Quality of life (QOL) was measured using EORTC QLQ-C30. **Results:** Of the 20 patients recruited, 40% had final pathology of stage III, 40% stage II and 20% stage I. All patients received intra-operative chemotherapy with no associated morbidity. Median length of stay was 2 days (range of 2-4). There was no intraoperative morbidity with 5% (N = 1) grade 3 complication. AC was administered to 65% of patients. The median time to AC was 14 days (range 14-36). Overall quality of life and health scores were similar before surgery and at 30-day postoperatively ($P < .05$). **Conclusions:** A protocol based on IAC starting at the time of surgical resection was found to be safe and feasible with no adverse effects on surgical morbidity or quality of life. Further prospective studies are needed to explore the oncologic benefit of this novel systemic treatment approach.

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Key Words: Peri Operative phase of care, early stage colon cancer, quality of life, early start of adjuvant treatment, colon resection

Introduction

Colorectal cancer is the third leading cause of cancer-related death worldwide.[1,2] Standard of care for patients with non-metastatic colon cancer includes surgical resection followed by adjuvant chemotherapy in high-risk patients.[3] Surgical intervention is intended as a curative treatment and staging modality, as accurate lymph node assessment depends on review of the surgical pathology. However, despite adequate resection and adjuvant chemotherapy, colon cancer recurrence occurs even in cases of early-stage disease. Despite improvement in surgical techniques and chemotherapy regimens over time, the rate of metastatic failure continues to be high at 35% among non-metastatic lymph node positive colon cancer patients.[4-7]

We hypothesize that, among other factors, the high metastatic failure rate may be due to delays in chemotherapy as well as systemic changes that occur during the perioperative phase of care.[8-13] Currently, the National Comprehensive Cancer Network (NCCN) guidelines have no recommendations with regard to timing of the

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initiation of AC. However, the gap between surgical resection and initiation of adjuvant chemotherapy has been shown to be an independent risk factor for cancer relapse.[14,15] Moreover, the early postoperative period in itself can lead to many systemic changes, including impairment of tissue integrity, establishment of a significant stress response, and ultimately immune suppression.[8-10] These changes can lead to an environment that enables cancer spread and recurrence.[16,17] This has been established both in the animal model and in clinical trials investigating the role of portal vein infusion in colon cancer.[17,18] Therefore we believe that the perioperative period represents an underutilized window of opportunity for therapies aimed at reducing micrometastatic spread.[16]

Treatments directed at minimizing recurrence during the perioperative period may have beneficial effects on clinical outcomes. We hypothesize that given the systemic changes occurring during the perioperative period, effective cytotoxic treatments may be considered at this time in order to reduce circulating tumor cells and ultimately blunt the possibility of systemic spread of malignant cells. We therefore conducted a phase I feasibility and safety protocol in which immediate adjuvant chemotherapy (IAC) is given to non-metastatic colon cancer patients at the time of surgical resection and standard adjuvant therapy is started early in the postoperative period.

Patients and Methods

The immediate adjuvant chemotherapy treatment trial was a single institution phase I trial to examine the safety and feasibility of administering intraoperative chemotherapy and early adjuvant (<2 weeks) chemotherapy in non-metastatic colon cancer. The study was given full approval by the IRB committee of University of California, Irvine (UCI IRB# 2017-3421) and all patients were provided informed consent in their native language before enrollment.

Eligible patients were age ≥ 18 years old and had non-metastatic, Microsatellite Stable (MSS) and/or Mismatch Repair Proficient (MMR-p) colon cancer (according to TNM staging defined by the American Joint Cancer Committee). Biopsy proven colon adenocarcinoma defined as above the peritoneal reflection and not amenable to colonoscopy resection were included. Only tumors ≥ 2 cm in size based on imaging and/or colonoscopy findings were included, in an attempt to minimize the number of patients ultimately diagnosed with early stage disease (ie stage I, low-risk stage II). Patients with Microsatellite Instability High (MSI-High) and/or Mismatch Repair Deficient (MMR-d) colon cancer, metastatic disease, ASA Score (American Society of Anesthesiologists) ≥ 4 and/or ECOG (Eastern Cooperative Oncology Group) score ≥ 2 were excluded from the study (Appendix A). All patients had appropriate staging prior to enrollment in adherence with NCCN guidelines [3].

Protocol

All patients who met the above criteria had consultation with a medical oncologist prior to surgical resection at which time discussion regarding potential indications for adjuvant chemotherapy and early adjuvant chemotherapy start date was initiated. On the day of surgery (Day 0): Patients underwent initial liquid biopsy (ctDNA, Circulating tumor cells) and standard laboratory testing including CEA, chemistry profile, and Complete Blood Count (to allow calculation of the neutrophil lymphocyte ratio) prior to the start of surgery. Intraoperatively, after vascular ligation and division of the bowel, patients received intravenous (IV) piggyback of Leucovorin 20 mg/m2 followed by a single dose of 5-Flurouracil 400 mg/m2 IV Push (Cycle 0, Day 0). Quality of Life Questionnaires (QLQ-CR30) were completed by the study patients on the day surgery (Day 0) and on Follow-up day 30.[19] All surgical-related complications were tracked postoperatively (Appendix C). Postoperative care was our current Enhanced Recovery After Surgery (ERAS) protocol, with regular diet on POD0, minimization of narcotics, elimination of Foley catheter and fluids POD 0. There was no other changes to our standard colectomy preoperative, intraoperative and postoperative care Fig. 1.

Pathology reports were reviewed by the medical oncologist on Day 7, and patients' adjuvant treatment, when indicated, was planned to start on Day 14. At the time of pathology review (approximately day 7), patients received a call from medical oncology informing them of pathology results, plan of care, and (when chemotherapy was recommended) a review of the risks, benefits to chemotherapy with plans for chemotherapy consenting procedures to occur prior to infusion. Patients in which final pathology revealed either lymph node involvement (Stage III), or high-risk stage II colon cancer received standard adjuvant chemotherapy as per choice of the treating oncologist and within standard recommendations of NCCN guidelines (CAPOX and/or FOLFOX).[20] This Day 14 dose initiated the planned treatment course (3-months or 6-months, as per treating physician). Patients with Stage I and low-risk Stage II disease received no further chemotherapy. All patients underwent a second liquid biopsy draw on Day 14.

On Day 28-35, depending on whether or not the patient was receiving a every 14 day or every 21 day regimen: Eligible patients (stage III or high-risk stage II) received the 2nd standard dose of chemotherapy (Cycle 2, Day 1, which was be the 3rd total dose on-study, including the assigned study intervention on Day 0). All patients underwent a third liquid biopsy on day 30.

After the Day 0 (intraoperative) dose of chemotherapy, the treatment algorithm conformed to established standard of care for postoperative adjuvant chemotherapy in colonic adenocarcinoma (ie 3-months-6-months, based on recommendation of the treating medical oncologist).

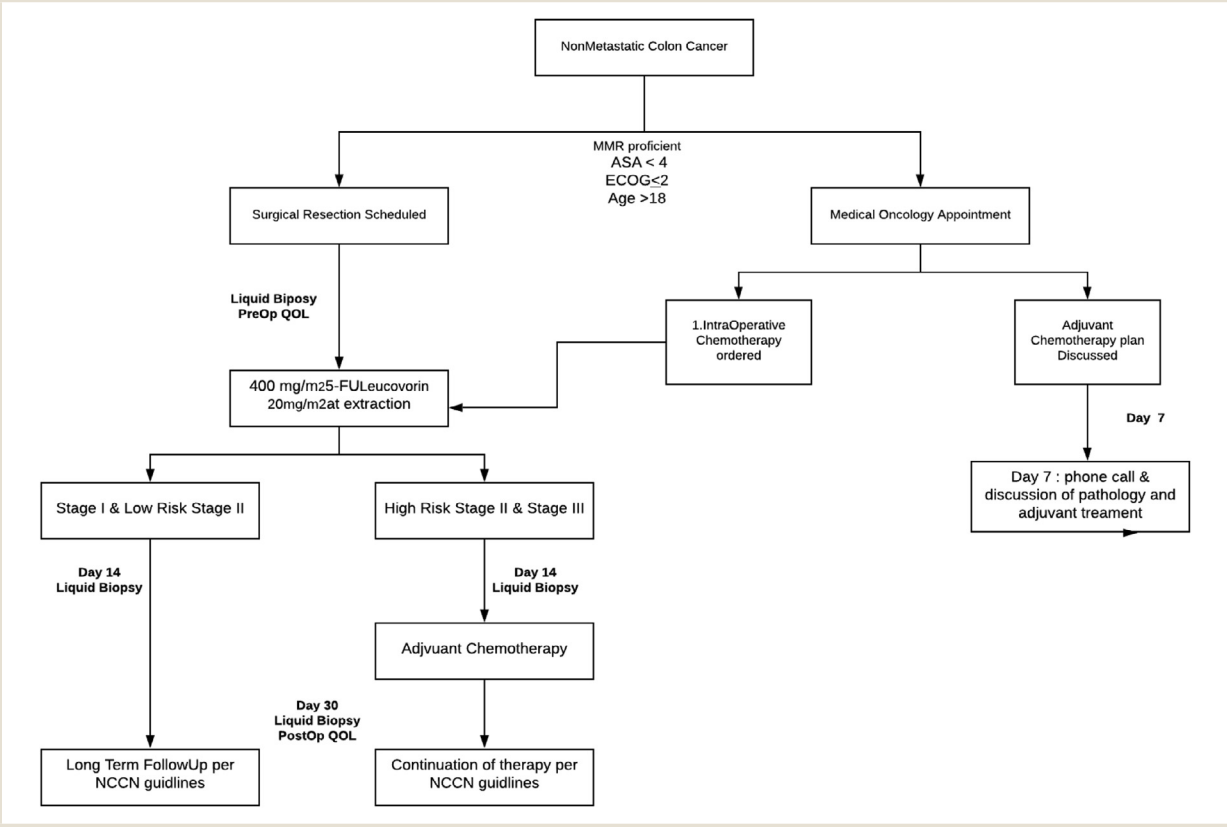
Objectives

The primary objective of this trial was safety and feasibility of administering chemotherapy in the immediate adjuvant setting. The primary endpoint was intraoperative and postoperative complications. Secondary objectives included quality of life analysis using the EORTC QLQ-C30.[19]

Statistical Analysis

As the primary objective of this study was the safety and feasibility of administrating chemotherapy in the immediate adjuvant setting, our statistics are descriptive and qualitative in nature.[38] The collection of blood biomarkers was used for exploratory purposes and to guide our next phase of the study. A paired-samples *t* test was conducted to compare patients' quality of life scores before and after surgery. All analyses were two-tailed and a difference was considered

Figure 1 Immediate Adjuvant Chemotherapy Protocol.



statistically significant if the *P* value was less than or equal to .05. The statistical data analyses were performed with the IBM SPSS Statistics 25.0. The EORTC subscales were analyzed using a split-plot ANOVA with gender, age, and chemotherapy treatment as the between-subjects factors and pre/post-surgery as the within subjects factor.

Results

During the period of November 2017-April 2019, 24 patients were recruited. Four patients were ineligible due to MMR-deficient status based on immunohistochemistry. Among 20 eligible patients, the median age was 57 years (Range: 36-79) and 60% of patients were female; 20% (n = 4) were stage I, 40% stage II (n = 8) and 40% stage III (n = 8). Table 1 lists patient demographics. Ascending colon cancer comprised 50% (n = 10) of patients, sigmoid in 30% (n = 6) and 15% (n = 3) had rectosigmoid cancers. One patient had a synchronous right (T3), transverse (T3) and sigmoid (T3) node negative colon cancer. All patients underwent laparoscopic surgery, with one patient (5%) requiring conversion to open due to malrotation and dense adhesions. This patient required readmission due postoperative ileus which resolved with no intervention (only grade 3 adverse event). There were no intraoperative complications (Table 2).

Table 1 Patient Demographics

Age (years, median)	58	range (39-76)
Gender (Female, N; %)	9	45
Stage (N; %)		
T1	3	15
T2	2	10
T3	10	50
T4	5	25
N0	11	55
N1	5	25
N2	4	20
Adjuvant chemotherapy (N; %)	13	65
Date to chemotherapy (days, median)	14	range (14-36)

All patients successfully received intraoperative chemotherapy. Median time to start of adjuvant chemotherapy was 14 days (range 14-36). Delays in two patients with T3N0 tumors lacking high-risk features were due to additional gene profile testing, chemotherapy start dates of 30 and 36 days. Three patients had delays due to port placement and started chemotherapy on day 18 and 21. One patient

Table 2 Operative Characteristics

	N	%
Surgical Procedure		
Sigmoid Colectomy	2	10
low anterior	5	25
Right Colectomy	10	50
Total colectomy	1	5
Length of stay (median)	2 d	Range (2-4 d)
Conversion to Open	1	5
Intraoperative Complications	0	0
Postoperative Complication	1	5

had insurance delays and was started on day 23. Table 3 lists all adverse events.

Quality of Life

We observed a statistically significant increase of roughly 14 points (SD = 26.2, $P = 0.038$) using the Emotional Functioning Scale between Preop (M = 76.39, SD = 25.0) and Postop (M = 90.28, SD = 11.9) EORTC QLQ-C30[19] scores (higher scores indicate improvement in quality of life) (Table 4). Cohen's *d* was estimated at 0.529, which also represents a medium effect[21] for emotional functioning. No other differences in EORTC scales or items were statistically significant. Although global health scores improved over time this was not statistically significant. Patients who received adjuvant therapy had a higher dyspnea scores dyspnea ($P = .025$) over time. A significant interaction was also observed between gender and surgery for pain ($P = .003$) (Table 5).

Median Neutrophil/lymphocyte ratio (NLR) was essentially unchanged over the course of study: 3.0 preoperatively compared to 3.6 on day 14 and 2.31 on postop day 30. Median preoperative CEA was 4.1ng/ML (range 0.8-12.2ng/ML).

Discussion

In this phase I "immediate adjuvant chemotherapy" trial we demonstrated that initiation of cytotoxic agents at the time of colon resection and administration of very early adjuvant chemotherapy) is safe and feasible. Within our institution, we were successful in establishing a new approach to multidisciplinary care of colon cancer patients. There were no intraoperative and/or postoperative chemotherapy related complications. The majority of patients started their adjuvant treatment (where indicated, as per NCCN guidelines[20]) at postoperative day 14, which, to the authors' knowledge, is the earliest median time to colon cancer adjuvant chemotherapy reported in the literature. There was a statistically significant overall improvement in emotional wellbeing postoperative compared to preoperatively and a trend towards global quality of life improvement. As such, these results validate a novel approach to the perioperative phase of care in the colon cancer treatment paradigm that may be evaluated for therapeutic advantages in future clinical trials.

Despite optimal treatment, systemic recurrence in colon cancer remains high.[22] It is well established that patients who ultimately recur harbor tumor cells (ie micrometastases) during their perioperative phase of care. It is hypothesized that patients are most vulnerable to micrometastasis during the perioperative period as they are immunocompromised from the trauma of surgery.[16,23-27] Introducing cytotoxic agents during this vulnerable period may decrease systemic failures.[28] This hypothesis directly correlates to clinical findings that delays in adjuvant treatment have been shown to be an independent risk factor for relapse with reported 14% relative risk reduction in overall survival for every 4-week delay in chemotherapy administration.[14,15] While it is generally agreed that early postoperative chemotherapy administration is better than delayed treatment, in clinical practice patients do not commonly start postoperative therapy until week 6-8, or later.[14,15] We have demonstrated that early initiation of adjuvant chemotherapy is safe and feasible within a multidisciplinary approach. The median start time to chemotherapy for the 65% of patients who received adjuvant chemotherapy was just 14 days. There were no intraoperative complications and only 5% postoperative complication rate, which was not related to early chemotherapy administration.

There is much apprehension both in the surgical and medical oncology community that starting chemotherapy too early may adversely affect patient outcomes.[29,30] However, the concern appears to be based on hypothesized rather than published data. In fact, we demonstrated that early initiation of chemotherapy is feasible after successful minimally invasive surgery and did not

Table 3 Adverse Event

System Organ Class	Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Blood and lymphatic	Anemia	1 (5%)	0	0	0	0
General	Fatigue	1 (5%)	0	0	0	0
Gastrointestinal			0	0	0	0
	Diarrhea	1 (5%)	0	0	0	0
	Mucositis Oral	1 (5%)	0	0	0	0
	small bowel obstruction		0	1 (5%)	0	0
Nervous system	Syncope	1 (5%)	0	0	0	0
Skin & subcutaneous tissue	Palmar-plantar erythrodysesthesia	1 (5%)	0	0	0	0
Psychiatric	Insomnia	1 (5%)	0	0	0	0
Reproductive & breast	Penile pain	1 (5%)	0	0	0	0

Table 4 Quality of Life: Mean Preoperative and Postoperative scores for EORTC-QLQ C-30

Scales/Items	N	Preop Mean (SD)	Postop Mean (SD)	*P* value
Global Health Status				
General QOL	18	72.69 (22.1)	77.31 (18.7)	.243
Functional Scales				
Physical Functioning	18	86.67 (16.0)	86.67 (15.5)	1.000
Role Functioning	18	87.96 (17.9)	87.04 (17.7)	.834
Emotional Functioning	**18**	**76.39 (25.0)**	**90.28 (11.9)**	**.038**
Cognitive Functioning	18	88.89 (16.2)	89.8 (14.2)	.805
Social Functioning	18	87.96 (16.0)	87.96 (20.5)	1.000
Symptoms Scales/Items				
Fatigue	18	21.60 (24.2)	30.25 (21.8)	.067
Nausea and Vomiting	18	12.04 (14.9)	16.67 (28.0)	.508
Pain	18	15.74 (18.5)	11.00 (19.0)	.331
Dyspnea	18	7.41 (14.3)	9.2 (15.4)	.668
Insomnia	18	18.52 (30.7)	5.56 (12.8)	.130
Appetite Loss	18	16.67 (30.8)	16.67 (26.2)	1.000
Constipation	17	7.84 (14.6)	15.69 (17.1)	.104
Diarrhea	18	27.78 (32.8)	18.52 (28.5)	.236
Financial Difficulties	18	14.81 (28.5)	16.67 (28.6)	.772

EORTC = European Organization for Research and Treatment of Cancer

Table 5 Interactions from Split-Plot ANOVA with EORTC Subscales and Gender, Age, or Chemotherapy

Scales/Items	N	Preop Mean (SD)	Postop Mean (SD)	*df*	MS	*F*	*P*-value	η2
Pain								
Male	10	6.67 (11.7)	13.33 (22.0)	–	–	–	–	–
Female	8	27.08 (19.8)	8.33 (15.4)	–	–	–	–	–
Gender*Pain	–	**–**	**–**	**1**	**1435.571**	**12.458**	**.003**	**0.438**
Fatigue								
Did NOT receive adj chemo	6	20.37 (21.6)	14.81 (11.5)	–	–	–	–	–
DID receive adj chemo	12	22.22 (26.4)	37.96 (21.9)	–	–	–	–	–
Chemo*Fatigue	–	–	–	**1**	**907.064**	**7.253**	**.016**	**0.312**
Dyspnea								
Did NOT receive adj chemo	6	16.67 (18.3)	5.56 (13.6)	–	–	–	–	–
DID receive adj chemo	12	2.78 (9.6)	11.11 (15.4)	–	–	–	–	–
Chemo*Dyspnea	–	–	–	**1**	**756.173**	**6.078**	**.025**	**0.275**
Physical Functioning (PF)								
60 y and Under	10	89.33 (14.8)	84.00 (18.9)	–	–	–	–	–
Above 60 y	8	83.333 (17.8)	90.00 (10.1)	–	–	–	–	–
Age*PF	–	–	–	**1**	**320.00**	**3.866**	**.067**	**0.195**

result in postoperative complications. Moreover, all patients in this study received an intraoperative dose of 5FU/LV with no surgical related complication related to chemotherapy. Although we are the first to study this new treatment paradigm, there is ample data demonstrating that perioperative systemic (intravenous) chemotherapy for patients with advanced colon cancer undergoing cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC) is safe.[31-36] HIPEC/CRS often includes administering IV chemotherapy intra-operatively in addition to intraperitoneal heated chemotherapy (bidirectional chemotherapy) after extensive surgery. The majority of the morbidity incurred during cases involving HIPEC administration is secondary to the peritonectomy and extensive surgery required to clear the disease. A standard minimally invasive colectomy has a much lower morbidity and mortality compared to CRS/HIPEC (which may include colectomy along with resection of any peritoneal surface deposits on various intra-abdominal structures). There is also data regarding the administration of cytotoxic drugs into the liver via portal vein infusion

(PVI) in the adjuvant setting to enhance the delivery of chemotherapeutic agents within the liver. A meta-analysis of 10 randomized clinical trials reported low rates of postoperative mortality (<2%) with a 5-year overall survival improvement of 5% ($P > .05$).[37] It has been suggested that the added benefits of 5-FU administration via PVI was because the drug was given perioperatively rather than the particular route of the administration. This is hypothesis is supported by the findings that the apparent reduction in recurrence was confined to non-liver metastasis.[17]

In the era of minimal invasive surgery and enhanced recovery programs, which is associated with improved postoperative complications,[38-41] we demonstrated a 2-day median LOS, with one complication of small bowel obstruction requiring readmission. Even in this patient, adjuvant chemotherapy was started on postoperative day 30. We also reviewed all colon cancer cases undergoing resection at our tertiary center during the study period and found a comparable median length of stay of 2 days (Average 4.5±3.3) and similar morbidity rate for our colon cancer colectomies (internal communication, full data not shown). In this small pilot study, we have successfully demonstrated that given the low morbidity burden of minimal invasive surgery the likelihood of surgical complications due to early administration of chemotherapy are low. This should lead us to question the age-old dogma that chemotherapy must be delayed postoperatively.

Our protocol most importantly established a new multidisciplinary approach between the oncologist and the surgeon, which is lacking in current colon cancer care. The advantages of this approach are 2-fold. First, there is the potential for improvement in quality of life for patients by completing their overall treatment much earlier than current paradigms. Second, it is well established that multidisciplinary care improves overall outcomes.[42-45] Meeting and discussing plans for postoperative chemotherapy prior to resection potentially allows patients to be more compliant with treatment, and potentially alleviate anxiety during the postoperative period. It will also allow a team-based discussion between the surgeon and medical oncologist. This improvement in outcomes was seen in the FOxTROT trial which did not find a difference in disease free survival between the neoadjuvant chemotherapy group and the adjuvant group. Their hypothesis was that the multidisciplinary care of all patients in this study could have perhaps led to this nonsuperiority of neoadjuvant therapy in colon cancer. However, it should be noted that FOxTROT had a higher rate of anastomotic leak rates in the neoadjuvant group (7.4% compared to 4.7%).[46] In our study, we demonstrated that the one dose of chemotherapy administration during surgery and then postoperative did not affect postoperative outcomes. In fact, 30% of patients had colorectal anastomosis due to an upper rectal/rectosigmoid lesion.

Clearly there is renewed interest in neoadjuvant chemotherapy for colon cancer as described in the FOxTROT trial. The essential hypothesis of FOxTROT and IAC protocol are similar in that both were designed to overcome the inherent delays in standard postoperative chemotherapy, potentially leading to poor survival outcomes. However, current imaging modalities are not accurate enough to predict colon cancer staging prior to operation. Unlike, gastric, esophageal, and rectal cancer, the preoperative staging of colon cancer has low yield in nonmetastatic disease**.** Smith et al reported a 60% accuracy for T staging and 50% accuracy for N staging. This is further confirmed by the results of FOxTROT Collaborative Group's pilot randomized trial demonstrated that 24% of patients did not have lymph node positive disease in the control group when comparing preoperative imaging versus postoperative path results.[26] This can lead to over treatment of a quarter of patients who may never have received adjuvant treatment. We report similarly that 35% of our patients did not require adjuvant chemotherapy based on NCCN guidelines. Although these patients did receive a single dose of chemotherapy in the operating room, our clinical trial revealed essentially no harm to these patients.

It is known that adjuvant chemotherapy contributes to worsening fatigue and dyspnea. Despite these well-known side effects of treatment, we observed a significant improvement in emotional functioning and non-significant, but important, increases in global well-being. We hypothesize that our protocol can lead to quality-of-life improvements in two ways. First, early introduction to the oncologist can eliminate some anxiety and fears about chemotherapy; secondly, the early completion of treatment in patients requiring adjuvant treatment may lead to improvement in overall well-being.

This study has limitations which are inherent to small single-arm pilot study. Although surgical outcomes were similar to our overall colon cancer patient population- as tracked by prospective databases such as the National Surgical Quality Improvement Program (NSQIP) data during the same time period at our institution-, we cannot exclude inherent patient selection biases. This study is also limited by small sample size, and lack of a control group. We also lack translational endpoints such as ctDNA [47] which is a biomarker of micrometastasis and minimal residual disease to guide treatment; however, we plan to include ctDNA analyses in a future report when data are available.

Given the positive findings of our phase I trial, we plan to proceed to a phase IIB trial. We are currently in the process of completing the biomarker portion of this study. As our ultimate goal is 3-fold: clinical outcomes, biomarker analysis and quality of life.

Conclusion

As proof of principle, the results of our study demonstrate that intraoperative chemotherapy for colon cancer followed by early postoperative therapy is well-tolerated, and safe. As a next step, we aim to study the impact of this novel treatment paradigm on both quality of life and disease-free survival for patients with nonmetastatic colon cancer in a randomized clinical trial. Such a strategy may justify earlier cancer treatment, and ultimately improve patient outcomes by decreasing systemic recurrence.

Clinical Practice Points

It is well established through retrospectives studies that delays in chemotherapy will lead to overall worse survival in colon cancer. Currently there are no guidelines for timing of the initiation of adjuvant chemotherapy.

This study aims to launch a phase II trial based on our finding that initiation of chemotherapy at the time of operation is both feasible.

This early start to chemotherapy will not only have potential impact in patient survival, but we hypothesize quality of life.

Author Contribution

Jafari, Mehraneh D MD: Conceptualization; methodology; formal analysis; investigation; writing; acquisition of financial support; editing. Carmichael, Joseph C MD: investigation; editing. Dayyani, Farshid MD: investigation; editing. McKinney, Chelsea PhD MPH: investigation; methodology; formal analysis; editing. Wenzel, Lari PhD: investigation; methodology; formal analysis; editing. Zell, Jason A DO: Conceptualization; methodology; formal analysis; investigation; editing. MPH; Pigazzi A MD PhD: Conceptualization; methodology; formal analysis; investigation; editing.

Disclosures

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Appendix A

Inclusion Criteria

- Male and Female subjects ≥ 18 years old.
- Subjects with biopsy proven adeno carcinoma > 2 cm based on prior imaging study or colonoscopy and are NOT amenable to colonoscopic resection (i.e., Not malignant polyps).
- Have Microsatellite Stable (MSS) and/or Mismatch Repair Proficient (MMR-p) colon cancer.
- Understand and give informed consent.

Exclusion Criteria

- Have Microsatellite Instability High (MSI-High) and/or Mismatch Repair Deficient (MMR-d) colon cancer.
- Subjects with metastatic disease will be excluded.
- Subjects with ASA Score (American Society of Anesthesiologists) ≥ 4 and/or ECOG (Eastern Cooperative Oncology Group) score ≥ 2 will be excluded from the study due to concern for immediate adjunct chemotherapy tolerance.
- Pregnancy

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