# N9741:

# A Randomized Phase III Trial of Combinations of Oxaliplatin (OXAL), 5-Fluorouracil (5-FU), and Irinotecan (CPT-11) as Initial Treatment of Patients With Advanced Adenocarcinoma of the Colon and Rectum

**ClinicalTrials.gov Identifier:** NCT00003594

## Study Background

**Trial Design:**

This is a randomized, multicenter study. Patients are stratified according to ECOG performance status (0-1 vs 2), prior adjuvant chemotherapy (yes vs no), prior immunotherapy (yes vs no), and age (under 65 vs 65 and over). Patients are randomized to one of three treatment arms.

- Arm I (Saltz regimen): Patients receive irinotecan IV over 90 minutes followed by leucovorin calcium IV over 15 minutes and fluorouracil IV once a week for 4 weeks followed by 2 weeks of rest. Courses repeat every 6 weeks. (Arm I closed to accrual as of March 15, 2002.)
- Arm II (FOLFOX4 regimen): Patients receive oxaliplatin IV over 2 hours on day 1 and leucovorin calcium IV over 2 hours plus fluorouracil IV over 22 hours on days 1 and 2. Courses repeat every 2 weeks.
- Arm III (oxaliplatin plus irinotecan): Patients receive oxaliplatin IV over 2 hours and irinotecan IV over 30 minutes on day 1. Courses repeat every 3 weeks. (Arm III closed to accrual as of March 15, 2002.) Treatment continues in the absence of disease progression or unacceptable toxicity.

Quality of life is assessed before treatment, during treatment (arm specific), and after completion of treatment.

Patients are followed every 3 months for 1 year, every 6 months for 2 years, and then annually thereafter.

**Objectives:**

Primary:

- The primary objective of this trial is to compare the time to progression in patients with locally advanced or metastatic colorectal cancer (previously untreated for advanced disease) who receive OXAL + 5-FU + CF or CPT-11 + OXAL (the two experimental regimens) to those receiving CPT-11 + 5-FU + CF (the control regimen).

Secondary:

- A secondary objective of this trial is to compare the time to progression of patients receiving the two experimental regimens.

- The primary secondary outcome measure in this trial is overall survival.
- Other secondary objectives include evaluation of toxicity, response rate, and time to treatment failure.
- To compare quality-of-life parameters in patients on these regimens.

**Stratification Factors:**

- ECOG PS: 0, 1 vs. 2.
- Prior adjuvant chemotherapy: Yes vs. no.
- Prior immunotherapy: Yes vs. no.
- Age <65 vs. ≥65.
- Membership: Intergroup vs. Expanded Participation Project (EPP).

**Study History:**

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| 10/27/1998 | Activation Date |
| 7/19/2002 | Close Date |
| October 2004 | Primary Completion Date |
| October 2004 | Study Completion Date |

## Publication Information

**Analysis Type:** Primary Endpoint Analysis

**PubMed ID:** 14665611

**Citation:** Goldberg, R. M., Sargent, D. J., Morton, R. F., Fuchs, C. S., Ramanathan, R. K., Williamson, S. K., . . . Alberts, S. R. (2004). A Randomized Controlled Trial of Fluorouracil Plus Leucovorin, Irinotecan, and Oxaliplatin Combinations in Patients With Previously Untreated Metastatic Colorectal Cancer. Journal of Clinical Oncology, 22(1), 23-30. doi:10.1200/jco.2004.09.046

**Associated Datasets:**

NCT00003594_D1crse
NCT00003594_D2cycle
NCT00003594_D3cytox
NCT00003594_D4end_at

**Note: These datasets have been updated since the primary publication and may not match the exact results reported in the primary manuscript.**

## Dataset Information

**Dataset Name:** NCT00003594_D2cycle

**Description:** The NCT00003594_D2cycle dataset is one of 4 datasets associated with PubMed ID 14665611. This dataset contains information per patient, per cycle regarding dosing and overall response assessment status.

## NCT00003594_D2cycle Data Dictionary

| Variable Description | Variable Name | Code | Notes |
|---|---|---|---|
| Unique identifier for each patient | patref | | |
| Primary reason for 5FU Adjustment | adjrsn1 | 39=Neutropenia<br>40=Neutropenic fever<br>41=Thrombocytopenia<br>42=Diarrhea<br>44=Mucositis/Stomatitis<br>45=Dermatitis<br>46=Nausea<br>47=Vomiting<br>51=Sensory-Neuropathy<br>88=Pharyngo-Laryngeal dysesthesias<br>99=Other | If missing then no adjustment was recorded. |
| Primary reason for CF Adjustment | adjrsn2 | See adjrsn1. | See adjrsn1. |
| Primary reason for CPT-11 Adjustment | adjrsn3 | See adjrsn1. | See adjrsn1. |
| Primary reason for OXAL Adjustment | adjrsn4 | See adjrsn1. | See adjrsn1. |
| Primary reason for 5FU Bolus Adjustment | adjrsn5 | See adjrsn1. | See adjrsn1. |

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|---|---|---|---|
| Primary reason for 5FU Infusion Adjustment | adjrsn6 | See adjrsn1. | See adjrsn1. |
| Agent: 5FU | agent1 | | If missing then agent was not given in the cycle. |
| Agent: CF | agent2 | | See agent 1. |
| Agent: CPT-11 | agent3 | | See agent 1. |
| Agent: OXAL | agent4 | | See agent 1. |
| Agent: 5FU Bolus | agent5 | | See agent 1. |
| Agent: 5FU Infusion | agent6 | | See agent 1. |
| Experimental arm: A, F, G | arm | A = CPT-11, 5-FU, CF<br>F = OXAL<br>G = OXAL + CPT-11 | For the purposes of matching the study background and clinicaltrials.gov registration information, Arm I, Arm II, and Arm III are synonymous with Arm A, Arm F and Arm G, respectively. |
| Days from randomization until tumor assessment | assess_time | | If missing then no assessment date was recorded. |
| Days from randomization until date treatment was given this cycle | chemo_time | | If missing then no treatment date was recorded. |
| Number of protocol treatment regimens received | course | 1 = 1$^{st}$ treatment regimen<br>2 = 2$^{nd}$ treatment regimen | If missing then no treatment was given. |
| Protocol specific interval (typically based on treatment delivery times) | cycle | | If missing then no treatment was given. |
| 5FU dose level this cycle (mg/m$^2$) | dlevel_1 | | See agent 1. |
| CF dose level this cycle (mg/m$^2$) | dlevel_2 | | See agent 1. |

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| CPT-11 dose level this cycle ($mg/m^2$) | dlevel_3 | | See agent 1. |
| OXAL dose level this cycle ($mg/m^2$) | dlevel_4 | | See agent 1. |
| 5FU Bolus dose level this cycle ($mg/m^2$) | dlevel_5 | | See agent 1. |
| 5FU Infusion dose level this cycle ($mg/m^2$) | dlevel_6 | | See agent 1. |
| Primary reason for treatment delay | dly_reas | 81=Toxicity<br>99=Other | If missing then no delay was recorded. |
| Days from randomization until start of 5FU | dose1_time | | If missing then no date was recorded. |
| Days from randomization until start of CF | dose2_time | | See dose1_time. |
| Days from randomization until start of CPT-11 | dose3_time | | See dose1_time. |
| Days from randomization until start of OXAL | dose4_time | | See dose1_time. |
| Days from randomization until start of 5FU Bolus | dose5_time | | See dose1_time. |
| Days from randomization until start of 5FU Infusion | dose6_time | | See dose1_time. |
| Days from randomization until adverse event evaluation | eval_time | | If missing no adverse event evaluation date recorded. |
| Indicator if patient has been determined to be | excluded | 9=Ineligible<br>8=Violation<br>7=Cancel<br>Missing = otherwise | |
| Objective Status | obj_stat | 1=Complete Response<br>2=Partial Response<br>3=Regression<br>5=Stable Disease<br>6=Progression | If missing then objective status was not recorded in the cycle. |
| ECOG Performance Status used for this cycle (0,1,2,3,4) | ps | | If missing then performance status was not recorded in the cycle. |

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| BSA used for this cycle ($m^2$) | rep_bsa | | If missing then BSA was not recorded in the cycle. |
| Arm to which patient was originally randomized | rnd_arm | | If missing then no treatment was given. |
| Was dose level adjusted this cycle (5FU)? | rxreduc1 | 1=Yes<br>2=No | If missing then adjustment for corresponding agent was not recorded. |
| Was dose level adjusted this cycle (CF)? | rxreduc2 | 1=Yes<br>2=No | See rxreduc1. |
| Was dose level adjusted this cycle (CPT-11)? | rxreduc3 | 1=Yes<br>2=No | See rxreduc1. |
| Was dose level adjusted this cycle (OXAL)? | rxreduc4 | 1=Yes<br>2=No | See rxreduc1. |
| Was dose level adjusted this cycle (5FU Bolus)? | rxreduc5 | 1=Yes<br>2=No | See rxreduc1. |
| Was dose level adjusted this cycle (5FU Infusion)? | rxreduc6 | 1=Yes<br>2=No | See rxreduc1. |
| Total dose ($mg/m^2$) this cycle (5FU) | tdose1 | | If missing then corresponding agent was not given in the cycle. |
| Total dose ($mg/m^2$) this cycle (CF) | tdose2 | | See tdose1. |
| Total dose ($mg/m^2$) this cycle (CPT-11) | tdose3 | | See tdose1. |
| Total dose ($mg/m^2$) this cycle (OXAL) | tdose4 | | See tdose1. |
| Total dose ($mg/m^2$) this cycle (5FU Bolus) | tdose5 | | See tdose1. |
| Total dose ($mg/m^2$) this cycle (5FU Infusion) | tdose6 | | See tdose1. |