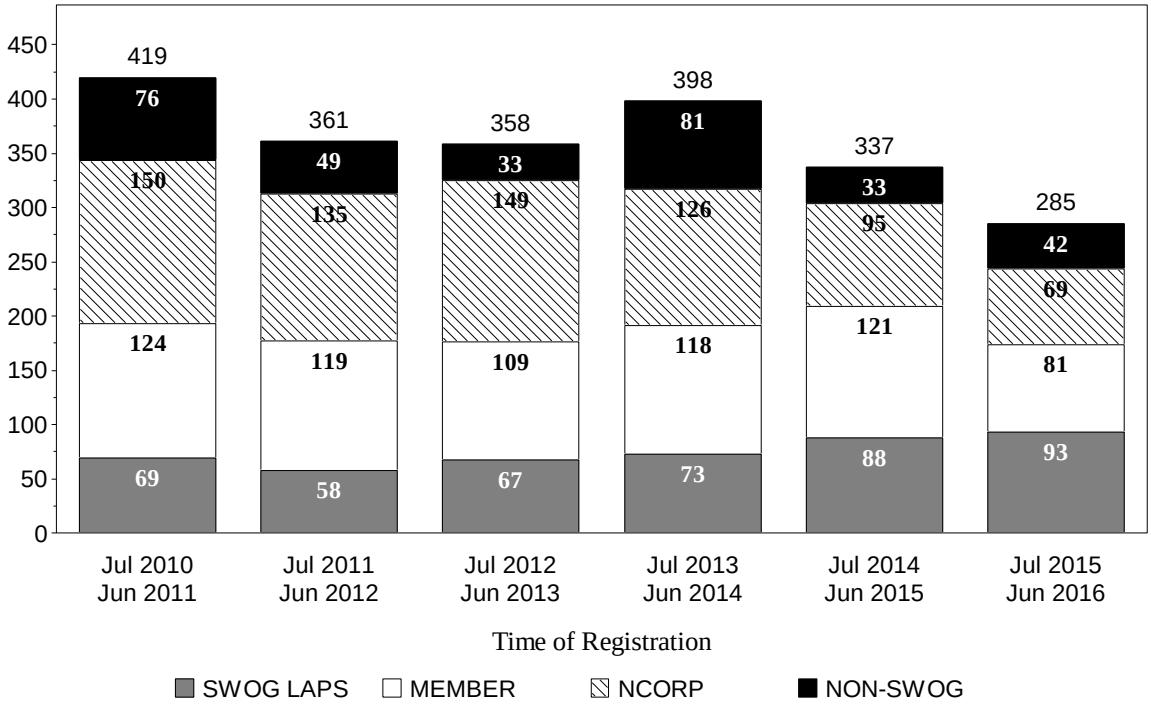
GASTROINTESTINAL COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
GASTROINTESTINAL COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

GASTROINTESTINAL COMMITTEE

	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
S1201 Gas/Esoph/GEJ, Adv, ERCC1-based				
Initial Marker Testing	0	0	28	264
Randomization				
FOLFOX	0	0	11	106
Irinotecan + Docetaxel	0	0	14	107
	0	0	25	213
S1310 Biliary, Ref. Adv, GSK1120212 vs Chemo				
Trametinib	0	0	9	27
5-FU+Leucovorin/Capecitabine	0	0	12	26
	0	0	21	53
S1313 Panc, Met, mFolfirinox +/- PEGPH20				
Phase I				
PEGPH20 Dose Level 1 + mFOLFIRINOX	0	0	0	5
PEGPH20 Dose Level 2 + mFOLFIRINOX	0	0	6	7
Phase II				
mFOLFIRINOX	15	16	1	32
PEGPH20 + mFOLFIRINOX	11	16	1	28
	26	32	8	72
S1406 CRC, Met, BRAF mut, Irino + Cetux ± Vem				
Initial Registration	23	62	51	142
Randomization				
Cetuximab + Irinotecan	10	25	15	52
Vemurafenib + Cetux + Irinotecan	12	24	16	54
	22	49	31	106
Crossover				
Vemurafenib + Cetux + Irinotecan	11	7	4	22
S1505 Panc, Resect, Perioperative Chemo				
mFOLFIRINOX->Surg->mFOLFIRINOX	19	0	0	19
Gem/nab-P->Surg->Gem/nab-P	16	0	0	16
	35	0	0	35
A021202 Carcinoid, Pazopanib vs Placebo*				
Total Registrations	0	12	10	35
C80702 Adj FOLFOX+Celecoxib or Placebo*				
Total Registrations	0	53	49	540
C80802 HCC, Adv, Sorafenib +/- Doxorubicin*				
Total Registrations	0	0	4	46

	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
E2211 Panc, Adv, Temozolomide +/- Cape*				
Total Registrations	6	12	17	55
E7208 CRC, Adv, Irino/Cet +/- Ramucirumab*				
Total Registrations	4	4	5	16
N1048 Rectal, Local Adv, ChemoRT +/- FOLFOX*				
Total Registrations	17	8	15	86
R0848 Panc, Adj, Erlotinib vs ChemoRT*				
Total Registrations	1	3	0	20
R1201 Panc, Local. Adv, Gem/nab-Paclitaxel +/- RT*				
Total Registrations	1	0	0	1

* For non-SWOG coordinated studies only SWOG registrations are shown.

S0820 Phase III

A Double Blind Placebo-Controlled Trial of Eflornithine and Sulindac to Prevent Recurrence of High Risk Adenomas and Second Primary Colorectal Cancers in Patients with Stage 0-III Colon or Rectal Cancer, Phase III - Preventing Adenomas of the Colon with Eflornithine and Sulindac (PACES)

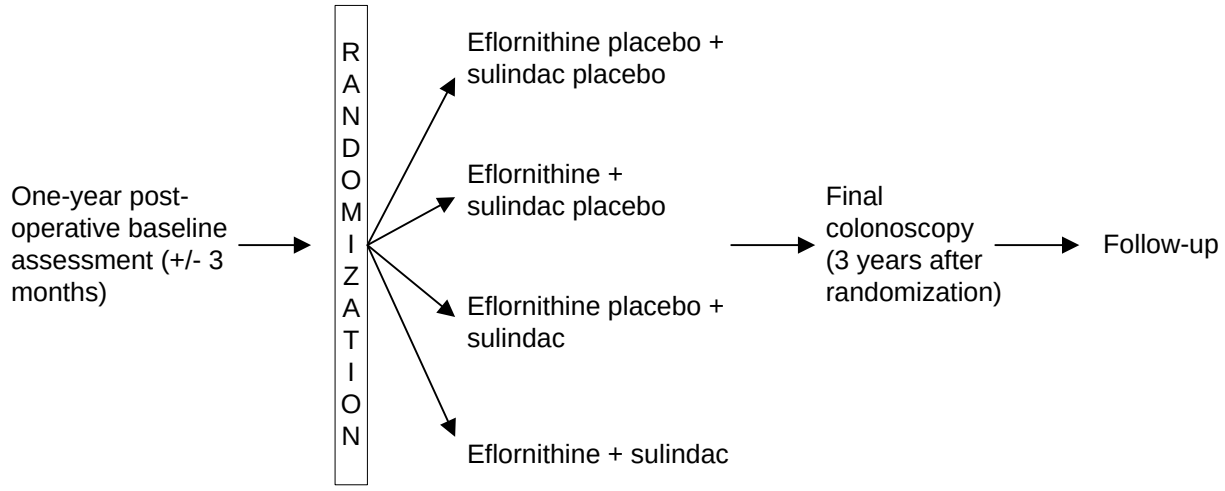
Study Chairs:
J Zell, P Brown

Date Activated:
03/01/2013

Statisticians:
J Unger, G Anderson, K Arnold

Data Coordinator:
M Yee

SCHEMA



Objectives

To assess whether eflornithine (+/- sulindac), sulindac (+/- eflornithine) or the combination are effective in reducing the three-year combined event rate (high-risk adenomas and second primary colorectal cancers) in patients with previously treated Stage 0-III colon or rectal cancer.

To assess whether eflornithine, sulindac or the combination has efficacy against colorectal lesions with respect to high-grade dysplasia, adenomas with villous features, adenomas 1 cm or greater, multiple adenomas, any adenomas 0.3 cm, total advanced colorectal events, or total colorectal events.

To assess quantitative and qualitative toxicities of patients when treated with eflornithine, sulindac, or the combination compared to placebo.

To evaluate a minimal set of tagging single nucleotide polymorphisms across multiple genes relevant to eflornithine and sulindac, in order to characterize associations with decreased

adenoma/second primary colorectal cancer (CRC) risk and adverse events.

To examine the interaction of intervention arm and baseline statin use with respect to the three-year event rate.

To examine the interaction of the intervention arm and patient-reported meat consumption with respect to the 3-year event rate.

To perform pharmacokinetic (PK) analysis of eflornithine and sulindac in patients with previously treated Stage 0-III colon or rectal cancer.

Patient Population

Patients must have a history of Stage 0, I, II or III colon or rectal adenocarcinoma that has been treated per standard care with resection alone or in combination with radiation or chemotherapy. Adjuvant chemotherapy and/or radiation treatment must have been completed at least 30 days prior to registration.

Patients must be registered between 180 days and 456 days (inclusive) of primary resection. Patients must show no evidence of disease based on post-operative colonoscopy (performed at least 180 days after the colon resection date or at least 120 days after the rectal resection date and prior to registration) and CT or MRI scans (at the discretion of the treating physician for high risk patients, per NCCN guidelines) of chest, abdomen and pelvis (performed at least 180 days after the colon resection date or at least 120 days after the rectal resection date and prior to registration). Patients with adenomas detected at the one-year postoperative colonoscopy are eligible if all adenomas have been completely removed.

Patients must be at least 18 years of age and must not have cardiovascular risk factors as outlined in the protocol. Patients must have Zubrod performance status of 0-1 and adequate hematologic, hepatic and renal function. Patients must not have a known history of familial adenomatous polyposis, hereditary nonpolyposis colorectal cancer, or inflammatory bowel disease. Patients must have a pure tone audiometry evaluation within 30 days prior to registration: patients with at least 40 dB hearing loss of any of the tested frequencies are not eligible. Patients must not be hypersensitive to selective inhibitors of cyclooxygenase-2, non-steroidal anti-inflammatory drugs, salicylates, or sulfonamides. Patients must not have documented history of gastric/duodenal ulcer within the last 12 months.

Stratification/Descriptive Factors

At randomization, patients will be stratified by risk of recurrence: Stage 0/I vs Stage II with no prior chemotherapy vs Stage II with prior chemotherapy vs Stage III.

Accrual Goals

A total of 1488 patients will be randomized, 372 to each study arm, to achieve 1,340 eligible patients.

Summary Statement

For the current status of this study, please refer to the Prevention and Epidemiology chapter.

S1013 Validation

A Prospective Study of Epidermal Growth Factor Receptor (HER-1/EGFR) Inhibitor-Induced Dermatologic Toxicity: Validation of the Functional Assessment of Cancer Therapy-EGFRI 18 (FACT-EGFRI 18) Questionnaire for EGFRI-Induced Skin Toxicities

Study Chairs:
S Wong, C Moinpour, J Wade

Statisticians:
J Unger, K Arnold

Data Coordinator:
J Patterson

Date Activated:
11/15/2011

Objectives

To establish psychometric properties for the Functional Assessment of Cancer Therapy Epidermal Growth Factor Receptor Inhibitor (FACT-EGFRI 18) module (based on criterion validity, known group's validity, internal consistency reliability, and responsiveness to change) as a patient-reported outcome (PRO) measure of EGFRI-induced skin-related toxicity.

To document minimally important differences over time for the FACT-EGFRI 18 by comparing mean changes in this PRO measure to the patient's direct assessment of change using two anchor items (change in skin condition severity and impact).

To examine the association between toxicity profiles (severity and time to onset), and treatment profiles (e.g., delays and discontinuation) and the FACT-EGFRI 18 scores.

To assess degree of concordance between FACT-EGFRI 18 ratings and study site physician CTCAE Version 4.0 EGFRI-Induced Dermatologic Toxicity Grading Assessment ratings.

To evaluate feasibility outcomes.

Patient Population

Patients must have a diagnosis of colorectal or lung cancer and be planning to receive one of the following HER1/EGFR inhibitor therapies listed below for at least 6 weeks: (a) cetuximab 400 mg/m^2 loading dose, 250 mg/m^2 weekly; (b) cetuximab 500 mg/m^2 every 2 weeks; (c) panitumumab 6 mg/kg every 2 weeks; (d) erlotinib 100-150 mg daily. Other HER1/EGFR inhibitor therapies, schedules, or doses of the above listed agents are not allowed.

Concurrent chemotherapy and other anti-cancer therapies (such as carboplatin, paclitaxel, and bevacizumab) are allowed EXCEPT for the following chemotherapeutic agents which are known to cause skin rash that could interfere with EGFRI-induced skin toxicity assessment: gemcitabine, capecitabine, and topical fluorouracil. Patients may have had prior HER1/EGFR inhibitor therapy but must have fully recovered from any skin toxicities prior to registration. Patients must not have any of the serious concomitant skin disorders specified in the protocol that, in the investigator's opinion, could interfere with assessment of EGFRI induced skin toxicity. Patients must not be planning to receive any of the concomitant medications specified in the protocol that can cause skin rash or other dermatologic reactions that could interfere with the EGFRI-induced skin toxicity assessments, for the duration of the study. Patients must not be planning to receive concurrent external beam radiation therapy, including prophylactic cranial radiation.

Patients must have a Zubrod performance status of 0-2. Patients must be able to complete questionnaires in

English. Patients may concurrently participate in other therapeutic clinical trials. Patients must have completed the baseline S1013 FACT-EGFRI 18 within seven days prior to registration.

Accrual Goals

This study will enroll 156 patients.

Summary Statement

For the current status of this study, please refer to the Symptom Control and QOL chapter.

S1204 Surveillance

A Sero-Epidemiologic Survey and Cost-Effectiveness Study of Screening for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Among Newly Diagnosed Cancer Patients

Study Chairs:
S Ramsey, R Loomba, R Chugh, D Hershman, J Hwang

Date Activated:
08/29/2013

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Objectives

Among newly diagnosed cancer patients presenting to SWOG-affiliated community and academic oncology clinics, estimate the prevalence of human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) infection.

Evaluate known sociodemographic, clinical, and behavioral factors that are significantly associated with previously undiagnosed HIV, HBV, and/or HCV infection in a population of people with newly diagnosed cancer.

Among patients who are identified as having HIV, HBV, and/or HCV, evaluate the timing and type of treatments received, both for the viral infections and the cancers.

Evaluate type and rate of cancer treatment-related adverse events in patients with HIV, HBV, and/or HCV infection.

Determine the cost-effectiveness of (1) routine, universal screening and (2) risk factor-directed screening of newly diagnosed cancer patients for HIV, HBV and/or HCV versus current care.

Create a biorepository of stored serum for future translational medicine studies that may include identifying genomic and viral factors that increase the risk of serious adverse effects among participants infected with HIV, HBV, and/or HCV being treated for invasive cancers.

Patient Population

Patients must be presenting for evaluation or treatment for the first diagnosis of a new solid or hematologic cancer malignancy. Confirmed diagnosis date must be within 120 days prior to first clinic visit as a newly diagnosed cancer patient at the registering clinic. Patients presenting for "second opinions" of confirmed malignancies are eligible, including those who have started cancer treatment at other facilities. Patients must be registered within 90 days after their first clinic visit. Patients must not have been diagnosed with a malignancy other than the current malignancy within the past five years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer. Patients must have no evidence of disease for a prior malignancy for at least five years prior to randomization except as noted above.

Patients must be 18 years of age or older. Patients must have had their blood drawn for viral status testing for HIV, HBV and HCV or provide acceptable viral status documentation prior to registration, as defined in the protocol. Note that patients must have blood drawn for testing prior to registration for any of the three viruses not covered by the documentation. Patients are allowed to participate in other clinical trials.

Accrual Goals

A total of 3,061 patients will be accrued to achieve 3,000 eligible patients.

Summary Statement

For the current status of this study, please refer to the Cancer Care Delivery chapter.

S1313 Phase I-II

A Phase IB/II Randomized Study of Modified Folfirinox + Pegylated Recombinant Human Hyaluronidase (PEGPH20) Versus Modified Folfirinox Alone in Patients with Good Performance Status Metastatic Pancreatic Adenocarcinoma

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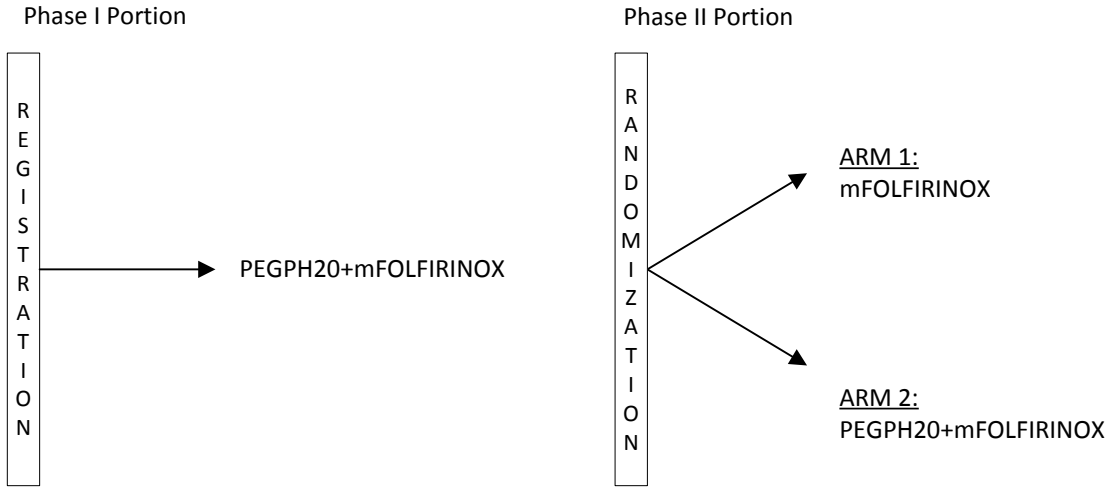
Study Chairs:
R Ramanathan, S Hingorani, P Philip

Date Activated:
01/06/2014

Statisticians:
S McDonough, K Guthrie

Data Coordinator:
B Zeller

SCHEMA



Patients will be enrolled into either the Phase I portion or the Phase II portion, not both

Objectives

Phase I Portion:
To assess the safety of mFOLFIRINOX in combination with PEGPH20 and select the optimal dose of PEGPH20 for the phase II portion in patients with metastatic pancreatic adenocarcinoma.

Phase II Portion:
To assess the overall survival of patients with metastatic pancreatic adenocarcinoma treated with mFOLFIRINOX + PEGPH20 compared to those treated with mFOLFIRINOX alone.

To assess progression free survival (PFS) in patients receiving mFOLFIRINOX with PEGPH20 and patients receiving mFOLFIRINOX alone in this patient population.

To assess objective tumor response (confirmed and unconfirmed, complete and partial) in patients with measurable disease treated with mFOLFIRINOX with PEGPH20 and patients receiving mFOLFIRINOX alone in this patient population.

To determine the frequency, severity, and tolerability of adverse events of mFOLFIRINOX with PEGPH20.

Patient Population

Patients must have newly diagnosed, untreated metastatic histologically or cytologically documented pancreatic adenocarcinoma. Patients must not have known history of brain metastases. Patients must have measurable metastatic disease.

Patients must not have had any prior treatment with oxaliplatin or irinotecan within 3 years prior to registration. Patients must not have had prior chemotherapy in metastatic setting or abdominal radiation therapy.

Patients must be between 18 and 75 years of age (inclusive) and have a Zubrod performance status of 0-1. Patients must have adequate hematologic, hepatic, and renal function. Patients must have normal clotting function. Patients must not have liver disease, chronic active hepatitis or chronic persistent hepatitis. Patients must not have active bleeding or a pathological condition that is associated with a high risk of bleeding. Patients known to be HIV-positive must not be on active treatment.

Stratification/Descriptive Factors

Phase I Portion: Stratification factors are not applicable to this portion.

Phase II Portion: Patients will be stratified according to Zubrod Performance Status: 0 vs 1.

Accrual Goals

The phase I portion of the trial will accrue 6-18 eligible and evaluable patients. The phase II portion of the trial will accrue 152 patients to yield 138 eligible patients. An interim futility analysis on the phase II trial will be performed when one-third of the deaths have been observed. Interim analyses for safety will also be conducted.

Summary Statement

The Phase I portion of this trial was closed to accrual on April 1, 2015 and Dose Level 2 (mFOLFIRINOX + PEGPH20 3 mcg/kg on day 1 only) was established as the appropriate dose level for the Phase II portion of the trial. The following summary contains only Phase II patients.

The Phase II portion of the trial was opened to accrual on May 22, 2015 and as of June 30, 2016, 60 patients have enrolled. One patient is ineligible due to inadequate renal function. One patient refused the assigned treatment arm and did not receive any protocol treatment; this patient is not assessable for adverse events and is coded as a major protocol deviation.

One patient was removed from protocol treatment after treatment was held over four weeks to perform oral surgery. Another patient was removed from protocol treatment due to increased incidence of blood clots, in addition to financial and transportation issues. Both are coded as 'Other' in the Treatment Summary table. One patient received bolus 5-FU (not per protocol treatment) and one patient randomized to mFOLFIRINOX received the PEGPH20 + mFOLFIRINOX treatment arm. Both are coded as major protocol deviations.

Of the 28 patients assessed for adverse events on the mFOLFIRNOX arm, one suffered a treatment-related death due to sepsis. Three additional patients experienced Grade 4 treatment-related adverse events, including decreased neutrophils (2), hypokalemia, decreased platelets, and sepsis (1 patient each). An additional ten patients had Grade 3 toxicities. Of the 25 patients assessed for adverse events on the PEGPH20 + mFOLFIRINOX arm, four patients experienced Grade 4 treatment-related adverse events, including hypokalemia, infusion related reaction, decreased lymphocytes, thromboembolic event, and vomiting (1 patient each). Sixteen additional patients experienced Grade 3 adverse events, including three thromboembolic events.

Registration by Institution

Phase II Patients

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Yale University	21	Arizona MC, U of	1
Fred Hutchinson CRC	7	City of Hope Med Ctr	1
Wayne State Univ	7	Davis, U of CA	1
So Calif, U of	5	Heartland NCORP	1
Irvine, U of CA	4	Kansas City NCORP	1
PCRC NCORP	4	MUSC MU-NCORP	1
Southeast COR NCORP	3	**Total (14 Institutions)**	**60**
Sutter Cancer RC	3		

Registration, Eligibility, and Evaluability

Phase II Patients

Registrations ending June 30, 2016; Data as of July 18, 2016

	TOTAL	mFOLFIRINOX	PEGPH20 + mFOLFIRINOX
NUMBER REGISTERED	60	32	28
INELIGIBLE	1	1	0
ELIGIBLE	59	31	28
Analyzable, Pend. Elig.	17	10	7
BASELINE DISEASE STATUS			
Measurable	41	20	21
Non Measurable	1	1	0
Too Early	17	10	7
ADVERSE EVENT ASSESSMENT			
Evaluable	53	28	25
Not Evaluable	1	1	0
Too Early	5	2	3

Patient Characteristics

Phase II Patients

Registrations ending June 30, 2016; Data as of July 18, 2016

	mFOLFIRINOX (n=31)		PEGPH20 + mFOLFIRINOX (n=28)	
AGE				
Median	57.0		64.0	
Minimum	32.0		44.4	
Maximum	75.0		72.7	
SEX				
Males	18	58%	13	46%
Females	13	42%	15	54%
HISPANIC				
Yes	2	6%	1	4%
No	28	90%	24	86%
Unknown	1	3%	3	11%
RACE				
White	26	84%	21	75%
Black	1	3%	0	0%
Asian	2	6%	5	18%
Unknown	2	6%	2	7%
PERFORMANCE STATUS				
0	18	58%	18	64%
1	13	42%	10	36%

Treatment Summary

Phase II Patients

Registrations ending June 30, 2016; Data as of July 18, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	27
NUMBER OFF PROTOCOL TREATMENT	32
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	3
Refusal unrelated to adverse event	2
Progression/relapse	13
Death	2
Other - not protocol specified	2
Reason under review	10
MAJOR PROTOCOL DEVIATIONS	3

Number of Patients with a Given Type and Grade of Adverse Event

Phase II Patients

Adverse Events Unlikely or Not Related to Treatment Excluded

Adverse Events with No Entries for Grades 3 to 5 Have Been Suppressed

Registrations ending June 30, 2016; Data as of July 18, 2016

	mFOLFIRINOX (n=28) Grade				PEGPH20 + mFOLFIRINOX (n=25) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
Abdominal pain	27	1	0	0	25	0	0	0
Anemia	24	4	0	0	24	1	0	0
Anorexia	27	1	0	0	23	2	0	0
Arthralgia	28	0	0	0	24	1	0	0
Dehydration	26	2	0	0	24	1	0	0
Delirium	28	0	0	0	24	1	0	0
Diarrhea	22	6	0	0	18	7	0	0
Enterocolitis	28	0	0	0	24	1	0	0
Esophagitis	28	0	0	0	24	1	0	0
Fatigue	26	2	0	0	20	5	0	0
Generalized muscle weakness	28	0	0	0	24	1	0	0
Hypokalemia	26	1	1	0	22	2	1	0
Hyponatremia	28	0	0	0	24	1	0	0
Infections/infestations-Other	27	1	0	0	24	1	0	0
Infusion related reaction	28	0	0	0	24	0	1	0
Lymphocyte count decreased	28	0	0	0	23	1	1	0
Mucositis oral	28	0	0	0	24	1	0	0
Myalgia	28	0	0	0	24	1	0	0
Nausea	24	4	0	0	18	7	0	0
Neutrophil count decreased	26	0	2	0	24	1	0	0
Pain	27	1	0	0	25	0	0	0
Peripheral sensory neuropathy	28	0	0	0	22	3	0	0
Peritoneal infection	28	0	0	0	24	1	0	0
Platelet count decreased	25	2	1	0	25	0	0	0
Sepsis	26	0	1	1	25	0	0	0
Small intestine infection	28	0	0	0	24	1	0	0
Soft tissue infection	28	0	0	0	24	1	0	0
Thromboembolic event	27	1	0	0	21	3	1	0
Ventricular tachycardia	27	1	0	0	25	0	0	0
Vomiting	25	3	0	0	20	4	1	0
White blood cell decreased	28	0	0	0	24	1	0	0
MAX. GRADE ANY ADVERSE EVENT	14	10	3	1	5	16	4	0

S1316 Pilot

Coordinating Group: SWOG

Prospective Comparative Effectiveness Trial For Malignant Bowel Obstruction

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Participants:
SWOG, Alliance

Date Activated:
03/09/2015

Study Chairs:
R Krouse, B Bagwell, A Secord (Alliance)

Statisticians:
G Anderson, K Arnold

Data Coordinator:
R Topacio

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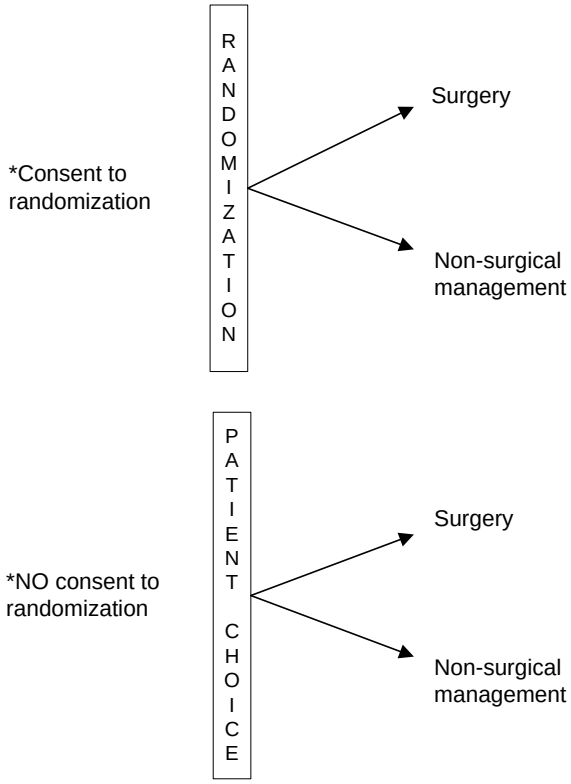

*Patients will be enrolled into either the randomized or patient choice portion, not both

Objectives

To compare quality of life, as assessed by the number of days alive and residing outside of the hospital within the first 91 days (13 weeks) after registration, among patients with malignant bowel obstruction (MBO) who receive surgical intervention and similar patients treated non-surgically.

To explore whether there are differences in other health related quality of life (HRQOL) factors of particular interest in this population, including ability to eat, days with nasogastric tube, development of nausea, days of intravenous hydration, days eating solid foods and days drinking that are different for patients with MBO who receive surgical intervention as compared to non-surgical intervention.

To explore whether overall survival is different for patients with MBO who receive surgical intervention as compared to non-surgical intervention. To estimate the effects of surgical versus non-surgical management on quality of life after adjustment for non-adherence to initially assigned/chosen treatment.

To explore whether there are clinical factors (e.g., ascites, albumin, carcinomatosis) that predict better quality of life outcomes for patients with MBO who receive surgical intervention as compared to non-surgical intervention.

Patient Population

Patients must have clinical evidence of a small bowel obstruction (via history, physical, and radiographic examination) distal to ligament of Treitz, with radiographic confirmation prior to registration. Patients must have intra-abdominal primary cancer with incurable disease. Patients may still have primary tumor as long as it is not a primary large bowel obstruction from colorectal cancer. Patients must not have signs of bowel perforation necessitating surgery or "acute" abdomen as evidenced by peritonitis on physical exam within two days prior to registration.

Patients must be registered to the study within three days after being seen by surgical team for MBO or within three days after completion of indicated treatment (e.g. TPN, anticoagulation reversal) to make them eligible for surgical intervention, whichever is later, and prior to any treatment (surgical or non-surgical) for MBO. Somatostatin analogues may be used prior to registration if that use is limited to not more than the two days just prior to registration.

Patients must be able to tolerate a major surgical procedure based on clinical evaluation, status of their cancer, and any other underlying medical problems. A member of the patient's surgical team must indicate equipoise for the benefit of the surgical treatment for MBO. Patients must be 18 years or older and have Zubrod performance status of 0-2 within seven days prior to hospitalization. Serum albumin must be planned to be collected after hospital admission, but prior to treatment. History and physical must be obtained within three days prior to registration. Patients must be able to complete the study questionnaires in English or Spanish.

Stratification/Descriptive Factors

Patient randomization will be stratified by primary tumor type: colorectal cancer vs ovarian cancer vs other cancer.

Accrual Goals

A total of 200 patients will be accrued to achieve 180 eligible patients, with a target of at least 50 eligible patients in the randomized component.

Summary Statement

For the current status of this study, please refer to the Cancer Survivorship chapter.

S1406 Phase II

Coordinating Group: SWOG

A Randomized Phase II Study of Irinotecan and Cetuximab With or Without Vemurafenib in BRAF Mutant Metastatic Colorectal Cancer

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Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, and NRG)

Study Chairs:
S Kopetz, H Lenz, C Atreya (Alliance), L Diaz (ECOG-ACRIN), C Allegra (NRG)

Statisticians:
S McDonough, K Guthrie

Data Coordinator:
J Scurlock

Date Activated:
11/13/2014

Date Closed:
04/01/2016

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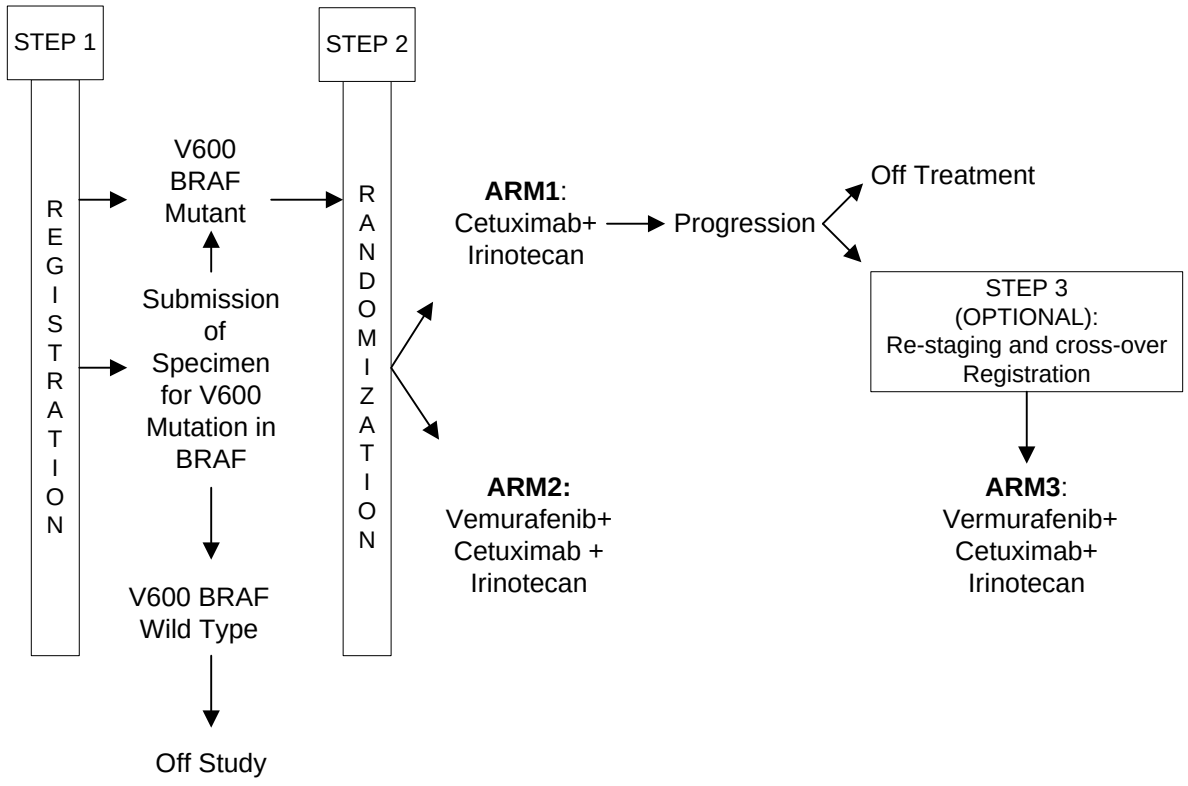


Objectives

To evaluate the progression-free survival (PFS) of BRAF mutant metastatic colorectal cancer patients treated with irinotecan, cetuximab, and vemurafenib compared to a control arm of irinotecan and cetuximab.

To evaluate the frequency and severity of toxicity associated with each of the treatment arms in this patient population.

To evaluate overall survival (OS) in treatment Arms 1 and 2.

To evaluate the overall response rate (ORR), including confirmed and unconfirmed, complete and partial response, in treatment Arms 1 and 2 in the subset of patients with measurable disease.

To estimate rates of OS, ORR, and PFS in patients who register to Arm 3 after disease progression on Arm 1.

Patient Population

Patients must have histologically or cytologically documented adenocarcinoma of the colon or rectum that is either metastatic, or locally advanced and unresectable. Patients must have measurable or non-measurable metastatic disease. Patients must have a $BRAF^{V600E}$ mutation and have tissue available for central $BRAF^{V600E}$ testing. Brain metastases are allowed if they have been adequately treated with radiotherapy or surgery and stable for at least 90 days prior to Step 1 initial registration. Patients must not have a tumor with a mutation detected in codons 61, 117, or 146 of KRAS or 12, 13, 61, 117 or 146 of NRAS.

Patients must have had one or two prior regimens of systemic chemotherapy for metastatic disease. Prior treatment with irinotecan is allowed. Prior treatment for metastatic disease is not required for patients who experienced disease recurrence during or within 6 months of completion of adjuvant chemotherapy. Patients must not have been treated with any of the following prior to Step 2 randomization: (1) cetuximab, panitumumab, or other monoclonal antibody against EGFR or inhibitor of EGFR, (2) BRAF inhibitor including, but not limited to, vemurafenib or dabrafenib (regorafenib is not considered a BRAF inhibitor for the purpose of trial eligibility), or (3) MEK inhibitor including, but not limited to, trametinib or selumetinib. Previous chemotherapy, immunotherapy, or radiation therapy must have been completed at least 14 days prior to Step 1 initial registration.

Patients must have adequate hepatic, renal, hematologic, and cardiac function and have a Zubrod performance status of 0-1. Patients must not have a known history of Gilbert's Syndrome or known homozygosity for the UGT1A*28 allele. Patients must not have interstitial pneumonia or extensive symptomatic interstitial fibrosis of the lung. Patients must not have any uncontrolled intercurrent illness.

Stratification/Descriptive Factors

Patients will be stratified by prior treatment with irinotecan: yes vs no.

Accrual Goals

A total of 94 eligible patients will be randomized to this study. An interim analysis will be performed when half of the expected events (approximately 44 PFS failures) have been observed.

Summary Statement

This study closed as of April 1, 2016 after meeting the accrual goal with 142 patients registered to the initial screening. Thirty-one patients were found to be BRAF wild-type. Three patients were not tested for BRAF due to: no invasive cancer in submitted tissue (2) and misplaced tissue (1). Two patients were found to be BRAF mutant, but were not randomized to protocol treatment. One hundred six patients were randomized to protocol treatment. The interim futility analysis was reviewed by the DSMC in the Spring of 2016 and it was recommended that the study continue as planned.

Eight patients were deemed ineligible due to: inadequate hematologic function (3), receiving chemotherapy within 14 days prior to randomization (2), not having BRAF V600E mutation (2), and performance status (1).

Six patients did not begin protocol treatment due to: symptomatic deterioration (3), poor prognosis (coded as 'Other' in the Treatment Summary table), elevated AST after a delay in starting treatment due to fever (coded as 'Other' in the Treatment Summary table), and patient refusal due to the size of the tablets (1 patient each). All six are considered major protocol deviations and are not assessable for adverse events.

One patient came off protocol treatment to undergo HIPEC surgery. Another patient came off protocol treatment due to increasing disease, not meeting

RECIST criteria for progression. Both are coded as 'Other' in the Treatment Summary table.

Of the 45 patients assessed for adverse events on the cetuximab + irinotecan arm, two patients have experienced Grade 4 treatment-related hematologic events and 21 additional patients have experienced Grade 3 treatment-related adverse events, including metabolic acidosis (reported as Metab/nutrition disorders-Oth). Of the 44 patients assessed for adverse events on the vemurafenib + cetuximab + irinotecan arm, there has been one treatment-related death due to sepsis. Seven additional patients have experienced Grade 4 treatment-related adverse events, primarily hematologic, and 27 patients have experienced Grade 3 treatment-related adverse events.

Twenty-two patients randomized to the cetuximab + irinotecan arm have enrolled to crossover for treatment with vemurafenib + cetuximab + irinotecan. One patient did not have documented progression per RECIST criteria on the cetuximab + irinotecan arm and thus is not eligible for crossover. Of 18 patients assessed for adverse events, one patient has experienced Grade 4 decrease in neutrophils and eleven additional patients have experienced Grade 3 treatment-related events, including atrial fibrillation with rapid ventricular response (reported as Cardiac disorder-Other, spec).

Registration by Institution

Initial Registration

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Alliance	25	Ozarks NCORP	2
MD Anderson CC	18	Arnot Ogden Med Ctr/Rochester, Univ of	1
ECOG-ACRIN	15	Baptist MU-NCORP	1
Kaiser Perm NCORP	11	Essentia Hlth NCORP	1
NRG	9	Fred Hutchinson CRC	1
Southeast COR NCORP	7	Greenville NCORP	1
Kansas, U of	6	Hawaii MU-NCORP	1
Yale University	5	Irvine, U of CA	1
Cleveland Clinic OH	4	Kadlec Clinic Hem/Fred Hutchinson CRC	1
Colorado, U of	4	McLaren Cancer Inst/Wayne State Univ	1
Columbus NCORP	4	Northwest NCORP	1
City of Hope Med Ctr	3	PCRC NCORP	1
Wayne State Univ	3	Providence Hosp	1
CORA NCORP	2	San Antonio, U of TX	1
Gulf South MU-NCORP	2	So Calif, U of	1
Heartland NCORP	2	Sutter Cancer RC	1
Michigan CRC NCORP	2	Thompson Ca Surv Ctr/San Antonio, U of TX	1
Michigan, U of	2	**Total (35 Institutions)**	**142**

Registration, Eligibility, and Evaluability

Randomization

Registrations ending June 30, 2016; Data as of July 18, 2016

	TOTAL	Cetuximab + Irinotecan	Vemurafenib + Cetux + Irinotecan
NUMBER REGISTERED	106	52	54
INELIGIBLE	8	2	6
ELIGIBLE	98	50	48
BASELINE DISEASE STATUS			
Measurable	89	47	42
Non Measurable	5	1	4
Not Evaluable	1	1	0
Too Early	3	1	2
ADVERSE EVENT ASSESSMENT			
Evaluable	89	45	44
Not Evaluable	6	3	3
Too Early	3	2	1

Patient Characteristics

Randomization

Registrations ending June 30, 2016; Data as of July 18, 2016

	Cetuximab + Irinotecan (n=50)		Vemurafenib + Cetux + Irinotecan (n=48)	
AGE				
Median	61.9		60.0	
Minimum	30.5		34.4	
Maximum	82.9		82.9	
SEX				
Males	13	26%	27	56%
Females	37	74%	21	44%
HISPANIC				
Yes	2	4%	2	4%
No	48	96%	45	94%
Unknown	0	0%	1	2%
RACE				
White	49	98%	42	88%
Black	0	0%	1	2%
Asian	1	2%	4	8%
Unknown	0	0%	1	2%
PRIOR TREATMENT WITH IRINOTECAN				
Yes	19	38%	20	42%
No	31	62%	28	58%

Treatment Summary

Randomization

Registrations ending June 30, 2016; Data as of July 18, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	15
NUMBER OFF PROTOCOL TREATMENT	83
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	9
Refusal unrelated to adverse event	10
Progression/relapse	50
Death	1
Other - not protocol specified	4
Reason under review	9
MAJOR PROTOCOL DEVIATIONS	6

Number of Patients with a Given Type and Grade of Adverse Event

Randomization

Adverse Events Unlikely or Not Related to Treatment Excluded

Adverse Events with No Entries for Grades 3 to 5 Have Been Suppressed

Registrations ending June 30, 2016; Data as of July 18, 2016

	Cetuximab + Irinotecan (n=45) Grade					Vemurafenib + Cetux + Irinotecan (n=44) Grade				
ADVERSE EVENTS	**<=1**	**2**	**3**	**4**	**5**	**<=1**	**2**	**3**	**4**	**5**
Abdominal pain	43	2	0	0	0	40	3	1	0	0
Alkaline phosphatase increased	42	2	1	0	0	43	1	0	0	0
Allergic reaction	44	0	1	0	0	44	0	0	0	0
Anaphylaxis	44	0	1	0	0	44	0	0	0	0
Anemia	41	4	0	0	0	31	7	6	0	0
Anorexia	42	2	1	0	0	40	1	3	0	0
Arthralgia	45	0	0	0	0	38	3	3	0	0
Blood bilirubin increased	44	0	1	0	0	44	0	0	0	0
Colonic obstruction	44	0	1	0	0	44	0	0	0	0
Creatinine increased	44	1	0	0	0	43	0	1	0	0
Dehydration	38	5	2	0	0	39	0	5	0	0
Diarrhea	32	8	5	0	0	30	4	10	0	0
ECG QT corrected int prolong	45	0	0	0	0	42	1	1	0	0
Fatigue	33	6	6	0	0	29	8	7	0	0
Febrile neutropenia	43	0	1	1	0	39	0	4	1	0
Generalized muscle weakness	43	1	1	0	0	44	0	0	0	0
Hypokalemia	42	2	1	0	0	39	1	4	0	0
Hypomagnesemia	40	3	2	0	0	44	0	0	0	0
Hyponatremia	44	0	1	0	0	42	0	2	0	0
Infusion related reaction	43	1	1	0	0	42	1	1	0	0
Lung infection	44	1	0	0	0	42	1	1	0	0

	Cetuximab + Irinotecan (n=45) Grade					Vemurafenib + Cetux + Irinotecan (n=44) Grade				
ADVERSE EVENTS	**<=1**	**2**	**3**	**4**	**5**	**<=1**	**2**	**3**	**4**	**5**
Lymphocyte count decreased	45	0	0	0	0	42	1	1	0	0
Metab/nutrition disorders-Oth	44	0	1	0	0	44	0	0	0	0
Mucositis oral	45	0	0	0	0	37	6	1	0	0
Myalgia	45	0	0	0	0	40	2	2	0	0
Nausea	37	8	0	0	0	33	4	7	0	0
Neutrophil count decreased	35	7	2	1	0	28	3	6	7	0
Pain	45	0	0	0	0	43	0	1	0	0
Pancreatitis	45	0	0	0	0	43	0	1	0	0
Papulopustular rash	44	0	1	0	0	44	0	0	0	0
Photosensitivity	45	0	0	0	0	43	0	1	0	0
Platelet count decreased	43	2	0	0	0	43	0	1	0	0
Pruritus	43	1	1	0	0	44	0	0	0	0
Rash acneiform	39	3	3	0	0	37	7	0	0	0
Rash maculo-papular	44	1	0	0	0	42	1	1	0	0
Rash pustular	43	2	0	0	0	42	1	1	0	0
Sepsis	45	0	0	0	0	42	0	0	1	1
Urinary tract infection	44	0	1	0	0	44	0	0	0	0
Vomiting	43	2	0	0	0	36	4	4	0	0
White blood cell decreased	42	3	0	0	0	33	4	4	3	0
MAX. GRADE ANY ADVERSE EVENT	8	14	21	2	0	2	7	27	7	1

Registration, Eligibility, and Evaluability

Crossover

Registrations ending June 30, 2016; Data as of July 18, 2016

	Crossover: Vem + Cetux + Irinotecan
NUMBER REGISTERED	22
INELIGIBLE	1
ELIGIBLE	21
Analyzable, Pend. Elig.	1
BASELINE DISEASE STATUS	
Measurable	19
Non Measurable	1
Too Early	1
ADVERSE EVENT ASSESSMENT	
Evaluable	18
Not Evaluable	1
Too Early	2

Treatment Summary

Crossover

Registrations ending June 30, 2016; Data as of July 18, 2016

	Crossover: Vem + Cetux + Irinotecan
NUMBER ON PROTOCOL TREATMENT	9
NUMBER OFF PROTOCOL TREATMENT	12
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	2
Refusal unrelated to adverse event	1
Progression/relapse	6
Death	1
Other - not protocol specified	0
Reason under review	2
MAJOR PROTOCOL DEVIATIONS	1

Number of Patients with a Given Type and Grade of Adverse Event

Crossover

Adverse Events Unlikely or Not Related to Treatment Excluded

Adverse Events with No Entries for Grades 3 to 5 Have Been Suppressed

Registrations ending June 30, 2016; Data as of July 18, 2016

	Crossover: Vem + Cetux + Irinotecan (n=18) Grade				
ADVERSE EVENTS	**<=1**	**2**	**3**	**4**	**5**
AST increased	17	0	1	0	0
Arthritis	17	0	1	0	0
Cardiac disorder-Other, spec	17	0	1	0	0
Colitis	17	0	1	0	0
Diarrhea	11	0	7	0	0
ECG QT corrected int prolong	16	1	1	0	0
Fatigue	11	2	5	0	0
Gastric hemorrhage	17	0	1	0	0
Generalized muscle weakness	17	0	1	0	0
Hand-Foot syndrome	16	1	1	0	0
Hypocalcemia	17	0	1	0	0
Hypokalemia	17	0	1	0	0
Hypomagnesemia	16	1	1	0	0
Insomnia	17	0	1	0	0
Lower GI hemorrhage	17	0	1	0	0
Nausea	13	4	1	0	0
Neutrophil count decreased	14	1	2	1	0
Rash maculo-papular	17	0	1	0	0
Thromboembolic event	17	0	1	0	0
Urinary tract infection	17	0	1	0	0
White blood cell decreased	14	3	1	0	0
MAX. GRADE ANY ADVERSE EVENT	2	4	11	1	0

S1415CD Phase III

Pragmatic Trial to Evaluate a Guideline-Based Colony Stimulating Factor Standing Order Intervention and to Determine the Effectiveness of Colony Stimulating Factor Use as Prophylaxis for Patients Receiving Chemotherapy with Intermediate Risk for Febrile Neutropenia – Trial Assessing CSF Prescribing Effectiveness and Risk (TrACER)

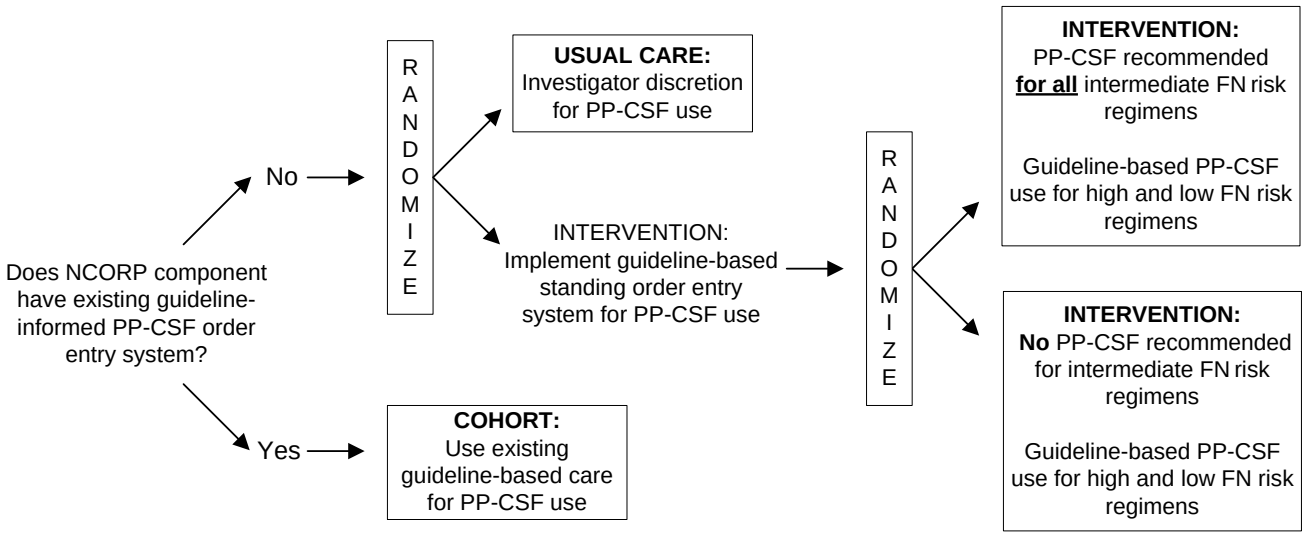
Study Chairs:
S Ramsey, D Hershman

Statisticians:
A Bansal (US), W Barlow, K Arnold

Project Manager:
K Watabayashi (HICOR)

Data Coordinator:
M Yee

SCHEMA



Randomization is at the NCORP component level. All patients at participating components will be subject to the PP-CSF use care as determined by component assignment (Usual Care, Intervention, or Cohort). Only consented patients registered to the study will participate in the data collection.

Objectives

To compare the use of primary prophylactic colony stimulating factor (PP-CSF) according to recommended clinical practice guidelines among patients registered at Intervention components versus Usual Care components.

To compare the rate of febrile neutropenia (FN) among patients registered at Intervention components versus Usual Care components.

To compare the rate of FN among intermediate risk patients registered at Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare the rate of FN among low-risk patients registered at Intervention components versus Usual Care components.

To compare the FN-related health-related quality of life (HRQL) among low-risk patients registered at Intervention components versus Usual Care components.

To compare patient adherence to PP-CSF prescribing among patients registered at Intervention components versus Usual Care components.

To compare patient knowledge of the indications for, efficacy of, and side effects associated with PP-CSF between the initiation and conclusion of the first cycle of myelosuppressive systemic therapy among patients registered at Intervention components versus Usual Care components.

To compare the proportion of patients completing the initial systemic therapy regimen at planned duration and at planned dose intensity among patients registered at Intervention components versus Usual Care components.

To compare antibiotic use both as prophylaxis and as treatment for FN among patients registered at Intervention components versus Usual Care components.

To compare the rate of FN-related emergency department visits and hospitalizations among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare the FN-related health-related quality of life (HRQL) among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare overall survival among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

Patient Population

Patients must have a current diagnosis of breast cancer, non-small cell lung cancer, or colorectal cancer. Cancer may be metastatic or non-metastatic.

Patients must be planning to receive one of the study-allowed regimens as their initial treatment for their current diagnosis. Patients must be registered prior to their first cycle of systemic therapy (chemotherapy, immunotherapy, biologic therapy, or combination regimens). Prior systemic therapy must have been completed at least 180 days prior to registration. Patients must not have any known contraindication to CSFs, including prior hypersensitivity to Escherichia coli-derived proteins, filgrastim, pegfilgrastim, or tbo-filgrastim.

Patients must be able to understand and provide information for the patient-completed study forms in either English or Spanish. Patients may have had a prior malignancy. Patients must not be participating or plan to participate in other clinical trials that involve investigational systemic cancer treatments or investigational uses of CSF.

Stratification/Descriptive Factors

NCORP components eligible for randomization will be randomly assigned to Usual Care or Intervention with stratification by component size (number of patients at that component) and type of NCORP component (minority/underserved vs not).

Accrual Goals

A total of 3,960 patients will be accrued to achieve 3,600 eligible patients. The Intervention components will accrue 2,376 patients, the Usual Care components will accrue 792 patients and the Cohort components will accrue 792 patients.

One interim analysis will be conducted when 360 patients in the intermediate risk group at Intervention components have complete outcome information. A second interim analysis will be conducted when 650

patients in the intermediate risk group at Intervention components have complete outcome information.

Summary Statement

For the current status of this study, please refer to the Cancer Care Delivery chapter.

S1417CD Survey

Coordinating Group: SWOG

Implementation of a Prospective Financial Impact Assessment Tool in Patients with Metastatic Colorectal Cancer

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Participants:
SWOG, CTSU

Date Activated:
05/13/2016

Study Chairs:
V Shankaran, S Ramsey, D Hershman

Statisticians:
J Unger, A Darke

Data Coordinators:
M Yee, D Liggett

Objectives

To estimate the incidence of treatment-related major financial hardship over 12 months, among patients with newly diagnosed metastatic colorectal cancer (mCRC) treated at SWOG-affiliated NCI Community Oncology Research Program (NCORP) Cancer Care Delivery Research (CCDR) components.

To describe the association of major financial hardships with mCRC treatment by demographic factors, including age, race, marital status, employment status, and income.

To explore whether occurrence of major financial hardship is associated with poorer health-related quality of life over time.

To profile the magnitude and timing of treatment-related changes in patients' income, assets, debt, and employment, and to quantify major out-of-pocket expenses during the 12 months following registration.

To explore the extent to which health insurance factors (e.g., high copayments, deductibles, premiums, loss/change of insurance plan) are associated with major financial hardship and treatment adherence.

To determine feasibility of recruiting primary caregivers and measuring caregiver burden and caregivers' perceptions about cancer treatment costs.

To determine the feasibility of conducting a prospective multi-site longitudinal cohort study assessing financial outcomes in patients with mCRC undergoing treatment within the NCORP network.

Patient Population

Patients must have newly diagnosed metastatic colon or rectal cancer (de novo metastatic diagnosis or metastatic recurrence after prior treatment for stage I-III disease), with registration within 90 days of diagnosis. Patients must plan to begin systemic chemotherapy and/or biologic therapy at the registering institution within 30 days after registration. Patients must not have been diagnosed with any malignancy other than colorectal cancer within the past five years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer.

Patients may have received prior chemotherapy, biologic therapy, radiation therapy, or surgery for non-metastatic colorectal cancer.

Patients must provide full name, address, and social security number at registration and be able to

complete questionnaires in English. Patients must not be currently enrolled in any clinical treatment trials at time of registration. Patients may enroll in treatment trials or other clinical trials following completion of baseline surveys.

Accrual Goals

A total of 374 patients will be enrolled to achieve 320 eligible patients.

Summary Statement

For the current status of this study, please refer to the Cancer Care Delivery chapter.

S1505 Phase II

Coordinating Group: SWOG

A Randomized Phase II Study of Perioperative mFOLFIRINOX versus Gemcitabine/nab-Paclitaxel as Therapy for Resectable Pancreatic Adenocarcinoma

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Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, and NRG)

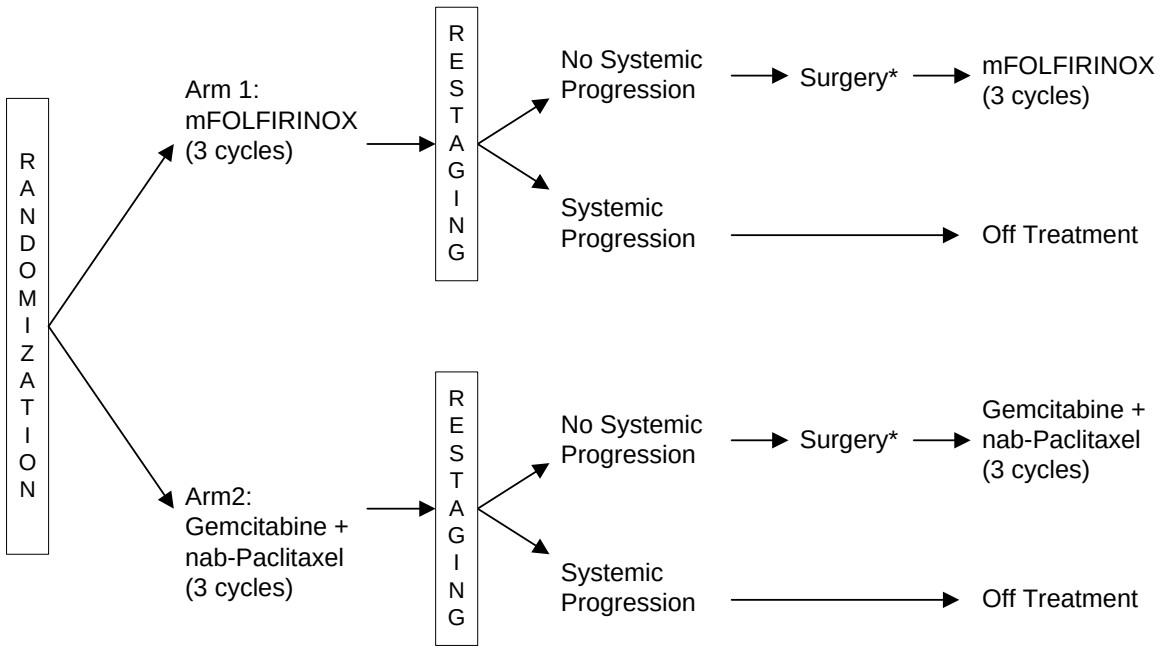
Date Activated:
10/12/2015

Study Chairs:
D Sohal, S Ahmad, A Wang-Gillam (Alliance), M Beg (ECOG-ACRIN), P Das (NRG),

Statisticians:
K Guthrie, S McDonough

Data Coordinator:
B Zeller

SCHEMA



*If patient is unable to undergo R0 or R1 surgical resection, he or she must be taken off protocol treatment.

Objectives

To assess 2-year overall survival in each treatment arm (mFOLFIRINOX and gemcitabine/nab-paclitaxel) in patients with resectable pancreatic cancer.

To choose the better regimen with respect to 2-year overall survival.

To estimate the frequency and severity of adverse events associated with chemotherapy in the perioperative setting, for all patients and within treatment arms.

To estimate the proportion of patients going to surgery for resection after preoperative chemotherapy, for all patients and within treatment arms.

To estimate the proportion of patients achieving R0 resection after preoperative chemotherapy, for all patients and within treatment arms.

To estimate the overall response rate following preoperative chemotherapy, including confirmed and unconfirmed, complete and partial response, per RECIST 1.1, for all patients and within treatment arms.

To estimate the pathologic response rates after R0 or R1 resection, for all patients and within treatment arms.

To estimate the patterns of recurrence (loco-regional, distant) after R0 or R1 resection, for all patients and within treatment arms.

To estimate disease-free survival from the time of R0 or R1 resection, for all patients and within treatment arms.

Patient Population

Patients must have histologically or cytologically proven pancreatic adenocarcinoma. Patients must have measurable disease in the pancreas. Patients must have resectable primary tumor, as defined in the protocol, based on contrast-enhanced CT or MRI. CT scans or MRIs used to assess disease at baseline must be submitted for central review. Patients must have a surgical consult to verify patient is a surgical candidate.

Patients must not have received prior surgery, radiation therapy, chemotherapy, targeted therapy, or any investigational therapy for pancreatic cancer.

Patients must be between 18 and 75 years of age (inclusive) and have a Zubrod performance status of 0-1. Patients must have adequate hematologic, hepatic and renal function.

Stratification/Descriptive Factors

Patients will be stratified by Zubrod performance status: 0 vs 1.

Accrual Goals

A total of 100 eligible patients will be randomized to this study. The rate of resection will be examined after the 40^{th} and 80^{th} enrolled patient becomes evaluable.

Summary Statement

The trial opened to accrual on October 12, 2015. As of June 30, 2016, 35 patients have enrolled. Four patients are ineligible due to evidence of metastatic disease.

On the mFOLFIRINOX arm, 13 patients have been assessed for chemotherapy-related adverse events. One patient has experienced Grade 4 decrease in platelet counts and four additional patients have experienced Grade 3 treatment-related adverse events. On the gemcitabine + nab-paclitaxel arm, nine patients have been assessed for chemotherapy-related adverse events. One patient has experienced Grade 4 decrease in neutrophils and two additional patients have experienced Grade 3 treatment-related adverse events.

Three patients have received protocol surgery and two have been assessed for adverse events related to surgery. One patient experienced Grade 3 anemia and generalized muscle weakness, both possibly related to the procedure. One patient experienced treatment-related Grade 2 nausea, abdominal pain, and vomiting.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
NRG	7	Cincinnati MC, U of	1
ECOG-ACRIN	5	Cleveland Clinic OH	1
Alliance	4	Dayton NCORP	1
Heartland NCORP	4	Greenville NCORP	1
Kaiser Perm NCORP	3	Kentucky, U of	1
Carle CC NCORP	2	MUSC MU-NCORP	1
Michigan, U of	2	**Total (14 Institutions)**	**35**
PCRC NCORP	2		

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2016; Data as of July 19, 2016

	TOTAL	mFOLFIRINOX	Gem/nab-paclitaxel
NUMBER REGISTERED	35	19	16
INELIGIBLE	4	3	1
ELIGIBLE	31	16	15
Analyzable, Pend. Elig.	31	16	15
BASELINE DISEASE STATUS			
Measurable	28	15	13
Too Early	3	1	2
ADVERSE EVENT ASSESSMENT			
Evaluable	22	13	9
Too Early	9	3	6

Patient Characteristics

Registrations ending June 30, 2016; Data as of July 19, 2016

	mFOLFIRINOX (n=16)		Gem/nab-paclitaxel (n=15)	
AGE				
Median	63.6		59.2	
Minimum	52.7		45.1	
Maximum	73.8		75.5	
SEX				
Males	12	75%	8	53%
Females	4	25%	7	47%
HISPANIC				
No	15	94%	15	100%
Unknown	1	6%	0	0%
RACE				
White	16	100%	14	93%
Black	0	0%	1	7%
PERFORMANCE STATUS				
0	12	75%	11	73%
1	4	25%	4	27%

Treatment Summary

Registrations ending June 30, 2016; Data as of July 19, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	28
NUMBER OFF PROTOCOL TREATMENT	3
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	0
Refusal unrelated to adverse event	1
Progression/relapse	1
Death	0
Other - not protocol specified	0
Reason under review	1
MAJOR PROTOCOL DEVIATIONS	0

Number of Patients with a Given Type and Grade of Adverse Event

Chemotherapy Related Adverse Events

Adverse Events Unlikely or Not Related to Treatment Excluded

Adverse Events with No Entries for Grades 2 to 5 Have Been Suppressed

Registrations ending June 30, 2016; Data as of July 19, 2016

	mFOLFIRINOX (n=13) Grade					Gem/nab-paclitaxel (n=9) Grade				
ADVERSE EVENTS	**<=1**	**2**	**3**	**4**	**5**	**<=1**	**2**	**3**	**4**	**5**
ALT increased	12	1	0	0	0	9	0	0	0	0
Alopecia	12	1	0	0	0	7	2	0	0	0
Anemia	13	0	0	0	0	8	1	0	0	0
Anorexia	13	0	0	0	0	8	1	0	0	0
Arthralgia	12	1	0	0	0	9	0	0	0	0
Constipation	13	0	0	0	0	8	1	0	0	0
Dehydration	13	0	0	0	0	8	0	1	0	0
Diarrhea	11	1	1	0	0	8	0	1	0	0
Dyspepsia	13	0	0	0	0	8	1	0	0	0
Fatigue	12	1	0	0	0	9	0	0	0	0
Febrile neutropenia	13	0	0	0	0	8	0	1	0	0
Generalized muscle weakness	12	1	0	0	0	9	0	0	0	0
Hand-Foot syndrome	13	0	0	0	0	8	1	0	0	0
Hyperglycemia	12	0	1	0	0	9	0	0	0	0
Hyperuricemia	12	0	1	0	0	9	0	0	0	0
Hypoglycemia	12	1	0	0	0	9	0	0	0	0
Hypokalemia	13	0	0	0	0	8	0	1	0	0
Hypotension	12	1	0	0	0	8	0	1	0	0
Infections/infestations-Other	13	0	0	0	0	8	1	0	0	0
Localized edema	12	1	0	0	0	9	0	0	0	0
Lymphocyte count decreased	13	0	0	0	0	8	1	0	0	0
Neutrophil count decreased	9	2	2	0	0	6	1	1	1	0
Paresthesia	12	1	0	0	0	9	0	0	0	0
Platelet count decreased	12	0	0	1	0	9	0	0	0	0
TTP	13	0	0	0	0	8	0	1	0	0
Weight loss	12	1	0	0	0	9	0	0	0	0
White blood cell decreased	13	0	0	0	0	6	2	1	0	0
MAX. GRADE ANY ADVERSE EVENT	6	2	4	1	0	3	3	2	1	0

S1513 Phase II

Coordinating Group: SWOG

Randomized Phase II Study of 2nd Line FOLFIRI versus Modified FOLFIRI With PARP Inhibitor ABT-888 (Veliparib) (NSC-737664) in Metastatic Pancreatic Cancer

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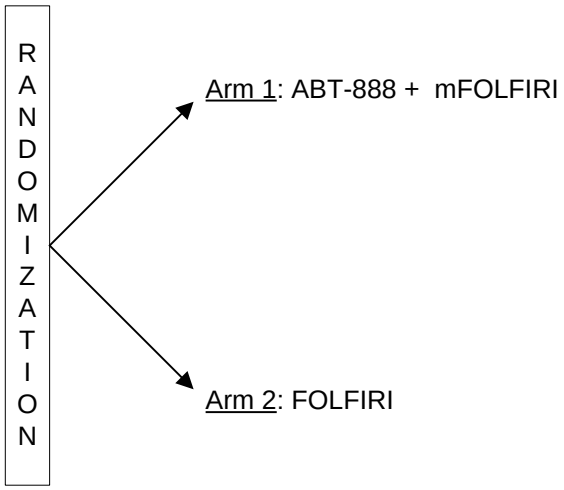
Participants:
SWOG, CTSU

Study Chairs:
E Chiorean, P Philip, E Swisher

Statisticians:
S McDonough, K Guthrie

Data Coordinator:
J Scurlock

SCHEMA



Objectives

To evaluate the overall survival (OS) of metastatic pancreatic cancer patients treated with fluorouracil, irinotecan, leucovorin (modified FOLFIRI) and ABT-888 comapared to a control arm of fluorouracil, irinotecan, and leucovorin (FOLFIRI).

To evaluate the frequency and severity of toxicity associated with each of the treatment arms in this patient population.

To evaluate the progression-free survival (PFS) in each of the treatment arms in this patient population.

To evaluate the response rate (confirmed and unconfirmed; complete response + partial response), disease control rate (confirmed and unconfirmed; complete response + partial response + stable disease), and duration of response in each of the treatment arms in this patient population.

Patient Population

Patients must have histologically or cytologically documented pancreatic adenocarcinoma. Patients with pancreatic neuroendocrine tumors, lymphoma of the pancreas, or ampullary cancer are not eligible. Patients must have metastatic disease that is measurable. Patients must not have a history of brain metastases.

Patients must have had one and only one prior regimen of systemic therapy for metastatic disease. However, patients who received systemic therapy with gemcitabine/nab-paclitaxel for resectable or borderline/locally advanced unresectable disease and progressed with metastatic disease within three months of the last dose of therapy are eligible. Patients must have completed systemic therapy at least 14 days prior to registration, any surgical procedure must have been performed at least 14 days prior to registration, and radiation therapy must be completed at least 7 days prior to registration. Patients must have recovered from major side effects of prior therapies or procedures. Patients must not have received prior irinotecan-based chemotherapy. Patients must not have received prior PARP inhibitor therapy including, but not limited to ABT-888, olaparib, rucaparib, and BMN637.

Patients must have a Zubrod performance status of 0-1. Patients must have adequate hematologic, hepatic, renal, and cardiac function. Patients must not have any clinically significant and uncontrolled major medical conditions. Patients must not have known Gilbert's Syndrome. Patients must not have known hypersensitivity to irinotecan, fluorouracil, or leucovorin.

Stratification/Descriptive Factors

Patients will be stratified by prior systemic treatment for metastatic disease: yes vs no.

Accrual Goals

A total of 128 eligible patients will be randomized to this study. An interim futility analysis of progression-free survival (PFS) will be performed when 35% (approximately 40 events) of the expected PFS events have been observed.

A021202 Phase II SWOG Supported CTSU Study

Coordinating Group: Alliance

Prospective Randomized Phase II Trial of Pazopanib (NSC #737754, IND #75648) Versus Placebo in Patients with Progressive Carcinoid Tumors

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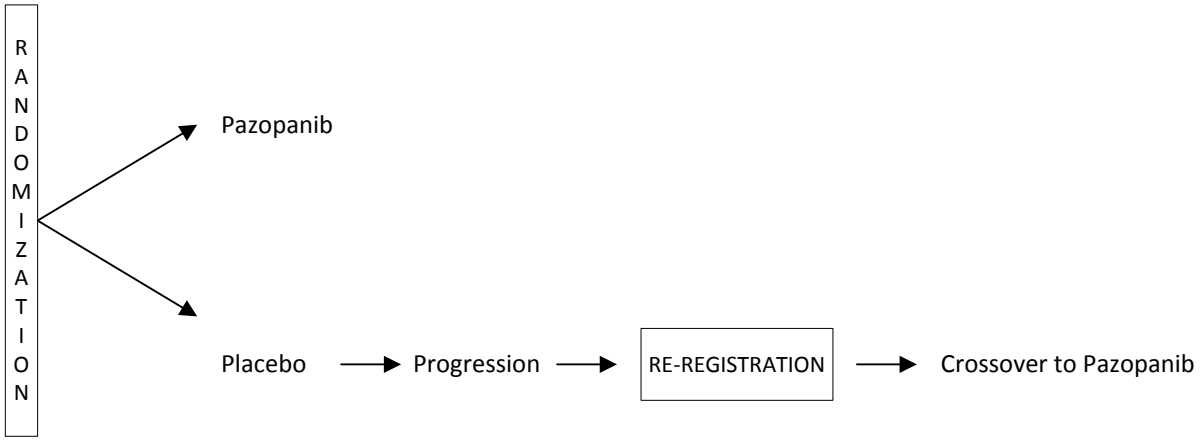
Participants:
Alliance, CTSU

Date Activated:
06/21/2013

Study Chairs:
E Bergsland (Alliance), A Phan (SWOG)

SCHEMA



Objectives

To compare centrally reviewed progression-free survival (PFS) between patients with progressive carcinoid tumors randomized to treatment with pazopanib versus placebo.

To compare overall survival between treatment arms.

To compare objective response rate, duration of response, and time to treatment failure between treatment arms.

To compare PFS as assessed by central radiology review and local radiology review overall and within treatment arms.

To estimate PFS at 6 months and 12 months within each treatment arm.

To evaluate safety and tolerability of treatment with pazopanib/placebo.

To compare biochemical response between treatment arms among patients with elevated baseline levels of CGA and 5-HIAA.

To assess differences in QOL-related domains between the two treatment groups.

To determine if the more brief measures of QOL-related domains provide comparable information to that which is provided by the longer assessments.

To provide validation data for the EORTC NET21 module in terms of responsiveness over time and differences across arms.

Patient Population

Patients must have low- or intermediate-grade neuroendocrine carcinoma, including the following subtypes: carcinoid tumor, low- to intermediate-grade or well- to moderately-differentiated neuroendocrine carcinoma or tumor, or atypical carcinoid tumor. Patients must have locally unresectable or metastatic carcinoid tumors arising in the foregut, midgut, hindgut, or other non-pancreatic site. Patients must have radiological evidence for progressive disease within 12 months prior to registration. Patients must have measurable disease per RECIST 1.1. Patients with tumors arising in the midgut must have progressed on octreotide. Patients must not have known endobronchial lesions and/or lesions infiltrating major pulmonary vessels that increase the risk of pulmonary hemorrhage. Patients must not have clinical evidence of brain metastases or carcinomatous meningitis.

Patients must not have received prior treatment with an inhibitor of VEGF or VEGFR. Treatment with strong inhibitors of CYP3A4 must be discontinued 14 days prior to start of study treatment. Other prior treatment must be completed at least four weeks prior to registration, and any treatment-related toxicities must have improved to Grade 1 or lower. Prior treatment with embolization or ablative therapies is allowed if measurable disease remains outside of the treated area or there is documented disease progression in a treated site. Patients should have completed any major surgery at least four weeks prior to registration and must have completed any minor surgery at least two weeks prior to registration.

Patients must be at least 18 years of age and have ECOG performance status of 0-1. Patients must have adequate cardiac, hematologic, hepatic, renal, immunologic, and clotting function. Patients with symptomatic peripheral vascular disease are not eligible.

Stratification/Descriptive Factors

Patients are stratified by (1) site of primary: small bowel (defined as tumors arising in the small bowel, cecum, appendix, or unknown primary site) vs other; and (2) concurrent somatostatin analog: yes vs no.

Accrual Goals

The accrual goal for this study is 150 patients. Interim analyses for futility will be conducted when 38% and 75% of the expected number of events have been observed.

Summary Statement

Alliance reported that 171 patients had registered to this study as of June 30, 2016, 35 from SWOG institutions. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
H Lee Moffitt CC	22	Kansas, U of	1
Cedars-Sinai Med Ctr	4	Methodist Hospital	1
Baylor Univ Med Ctr	2	Poudre Valley Hosp/Colorado, U of	1
San Antonio, U of TX	2	Rochester, Univ of	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	1	**Total (9 Institutions)**	**35**

A021302 Phase II SWOG Supported CTSU Study

Coordinating Group: Alliance

Impact of Early FDG-PET Directed Intervention on Preoperative Therapy for Locally Advanced Gastric Cancer: A Random Assignment Phase II Study

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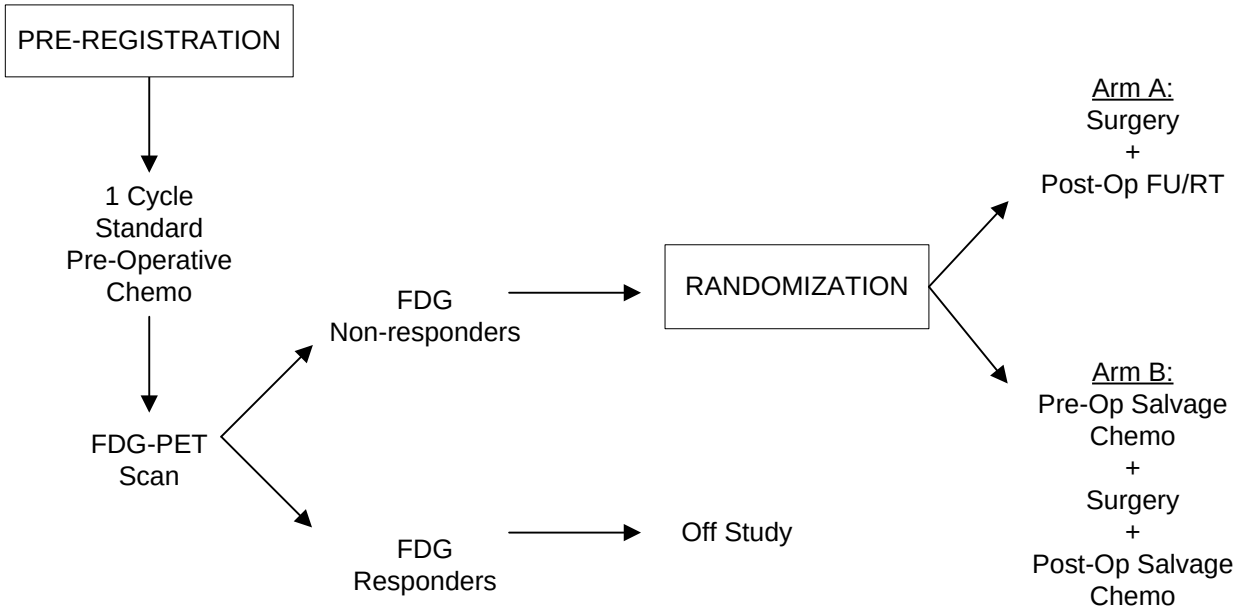
Participants:
Alliance, CTSU

Date Activated:
08/01/2015

Study Chairs:
M Shah (Alliance), S Iqbal (SWOG)

SCHEMA



Objectives

To assess and compare the overall survival (OS) of patients with locally advanced gastric cancer classified as FDG-PET non-responders after one cycle of pre-operative chemotherapy randomly assigned to receive either salvage chemotherapy before and after surgery or immediate surgery followed by fluorouracil sensitized radiotherapy.

To assess and compare progression-free survival (PFS) between the treatment arms (Arms A and B).

To assess and compare R0 resection rate between the treatment arms (Arms A and B).

To assess and compare pathologic complete response (pCR) rate between the treatment arms (Arms A and B).

To assess the adverse events (AE) profile and safety of each treatment arm (Arms A and B), including post-operative mortality rate and 30-day post-operative targeted adverse events (i.e., dehiscence, significant infection, and re-operation rate).

To examine the changes of FDG-PET SUV induced by pre-operative chemotherapy at different time points (from baseline to completion of one cycle of treatment before randomization, and 2 cycles of salvage treatment) in patients randomized to salvage treatment (Arm B).

To collect measurement of fatigue and overall perception of QOL at registration of the study. (Alliance registration QOL assessment study)

Patient Population

Patients must have histologically confirmed adenocarcinoma of the stomach or gastroesophageal junction (Siewert type II, III). Patients must have clinical stage of T3-4NanyM0 or TanyNpositiveM0 as determined by laparoscopy, CT scan (or PET/CT), or endoscopic ultrasound. Patients must be eligible for curative intent surgical resection. Patients must have an FDG avid tumor(s) as defined in the protocol.

Patients must not have known hypersensitivity to epirubicin, oxaliplatin, and cisplatin, capecitabine and 5-flurouracil, docetaxel, or irinotecan.

Patients must be at least 18 years of age and have ECOG performance status of 0-1. Patients must have adequate hematologic, hepatic, and renal function.Patients must not have a prior history of congestive heart failure or known DPD deficiency. Patients must not have current Grade 2, 3 or 4 neuropathy.

Stratification/Descriptive Factors

Patients are stratified by (1) tumor location: stomach vs gastroesophageal junction (Siewert type II, III); and (2) pre-op chemo regimen: cisplatin vs oxaliplatin.

Accrual Goals

The accrual goal for this study is 162 FDG-PET non-responding patients. An interim analyses for futility will be conducted after the first 60 events have been observed.

Summary Statement

Alliance reported that three patients had registered to this study as of June 30, 2016, none from SWOG institutions. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

E7208 Phase II SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Randomized Phase II Study of Irinotecan and Cetuximab with or without the Anti-Angiogenic Antibody, Ramucirumab (IMC-1121B), in Advanced, K-ras Wild-Type Colorectal Cancer Following Progression on Bevacizumab-Containing Chemotherapy

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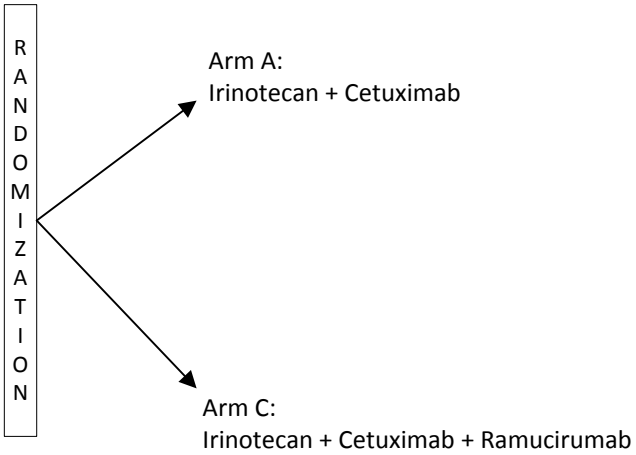
Participants:
ECOG-ACRIN, CTSU

Date Activated:
02/20/2014

Study Chair:
H Hochster (ECOG-ACRIN and SWOG)

SCHEMA



Note: Arm B closed to new accrual effective 6/2014

Objectives

To evaluate the progression free survival (PFS) for the addition of the anti-angiogenic antibody, ramucirumab, in combination with irinotecan and cetuximab as second line therapy for patients with K-ras wild-type colorectal cancer, as compared to the patients without the antibody.

To evaluate the response rate for irinotecan, cetuximab and ramucirumab in this patient population.

To evaluate the Grade 3-4 toxicity rates for the combination in this patient population.

To evaluate the overall survival for irinotecan, cetuximab, and ramucirumab in this patient population.

Patient Population

Patients must have histologically documented metastatic or advanced adenocarcinoma of the colon or rectum. Patients must not have brain or CNS

metastases, or other cancer requiring therapy within the last three years.

Patients must have had prior first-line therapy with oxaliplatin-based fluoropyrimidine-containing chemotherapy and bevacizumab for metastatic colorectal cancer. Patients must not have had any other prior therapy. Patients must not have had any major surgery within 28 days prior to randomization, or subcutaneous venous access device placement within seven days prior to registration.

Patients must have a performance status 0-1 and be at least 18 years of age. Patients must have adequate coagulation, hematologic, hepatic and renal function. Patients must not have had Grade 3-4 bleeding episodes within three months prior to registration.

Stratification/Descriptive Factors

Randomization will be stratified by (1) performance status: 0 vs 1; (2) discontinuation of oxaliplatin before disease progression: yes vs no; and (3) time frame of progression: within six months of last treatment vs more than 6 months since last treatment.

Accrual Goals

This study requires 135 patients to achieve a goal of 130 eligible patients.

Summary Statement

ECOG-ACRIN reported that 101 patients had registered to this study as of June 30, 2016, 16 from SWOG institutions. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg
Yale University	6
So Calif, U of	5
CORA NCORP	1
Michigan, U of	1
Northwestern Univ	1
Providence Hosp	1
Wayne State Univ	1
Total (7 Institutions)	**16**

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

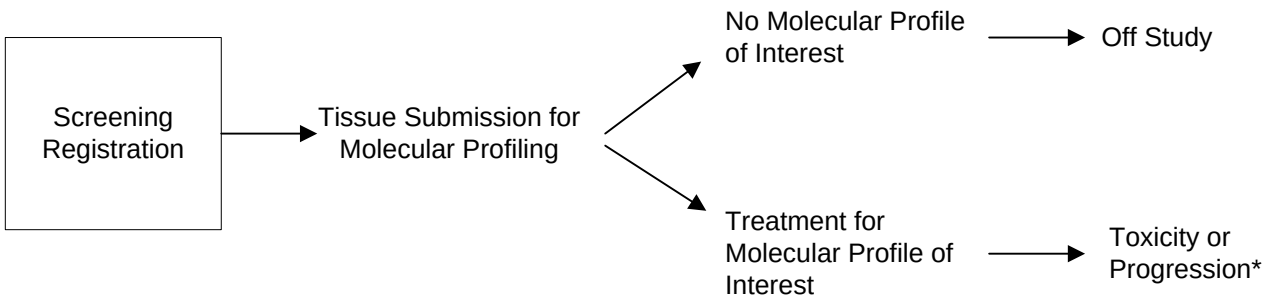
NCI-MATCH: Molecular Analysis for Therapy Choice

Participants:
ECOG-ACRIN, CTSU

Date Activated:
08/12/2015

Study Chairs:
K Flaherty (ECOG-ACRIN), P O'Dwyer (ECOG-ACRIN), A Chen (NCI), B Conley (NCI), V Villalobos (SWOG)

SCHEMA



*Upon progression or inability to tolerate protocol treatment, patients may be re-screened for additional molecular profiles of interest and corresponding protocol treatment.

Objectives

To evaluate the proportion of patients with objective response (OR) to targeted study agent(s) in patients with advanced refractory cancers/lymphomas/multiple myeloma.

To evaluate the proportion of patients alive and progression free at six months of treatment with targeted study agent in patients with advanced refractory cancers/lymphomas/multiple myeloma.

To evaluate the time until death or disease progression.

To identify potential predictive biomarkers beyond the genomic alteration by which treatment is assigned or resistance mechanisms using additional genomic, RNA protein and imaging-based assessment platforms.

To assess whether radiomic phenotypes obtained from pre-treatment imaging and changes from pre- through post-therapy imaging can predict objective response and progression free survival and to evaluate the association between pre-treatment radiomic phenotypes and targeted gene mutation patterns of tumor biopsy specimens.

Patient Population

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma or multiple myeloma that has progressed following at least one line of standard systemic therapy and/or for whose disease no standard treatment exists that has been shown to prolong survival. Patients must have measurable disease and meet one of the criteria in the protocol regarding tissue procurement.

Patients must not currently be receiving any other investigational agents. Any prior therapy, radiotherapy (except palliative radiation therapy of 30 Gy or less), or major surgery must have been completed at least four weeks prior to treatment on NCI-MATCH and patient must be recovered from adverse events due to prior therapy (except alopecia and lymphopenia). Palliative radiation therapy must have been completed at least two weeks prior to enrollment on a NCI-MATCH treatment subprotocol, and patient must have recovered from any adverse events of this therapy. Patients with brain metastases or primary brain tumors must have completed treatment, surgery, or radiation therapy at least four weeks prior to start of treatment. Patients must not require the use of full dose coumarin-derivative anticoagulants. Factor X inhibitors are permitted. Patients may receive non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results, but patients may not enroll in another investigational study during this time and the therapy cannot be an arm in this trial.

Patients must be at least 18 years of age, have an ECOG performance status of 0 or 1 and must be able to swallow tablets. Patients must have adequate hematologic, hepatic, renal, cardiac and marrow function. Patients must not have any uncontrolled intercurrent illness. HIV-positive patients are eligible provided they meet protocol criteria. Each subprotocol will have additional eligibility criteria that will be outlined in Section 2.0 of the agent-specific subprotocol.

Accrual Goals

The target screening accrual for this study is approximately 3,000 patients, with the goal of accruing 35 patients in each treatment subprotocol. If after screening 500 patients, the total number of patients with actionable tumor alteration (therefore qualifying for treatment) is below 50, results will be presented to the steering committee for consideration of terminating the trial. Within any given subprotocol, if rate of enrollment is such that it is unlikely accrual can reach 25 patients by the time the overall study screening accrual goal is met, and if 13 patients have been treated and no responses have been observed, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. After 500 patients are screened, the study design will be reassessed to assure its appropriateness. An interim analysis of the assay results will be performed after biopsies from approximately the first 200 patients are processed.

Summary Statement

This study activated on January 26, 2015, with 10 subprotocols included in the activation. Only sites utilizing the CIRB as their IRB of record are able to participate in the trial. The study was temporarily closed to accrual on November 11, 2015, after rapid accrual of 795 patients to the screening step in only three months, including 119 SWOG registrations. This pause in patient enrollment for assessment of study design appropriateness was lifted on May 31, 2016, when this study reopened to enrollment with an additional 14 new subprotocols.

Patients with multiple myeloma will be allowed to enroll in the MATCH protocol at a future amendment. The screening sample collection, processing and assay are currently being validated for the marrow specimens for patients with myeloma. Once this is completed, an amendment allowing these patients to enroll will be submitted. Patients with myeloma cannot be entered on the trial until that is completed.

ECOG-ACRIN reported a total of 1,013 screened patients and 29 molecularly matched patients as of June 30, 2016. This includes 139 screened and two molecularly matched SWOG registrations. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

N1048 Phase II/III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Phase II/III Trial of Neoadjuvant FOLFOX with Selective Use of Combined Modality Chemoradiation versus Preoperative Combined Modality Chemoradiation for Locally Advanced Rectal Cancer Patients Undergoing Low Anterior Resection with Total Mesorectal Excision

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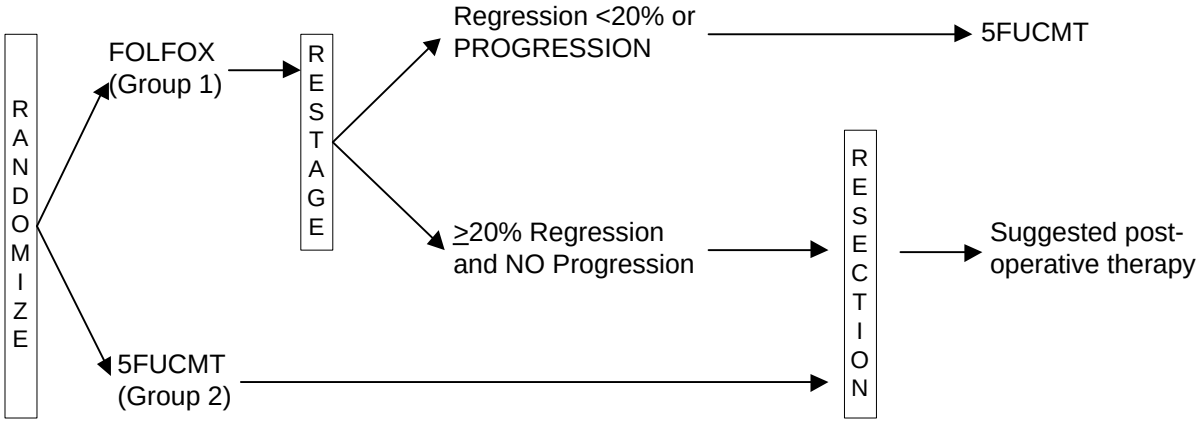
Participants:
Alliance, CTSU

Date Activated:
01/13/2012

Study Chairs:
D Schrag (Alliance), C Eng (SWOG)

SCHEMA



Objectives

Phase II component primary objective:
To assure that neoadjuvant FOLFOX followed by selective use of 5FUCMT group (Group 1) maintains the current high rate of pelvic R0 resection and is consistent with non-inferiority for time to local recurrence (TLR).

Phase III component primary objective:
To compare neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) to standard 5FUCMT (Group 2) with respect to the co-primary endpoints of the Time to Local Recurrence (TLR) and Disease-free Survival (DFS).

Secondary Objectives:
To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-inferior to the standard group 5FUCMT (Group 2) with respect to the proportion of patients who achieve a pathologic complete response (pCR) at the time of surgical resection.

To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-inferior to the standard 5FUCMT (Group 2) with respect to overall survival.

To evaluate and compare the adverse event profile and surgery complications between two groups.

To estimate the proportion of patients in the selective (Group 1) who receive: 1) pre-operative 5FUCMT; 2) post-operative 5FUCMT; 3) either pre- or post-operative 5FUCMT.

Patient Population

Patients must have rectal adenocarcinoma of clinical stage T2N1, T3N0 or T3N1. Patients must have radiologically measurable or clinically evaluable disease with tumor tissue evident between 5 and 12 cm from the anal verge. Tumor must not be adjacent to (within 3 mm of) the mesorectal fascia. Patients must not need abdominaloperineal (APR) at baseline.

Patients must not have had chemotherapy within five years prior to registration. Hormonal therapy is allowable if the disease free interval is five years or longer. Patients must not have had any prior pelvic radiation.

Patients must have an ECOG performance status 0-2 and be at least 18 years of age. Patients must have adequate hematologic, hepatic and renal function.

Stratification/Descriptive Factors

Patients will be stratified by ECOG performance status: 0 or 1 vs 2.

Accrual Goals

There will be total of 500 patients randomized to each group of this study (total of 1060 to get 1000 evaluable patients) if the trial completes the full phase III accrual. The phase II portion is defined as the first 366 randomized patients.

Summary Statement

Alliance reported that 593 patients had registered to this study as of June 30, 2016, including 86 from SWOG institutions. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	13	Boston Medical Ctr	2
Rochester, Univ of	13	Davis, U of CA	2
Baylor College	10	Michigan, U of	2
Methodist Hospital	7	CORA NCORP	1
Irvine, U of CA	6	Good Samaritan Hosp/CORA NCORP	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	6	Northwestern Univ	1
Lahey Hosp & Med Ctr	6	Ozarks NCORP	1
Fred Hutchinson CRC	5	PCRC NCORP	1
Arizona MC, U of	4	Utah, U of	1
San Diego, U of CA	4	**Total (19 Institutions)**	**86**

R0848 Phase III SWOG Supported CTSU Study

Coordinating Group: NRG

A Phase III Trial Evaluating Both Erlotinib and Chemoradiation as Adjuvant Treatment for Patients with Resected Head of Pancreas Adenocarcinoma

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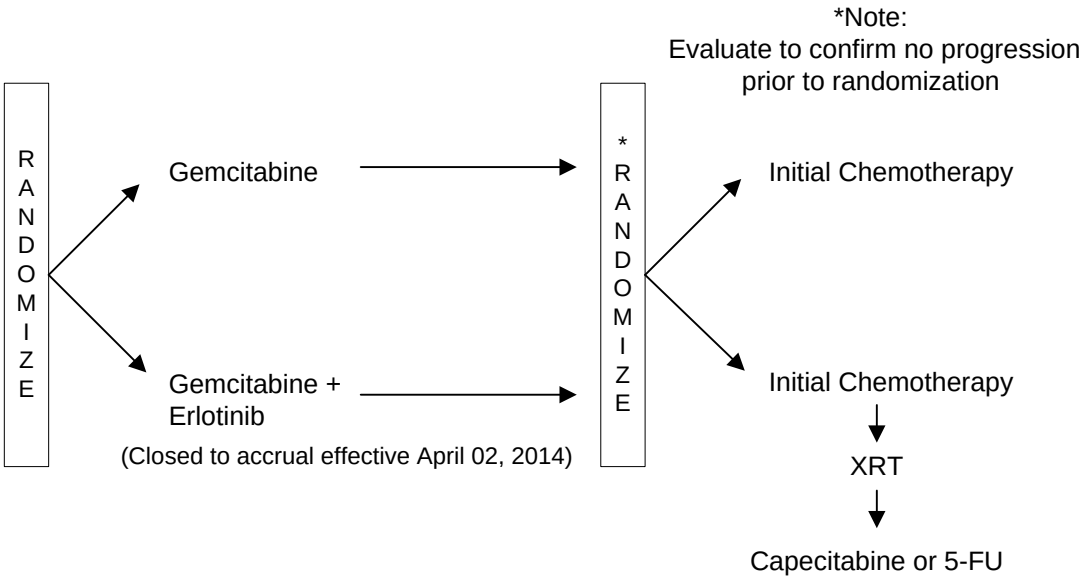
Participants:
NRG, CTSU

Date Activated:
03/01/2014

Study Chairs:
R Abrams (NRG), P Philip (SWOG)

Statistician:
K Guthrie

SCHEMA



Objectives

To determine whether the addition of erlotinib to gemcitabine adjuvant chemotherapy improves survival as compared to gemcitabine alone following R0 or R1 resection of head of pancreas adenocarcinoma (including adenocarcinoma of the head, neck and uncinate process).

To determine whether the use of concurrent fluoropyrimidine and radiotherapy following adjuvant gemcitabine-based chemotherapy further enhances survival for such patients who are without evidence of progressive disease after five cycles of gemcitabine-based chemotherapy.

To evaluate disease-free survival of adjuvant chemotherapy followed by radiotherapy and concurrent fluoropyrimidine for patients with resected head of pancreas adenocarcinoma who are disease-free after five cycles of adjuvant chemotherapy.

To evaluate disease-free survival of standard adjuvant gemcitabine chemotherapy with and without erlotinib for patients with resected head of pancreas adenocarcinoma.

To evaluate the disease-free and overall survival of standard adjuvant treatment with and without erlotinib for patients with resected head of pancreas adenocarcinoma by wild-type and mutant KRAS status.

To evaluate adverse events with and without erlotinib for patients with resected head of pancreas adenocarcinoma.

To evaluate adverse events of adjuvant chemotherapy with or without radiation therapy and concurrent fluoropyrimidine for patients with resected head of pancreas adenocarcinoma who are disease-free after adjuvant chemotherapy.

To evaluate preoperative cross-sectional imaging of the primary head of pancreas adenocarcinoma in order to determine the frequency with which objective criteria of resectability are present.

To determine if patients reporting low baseline fatigue, as measured by the FACIT-Fatigue, predicts survival and to explore correlations between baseline fatigue, as measured by PROMIS, and survival.

Patient Population

Patients must have histologic proof of primary head of pancreas invasive adenocarcinoma managed with a potentially curative resection. Patients with invasive adenocarcinoma that also contains a component of intraductal papillary mucinous neoplasm (IPMN) are eligible. Patients must have pathologic stage T1-3, N0-1 and M0 according to the 6th edition AJCC staging system. Patients with non-adenocarcinomas, adenosquamous carcinomas, islet cell tumors, cystadenomas, cystadenocarcinomas, carcinoid tumors, duodenal carcinomas, distal bile duct or ampullary carcinomas are not eligible.

Patients must have had removal of all gross tumor involving a classic pancreaticoduodenectomy, or a pylorus preserving pancreaticoduodenectomy. This surgery must have occurred within 21 and 56 days of registration. Patients managed with a total pancreatectomy, distal pancreatectomy, or central pancreatectomy are not eligible. Prior chemotherapy for pancreas cancer is not allowed. Patients with prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields are not eligible.

Patients must have adequate hematologic, hepatic and renal function and be at least 18 years of age. Patients must have a Zubrod performance status of 0 or 1. Patients with active HIV infection are eligible if their CD4 count is 499/mm^3 or greater and their viral load is 50 copies/ml or less (use of HAART is allowed).

Stratification/Descriptive Factors

At initial randomization patients will be stratified by (1) nodal status: involved vs uninvolved; (2) CA 19-9 results: 90 or less vs > 90-180; and (3) surgical margins: positive vs negative.

Accrual Goals

This study will accrue 950 patients to reach the 640 patients required to be randomized to answer the radiation therapy question. Three interim analyses will be performed.

Summary Statement

NRG reported that as of June 30, 2016, 234 patients had been accrued, including 20 patients from SWOG institutions. The complete January 2016 summary of this study from NRG is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Irvine, U of CA	6	Hawaii MU-NCORP	1
Edward Hospital/Loyola University	4	Stormont-Vail Health/Kansas, U of	1
Northwest NCORP	3	Valley Hospital/Columbia University	1
Columbia MU-NCORP	2	Wichita NCORP	1
Greenville NCORP	1	**Total (9 Institutions)**	**20**

R1112 Phase III SWOG Supported CTSU Study

Coordinating Group: NRG

Randomized Phase III Study of Sorafenib Versus Stereotactic Body Radiation Therapy Followed by Sorafenib in Hepatocellular Carcinoma

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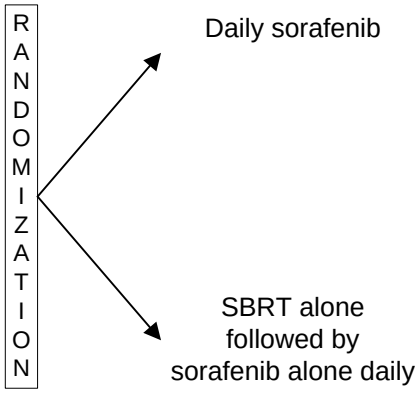
Participants:
NRG, CTSU

Date Activated:
04/24/2013

Study Chairs:
L Dawson (NRG), T Mitin (SWOG)

SCHEMA



Objectives

To determine if stereotactic body radiation therapy (SBRT) improves overall survival in hepatocellular carcinoma (HCC) patients treated with sorafenib.

To determine the difference in time to progression (TTP) and progression-free survival (PFS) in HCC patients treated with sorafenib compared to SBRT followed by sorafenib.

To measure differences in toxicity in HCC patients treated with sorafenib versus SBRT followed by sorafenib.

To measure vascular thrombosis response post sorafenib versus SBRT followed by sorafenib.

To measure differences in Health Related QOL and quality-adjusted survival in HCC patients treated with sorafenib compared to SBRT followed by sorafenib.

Patient Population

Patients must have an HCC diagnosis by at least one criterion listed in the protocol within 360 days prior to study entry. Patients must have CT/MRI prior to study entry. Patients must have measureable hepatic disease and/or presence of vascular tumor thrombosis. Patients must have Child-Pugh score A, and either intermediate (B) or advanced (C) stage BCLC. Patients must be unsuitable for resection or transplant or radiofrequency ablation (RFA). Patients must be unsuitable for or refractory to transarterial hepatic chemo-embolization (TACE) or drug eluting beads (DEB). Patients must not have any of the following disease characteristics: any one hepatocellular carcinoma greater than 15 cm; total maximal sum of hepatocellular carcinomas or a single conglomerate HCC greater than 20 cm; more than five discrete intrahepatic parenchymal foci of

HCC; direct tumor extension into the stomach, duodenum, small bowel or large bowel; measurable common or main branch biliary duct involvement with HCC; extrahepatic metastases or malignant nodes greater than 3 cm, in sum of maximal diameters.

Patients must not have received prior sorafenib for more than 60 days of duration, prior liver transplant, or radiotherapy to the region of the liver that would result in excessive doses to normal tissues due to overlap of radiation therapy fields. Patients must not have received selective internal radiotherapy/hepatic arterial Yttrium therapy. Patients must not be receiving combination anti-retroviral therapy for HIV.

Patients must be at least 18 years of age and have a Zubrod performance status of 0-2. Patients must have adequate hematologic, hepatic, renal, and coagulation function. Patients must not have severe, active co-morbidity as defined in the protocol.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) vascular involvement: IVC/main portal vein/right or left main branch portal vein vs other vascular involvement vs none; (2) hepatitis: B or B and C vs C vs other; (3) site: North American vs non-North American; and (4) HCC volume/liver volume: 10% vs 10-40% vs >40%.

Accrual Goals

This study requires 368 patients to achieve the accrual goal of 320 evaluable patients. Interim analyses will be conducted when 50% and 75% of the expected number of deaths have been observed.

Summary Statement

NRG reported that as of June 30, 2016, 84 patients have been randomized with none from SWOG. The complete January 2016 summary of this study from NRG is available on the SWOG web site.

R1201 Phase II SWOG Supported CTSU Study

Coordinating Group: NRG

A Phase II Randomized Trial Evaluating the Addition of High or Standard Intensity Radiation to Gemcitabine and nab-Paclitaxel for Locally Advanced Pancreatic Cancer

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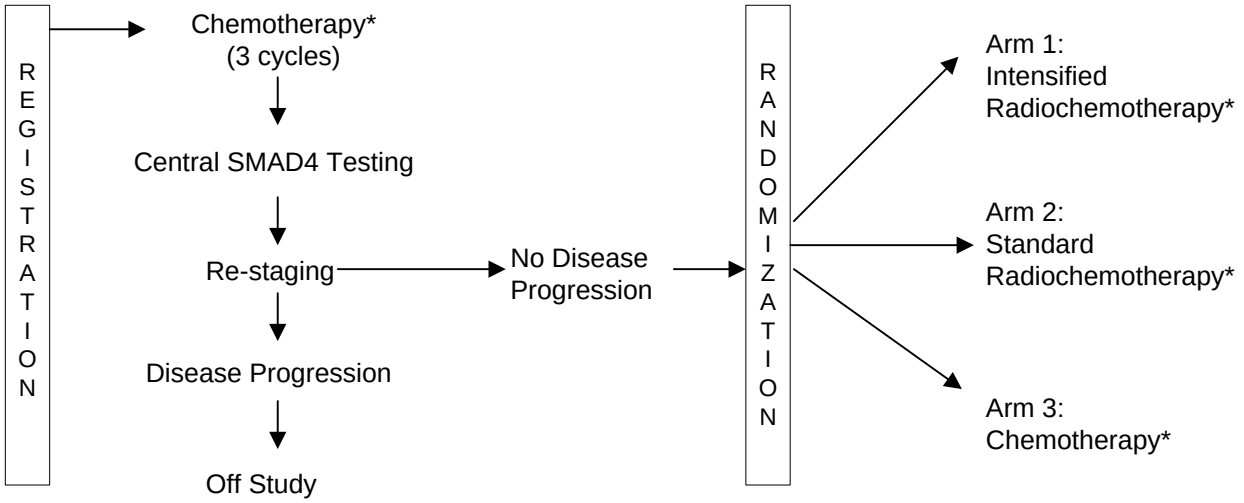
Participants:
NRG, CTSU

Date Activated:
08/14/2013

Study Chairs:
E Ben-Josef (NRG), J Murphy (SWOG)

Date Closed:
04/01/2016

SCHEMA



*Chemotherapy with gemcitabine + nab - paclitaxel

Objectives

To determine if intensified radiochemotherapy following gemcitabine and nab-paclitaxel in patients with unresectable pancreatic cancer will show a signal for improved 2-year overall survival (OS) from 10% to 22.5% as compared to chemotherapy with gemcitabine and nab-paclitaxel alone.

To determine if standard radiochemotherapy following gemcitabine and nab-paclitaxel in patients with unresectable pancreatic cancer will show a signal for improved 2-year OS from 10% to 22.5% as compared to chemotherapy with gemcitabine and nab-paclitaxel alone.

To evaluate patterns of failure (local and systemic progression) by SMAD4 status and intensity of radiation therapy.

To evaluate the impact of radiochemotherapy on OS for the subset of SMAD4 intact patients.

To evaluate adverse events associated with the treatments.

To evaluate correlation between SMAD4 status determined by IHC and genetic SMAD4 status.

Patient Population

Patients must have histologically or cytologically confirmed adenocarcinoma of the pancreas. Tumor diameter must be seven centimeters or less and unresectable as defined in the protocol. Patients must not have distant metastases or more than one primary lesion. Patients must have a cell block or core biopsy submitted for central SMAD4 testing.

Patients must not have received prior systemic anti-cancer therapy for pancreatic cancer or prior radiation therapy to the abdomen that results in overlap of radiation fields.

Patients must be at least 18 years of age and have a Zubrod performance status of 0-1. Patients must have adequate hematologic, hepatic, renal, and coagulation function. Patients must not have pre-existing Grade 2 or greater neuropathy.

Stratification/Descriptive Factors

At randomization, patients will be stratified by the following factors: (1) CA19-9 status: < 1 vs ≥ 1 to ≤ 90 vs > 90; and (2) SMAD4 status: intact vs loss vs undetermined.

Accrual Goals

This study is estimated to accrue 346 patients to randomize 288 eligible patients. For each comparison, there will be one interim analysis for futility performed when 50% of the total events (70 deaths) have been observed.

Summary Statement

NRG reported that as of June 30, 2016, 13 patients have been randomized, including one from SWOG (CORA NCORP). The complete January 2016 summary of this study from NRG is available on the SWOG web site.