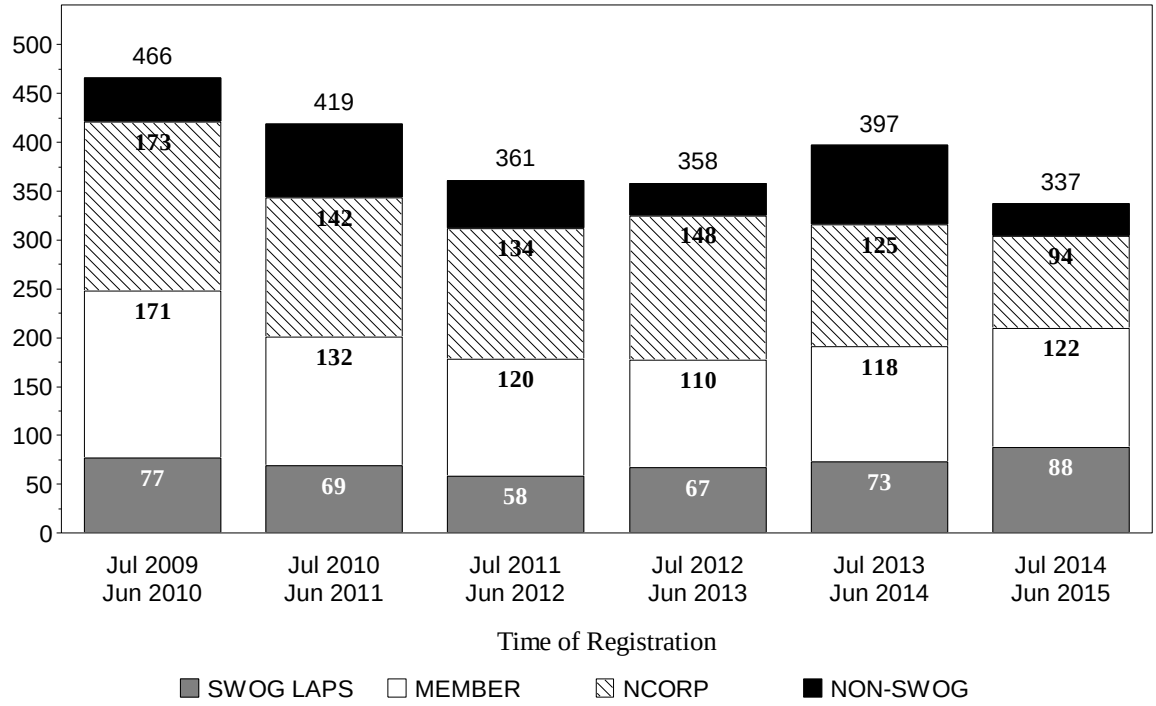
GASTROINTESTINAL COMMITTEE

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 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
S1115 Panc, Met, AZD6244 + MK2206 vs mFOLFOX				
mFOLFOX	0	0	27	70
AZD-6244 + MK-2206	0	0	25	67
	0	0	52	137
S1201 Gas/Esoph/GEJ, Adv, ERCC1-based				
Initial Marker Testing	28	42	59	264
Randomization				
FOLFOX	11	16	27	106
Irinotecan + Docetaxel	14	18	24	107
	25	34	51	213
S1310 Biliary, Ref. Adv, GSK1120212 vs Chemo				
Trametinib	9	16	2	27
5-FU+Leucovorin/Capecitabine	12	9	5	26
	21	25	7	53
S1313 Panc, Met, mFolfirinox +/- PEGPH20				
Phase I				
PEGPH20 Dose Level 1 + mFOLFIRINOX	0	3	2	5
PEGPH20 Dose Level 2 + mFOLFIRINOX	6	1	0	7
Phase II				
mFOLFIRINOX	1	0	0	1
PEGPH20 + mFOLFIRINOX	1	0	0	1
	8	4	2	14
S1406 CRC, Met, BRAF mutant, Irino + Cetux ± Vem				
Initial Registration	51	6	0	57
Randomization				
Cetuximab + Irinotecan	15	2	0	17
Vemurafenib + Cetux + Irinotecan	16	2	0	18
	31	4	0	35
Crossover				
Crossover:Vem + Cetux + Irinotecan	4	0	0	4
A021202 Carcinoid, Pazopanib vs Placebo*				
Total Registrations	10	8	5	23
C80702 Adj FOLFOX + Celecoxib or Placebo*				
Total Registrations	49	45	46	486
C80802 HCC, Adv, Sorafenib +/- Doxorubicin*				
Total Registrations	4	3	4	46
C80803 Esoph, PET-directed combined Tx*				
Total Registrations	0	1	3	5

	Jan 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
E1208 HCC, Unresec, Chemoembolization +/- Soraf*				
Total Registrations	0	3	15	72
E2211 Panc, Adv, Temozolomide +/- Cape*				
Total Registrations	17	3	15	37
E7208 CRC, Adv, Irino/Cet +/- Ramucirumab*				
Total Registrations	5	3	0	8
N1048 Rectal, Local Adv, ChemoRT +/- FOLFOX*				
Total Registrations	15	19	17	61
R1010 Esoph, HER2, TrimodalTx +/- Trastuz*				
Total Registrations	0	0	1	5

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

S0820 Phase III

Coordinating Group: SWOG

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)

Participants:
SWOG, CTSU

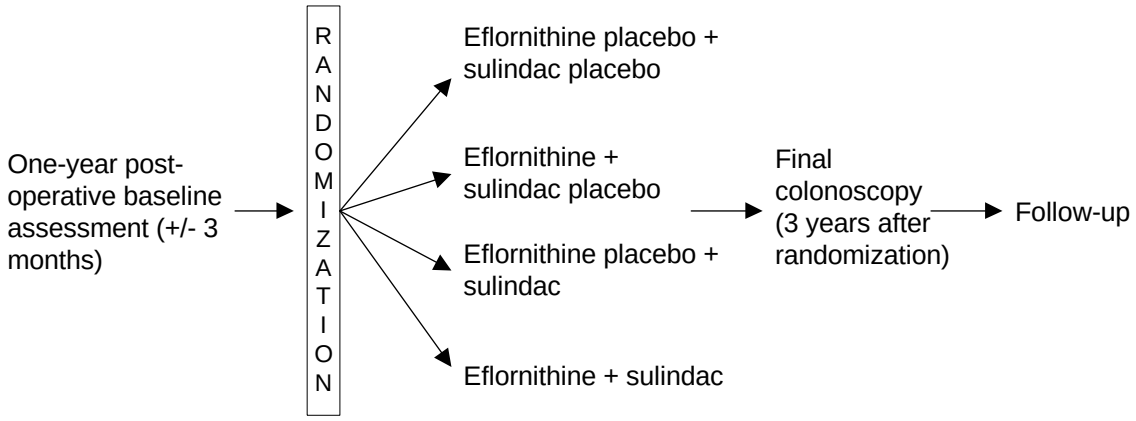
Date Activated:
03/01/2013

Study Chairs:
J Zell, P Brown

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 $\geq$ 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 30 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 1,340 eligible patients will be enrolled, 335 to each study arm.

Summary Statement

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

S1008 Phase II

Feasibility Study of a Physical Activity and Dietary Change Weight Loss Intervention in Breast and Colorectal Cancer Survivors, Phase II

Study Chairs:
H Greenlee, D Hershman

Statisticians:
D Lew, J Unger

Data Coordinator:
D Marrah

Date Activated:
03/01/2012

Date Closed:
07/01/2014

Objectives

To determine the feasibility of a 12-month community-situated combined physical activity and dietary change weight loss intervention in overweight and sedentary female breast and colorectal cancer survivors recruited via SWOG. Feasibility will be assessed based on study accrual, intervention adherence, and study retention. Analyses will be conducted separately for breast and colorectal cancer survivors.

To estimate the effect size of the intervention on weight loss at 12 months.

To measure changes from baseline to 6 and 12 months in anthropometric measures (body mass index [BMI], waist and hip circumference) and changes from baseline to 12 months in body composition (% body fat as assessed by DXA scan).

To measure changes from baseline to 6 and 12 months in minutes spent per week in moderate-to-vigorous aerobic activity using Curves® attendance records and a 7-day physical activity assessment.

To measure changes from baseline to 6 and 12 months in self-reported dietary intake via three separate 24-hour diet recalls at each time point.

To measure changes from baseline to 6 and 12 months in dietary intake of carotenoids via serum carotenoid measures.

To measure changes from baseline to 6 and 12 months in metabolic and hormonal biomarkers associated with breast and colorectal cancer recurrence risk (fasting insulin, fasting glucose, hemoglobin A1C, bioavailable estradiol, free testosterone, and adiponectin).

To assess changes from baseline to 6 and 12 months in anxiety, depression, fatigue, sleep, satisfaction with social roles, pain and physical function using the PROMIS-43.

To assess changes from baseline to 6 and 12 months in perceived benefit of dietary change, physical activity and weight loss after a cancer diagnosis.

To assess the diversity of subjects who enroll and complete the intervention.

To assess baseline predictors (medical history, health behaviors, quality of life) of subjects who adhere to and complete the intervention.

To assess the safety of the Curves® fitness centers for this population by assessing self-reported changes in lymphedema and any injuries as measured at 6 and 12 months.

To assess the availability and acceptability of the Curves® fitness centers at 12 months.

To assess the acceptability of the dietary change component of the intervention at 12 months.

To explore changes in DNA methylation.

To assess the intervention and study process via open-ended interviews with SWOG sites and Curves® franchises.

To measure changes in anthropometric measures and assess feasibility of extended follow-up at 24 and 36 months.

Patient Population

Participants must be women with a previous diagnosis of invasive breast cancer or colorectal cancer, Stage I, II, or III, with no evidence of metastatic disease (M0). Participants must have no evidence of disease at the time of registration and no history of metastases. Participants must be post-menopausal as defined in the protocol.

Participants must be 90 days to 7 years post-surgery, chemotherapy, and radiation therapy. Concurrent cytotoxic therapies, including Herceptin, are not allowed among breast cancer patients. Other concurrent therapies are allowed among breast cancer patients, including IV bisphosphonates (e.g., Zometa), RANK ligand inhibitors (e.g., Xgeva, Prolia), and anti-hormonal therapies (e.g., aromatase inhibitors). Participants must not have had weight loss surgery.

Participants must be considered sedentary as defined in the protocol, have a BMI $\geq$ 25 kg/m2 and a Zubrod performance status of 0. Participants must have no abnormal changes on cardiovascular exercise stress test as measured by EKG. Participants must not be active smokers or have evidence of uncontrolled hypertension. Participants with diabetes, pre-diabetes, and/or metabolic syndrome must have HgbA1C $\leq$ 8. Participants must be willing and able to attend a Curves® fitness center at least three times per week for 12 months and agree to participate in the behavioral counseling sessions and telephone interviews. Participants must be willing to submit blood samples for biomarkers. Participants must have physician clearance to participate, regular access to the internet, a home phone or cell phone, and be able to understand, speak and read English.

Stratification/Descriptive Factors

Participants will be stratified at time of registration by type of cancer: breast vs colorectal.

Accrual Goals

The accrual goal is 25 eligible breast cancer survivors and 25 eligible colorectal cancer survivors.

Summary Statement

For the current status of this study, please refer to the Cancer Survivorship 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:
D Marrah

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 112 analyzable patients.

Summary Statement

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

S1201 Phase II

Coordinating Group: SWOG

A Randomized Phase II Pilot Study Prospectively Evaluating Treatment for Patients Based on ERCC1 (Excision Repair Cross-Complementing 1) for Advanced/Metastatic Esophageal, Gastric or Gastroesophageal Junction (GEJ) Cancer

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

Study Chairs:
S Iqbal, H Lenz

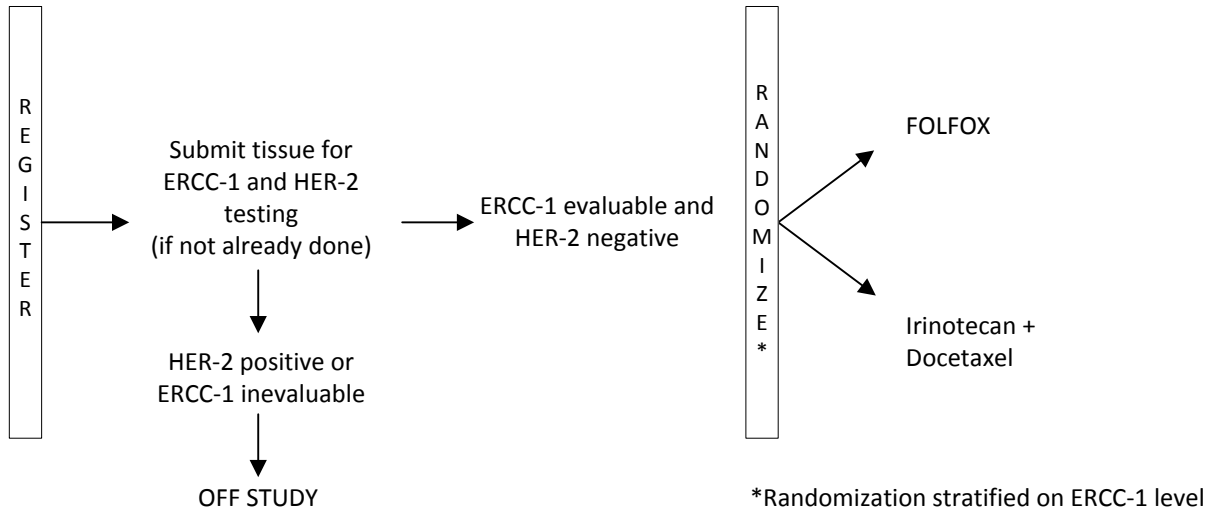
Statisticians:
S McDonough, K Guthrie

Data Coordinator:
C McLeod

Date Activated:
03/01/2012

Date Closed:
04/01/2015

SCHEMA



*Randomization stratified on ERCC-1 level

Objectives

To assess progression-free survival in high-ERCC1 patients with advanced or metastatic cancer of the esophagus, stomach, or GEJ treated with FOLFOX compared to those treated with irinotecan plus docetaxel.

To assess progression-free survival in low-ERCC1 patients with advanced or metastatic cancer of the esophagus, stomach, or GEJ treated with FOLFOX

compared to those treated with irinotecan plus docetaxel.

To assess progression-free survival in low-ERCC1 patients with advanced or metastatic cancer of the esophagus, stomach, or GEJ treated with FOLFOX compared to high-ERCC1 patients treated with FOLFOX.

To assess overall survival and toxicities in each of the two treatment arms in this group of patients.

To assess the response probability (confirmed and unconfirmed, complete and partial responses) in the subset of patients with measurable disease in each of the two treatment arms.

To explore whether there is evidence of interaction between treatment arm and ERCC1 expression in this group of patients.

To bank tissue and blood for these future translational medicine studies:

To explore the relationship of ERCC1 and ERCC2 single nucleotide polymorphism (SNP) genotypes with clinical outcome in these patients.

To explore the association between germline variations in these SNPs and ERCC1 mRNA expression in these patients.

Patient Population

Patients must have histologically or cytologically confirmed unresectable advanced or metastatic adenocarcinoma of the esophagus, stomach, or GEJ. Patients who have had prior HER-2 expression testing must be HER-2 negative. Patients must have tumor available for submission to assess ERCC1 and HER-2 (if not already performed).

Patients must not have received treatment for metastatic or unresectable disease. Patients must have completed any prior neoadjuvant and adjuvant therapy for resectable disease at least 180 days prior to registration.

Patients must have adequate hepatic, renal, and hematologic function and a Zubrod performance status of 0-1. Patients must not have Grade 2 (by CTCAE Version 4.0) or higher motor or sensory neuropathy.

Stratification/Descriptive Factors

Treatment randomization will be stratified based on (1) ERCC1 expression: high (≥1.7) vs low (< 1.7) and (2) disease site: esophageal vs gastric/GEJ.

Accrual Goals

A total of 200 eligible patients will be randomized to this study. Allowing for an ineligibility rate of 10%, it is anticipated that 225 patients will be enrolled to the initial registration. If a greater number of patients than expected are found to be HER-2 positive after initial screening registration, then additional patients will be enrolled to reach the goal of 200 eligible randomized patients.

Summary Statement

This study closed as of April 1, 2015 after meeting the accrual goal with 264 patients registered to the initial screening. Fifty-one patients were not randomized due to: inadequate specimens for testing (21), HER-2 positive expression (20), heterogeneous results with respect to HER-2 status (3), patient withdrawal prior to randomization (3), change in patient's status, moving to hospice, death prior to randomization, and insurance denial (1 patient each). Two-hundred thirteen patients have been randomized.

Four patients were deemed ineligible due to timing of baseline disease or laboratory assessment (3 patients) and diagnosis of squamous cell carcinoma. Per physician's discretion, two patients started non-protocol therapy prior to screening results/randomization and are not included in any of the following analyses. Thirteen additional patients are not included in assessment of adverse events (also recorded as major protocol deviations): five patients died prior to starting treatment, four patients refused randomization and chose to receive other therapy prior to starting protocol treatment, one lacked transportation and was unable to receive protocol treatment, one withdrew consent, one had decreasing performance status and did not start therapy, and one received the incorrect treatment arm. Six additional patients are recorded as major protocol deviations: three patients were inadvertently taken off protocol treatment prior to progression due to institutional error, two patients started protocol treatment prior to treatment arm randomization, and one patient received only 10 mg/m^2 of leucovorin, instead of the 400 mg/m^2 per protocol.

Twenty-four patients were removed from protocol therapy due to adverse events, primarily hematologic events. Seven patients were removed from protocol

therapy for reasons not specified in the protocol: lack of transportation (2 patients), removed inadvertently prior to progression (2), proceeded to surgery (1), started palliative radiation (1), and wanted to receive Herceptin after post-registration biopsy showed HER-2 positivity in liver metastases, even though original biopsy was HER-2 negative (1). Twenty-four patients refused to complete protocol therapy, primarily electing for no longer wanting any therapy.

One hundred ninety-one patients have been assessed for adverse events. Three treatment-related deaths have been reported on the FOLFOX arm, one each due to lung infection and oral mucositis, and a sudden death of unknown cause. Eight additional patients on the FOLFOX arm have experienced Grade 4 adverse events, primarily hematologic events. Three treatment-related deaths have been reported on the Irinotecan + Docetaxel arm, two due to multi-organ failure and one due to respiratory failure. Fourteen additional patients on the Irinotecan + Docetaxel arm have experienced Grade 4 adverse events, primarily sepsis and hematologic events. One patient reported Grade 3 colon infection (reported as 'Infections/infestations-Other').

Registration by Institution

Screening Registration

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	56	Rockwood Clinic, PS/PCRC NCORP	4
ECOG-ACRIN	37	Dayton NCORP	3
So Calif, U of	22	Hawaii MU-NCORP	3
Irvine, U of CA	14	Kansas City NCORP	3
Heartland NCORP	12	Montana NCORP	3
Michigan CRC NCORP	11	Northwest NCORP	3
Rochester, Univ of	11	CRC West MI NCORP	2
Baylor College	9	Henry Ford Hosp	2
Davis, U of CA	7	New Mexico MU-NCORP	2
NRG	7	Ozarks NCORP	2
Wichita NCORP	7	Arkansas, U of	1
Greenville NCORP	6	Broward Health MC/H Lee Moffitt CC	1
Kansas, U of	6	Loyola University	1
Oklahoma, Univ of	6	Prov Portland MC/PCRC NCORP	1
Southeast COR NCORP	6	Singing River Hosp/Mississippi, Univ of	1
Upstate Carolina	5	Sutter General Hosp/Sutter Cancer RC	1
Michigan, U of	4	VAMC Ann Arbor/Michigan, U of	1
PCRC NCORP	4	**Total (35 Institutions)**	**264**

Registration, Eligibility, and Evaluability

Randomization

Registrations ending June 30, 2015; Data as of July 9, 2015

	TOTAL	FOLFOX	Irinotecan + Docetaxel
NUMBER REGISTERED	213	106	107
INELIGIBLE	4	2	2
ELIGIBLE	209	104	105
Analyzable, Pend. Elig.	23	9	14
Not Analyzable	2	1	1
BASELINE DISEASE STATUS			
Measurable	150	77	73
Non Measurable	33	17	16
Too Early	24	9	15
ADVERSE EVENT ASSESSMENT			
Evaluable	191	93	98
Not Evaluable	13	8	5
Too Early	3	2	1

Patient Characteristics

Randomization

Registrations ending June 30, 2015; Data as of July 9, 2015

	FOLFOX (n=103)		Irinotecan + Docetaxel (n=104)	
AGE				
Median	62.3		62.4	
Minimum	21.5		33.8	
Maximum	85.6		84.9	
SEX				
Males	83	81%	83	80%
Females	20	19%	21	20%
HISPANIC				
Yes	14	14%	19	18%
No	85	83%	83	80%
Unknown	4	4%	2	2%

	FOLFOX (n=103)		Irinotecan + Docetaxel (n=104)	
RACE				
White	87	84%	80	77%
Black	7	7%	6	6%
Asian	5	5%	8	8%
Native American	1	1%	0	0%
Unknown	3	3%	10	10%
ERCC1				
High (≥1.7)	15	15%	15	14%
Low (<1.7)	88	85%	89	86%
SITE OF DISEASE				
Esophageal	35	34%	35	34%
Gastric/GEJ	68	66%	69	66%

Treatment Summary

Randomization

Registrations ending June 30, 2015; Data as of July 9, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	21
NUMBER OFF PROTOCOL TREATMENT	186
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	24
Refusal unrelated to adverse event	24
Progression/relapse	86
Death	14
Other - not protocol specified	7
Reason under review	31
MAJOR PROTOCOL DEVIATIONS	19

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, 2015; Data as of July 9, 2015

	FOLFOX (n=93) Grade				Irinotecan + Docetaxel (n=98) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
ALT increased	91	2	0	0	97	1	0	0
APTT prolonged	93	0	0	0	97	1	0	0
AST increased	91	1	1	0	93	5	0	0
Abdominal pain	92	1	0	0	98	0	0	0
Acute kidney injury	93	0	0	0	97	1	0	0
Alkaline phosphatase increased	92	1	0	0	97	1	0	0
Allergic reaction	92	1	0	0	98	0	0	0
Anemia	87	6	0	0	85	13	0	0
Anorexia	93	0	0	0	91	7	0	0
Bladder infection	93	0	0	0	97	1	0	0
Blood bilirubin increased	92	1	0	0	97	1	0	0
Bone pain	92	1	0	0	98	0	0	0
CD4 lymphocytes decreased	93	0	0	0	95	3	0	0
Confusion	92	1	0	0	98	0	0	0
Death NOS	92	0	0	1	98	0	0	0
Dehydration	91	2	0	0	80	17	1	0
Depression	92	1	0	0	98	0	0	0
Diarrhea	89	4	0	0	70	24	4	0
Dry mouth	92	1	0	0	98	0	0	0

	FOLFOX (n=93) Grade				Irinotecan + Docetaxel (n=98) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
Dysphagia	92	1	0	0	97	1	0	0
Edema limbs	93	0	0	0	97	1	0	0
Esophageal hemorrhage	93	0	0	0	97	1	0	0
Esophagitis	93	0	0	0	97	1	0	0
Fatigue	87	6	0	0	85	13	0	0
Febrile neutropenia	92	1	0	0	92	6	0	0
Gastrointestinal pain	93	0	0	0	97	1	0	0
Generalized muscle weakness	91	2	0	0	96	2	0	0
Hand-Foot syndrome	92	1	0	0	98	0	0	0
Headache	93	0	0	0	97	1	0	0
Hyperglycemia	92	1	0	0	97	1	0	0
Hypertension	92	1	0	0	97	1	0	0
Hypoalbuminemia	92	1	0	0	94	4	0	0
Hypocalcemia	93	0	0	0	96	2	0	0
Hypokalemia	91	1	1	0	90	8	0	0
Hypomagnesemia	93	0	0	0	96	2	0	0
Hyponatremia	91	1	1	0	93	5	0	0
Hypotension	92	1	0	0	96	1	1	0
INR increased	93	0	0	0	97	1	0	0
Infections/infestations-Other	93	0	0	0	97	1	0	0
Infusion related reaction	92	1	0	0	98	0	0	0
Leukocytosis	93	0	0	0	97	1	0	0
Lung infection	92	0	0	1	97	1	0	0
Lymphocyte count decreased	84	8	1	0	92	5	1	0
Mucositis oral	91	1	0	1	97	0	1	0
Multi-organ failure	93	0	0	0	96	0	0	2
Nausea	86	7	0	0	86	12	0	0
Neutrophil count decreased	66	22	5	0	80	10	8	0
Non-cardiac chest pain	93	0	0	0	97	1	0	0
Obstruction gastric	92	1	0	0	98	0	0	0
Peripheral motor neuropathy	92	1	0	0	98	0	0	0
Peripheral sensory neuropathy	85	7	1	0	97	1	0	0
Platelet count decreased	88	5	0	0	97	1	0	0
Pneumonitis	93	0	0	0	97	1	0	0
Respiratory failure	93	0	0	0	96	0	1	1
Sepsis	92	0	1	0	92	0	6	0
Stomach pain	93	0	0	0	97	1	0	0
Syncope	92	1	0	0	97	1	0	0
Thromboembolic event	92	1	0	0	98	0	0	0
Upper GI hemorrhage	93	0	0	0	97	1	0	0
Urinary tract infection	93	0	0	0	97	1	0	0
Vascular access complication	93	0	0	0	97	1	0	0
Vomiting	88	5	0	0	90	8	0	0
Weight loss	93	0	0	0	96	2	0	0
White blood cell decreased	85	7	1	0	85	7	6	0
MAX. GRADE ANY ADVERSE EVENT	37	45	8	3	37	44	14	3

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

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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 3,000 eligible patients will be accrued.

Summary Statement

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

S1310 Phase II

Randomized Phase II Trial of Single Agent MEK Inhibitor Trametinib (GSK1120212) vs. 5-Fluorouracil or Capecitabine in Refractory Advanced Biliary Cancer

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Study Chairs:
R Kim, A El-Khoueiry

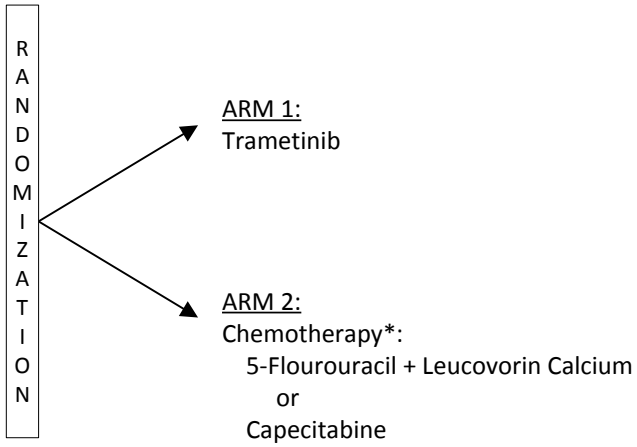
Statisticians:
S McDonough, K Guthrie

Data Coordinator:
S Edwards

Date Activated:
02/15/2014

Date Closed:
05/15/2015

SCHEMA



*If randomized to Arm 2, patient and physician may select regimen.

Objectives

To assess overall survival (OS) in patients with refractory advanced biliary cancer randomized to Arm 1: trametinib compared to those randomized to Arm 2: chemotherapy (either 5-fluorouracil and leucovorin or capecitabine).

To determine the frequency and severity of adverse events of trametinib in this patient population.

To assess response rate (RR) and progression-free survival (PFS) in patients randomized to Arm 1: trametinib and patients randomized to Arm 2: chemotherapy (5-FU or capecitabine) in this patient population.

To determine if a 16-gene expression signature is predictive of MEK efficacy as evidenced by improved RR, PFS, and OS.

To evaluate the effects of trametinib on the inflammatory cytokine and explore potential associations with response rate and survival.

To estimate lean soft tissue and fat mass weight gain as a result of treatment with trametinib vs. chemotherapy in patients with advanced refractory biliary cancer.

To bank tissue samples for other future correlative studies including next generation sequencing and whole genome methylation assays.

Patient Population

Patients must have histologically or cytologically documented carcinoma primary to the intra- or extra-hepatic biliary system or gall bladder with clinical and/or radiologic evidence of unresectable, locally advanced or metastatic disease. Patients with ampullary carcinoma are not eligible. Patients must have measurable disease.

Patients must have completed any prior chemotherapy at least 21 days prior to registration and have recovered from any of the effects. Patients must have experienced progression to no more than one prior regimen of systemic chemotherapy for advanced biliary cancer. Patients who received adjuvant chemotherapy and had evidence of disease recurrence within 6 months of completion of the adjuvant treatment are also eligible. Patients must not have been treated with prior MEK inhibitors. Prior 5-FU or capecitabine treatment is allowed only if given as a radiosensitizer concurrently with radiation therapy at least 12 weeks prior to registration or if given as part of any adjuvant therapy regimen at least 12 months prior to study enrollment. For patients who have received prior cryotherapy, radiation therapy, radiofrequency ablation, therasphere, ethanol injection, transarterial chemoembolization (TACE) or photodynamic therapy, 28 days must have elapsed since that therapy.

Patients must have a Zubrod performance status of 0-1. Patients must have adequate hematologic, hepatic, renal and cardiac function. Patients with known history or current evidence of retinal vein occlusion (RVO) or central serous retinopathy (CSR) are not eligible. Patients must not have active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection. Patients with chronic or cleared HBV and HCV infection are eligible. HIV-positive patients on combination antiretroviral therapy are not eligible.

Stratification/Descriptive Factors

Patients are stratified by (1) planned chemotherapy if randomized to Arm 2: 5FU/LV vs Capecitabine; and (2) site: cholangiocarcinoma vs gall bladder.

Accrual Goals

A total of 80 eligible patients will be randomized to this study. An interim assessment of objective response will be performed on the first 14 patients registered to the trametinib arm (Arm 1). The study will not close during this assessment. If none of these first 14 patients respond to treatment then the study may be closed to further accrual.

Summary Statement

On April 24, 2015, the study statistician informed the study team that the interim analysis showed that the lack of measurable response in the trametinib arm ruled out the pre-specified treatment benefit with high confidence. The study permanently closed to accrual on May 15, 2015 with 53 patients enrolled. Eleven patients are ineligible due to: inadequate baseline labs (2 patients), receiving chemotherapy within 21 days of registration (2), not receiving prior chemotherapy (2), insufficient documentation of baseline data (2), receiving more than one line of systemic chemotherapy, baseline labs completed after registration, and no evidence of measurable disease (1 patient each). One patient withdrew consent prior to starting protocol therapy and is not included in any analyses. Two patients did not receive protocol treatment and thus are not assessable for adverse events. Both are considered major protocol deviations.

One patient refused further treatment and withdrew consent. One patient was hospitalized prior to starting protocol treatment (coded as 'Other' in the Treatment Summary table).

Twenty-one patients on the trametinib arm have been assessed for adverse events. One patient died due to vomiting and two additional patients reported treatment-related Grade 4 adverse events including bilirubin increase and sepsis. Four additional patients on this arm experienced Grade 3 events including duodenitis (reported as 'GI disorders-Other'). Seventeen patients on the chemotherapy arm have been assessed for adverse events. Six patients have experienced treatment-related Grade 3 adverse events including fever (reported as 'Infections/infestations-Other').

Six patients remain on protocol treatment. Institutions are encouraged to submit data in a timely fashion to ensure rapid reporting of the study results as the data mature. A complete report will be provided in the Spring 2016 Report of Studies.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
So Calif, U of	7	City of Hope Med Ctr	1
Yale University	5	CRC West MI NCORP	1
Michigan, U of	4	Greenville NCORP	1
Southeast COR NCORP	4	Heartland NCORP	1
Columbia MU-NCORP	3	Loyola University	1
Davis, U of CA	3	Michigan CRC NCORP	1
Sutter Cancer RC	3	Montana NCORP	1
Columbus NCORP	2	Oklahoma, Univ of	1
Florida, Univ of/Yale University	2	Oregon Hlth Sci Univ	1
Irvine, U of CA	2	Rochester, Univ of	1
KaiserPermanenteSCAL/Kaiser Vallejo NCORP	2	Utah, U of	1
Kansas, U of	2	Wayne State Univ	1
Ohio State Univ	2	**Total (25 Institutions)**	**53**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of July 23, 2015

	TOTAL	Trametinib	5-FU +Leucovorin /Capecitabine
NUMBER REGISTERED	53	27	26
INELIGIBLE	11	4	7
ELIGIBLE	42	23	19
Analyzable, Pend. Elig.	1	0	1
Not Analyzable	1	1	0
BASELINE DISEASE STATUS			
Measurable	40	22	18
Too Early	1	0	1
ADVERSE EVENT ASSESSMENT			
Evaluable	38	21	17
Not Evaluable	2	1	1
Too Early	1	0	1

Patient Characteristics

Registrations ending June 30, 2015; Data as of July 23, 2015

	Trametinib (n=22)		5-FU +Leucovorin /Capecitabine (n=19)	
AGE				
Median	62.9		65.1	
Minimum	39.6		40.5	
Maximum	77.5		81.4	
SEX				
Males	5	23%	9	47%
Females	17	77%	10	53%
HISPANIC				
Yes	3	14%	0	0%
No	19	86%	19	100%

	Trametinib (n=22)		5-FU +Leucovorin /Capecitabine (n=19)	
RACE				
White	15	68%	15	79%
Black	4	18%	2	11%
Asian	2	9%	2	11%
Unknown	1	5%	0	0%
PLANNED CHEMOTHERAPY				
5-FU+Leucovorin	7	32%	6	32%
Capecitabine	15	68%	13	68%
SITE				
Cholangiocarcinoma	17	77%	15	79%
Gall bladder	5	23%	4	21%

Treatment Summary

Registrations ending June 30, 2015; Data as of July 23, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	6
NUMBER OFF PROTOCOL TREATMENT	35
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	1
Refusal unrelated to adverse event	1
Progression/relapse	32
Death	0
Other - not protocol specified	1
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	2

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

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, 2015; Data as of July 23, 2015

	Trametinib (n=21) Grade						5-FU+Leucovorin/Capecitabine (n=17) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	19	1	0	1	0	0	17	0	0	0	0	0
AST increased	19	0	1	1	0	0	15	2	0	0	0	0
Anemia	18	1	1	1	0	0	11	3	3	0	0	0
Ascites	20	0	0	1	0	0	17	0	0	0	0	0
Blood bilirubin increased	20	0	0	0	1	0	16	0	1	0	0	0
Colitis	21	0	0	0	0	0	16	0	0	1	0	0
Fatigue	16	2	3	0	0	0	11	3	2	1	0	0
GI disorders-Other, specify	20	0	0	1	0	0	17	0	0	0	0	0
Gastric ulcer	20	0	0	1	0	0	17	0	0	0	0	0
Gastritis	20	0	0	1	0	0	17	0	0	0	0	0
Generalized muscle weakness	21	0	0	0	0	0	16	0	0	1	0	0
Hyponatremia	20	0	0	1	0	0	16	0	0	1	0	0
Infections/infestations-Other	21	0	0	0	0	0	16	0	0	1	0	0
Mucositis oral	20	1	0	0	0	0	14	1	1	1	0	0
Neutrophil count decreased	20	1	0	0	0	0	15	0	1	1	0	0
Pain in extremity	21	0	0	0	0	0	16	0	0	1	0	0
Sepsis	20	0	0	0	1	0	17	0	0	0	0	0
Thromboembolic event	20	0	0	1	0	0	17	0	0	0	0	0
Urinary tract infection	20	0	0	1	0	0	17	0	0	0	0	0
Vomiting	15	4	1	0	0	1	15	2	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	2	7	5	4	2	1	1	2	8	6	0	0

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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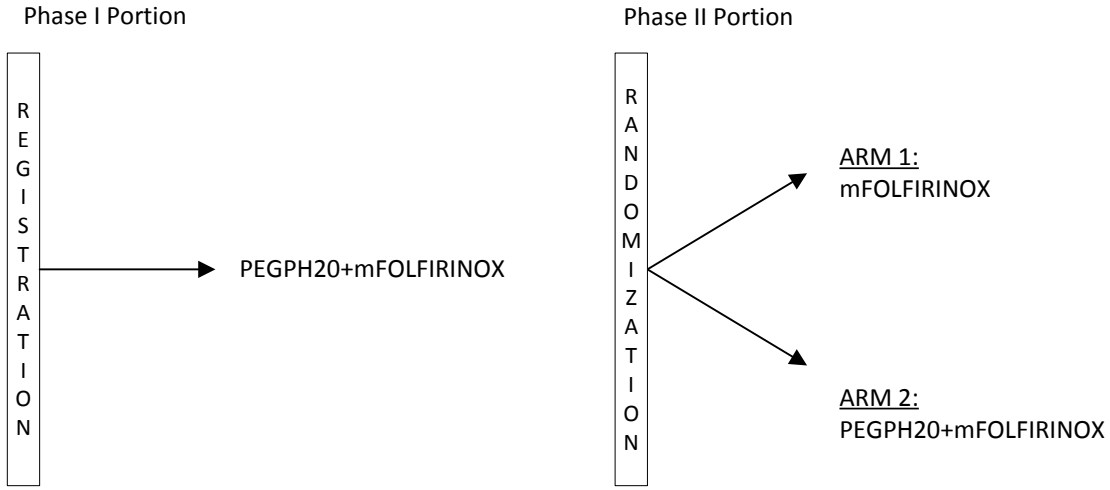
Study Chairs:
R Ramanathan, S Hingorani, P Philip

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.

To explore the correlation of maximum decrease in CA 19-9 levels and time to maximum decrease in CA 19-9 levels with overall survival, progression-free survival and response.

To explore the correlation of plasma hyaluronan (HA) and tumor expression of HA with overall survival, progression-free survival and response.

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 138 eligible patients. An interim analysis will be performed when one-third of the events have been observed. Evidence suggesting early termination would consist of rejection at a one-sided 0.07 level of the test for the alternative hypothesis.

Summary Statement

The Phase I portion of this trial was closed to accrual on April 1, 2015 with five patients enrolled on the first cohort (mFOLFIRINOX + PEGPH20 3 mcg/kg on day 1 and day 3 or 4), and seven patients on the second cohort (mFOLFIRINOX + PEGPH20 3 mcg/kg on day 1 only).

Five patients on the first cohort were assessed for dose-limiting toxicities (DLT). Two patients experienced a DLT, one due to Grade 3 myalgia, and the other due to Grade 3 fatigue and mucositis oral. Six patients on the second cohort were assessed for DLTs. One additional patient was not evaluable for DLTs due to confounding factors. One patient experienced a DLT due to Grade 3 elevated alkaline phosphatase. Per protocol, the recommended Phase II dose is mFOLFIRINOX + PEGPH20 3 mcg/kg on Day 1.

The Phase II portion of the trial was opened to accrual on May 22, 2015. As of June 30, 2015, 2 patients have enrolled to the Phase II portion of the trial, both from Yale University.

S1316 Pilot

Prospective Comparative Effectiveness Trial For Malignant Bowel Obstruction

---

Participants:
SWOG, Alliance

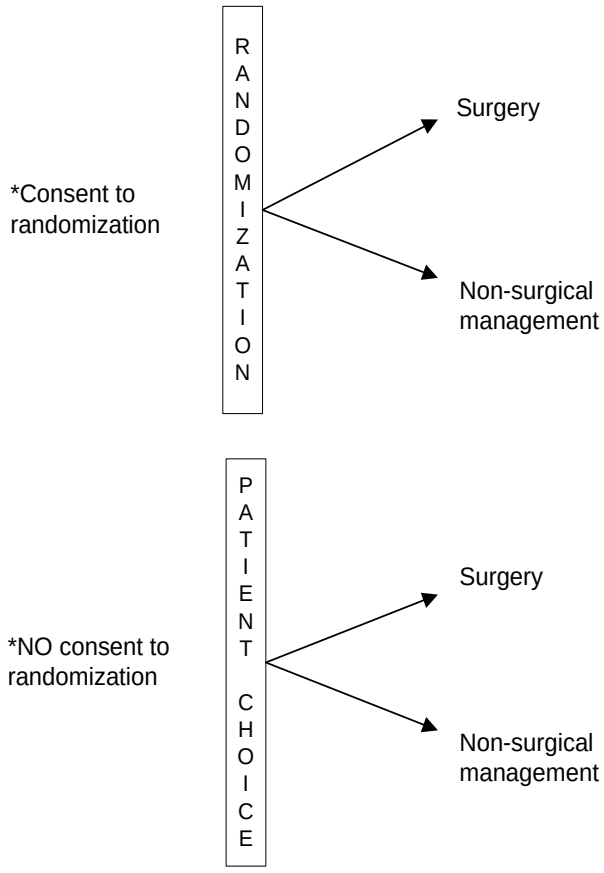
Date Activated:
03/09/2015

Study Chairs:
R Krouse, B Bagwell, A Abernethy

Statisticians:
G Anderson, K Arnold

Data Coordinator:
R Topacio

SCHEMA



*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 surgical consult for MBO 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

Participant 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 with a target of at least 50 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

---

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

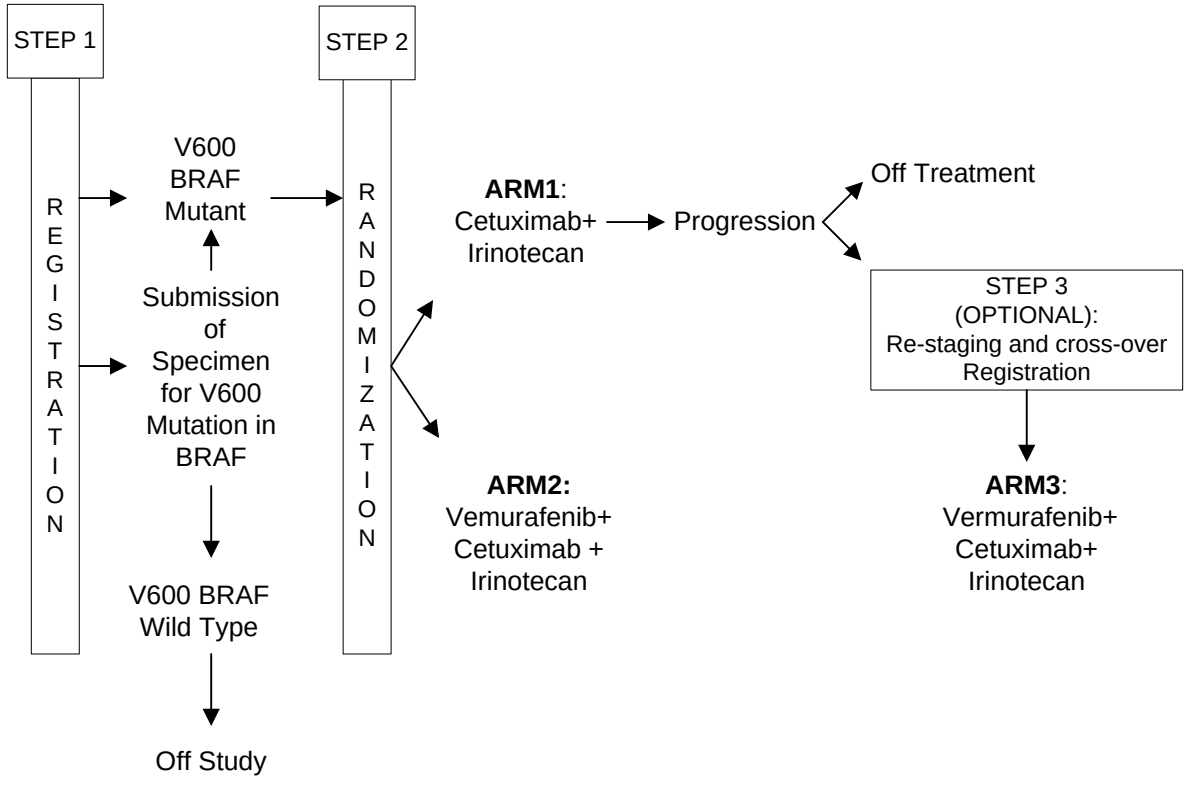
Date Activated:
11/13/2014

Study Chairs:
S Kopetz, H Lenz

Statisticians:
S McDonough, K Guthrie

Data Coordinator:
C McLeod

SCHEMA



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.

To evaluate genetic alterations, including low-frequency KRAS or NRAS mutations (definitive list of genes to be finalized after completion of enrollment based on latest scientific knowledge) as detected by high-depth sequencing as predictive biomarkers of efficacy.

To evaluate PIK3CA pathway activation through PIK3CA mutations or PTEN protein loss as a predictive biomarker of innate resistance to this regimen.

To evaluate gene expression signatures from screened patients with BRAF wild-type and BRAF V600E tumors.

To provide validation of BRAF IHC using complementary sequencing methodology from screened patients with BRAF wild-type and BRAF V600E tumors.

To confirm the estimated sensitivity of detectable BRAF V600E circulating cell-free DNA as a non-invasive biomarker for BRAF V600E mutation as detected by IHC in the primary tumor.

To correlate radiographic tumor response with change in quantification of BRAF V600E alleles in circulating cell-free DNA.

To monitor for known mechanisms of acquired resistance to EGFR inhibition in circulating cell-free DNA (KRAS, NRAS mutations).

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 72 eligible patients will be randomized to this study. An interim analysis will be performed when half of the expected events have been observed.

Summary Statement

As of June 30, 2015, 57 patents have been enrolled to the initial screening. Eighteen 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). One patient was found to be BRAF mutant, but was not randomized to protocol treatment. Thirty-five patients were randomized to protocol treatment.

One patient did not start protocol treatment due to poor prognosis (coded as 'Other' in the Treatment Summary Table). This is considered a major protocol deviation and the patient is not assessable for adverse events.

On the cetuximab + irinotecan arm, eleven patients have been assessed for adverse events. No patients have experienced Grade 4 adverse events and five have experienced Grade 3 treatment-related adverse events. On the vemurafenib + cetuximab + irinotecan arm, eleven patients have been assessed for adverse events and three have experienced Grade 4 treatment-related adverse events. Five additional patients on this arm experienced Grade 3 treatment-related adverse events.

Four patients have enrolled to crossover for treatment with vemurafenib + cetuximab + irinotecan. Of the 3 patients that have been assessed for adverse events, one has experienced Grade 3 treatment-related adverse events.

Registration by Institution

Initial Registration

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	9	Arnot Ogden Med Ctr/Rochester, Univ of	1
MD Anderson CC	8	Columbus NCORP	1
Kaiser Vallejo NCORP	7	Fred Hutchinson CRC	1
ECOG-ACRIN	5	Hawaii MU-NCORP	1
Kansas, U of	5	Michigan, U of	1
NRG	3	Ozarks NCORP	1
Southeast COR NCORP	3	PCRC NCORP	1
City of Hope Med Ctr	2	San Antonio, U of TX	1
Colorado, U of	2	Wayne State Univ	1
Michigan CRC NCORP	2	**Total (20 Institutions)**	**57**
Yale University	2		

Registration, Eligibility, and Evaluability

Randomization

Registrations ending June 30, 2015; Data as of July 24, 2015

	TOTAL	Cetuximab + Irinotecan	Vemurafenib +Cetux +Irinotecan
NUMBER REGISTERED	35	17	18
ELIGIBLE	35	17	18
Analyzable, Pend. Elig.	25	12	13
BASELINE DISEASE STATUS			
Measurable	8	5	3
Too Early	27	12	15
ADVERSE EVENT ASSESSMENT			
Evaluable	22	11	11
Not Evaluable	1	1	0
Too Early	12	5	7

Patient Characteristics

Randomization

Registrations ending June 30, 2015; Data as of July 24, 2015

	Cetuximab + Irinotecan (n=17)		Vemurafenib +Cetux +Irinotecan (n=18)	
AGE				
Median	61.6		59.6	
Minimum	30.5		36.3	
Maximum	80.4		81.7	
SEX				
Males	4	24%	10	56%
Females	13	76%	8	44%
HISPANIC				
Yes	2	12%	0	0%
No	15	88%	18	100%
RACE				
White	17	100%	16	89%
Asian	0	0%	2	11%
PRIOR TREATMENT WITH IRINOTECAN				
Yes	8	47%	9	50%
No	9	53%	9	50%

Treatment Summary

Randomization

Registrations ending June 30, 2015; Data as of July 24, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	20
NUMBER OFF PROTOCOL TREATMENT	15
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	4
Refusal unrelated to adverse event	0
Progression/relapse	1
Death	0
Other - not protocol specified	1
Reason under review	9
MAJOR PROTOCOL DEVIATIONS	1

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

Randomization

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending June 30, 2015; Data as of July 24, 2015

	Cetuximab + Irinotecan (n=11) Grade						Vemurafenib+Cetux+Irinotecan (n=11) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	9	2	0	0	0	0	10	1	0	0	0	0
AST increased	8	3	0	0	0	0	11	0	0	0	0	0
Abdominal distension	10	1	0	0	0	0	11	0	0	0	0	0
Abdominal pain	9	2	0	0	0	0	10	0	1	0	0	0
Acute kidney injury	11	0	0	0	0	0	10	1	0	0	0	0
Alkaline phosphatase increased	8	3	0	0	0	0	11	0	0	0	0	0
Alopecia	9	2	0	0	0	0	8	2	1	0	0	0
Anemia	10	1	0	0	0	0	8	1	1	1	0	0
Anorexia	8	1	1	1	0	0	11	0	0	0	0	0
Arthralgia	11	0	0	0	0	0	5	2	0	4	0	0
Blood bilirubin increased	11	0	0	0	0	0	10	1	0	0	0	0
Chills	11	0	0	0	0	0	10	1	0	0	0	0
Constipation	9	2	0	0	0	0	11	0	0	0	0	0
Cough	10	1	0	0	0	0	11	0	0	0	0	0
Dehydration	10	0	1	0	0	0	10	0	1	0	0	0
Diarrhea	7	2	1	1	0	0	4	3	1	3	0	0
Dizziness	11	0	0	0	0	0	9	1	1	0	0	0
Dry skin	7	2	2	0	0	0	11	0	0	0	0	0
Dysgeusia	10	1	0	0	0	0	10	1	0	0	0	0
Dyspnea	10	1	0	0	0	0	11	0	0	0	0	0
Fatigue	4	3	3	1	0	0	4	4	3	0	0	0

	Cetuximab + Irinotecan (n=11) Grade						Vemurafenib+Cetux+Irinotecan (n=11) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Febrile neutropenia	11	0	0	0	0	0	10	0	0	1	0	0
Fever	11	0	0	0	0	0	8	3	0	0	0	0
GI disorders-Other, specify	11	0	0	0	0	0	10	0	1	0	0	0
Generalized muscle weakness	10	1	0	0	0	0	10	1	0	0	0	0
Headache	11	0	0	0	0	0	10	1	0	0	0	0
Hot flashes	11	0	0	0	0	0	10	1	0	0	0	0
Hypoalbuminemia	11	0	0	0	0	0	10	0	1	0	0	0
Hypokalemia	9	1	1	0	0	0	7	2	1	1	0	0
Hypomagnesemia	7	3	1	0	0	0	7	4	0	0	0	0
Hyponatremia	11	0	0	0	0	0	9	2	0	0	0	0
Hypophosphatemia	11	0	0	0	0	0	10	1	0	0	0	0
Infusion related reaction	9	1	0	1	0	0	11	0	0	0	0	0
Insomnia	10	1	0	0	0	0	11	0	0	0	0	0
Lipase increased	11	0	0	0	0	0	10	0	1	0	0	0
Lung infection	11	0	0	0	0	0	10	0	1	0	0	0
Mucositis oral	11	0	0	0	0	0	9	2	0	0	0	0
Myalgia	11	0	0	0	0	0	8	1	1	1	0	0
Nail loss	10	1	0	0	0	0	11	0	0	0	0	0
Nausea	6	3	2	0	0	0	9	2	0	0	0	0
Neutrophil count decreased	9	0	2	0	0	0	8	0	0	0	3	0
Pain	11	0	0	0	0	0	10	0	0	1	0	0
Papulopustular rash	10	0	0	1	0	0	11	0	0	0	0	0
Peripheral sensory neuropathy	11	0	0	0	0	0	10	1	0	0	0	0
Platelet count decreased	10	0	1	0	0	0	10	0	0	1	0	0
Pruritus	10	0	0	1	0	0	11	0	0	0	0	0
Rash acneiform	7	4	0	0	0	0	6	2	3	0	0	0
Rash maculo-papular	9	2	0	0	0	0	10	1	0	0	0	0
Sepsis	11	0	0	0	0	0	10	0	0	0	1	0
Skin/subq tissue ds-Other	11	0	0	0	0	0	7	2	2	0	0	0
Sore throat	9	2	0	0	0	0	11	0	0	0	0	0
Vaginal dryness	10	1	0	0	0	0	11	0	0	0	0	0
Vomiting	9	0	2	0	0	0	7	4	0	0	0	0
Weight loss	10	0	1	0	0	0	10	1	0	0	0	0
White blood cell decreased	9	1	1	0	0	0	8	0	1	0	2	0
MAX. GRADE ANY ADVERSE EVENT	1	2	3	5	0	0	0	0	3	5	3	0

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

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.

To obtain objective measures of expenses, debt and credit through linkage with individual patient credit reports (TransUnion) at enrollment (baseline) and end of follow up (12 months).

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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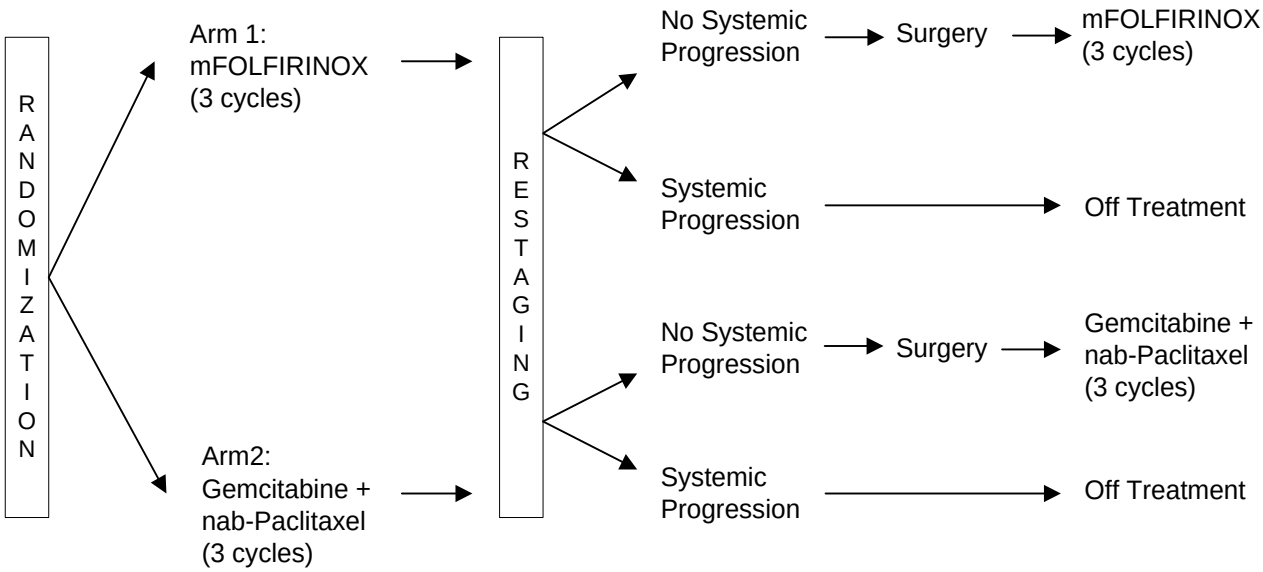
Participants:
SWOG, CTSU (supported by Alliance and NRG)

Study Chairs:
D Sohal, S Ahmad

Statisticians:
K Guthrie, S McDonough

Data Coordinator:
B Zeller

SCHEMA



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. Patients must have a surgical consult to verify that the 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.

CT scans or MRIs used to assess disease at baseline must be submitted for central review.

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. The study will be suspended pending further review if either of the following is observed: 10 failures in 40 patients or 17 failures in 80 patients.

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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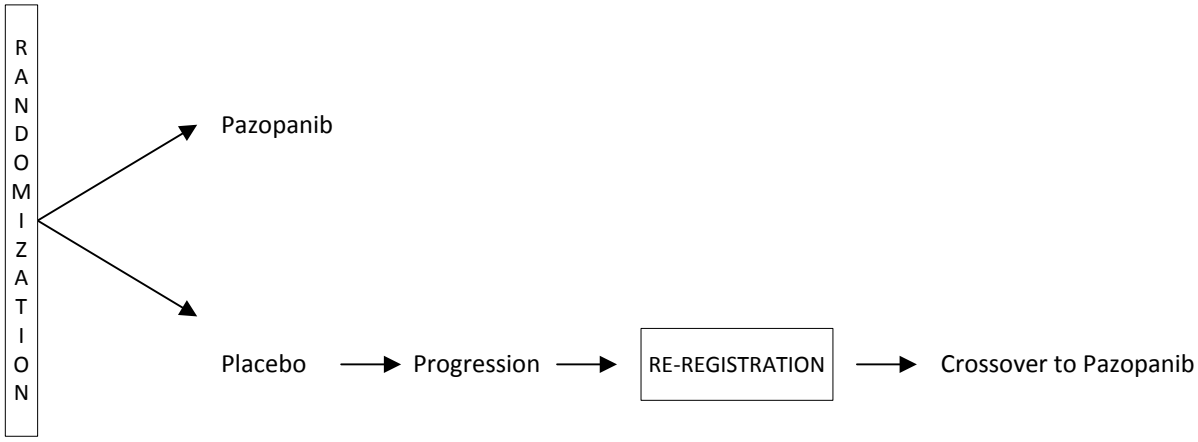
Participants:
Alliance, CTSU

Date Activated:
05/08/2013

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 estimate PFS and other indicators of efficacy in patients who crossover to pazopanib from placebo.

To estimate average time to submission of scans to the Alliance Imaging Core Laboratory (ICL) and average ICL "turn-around" time.

To estimate discordance between the local and central radiology review in assessment of progression.

To characterize the rates and quality of radiographic progression.

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 131 patients had registered to this study as of June 30, 2015, 22 from SWOG institutions. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
H Lee Moffitt CC	17
Cedars-Sinai Med Ctr	3
Methodist Hospital	1
Poudre Valley Hosp/Colorado, U of	1
San Antonio, U of TX	1
Total (5 Institutions)	**23**

C80702 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance and SWOG

A Phase III Trial of 6 Versus 12 Treatments of Adjuvant FOLFOX Plus Celecoxib or Placebo for Patients with Resected Stage III Colon Cancer

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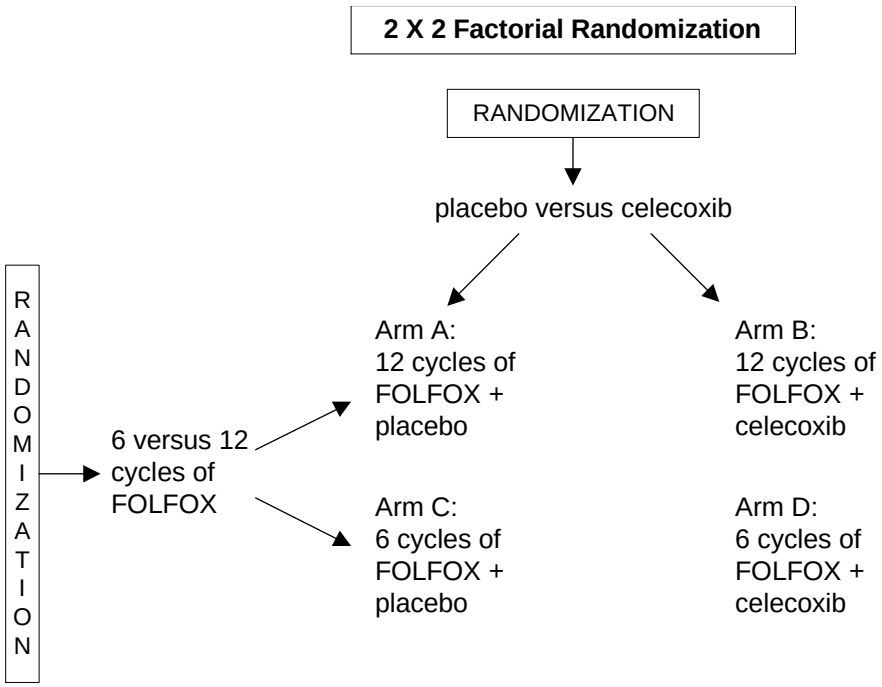
Participants:
Alliance, SWOG, CTSU

Date Activated:
06/22/2010

Study Chairs:
J Meyerhardt (Alliance), A Shields (SWOG)

Statistician:
K Guthrie

SCHEMA



Objectives

To compare disease-free survival of patients with Stage III colon cancer randomized to standard chemotherapy only (FOLFOX) or standard chemotherapy (FOLFOX) with three years of celecoxib 400 mg daily.

To contribute to an international prospective pooled analysis that will compare disease-free survival of patients with Stage III colon cancer randomized to six treatments of adjuvant FOLFOX chemotherapy or 12 treatments of adjuvant FOLFOX chemotherapy.

To compare overall survival of patients with Stage III colon cancer randomized to FOLFOX chemotherapy

only or FOLFOX chemotherapy with three years of celecoxib 400 mg daily.

To contribute to an international prospective pooled analysis that will compare overall survival of patients with Stage III colon cancer randomized to six treatments of adjuvant FOLFOX chemotherapy or 12 treatments of adjuvant FOLFOX chemotherapy.

To assess toxicities of celecoxib as maintenance adjuvant therapy in patients with Stage III colon cancer.

To assess differences in cardiovascular-specific events with celecoxib versus placebo in a population of Stage III colon cancer survivors.

To evaluate differences in toxicities, particularly cumulative peripheral neuropathy, for patients treated with six treatments of FOLFOX compared to those treated with 12 treatments of FOLFOX.

Patient Population

Patients must have histologically documented adenocarcinoma of the colon. Patients with rectal cancer are not eligible. There must be at least one pathologically confirmed positive lymph node.

Tumors must have been completely resected, with no evidence of residual involved lymph node disease or metastatic disease at the time of registration.

Patients must have an ECOG performance status 0-2 and be at least 18 years old. Patients must have adequate hematologic, cardiac, hepatic, and renal function. Patients must have no symptomatic pulmonary fibrosis, Grade 2 or higher interstitial pneumonitis, nor any Grade 2 or higher neurosensory or neuromotor toxicity. Patients must have no history of upper gastrointestinal ulceration, bleeding, or perforation within the past three years.

Stratification/Descriptive Factors

For the duration of adjuvant chemotherapy randomization (6 vs 12 cycles), treatment randomization will be stratified according to number of positive lymph nodes: 1-3 vs 4 or more.

For the randomization to celecoxib or placebo, treatment randomization will be stratified according to the following factors: (1) number of positive lymph nodes: 1-3 vs 4 or more; and (2) current regular low dose aspirin usage: yes vs no.

Accrual Goals

The accrual goal for this trial is 2,500 eligible patients. Formal interim analyses will begin when approximately 20% of the total expected events have occurred. Subsequently, interim analyses will be conducted every six months. Three interim analyses are expected during the accrual period and five during the follow-up period.

Summary Statement

Alliance reported that 2270 patients had registered to this study as of June 30, 2015, including 485 from SWOG institutions. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Kaiser Vallejo NCORP	64	Desert Hospital	5
Kansas, U of	32	Gulf South MU-NCORP	5
So Calif, U of	30	KaiserPermanenteCOL/Kaiser Vallejo NCORP	5
KaiserPermanenteSCAL/Kaiser Vallejo NCORP	29	Northwest NCORP	5
Heartland NCORP	25	Oregon Hlth Sci Univ	5
Cleveland Clinic OH	23	Wichita NCORP	5
Davis, U of CA	14	Columbia MU-NCORP	4
Wayne State Univ	14	Michigan, U of	4
Hawaii MU-NCORP	13	St Joseph Med Ctr/PCRC NCORP	4
Rochester, Univ of	12	Stormont-Vail Health/Kansas, U of	4
Baylor College	10	U of Tennessee MC/Tennessee, U of	4
Ozarks NCORP	10	Christian Hospital/St Louis University	3
MD Anderson CC	9	Cincinnati MC, U of	3
Providence Hosp	9	Harrison Bremerton/Harrison Medical Ctr	3
St Luke's Mt State/PCRC NCORP	9	LSU-Shreveport/Gulf South MU-NCORP	3
Michigan CRC NCORP	8	Poudre Valley Hosp/Colorado, U of	3
Presbyterian Hosp/Irvine, U of CA	8	Scott & White CCOP	3
Columbus NCORP	7	Singing River Hosp/Mississippi, Univ of	3
Thompson Ca Surv Ctr/San Antonio, U of TX	7	St Mary Med Ctr/PCRC NCORP	3
Salem Hospital/Oregon Hlth Sci Univ	6	All Other Institutions	61
Upstate Carolina	6	**Total (84 Institutions)**	**485**
Boston MC MBCCOP	5		

E2211 Phase II SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Randomized Phase II Study of Temozolomide or Temozolomide and Capecitabine in Patients with Advanced Pancreatic Neuroendocrine Tumors

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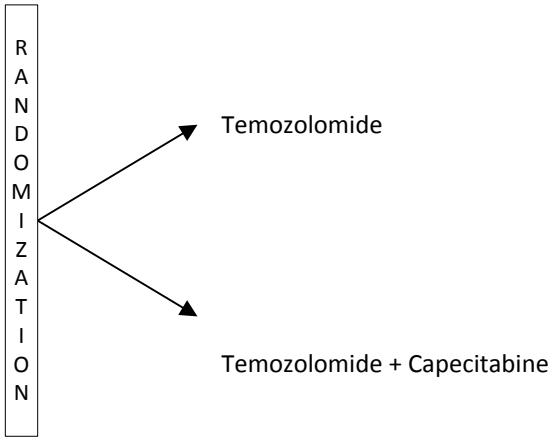
Participants:
ECOG-ACRIN, CTSU

Date Activated:
04/22/2013

Study Chairs:
P Kunz (ECOG-ACRIN), J Strosberg (SWOG)

SCHEMA



Objectives

To evaluate progression-free survival (PFS) associated with temozolomide alone or temozolomide and capecitabine in patients with advanced pancreatic neuroendocrine tumors.

To evaluate response rates (RR) associated with temozolomide alone or temozolomide and capecitabine treatment in patients with advanced pancreatic neuroendocrine tumors.

To evaluate overall survival (OS) associated with temozolomide alone or temozolomide and capecitabine in patients with advanced pancreatic neuroendocrine tumors.

To evaluate the toxicity associated with temozolomide alone or temozolomide and capecitabine in patients with advanced pancreatic neuroendocrine tumors.

To evaluate the usefulness of MGMT status (by IHC and promoter methylation) for predicting response in pancreatic neuroendocrine tumor patients treated with either temozolomide or temozolomide and capecitabine.

To bank radiology images for evaluation of quality, reproducibility, and compliance with CT methodology.

Patient Population

Patients must have histologically or pathologically confirmed locally unresectable or metastatic low or intermediate grade pancreatic neuroendocrine tumor, excluding small cell carcinoma. Patients must have measurable disease. Patients must have documented

disease progression within 12 months prior to randomization. Patients with either clinically apparent central nervous system metastases or carcinomatous meningitis are not eligible.

Patients must not have received prior temozolomide, DTIC, capecitabine, or 5-FU therapy. Prior everolimus or sunitinib therapy is allowed, provided therapy was discontinued at least four weeks prior to randomization.

Patients must be at least 18 years of age and have ECOG performance status 0-1. Patients must have adequate hematologic and hepatic function. Patients must not have active or uncontrolled infection or serious medical or psychiatric illness. Patients must not have a history of the following within 12 months prior to registration: arterial thromboembolic event, unstable angina, or myocardial infarction. Patients with symptomatic peripheral vascular disease are not eligible.

Stratification/Descriptive Factors

Treatment randomization will be stratified according to the following factors: (1) prior treatment with everolimus: yes vs no; (2) prior treatment with sunitinib: yes vs no; and (3) concurrent administration of octreotide: yes vs no.

Accrual Goals

The accrual goal for this study is 138 eligible patients. Allowing for an ineligibility rate of 5%, it is anticipated that 145 patients will be randomized.

Summary Statement

ECOG-ACRIN reported that 100 patients had registered to this study as of June 30, 2015, including 37 from SWOG institutions. The complete Spring 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
H Lee Moffitt CC	9	Kaiser Vallejo NCORP	1
Cedars-Sinai Med Ctr	7	KaiserPermanenteSCAL/Kaiser Vallejo NCORP	1
Kansas, U of	4	Kansas City NCORP	1
Rochester, Univ of	3	Lahey Hosp & Med Ctr	1
Cincinnati MC, U of	2	Loyola University	1
Kentucky, U of	2	Michigan, U of	1
Boston Medical Ctr	1	So Calif, U of	1
Cleveland Clinic OH	1	**Total (16 Institutions)**	**37**
Greenville NCORP	1		

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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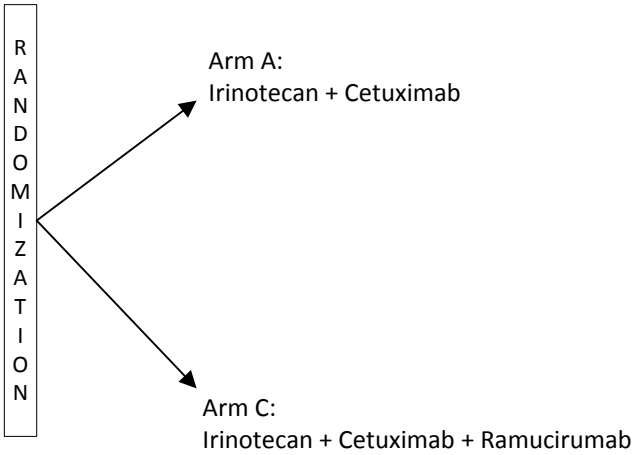
Participants:
ECOG-ACRIN, CTSU

Date Activated:
07/18/2012

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 67 patients had registered to this study as of June 30, 2015, eight from SWOG institutions. The complete Spring 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
Yale University	5
So Calif, U of	3
Total (2 Institutions)	**8**

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

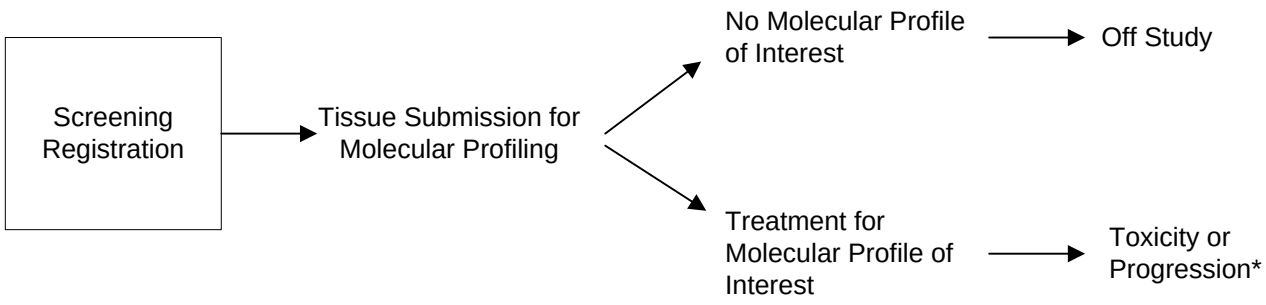
NCI-MATCH: Molecular Analysis for Therapy Choice

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)

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.

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.

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 and protein-based assessment platforms.

Patient Population

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma 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, have tumor amenable to image guided or direct vision biopsy, and be willing and able to undergo biopsy for molecular profiling.

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 initial registration. Patients must not require the use of full dose coumarin-derivative anticoagulants such as warfarin. Low molecular weight heparin is permitted for prophylactic or therapeutic use.

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. 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 be completed in 7.5 years, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. 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 August 12, 2015, with ten subprotocols included in the activation. Only sites utilizing the CIRB as their IRB of record will be able to participate in the trial.

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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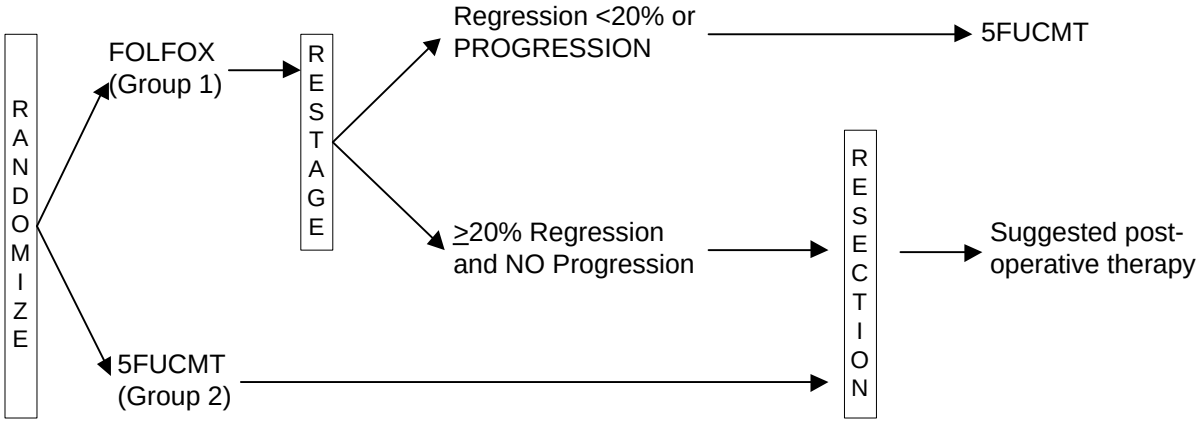
Participants:
Alliance, CTSU

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 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 (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 1000 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 369 patients had registered to this study as of June 30, 2015, including 61 from SWOG institutions. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Kaiser Vallejo NCORP	12	San Diego, U of CA	4
Rochester, Univ of	10	Davis, U of CA	2
Baylor College	6	Lahey Hosp & Med Ctr	2
Irvine, U of CA	5	Michigan, U of	1
KaiserPermanenteSCAL/Kaiser Vallejo NCORP	5	PCRC NCORP	1
Arizona MC, U of	4	Utah, U of	1
Fred Hutchinson CRC	4	**Total (14 Institutions)**	**61**
Methodist Hospital	4		

R0848 Phase III SWOG Supported CTSU Study

Coordinating Group: NRG and SWOG

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

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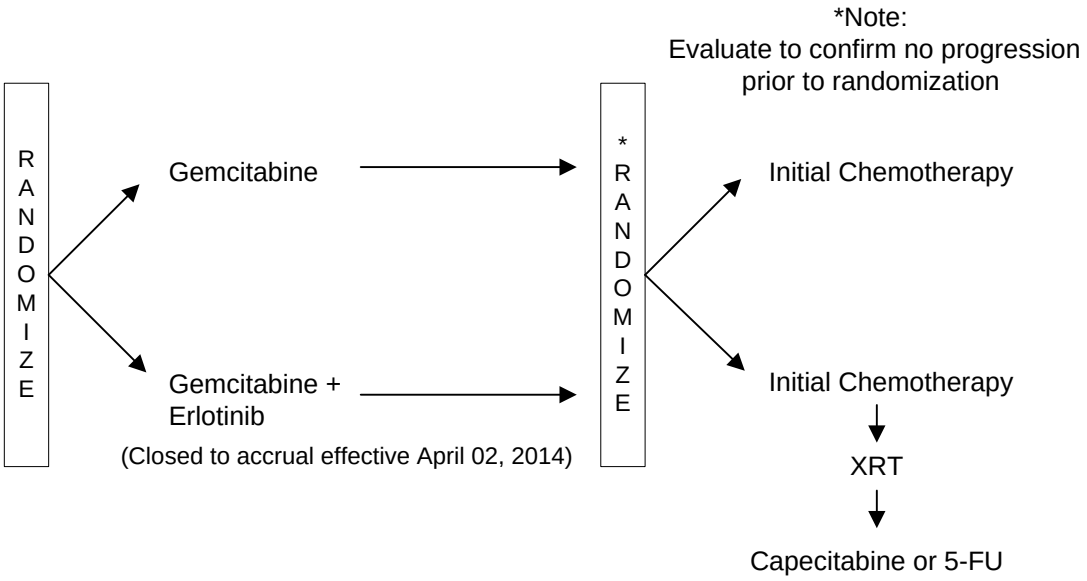
Participants:
NRG, SWOG, CTSU

Date Activated:
12/08/2009

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 the predictive roles of KRAS mutations and epithelial to mesenchymal transition (EMT) phenotype in response to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor in early-stage pancreas cancer.

To determine the frequency of EGFR-activated pathway and its influence on outcome in patients treated with gemcitabine and/or erlotinib, the association between developmental molecular markers and outcome of therapy, the phenotype and genotype of tumors in patients with recurrence after resection.

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. Three interim analyses will be performed.

Summary Statement

NRG reported that as of June 30, 2015, 413 patients had been accrued, including 16 patients from SWOG institutions. The complete July 2015 summary of this study from NRG is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
Edward Hospital/Loyola University	4
Irvine, U of CA	3
Northwest NCORP	3
Columbia MU-NCORP	2
Greenville NCORP	1
Stormont-Vail Health/Kansas, U of	1
Valley Hospital/Columbia University	1
Wichita NCORP	1
Total (8 Institutions)	**16**

R1010 Phase III SWOG Supported CTSU Study

Coordinating Group: NRG

A Phase III Trial Evaluating the Addition of Trastuzumab to Trimodality Treatment of HER2-Overexpressing Esophageal Adenocarcinoma

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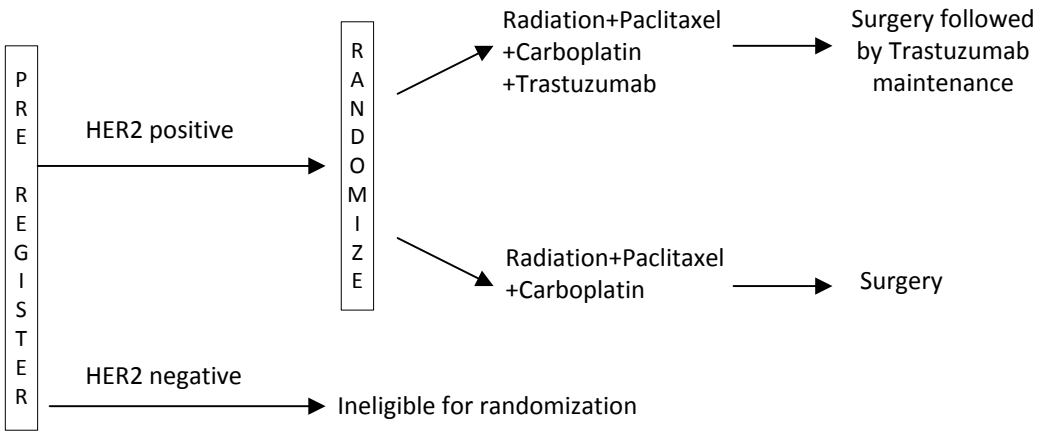
Participants:
NRG, CTSU

Date Activated:
01/07/2011

Study Chairs:
H Safran (NRG), L Leichman (SWOG)

SCHEMA



Objectives

To determine if trastuzumab increases disease-free survival when combined with trimodality treatment (radiation plus chemotherapy followed by surgery) for patients with HER2-over expressing esophageal adenocarcinoma.

To evaluate if the addition of trastuzumab to tri-modality treatment increases the pathologic complete response rate and overall survival for patients with HER2-overexpressing esophageal adenocarcinoma.

To develop a tissue bank of tumor tissue from patients with non-metastatic esophageal adenocarcinoma.

To determine molecular correlates of complete pathologic response, disease-free survival, and overall survival for patients with HER2-overexpressing esophageal adenocarcinoma treated with neoadjuvant and maintenance trastuzumab.

To evaluate predictors of cardiotoxicity in patients with esophageal cancer treated with trastuzumab and chemoradiation.

To evaluate adverse events associated with the addition of trastuzumab to trimodality treatment for patients with non-metastatic esophageal adenocarcinoma.

To determine if the addition of trastuzumab to trimodality treatment improves the patient-reported Functional Assessment of Cancer Therapy for Esophageal Cancer (FACT-E) Esophageal Cancer Subscale (ECS) score.

To determine if an improvement in the FACT-E ECS score at 6-8 weeks post completion of neoadjuvant chemoradiation correlates with pathologic complete response.

To determine if pathologic complete response correlates with the FACT-E ECS score at one year and/or two years from the start of chemoradiation.

To determine if the addition of trastuzumab to trimodality treatment improves the Swallow Index and Eating Index Subscale scores of the FACT-E.

To determine if the addition of trastuzumab to paclitaxel, carboplatin, and radiation impacts quality-adjusted survival.

Patient Population

Patients must have pathologically confirmed primary adenocarcinoma of the esophagus that involves the mid (up to 25 cm), distal, or esophagogastric junction. The cancer may involve the stomach up to 5 cm. Patients must have had an endoscopy with biopsy. Patients must be stage T1N1-2, T2-3N0-2 according to the American Joint Committee on Cancer (AJCC) seventh edition staging, based upon the following minimum diagnostic work-up: chest/abdominal/pelvic CT or whole-body PET/CT; patients must have regional adenopathy including paraesophageal, gastric, gastrohepatic and celiac nodes; patients with tumors at the level of the carina or above must undergo bronchoscopy to exclude fistula. Patients with evidence of tracheoesophageal fistula or invasion into the trachea or major bronchi are not eligible. Patients with cervical esophageal carcinoma are not eligible.

Patients may not have received any of the following prior therapies: systemic chemotherapy for esophageal cancer, radiation for esophageal cancer, chest radiotherapy, anthracycline, taxane, any agent targeting the HER2 pathway or HER1 (EGFR) pathway, or trastuzumab.

Patients must be at least 18 years of age and have Zubrod performance status of 0-2. Patients must have adequate renal, hepatic, cardiac and bone marrow function, as defined in the protocol. Patients with medical contraindications to esophagectomy or prior allergic reaction to the study drugs involved in this protocol or to a monoclonal antibody are not eligible. Patients with acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration are not eligible.

Stratification/Descriptive Factors

Patient randomization will be stratified by presence of adenopathy: no vs yes - celiac absent vs yes - celiac present up to 2 cm.

Accrual Goals

The study is estimated to accrue 480 patients to randomize a total of 160 eligible HER2-positive patients.

Summary Statement

NRG reported that 187 HER2-positive patients have been randomized to this study as of June 30, 2015, including five from SWOG institutions. The complete July 2015 summary of this study from NRG is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
Heartland NCORP	2
Salem Hospital/Oregon Hlth Sci Univ	2
Irvine, U of CA	1
Total (3 Institutions)	**5**

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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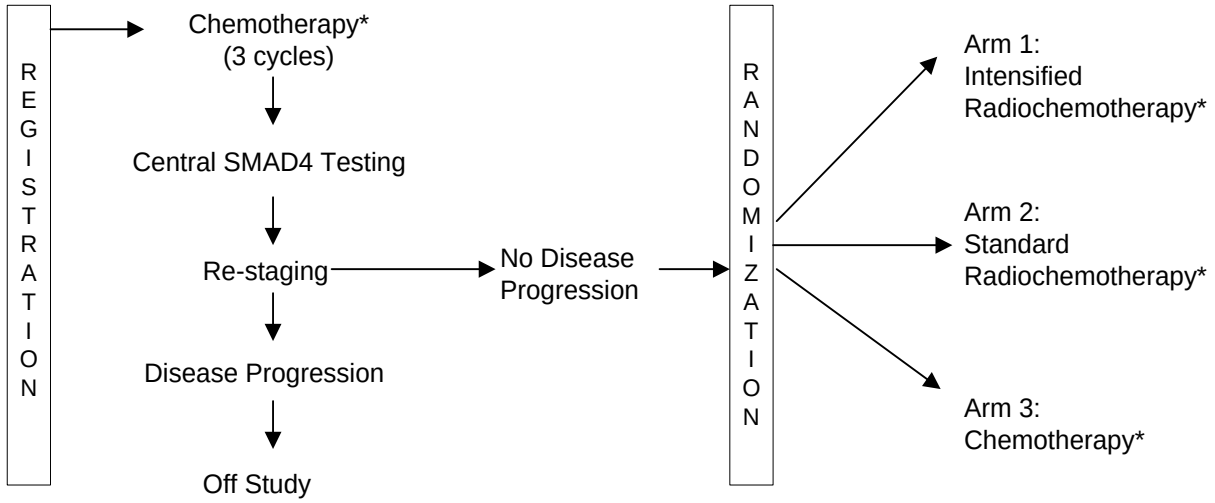
Participants:
NRG, CTSU

Date Activated:
08/14/2013

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

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
A total of 288 eligible patients will be randomized in this study. 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, 2015, one patient has been accrued (none from SWOG).