GASTROINTESTINAL COMMITTEE

CONTENTS

Patient Registrations to Studies

by 12 Month Intervals
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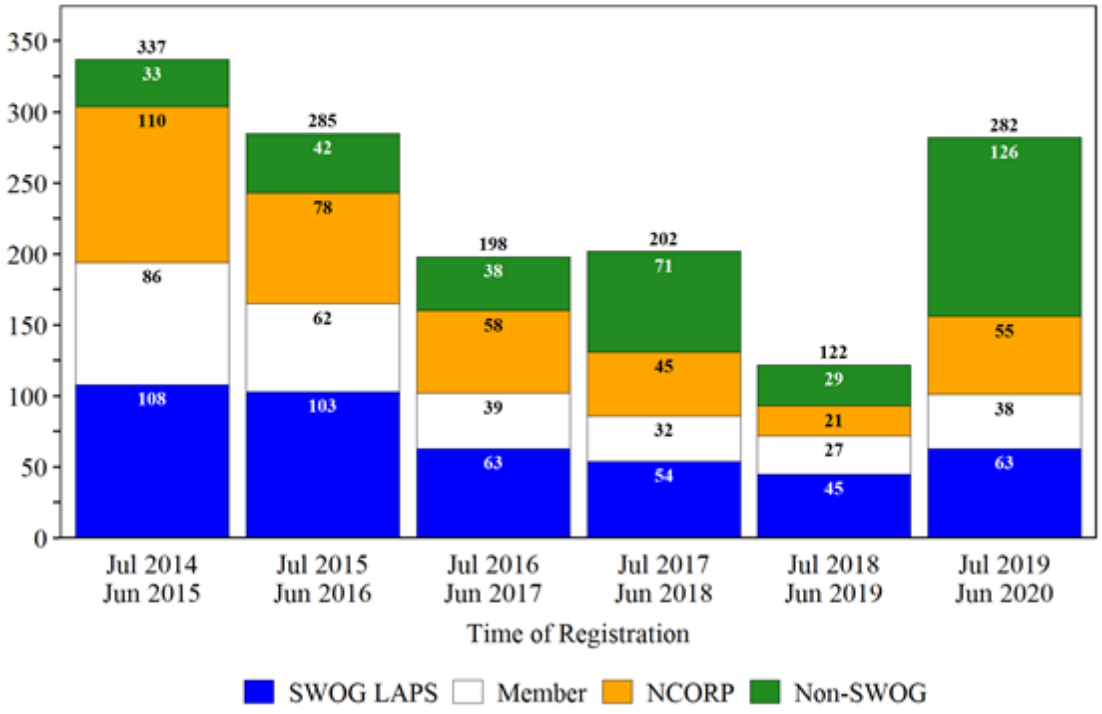

Screening registrations and registrations to Biologic only studies are excluded.

Patient Registrations by Study and Arm

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	Jan 2020 Jun 2020	Jul 2019 Dec 2019	Jan 2019 Jun 2019	All Patients
S1613 mCRC, Adv/Met, TP vs CETIRI				
Screening				
Screening	28	8	38	184
Randomization				
Trastuzumab + Pertuzumab	3	1	4	15
Cetuximab + Irinotecan	4	2	5	18
	7	3	9	33
Crossover				
Crossover: Trastuz + Pertuz	2	1	5	11
S1815 Biliary, Met/LocAdv, GC+CPT±Nab-paclitaxel				
Randomization				
Gem+Cisplatin+Nab-paclitaxel	55	95	29	179
Gemcitabine + Cisplatin	24	55	14	93
	79	150	43	272
S1922 Small Bowel,Ram+Pac vs FOLFIRI, mets/unresect				
Randomization				
FOLFIRI	1	0	0	1

Non-SWOG Studies with SWOG-Credited Registrations

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Studies with Accrual from January 2019 - June 2020

	SWOG Champion	SWOG Accrual Jan 2020 Jun 2020	SWOG Accrual Jul 2019 Dec 2019	SWOG Accrual Jan 2019 Jun 2019	SWOG Total	Total Accrued
A021501 Adeno Panc,Borderline Resect,Chemo vs ChemoRT		0	0	1	16	126
Date Activated: 12/01/16 Date Closed: 05/31/19						
Most Recent Progress Report						
A021502 Colon, Stg III, Chemo +/- Atezol, ATOMIC	C Lieu	6	6	7	28	321
Date Activated: 09/12/17						
Most Recent Progress Report						
A021602 PANC, Adv PNET Blinded Cabozantinib v Placebo	J Strosberg	2	5	1	8	62
Date Activated: 07/18/18						
Most Recent Progress Report						
A021703 COLON, Adv/Met, Chemo + Std v High dose V-D3	S Cohen	3	0	0	3	58
Date Activated: 09/30/19						
Most Recent Progress Report						
EA2142 GI NEC, Adv G3, EP vs TMZ + CAP	H Soares	0	1	0	5	52
Date Activated: 11/06/15						
Most Recent Progress Report						
EA2165 Anal, Stg II-III, Nivolumab after CMT	V Morris	9	5	6	22	198
Date Activated: 04/13/18						
Most Recent Progress Report						
NRGGI002 Rectal, Ph II, Sensitization using TNT	L Kachnic	0	0	6	20	6
Date Activated: 10/12/16 Date Closed: 07/02/18						
No Recent Progress Report						
NRGGI004 Colorectal, Stg IV, dMMR Immuno-Therapy	H Hochster	3	2	4	14	64
Date Activated: 11/07/17						
No Recent Progress Report						

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 (Supported by Alliance, ECOG-ACRIN, NRG)

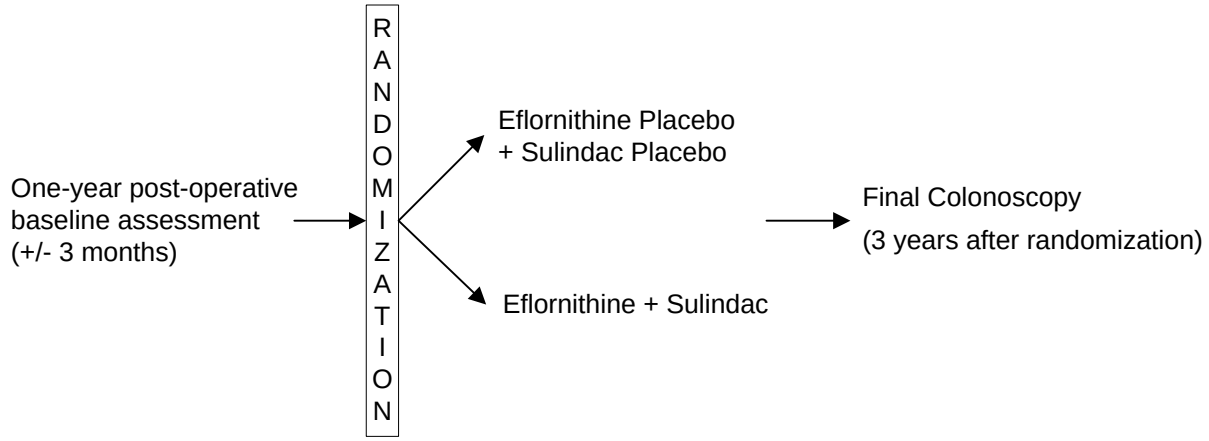
Date Activated:
03/01/2013

Study Chairs:
J Zell, P Brown, R Bergan (ECOG-ACRIN), J Dorth (NRG), Y You (Alliance)

Statisticians:
J Unger, G Anderson, K Arnold

Data Coordinator:
M Yee

SCHEMA



Objectives

To assess whether the combination of eflornithine and sulindac is effective in reducing the three-year 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 the combination of eflornithine and sulindac (compared to corresponding placebos)

has efficacy against colorectal lesions with respect to high-grade dysplasia, adenomas with villous features, adenomas 1 cm or greater, multiple adenomas, any adenomas ≥ 0.3 cm, total advanced colorectal events, or total colorectal events.

To assess quantitative and qualitative toxicities of patients when treated with the combination of eflornithine and sulindac compared to corresponding placebos.

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 (CRC) risk and adverse events.

To evaluate biomarker responses of treatment effect using novel microfluidics-based digital droplet detection system.

To explore the interaction of intervention arm and baseline statin use with respect to the 3-year event rate.

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

To perform population pharmacokinetic (PK) analysis of eflornithine and sulindac in patients with previously treated Stage 0-III colon or rectal cancer. (Sites participating in PK sampling are listed on page 1a of the protocol.)

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 120 days and 456 days (inclusive) of primary resection. Patients must show no evidence of disease based on post-operative colonoscopy (performed at least 120 days after the colon or 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, inflammatory bowel disease, biallelic mismatch repair deficiency syndrome, or constitutional mismatch repair deficiency syndrome. Patients must have a pure tone audiometry evaluation within 30 days prior to registration: patients with at least 40 dB hearing loss of any of the tested frequencies are not eligible. Patients must not be hypersensitive to selective inhibitors of cyclooxygenase-2, non-steroidal anti-inflammatory drugs, salicylates, or sulfonamides. Patients must not have documented history of gastric/duodenal ulcer within the last 12 months.

Stratification/Descriptive Factors

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

Accrual Goals

A total of 420 patients will be enrolled, 210 to each arm.

Summary Statement

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

S1316 Pilot

Coordinating Group: SWOG

Prospective Comparative Effectiveness Trial for Malignant Bowel Obstruction

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Participants:
SWOG, CTSU (Supported by Alliance)

Date Activated:
03/09/2015

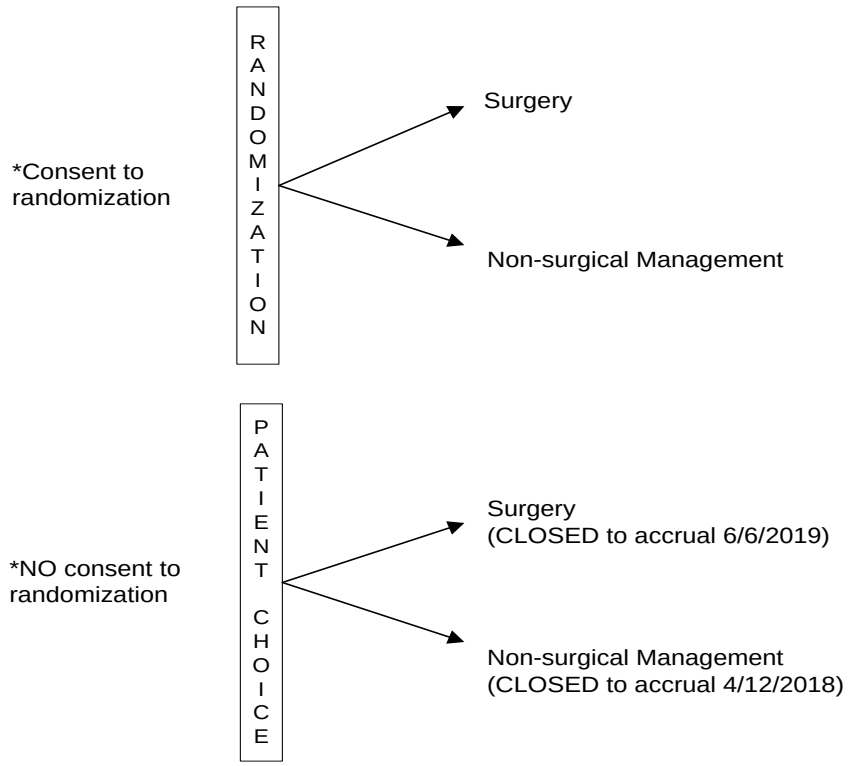
Study Chairs:
R Krouse, J Deneve, A Secord (Alliance)

Date Closed:
05/15/2020

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

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

Stratification/Descriptive Factors

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

Accrual Goals

A total of 220 patients will be accrued to achieve 200 eligible patients, with a target of 50 eligible patients in the randomized component.

Summary Statement

For the current status of this study, please refer to the Palliative and End of Life Care chapter.

S1415CD Phase III

Coordinating Group: SWOG

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

Participants:
SWOG, CTSU

Date Activated:
09/01/2016

Study Chairs:
S Ramsey, D Hershman

Date Closed:
04/15/2020

Statisticians:
A Bansa (UW)l, W Barlow, K Arnold

Project Manager:
K Watabayashi (HICOR)

Data Coordinator:
K Carvalho

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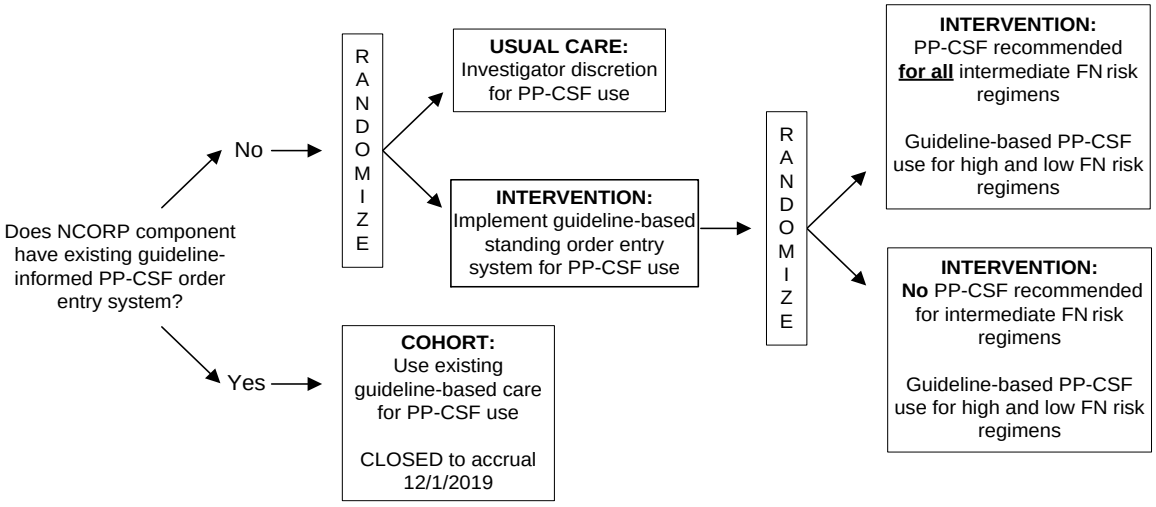

Randomization is at the NCORP component level. All patients at participating components will be subject to the PP-CSF use care as determined by component assignment (Usual Care, Intervention, or Cohort). Only consented patients registered to the study will participate in the data collection.

Objectives

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

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

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

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

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

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

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

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

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

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

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

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

Patient Population

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

Patients must be planning to receive one of the study-allowed regimens as their initial treatment for their current cancer diagnosis. Patients must be registered prior to or on the same day as their first cycle of chemotherapy. Patient must not have had any systemic therapy (chemotherapy or combination regimens) in the 180 days just prior to registration. Prior biologic therapy, immunotherapy, tyrosine kinase inhibitors, and hormonal therapy are allowed. Patients must not be receiving or planning to receive concurrent radiation therapy during systemic treatment. Patients must not have any known contraindication to CSFs, including prior hypersensitivity to *E. coli*-derived proteins, filgrastim, pegfilgrastim, or tbo-filgrastim.

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

Stratification/Descriptive Factors

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

Accrual Goals

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

One interim analysis will be conducted when 360 patients in the intermediate risk group at Intervention components have complete outcome information. A second interim analysis will be conducted when 650 patients in the intermediate risk group at Intervention components have complete outcome information. Complete outcome is defined as an assessment of FN after six months of follow-up after treatment commences.

Summary Statement

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

S1505 Phase II

Coordinating Group: SWOG

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

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

Date Activated:
10/12/2015

Study Chairs:
D Sohal, N Gandhi, A Lowy, P Philip, S Ahmad (CTSU), A Wang-Gillam (Alliance), M Beg (ECOG-ACRIN)

Date Closed:
04/20/2018

Statisticians:
K Guthrie, M Duong

Data Coordinator:
S Gurung

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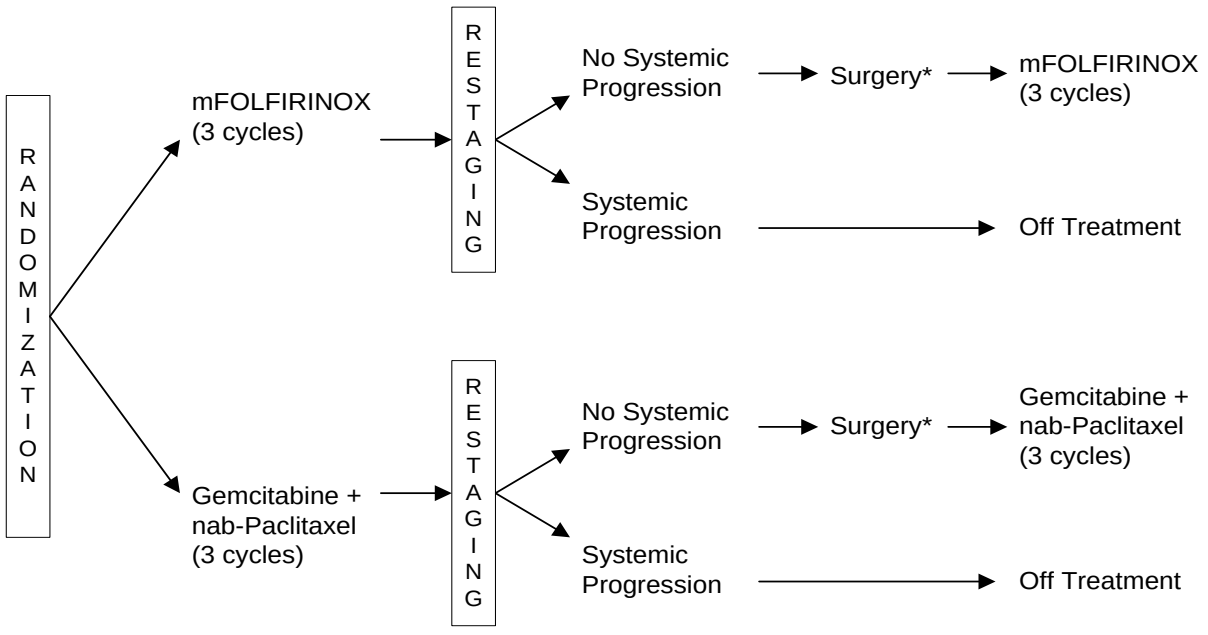


*If patient is unable to undergo R0 or R1 surgical resection, he or she must be taken off protocol treatment.

Objectives

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

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

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

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

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

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

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

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

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

Patient Population

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

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

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

Stratification/Descriptive Factors

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

Accrual Goals

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

Summary Statement

This study closed as of April 20, 2018, after meeting the accrual goal with 147 patients registered. Forty-four patients were ineligible; 43 of them were deemed unresectable by central radiology review and one was ineligible due to presence of distal bile duct cancer. One patient withdrew consent for further follow-up immediately after being randomized to gemcitabine + nab-paclitaxel and is not analyzable.

Four patients have been excluded from the adverse event analyses and were also coded as major deviations because they did not receive protocol treatment. Six patients are counted as "Other-not protocol specified" in the Treatment Summary table for going off treatment for the following reasons: unresectable following chemotherapy (2 patients), physician's discretion (1), insurance denial (1), presence of peritoneal deposits (1) and screen failure (1).

On the mFOLFIRINOX arm, 53 patients have been assessed for chemotherapy-related adverse events. There has been one treatment-related death due to sepsis; this patient also had Grade 4 neutrophil decrease. Five additional patients have experienced Grade 4 events; three with hematologic toxicities, one with hypokalemia and one with an allergic reaction. Thirty-two additional patients experienced Grade 3 events, including one with hepatic macrosteatosis (coded as 'Hepatobil disorders-Other') and another with a bacterial infection (coded as 'Infection/infestations-Other').

On the gemcitabine + nab-paclitaxel arm, 45 patients have been assessed for chemotherapy-related adverse events. There has been one treatment-related death due to respiratory failure. Six additional patients experienced Grade 4 events: sepsis (2 patients), colonic perforation (1), neutrophil count decreased (1); hematologic toxicities and hypokalemia (1); hypomagnesemia and dyspnea (1). Twenty-six additional patients experienced Grade 3 events, including cellulitis (coded as 'Investigations/ Infestations-Other').

Of the 69 patients (overall) that have been assessed for surgery-related adverse events, 10 patients have experienced Grade 3 events and one had a Grade 4 event.

Among the 40 mFOLFIRINOX arm and 33 gemcitabine + nab-paclitaxel arm patients undergoing surgical resection: R0 resection was achieved in 34 (85%) and 28 (85%) patients, node-negative resection in 16 (40%) and 15 (45%) patients, pathologic complete or major response in 10 (25%) and 14 (42%) patients respectively.

The estimated 2-year OS was 45% for mFOLFIRINOX and 47% for gemcitabine + nab-paclitaxel, with median OS of 23.2 months (95% CI: 17.6 - 41.4) and 23.6 months (95% CI: 17.8 - 39.3), respectively. Neither arm's 2-year OS estimate was significantly higher than the *a priori* threshold of 40% (p=0.42 in mFOLFIRINOX arm and p=0.12 in gemcitabine + nab-paclitaxel arm). Overall response rates were 9% (95% CI: 3 - 20%) and 21% (95% CI: 11 - 36%) in mFOLFIRINOX arm and gemcitabine + nab-paclitaxel arm correspondingly.

Estimates of median disease-free survival from resection were 10.9 (95% CI: 8.7 - 16.6) and 14.2 (95% CI: 7.3 - 18.6) months, respectively.

Registration by Institution

Institutions	Total Reg
Heartland NCORP	7
Cleveland Clinic OH	6
Michigan, U of	6
San Diego, U of CA	6
Kaiser Perm NCORP	5
PCRC NCORP	5
Greenville NCORP	4
Rochester, Univ of	4
Dayton NCORP	3
Kansas MU-NCORP	3
Kentucky, U of	3
MUSC MU-NCORP	3
Southeast COR NCORP	3
Wisconsin NCORP	3
Carle CC NCORP	2

Institutions	Total Reg
Cincinnati MC, U of	2
Michigan CRC NCORP	2
Ozarks NCORP	2
Arizona CC, Univ of	1
Baptist MU-NCORP	1
Columbus NCORP	1
New Mexico MU-NCORP	1
Oklahoma, Univ of	1
Salem Hospital	1
San Antonio, U of TX	1
ECOG-ACRIN	32
NRG	21
ALLIANCE	18
Total (28 Institutions)	**147**

Registration, Eligibility, and Evaluability

Data as of July 21, 2020

	TOTAL	mFOLFIRINOX	Gem/nab-P
NUMBER REGISTERED	147	74	73
INELIGIBLE	44	19	25
ELIGIBLE	103	55	48
Not Analyzable	1	0	1
BASELINE DISEASE STATUS			
Measurable	102	55	47
RESPONSE ASSESSMENT			
Determinable	92	48	44
Not Determinable	8	5	3
Not Applicable	2	2	0
ADVERSE EVENT ASSESSMENT			
Evaluable	98	53	45
Not Evaluable	4	2	2

Patient Characteristics

Data as of July 21, 2020

	mFOLFIRINOX (n=55)		Gem/nab-P (n=47)	
AGE				
Median	66.0		63.9	
Minimum	43.7		46.4	
Maximum	76.0		75.5	
SEX				
Males	36	65%	24	51%
Females	19	35%	23	49%
HISPANIC				
Yes	3	5%	4	9%
No	51	93%	43	91%
Unknown	1	2%	0	0%
RACE				
White	52	95%	39	83%
Black	2	4%	5	11%
Unknown	1	2%	3	6%
PERFORMANCE STATUS				
0	34	62%	31	66%
1	21	38%	16	34%

Treatment Summary

Data as of July 21, 2020

	TOTAL	mFOLFIRINOX	Gem/nab-P
NUMBER ON PROTOCOL TREATMENT	0	0	0
NUMBER OFF PROTOCOL TREATMENT	102	55	47
REASON OFF TREATMENT			
Treatment completed as planned	46	27	19
Adverse Event or side effects	21	7	14
Refusal unrelated to adverse event	8	7	1
Progression/relapse	18	8	10
Death	3	2	1
Other - not protocol specified	6	4	2
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	4	2	2

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

Chemotherapy Related Adverse Events (Pre- and Post-Operative Events Included)

Adverse Events Unlikely or Not Related to Treatment Excluded

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

Data as of July 21, 2020

	mFOLFIRINOX (n=53) Grade				Gem/nab-P (n=45) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
Abdominal infection	52	1	0	0	45	0	0	0
Acute kidney injury	53	0	0	0	44	1	0	0
Allergic reaction	52	0	1	0	45	0	0	0
ALT increased	50	3	0	0	43	2	0	0
Anemia	49	4	0	0	41	4	0	0
Anorexia	51	2	0	0	45	0	0	0
AST increased	51	2	0	0	44	1	0	0
Biliary tract infection	53	0	0	0	44	1	0	0
Blood bilirubin increased	52	1	0	0	42	3	0	0
Colonic perforation	53	0	0	0	44	0	1	0
Constipation	53	0	0	0	44	1	0	0
Dehydration	52	1	0	0	45	0	0	0
Diarrhea	45	8	0	0	42	3	0	0
Dysesthesia	52	1	0	0	45	0	0	0
Dyspnea	53	0	0	0	44	0	1	0
Fall	52	1	0	0	45	0	0	0
Fatigue	49	4	0	0	42	3	0	0
Febrile neutropenia	53	0	0	0	43	2	0	0
Hepatobil disorders-Other	52	1	0	0	45	0	0	0
Hyperglycemia	52	1	0	0	43	2	0	0
Hypertension	53	0	0	0	44	1	0	0
Hypoalbuminemia	53	0	0	0	44	1	0	0
Hypoglycemia	53	0	0	0	44	1	0	0

	mFOLFIRINOX (n=53) Grade				Gem/nab-P (n=45) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
Hypokalemia	50	2	1	0	44	0	1	0
Hypomagnesemia	53	0	0	0	43	1	1	0
Hyponatremia	51	2	0	0	43	2	0	0
Infections/infestations-Other	52	1	0	0	44	1	0	0
Infusion related reaction	52	1	0	0	45	0	0	0
Insomnia	53	0	0	0	44	1	0	0
Leukocytosis	52	1	0	0	45	0	0	0
Lung infection	52	1	0	0	43	2	0	0
Lymphocyte count decreased	53	0	0	0	43	2	0	0
Mucositis oral	53	0	0	0	44	1	0	0
Myocardial infarction	52	1	0	0	45	0	0	0
Nausea	50	3	0	0	44	1	0	0
Neutrophil count decreased	42	7	4	0	28	15	2	0
Non-cardiac chest pain	53	0	0	0	44	1	0	0
Pancreatitis	52	1	0	0	45	0	0	0
Papulopustular rash	53	0	0	0	44	1	0	0
Peripheral motor neuropathy	52	1	0	0	45	0	0	0
Peripheral sensory neuropathy	48	5	0	0	42	3	0	0
Platelet count decreased	50	2	1	0	43	2	0	0
Pneumonitis	53	0	0	0	44	1	0	0
Rectal hemorrhage	53	0	0	0	44	1	0	0
Respiratory failure	53	0	0	0	44	0	0	1
Sepsis	52	0	0	1	43	0	2	0
Skin infection	52	1	0	0	45	0	0	0
Thromboembolic event	51	2	0	0	45	0	0	0
Vomiting	51	2	0	0	45	0	0	0
Weight loss	52	1	0	0	45	0	0	0
White blood cell decreased	52	1	0	0	39	5	1	0
MAX. GRADE ANY ADVERSE EVENT	15	32	5	1	12	26	6	1

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

Surgery Related Adverse Events
Adverse Events Unlikely or Not Related to Treatment Excluded
Adverse Events with No Entries for Grades 2 to 5 Have Been Suppressed
Data as of July 21, 2020

	Total (n=69) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
Abdominal infection	68	1	0	0
Abdominal pain	68	1	0	0
Alkaline phosphatase increased	68	1	0	0
Alopecia	69	0	0	0
ALT increased	67	2	0	0
Anemia	63	6	0	0
Anorexia	67	2	0	0
Anxiety	69	0	0	0
AST increased	67	1	1	0
Back pain	68	1	0	0
Blood bilirubin increased	68	1	0	0
Colitis	68	1	0	0
Dehydration	68	1	0	0
Depression	69	0	0	0
Diarrhea	67	2	0	0
Dizziness	69	0	0	0
Dyspepsia	69	0	0	0
Esophagitis	68	1	0	0
Fatigue	68	1	0	0
Gastroparesis	68	1	0	0
Generalized muscle weakness	68	1	0	0
GERD	69	0	0	0
Hyperglycemia	69	0	0	0
Hypertension	67	2	0	0
Hypoalbuminemia	69	0	0	0
Hypocalcemia	69	0	0	0
Hypokalemia	68	1	0	0
Hypomagnesemia	69	0	0	0
Hypophosphatemia	68	1	0	0
Hypotension	69	0	0	0
Lymphocyte count decreased	69	0	0	0
Malabsorption	69	0	0	0
Metab/nutrition disorders-Oth	69	0	0	0
Nausea	68	1	0	0
Peripheral sensory neuropathy	68	1	0	0
Thromboembolic event	69	0	0	0
Vomiting	68	1	0	0
Weight loss	68	1	0	0
Wound infection	68	1	0	0
MAX. GRADE ANY ADVERSE EVENT	58	10	1	0

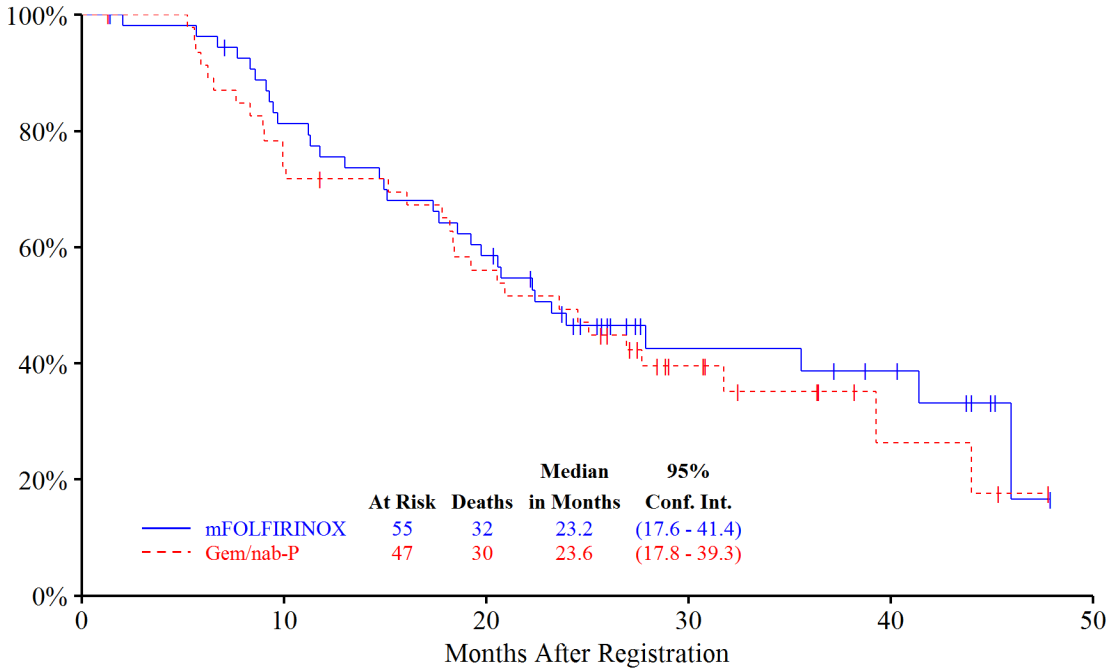
Response

Classified by Treatment Arm
Data as of July 21, 2020

	mFOLFIRINOX		Gem/nab-P	
	N	%	N	%
Complete Response	0	0	0	0
Partial Response	0	0	1	2
PR Non-measurable Disease	0	0	0	0
Unconfirmed Complete Response	2	4	0	0
Unconfirmed Partial Response	3	5	9	19
Unconfirmed PR NM Disease	0	0	0	0
Stable/No Response	38	69	24	51
Increasing Disease	3	5	10	21
Assessment Inadequate	9	16	3	6
Total	**55**	**100**	**47**	**100**

Overall Survival

Data as of July 21, 2020



S1609 Phase II

Coordinating Group: SWOG

DART: Dual Anti-CTLA-4 and Anti-PD-1 Blockade in Rare Tumors

Participants:
SWOG, CTSU

Date Activated:
01/13/2017

Study Chairs:
S Patel, Y Chae

Statisticians:
M Othus, M Plets, E Mayerson

Data Coordinators:
C Magner, S Gurung

Objectives

To evaluate the RECIST 1.1 overall response rate (ORR) in subsets of patients with advanced rare cancers treated with ipilimumab plus nivolumab combination immunotherapy.

To evaluate the overall response rate (ORR) in patients with gestational trophoblastic tumors treated with ipilimumab plus nivolumab combination immunotherapy.

To evaluate the RECIST 1.1 overall response rate (ORR) in patients PD-L1 amplified cancers treated with nivolumab immunotherapy.

To evaluate toxicities in each cohort.

To estimate overall survival (OS), progression-free survival (PFS), clinical benefit rate; and to estimate immune-related ORR (irORR), and immune-related PFS (irPFS) by unidimensional immune-related response criteria.

To collect specimens for banking for use in future correlative biomarker research studies.

Patient Population

Patients must have histologically confirmed rare cancer and/or cancer of unknown primary specified on the list of eligible rare cancer histologic cohorts in the S1609 protocol or with PD-L1 amplification only. As of September 11, 2017, patients are no longer required to have been enrolled in EAY131 (NCI-MATCH) to be eligible for this study.

Patients must have measurable disease and have progressed following at least one line of standard systemic therapy and there must not be other approved/standard therapy available that has been shown to prolong overall survival. Patients are also eligible if no standard treatment exists that has been shown to prolong overall survival. Patients in one of the histologically defined rare cancer cohorts maybe have received either prior anti-CTLA-4 or other prior anti-PD-1/anti-PD-L1 therapy, but not both, provided that it is completed at least 4 weeks prior to registration. Patients in the PD-L1 amplification cohort must not have received anti-PD-1/anti-PD-L1 therapy; prior anti-CTLA-4 is allowed provided that it is completed at least 4 weeks prior to registration. Patients who had a prior immune-related adverse event with prior immunotherapy are not eligible. Patients with brain metastases or primary brain tumors must have completed treatment, surgery or radiation therapy at least 28 days prior to registration and have stable disease at time of registration. Patients with metastatic brain parenchymal disease must have been treated and off steroids for seven days prior to registration. Patients must have been off

all other systemic anti-cancer therapy at least seven days prior to registration and any therapy-induced toxicity must have recovered to Grade 1 or less.

Patients must have a Zubrod performance status of 0-2 and have adequate hematologic, hepatic, renal, thyroid, and adrenal axis function. Patients must not have active autoimmune disease that has required systemic treatment in the past two years or any uncontrolled intercurrent illness. Patients must not have known active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection at time of registration. Patients with HBV or HCV that have an undetectable viral load, or in the opinion of the treating investigator are well controlled, are eligible. Patients who are known to be HIV-positive at registration are eligible if they meet the conditions outlined in the protocol.

Stratification/Descriptive Factors

Patients will be described by histologic cohorts, with the exception of PD-L1 amplification patients.

Accrual Goals

The maximum accrual for this study is 818 patients. A two-stage design will be used for all cohorts, with the exception of the NOC and "Cancer of Unknown Primary" (CuP) cohorts. Initially, six eligible patients will be registered to each histologic cohort. If at least one response is observed within a cohort, an additional 10 eligible patients will be registered to that cohort. Up to 16 eligible patients will be registered to the CuP cohort with no formal first stage response assessment. Up to 60 eligible patients will be enrolled to the NOC cohort, and data may be used to open additional cohorts.

Summary Statement

For the current status of this study, please refer to the Early Therapeutics and Rare Cancers chapter.

S1613 Phase II

Coordinating Group: SWOG

A Randomized Phase II Study of Trastuzumab and Pertuzumab (TP) Compared to Cetuximab and Irinotecan (CETIRI) in Advanced/Metastatic Colorectal Cancer (mCRC) with HER-2 Amplification

---

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

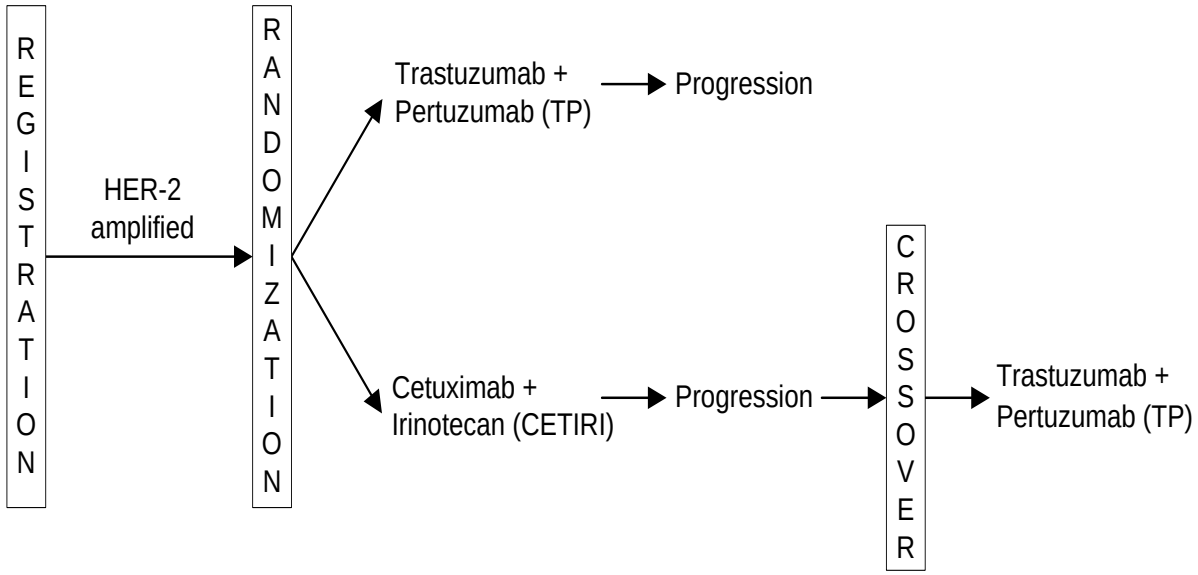
Date Activated:
10/09/2017

Study Chairs:
K Raghav, A Magliocco, S Kopetz, M Fakih (NRG), B Tan, Jr. (Alliance), C Denlinger (ECOG-ACRIN)

Statisticians:
K Guthrie, M Duong

Data Coordinator:
J Scurlock

SCHEMA



Objectives

To evaluate the efficacy of trastuzumab and pertuzumab (TP) in HER-2 amplified metastatic colorectal cancer (mCRC) by comparing progression-free survival on TP compared to control arm of cetuximab + irinotecan (CETIRI).

To evaluate the overall response rate, including confirmed and unconfirmed, complete and partial response per RECIST 1.1, in the TP and CETIRI treatment arms.

To evaluate the overall survival in the TP and CETIRI treatment arms.

To evaluate the safety and toxicity of TP compared to CETIRI.

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 disease. Brain metastases are allowed if they have been adequately treated with radiotherapy or surgery and stable for at least 30 days prior to randomization. Patients must not have any known activating mutation in exon 2 [codons 12 and 13], exon 3 [codons 59 and 61] and exon 4 [codons 117 and 146] of KRAS/NRAS genes, or in exon 15 (BRAFV600E mutation) of BRAF gene.

Patients must have had one or two prior regimens of systemic chemotherapy for metastatic disease or locally advanced unresectable disease. Patients must have progressed following the most recent therapy. Prior treatment with irinotecan is allowed. For patients that received adjuvant chemotherapy: prior treatment for metastatic disease is not required for patients who experienced disease recurrence during or within six months of completion of adjuvant chemotherapy. Patients must not have been treated with any of the following prior to Step 1 Initial Registration: (1) cetuximab, panitumumab, or other monoclonal antibody against EGFR or inhibitor of EGFR; or (2) HER-2 targeting for treatment of colorectal cancer. Patients must have completed prior chemotherapy, immunotherapy, or radiation therapy at least 14 days prior to Step 2 Randomization.

Patients must have adequate hepatic, renal, hematologic, and cardiac function and have a Zubrod performance status of 0-1. Patients must not have any uncontrolled intercurrent illness. Patients must not have any known previous or concurrent condition suggesting susceptibility to hypersensitivity or allergic reactions, including, but not limited to: known hypersensitivity to any of the study treatments or to excipients of recombinant human or humanized antibodies.

Patients must have tumor tissue available for submission for HER-2 testing, and must have HER-2 amplification as determined by central testing.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) prior use of irinotecan: yes vs no; and (2) HER-2/CEP17 ratio: > 5 vs ≤ 5.

Accrual Goals

This trial will randomize 130 patients to yield 122 eligible patients. An interim futility analysis of progression-free survival (PFS) will be performed when 49% (approximately 56 events) of the expected PFS events have been observed.

Summary Statement

As of June 30, 2020, 184 patients had been screened for HER-2 amplification with 33 patients randomized to therapy. Eleven patients on the CETIRI arm have crossed over to TP. The study was temporarily closed to accrual on May 16, 2019, pending the centralized HER-2 screening move to a new location, and reopened to accrual on November 18, 2019.

Among 33 randomized patients, two patients were deemed ineligible due to lack of progression after the most recent therapy (1) and receiving more than two prior therapies (1). One patient coded as "Major protocol deviations" was not assessable for response or adverse events due to refusal to receive treatment.

In 30 patients assessed for adverse events, no Grade 4 or 5 toxicities have been reported. Two patients on the TP arm have experienced Grade 3 events due to increased alkaline phosphatase and infusion related reaction. Six patients on the CETIRI arm have reported Grade 3 toxicities: anorexia (1 patient), fatigue (1), maculo-papular rash (1), hypomagnesemia (1), thromboembolic event (1), diarrhea and thickening of bladder wall (1).

Registration by Institution

Screening

Registrations ending June 30, 2020

Institutions	Total Reg	Institutions	Total Reg
Hawaii MU-NCORP	30	Wisconsin NCORP	2
Heartland NCORP	23	Yale University	2
Kansas MU-NCORP	17	Davis, U of CA	1
MD Anderson CC	16	Georgia NCORP	1
PCRC NCORP	7	Henry Ford Hospital	1
Michigan CRC NCORP	6	Kansas City NCORP	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	4	Lahey Hosp & Med Ctr	1
Sutter Cancer RC	4	Ozarks NCORP	1
Colorado, U of	3	Prov Portland MC/PCRC NCORP	1
CORA NCORP	3	So Calif, U of	1
Bay Area NCORP	2	Southeast COR NCORP	1
City of Hope Med Ctr	2	Utah, U of	1
Loyola University	2	ALLIANCE	19
Michigan, U of	2	NRG	14
Montana NCORP	2	ECOG-ACRIN	12
Nevada CRF NCORP	2	**Total (31 Institutions)**	**184**

Registration by Institution

Randomization

Registrations ending June 30, 2020

Institutions	Total Reg	Institutions	Total Reg
MD Anderson CC	11	Michigan, U of	1
Kansas MU-NCORP	3	So Calif, U of	1
PCRC NCORP	3	Southeast COR NCORP	1
Colorado, U of	1	ALLIANCE	4
Davis, U of CA	1	ECOG-ACRIN	3
Heartland NCORP	1	NRG	1
Lahey Hosp & Med Ctr	1	**Total (14 Institutions)**	**33**
Loyola University	1		

Registration, Eligibility, and Evaluability

Randomization

Registrations ending June 30, 2020; Data as of July 21, 2020

	TOTAL	Trastuzumab + Pertuzumab	Cetuximab + Irinotecan
NUMBER REGISTERED	33	15	18
INELIGIBLE	2	0	2
ELIGIBLE	31	15	16
Analyzable, Pend. Elig.	2	1	1
BASELINE DISEASE STATUS			
Measurable	30	14	16
Too Early	1	1	0
RESPONSE ASSESSMENT			
Determinable	29	14	15
Not Determinable	1	0	1
Too Early	1	1	0
ADVERSE EVENT ASSESSMENT			
Evaluable	30	15	15
Not Evaluable	1	0	1

Patient Characteristics

Randomization

Registrations ending June 30, 2020; Data as of July 21, 2020

	Trastuzumab + Pertuzumab (n=15)		Cetuximab + Irinotecan (n=16)	
AGE				
Median	52.7		57.1	
Minimum	32.1		38.9	
Maximum	75.6		75.2	
SEX				
Males	6	40%	8	50%
Females	9	60%	8	50%
HISPANIC				
Yes	1	7%	1	6%
No	13	87%	15	94%
Unknown	1	7%	0	0%
RACE				
White	13	87%	14	88%
Black	0	0%	1	6%
Asian	2	13%	0	0%
Unknown	0	0%	1	6%
PRIOR USE OF IRINOTECAN				
Yes	7	47%	7	44%
No	8	53%	9	56%
HER2/CEP17 RATIO				
> 5	11	73%	12	75%
<= 5	4	27%	4	25%

Treatment Summary

Randomization

Registrations ending June 30, 2020; Data as of July 21, 2020

	Total
NUMBER ON PROTOCOL TREATMENT	5
NUMBER OFF PROTOCOL TREATMENT	26
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	1
Refusal unrelated to adverse event	1
Progression/relapse	21
Death	1
Other - not protocol specified	0
Reason under review	2
MAJOR PROTOCOL DEVIATIONS	1

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

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, 2020; Data as of July 21, 2020

	Trastuzumab + Pertuzumab (n=15) Grade				Cetuximab + Irinotecan (n=15) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
Alkaline phosphatase increased	14	1	0	0	15	0	0	0
Anorexia	15	0	0	0	14	1	0	0
Diarrhea	15	0	0	0	14	1	0	0
Fatigue	15	0	0	0	14	1	0	0
Hypomagnesemia	15	0	0	0	14	1	0	0
Infusion related reaction	14	1	0	0	15	0	0	0
Rash maculo-papular	15	0	0	0	14	1	0	0
Renal/urinary disorders-Others	15	0	0	0	14	1	0	0
Thromboembolic event	15	0	0	0	14	1	0	0
MAX. GRADE ANY ADVERSE EVENT	13	2	0	0	9	6	0	0

S1614 Phase III

Coordinating Group: SWOG

A Phase III Randomized Trial of Prophylactic Antiviral Therapy in Patients with Current or Past Hepatitis B Virus (HBV) Infection Receiving Anti-Cancer Therapy for Solid Tumors

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

Study Chairs:
J Hwang, A Lok, E Mitchell (ECOG-ACRIN)

Statisticians:
J Unger, E Mayerson

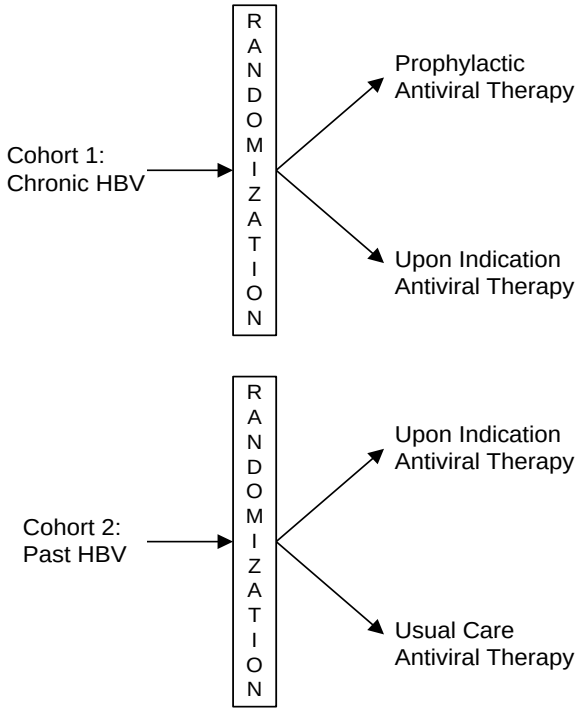
Data Coordinators:
S Dzingle, R Topacio

Date Activated:
02/21/2019

Date Closed:
05/20/2020

*Temporary closure

SCHEMA



Objectives
Co-primary objectives:

To compare the effect of prophylactic tenofovir alafenamide (TAF) therapy versus upon indication TAF therapy on time-to-adverse liver outcomes of liver failure or liver-related death in patients with chronic HBV infection (HBsAg+ and anti-HBc+) receiving anti-cancer therapy for solid tumors.

To compare the effect of upon indication TAF therapy versus usual care on time-to-adverse liver outcomes of liver failure or liver-related death in patients with past HBV infection (HBsAg- and anti-HBc+) receiving anti-cancer therapy for solid tumors.

Secondary objectives:

Using time-to-event analysis, to compare the effect of TAF therapy versus upon indication TAF therapy on HBV reactivation, on the combined endpoint of adverse liver outcomes (liver failure or liver-related death) and HBV reactivation, and on HBV flare by arm in patients with chronic HBV infection receiving anti-cancer therapy for solid tumors.

Using time-to-event analysis, to compare the effect of upon indication TAF therapy versus usual care on HBV reactivation, on the combined endpoint of adverse liver outcomes (liver failure or liver-related death) and HBV reactivation, and on HBV flare by arm in patients with past HBV infection receiving anti-cancer therapy for solid tumors.

Patient Population
Patients must be diagnosed with Stage I-III solid tumor malignancy not involving the liver. Patients must have HBV infection as indicated through positive HBsAG or anti-HBc tests. Patients must not have lymphoma, leukemia, or myeloma. Patients must not have primary liver cancer or evidence of any malignancy that involves the liver.

Patients must be planning to receive a new regimen of systemic anti-cancer therapy for their solid tumor malignancy and must have discontinued all previous therapies. Patients must not have received anti-CD20 cancer therapy regimens nor had a hematopoietic stem cell transplant. Patients must have discontinued any antiviral medications active against HBV at least 90 days prior to registration, and discontinue any contraindicated medications as identified in the protocol at time of registration.

Patients must have a Zubrod performance status of 0-2, and have adequate liver, renal, and coagulation function. Patients must not have known cirrhosis, known hepatitis-C infection, or history of human immunodeficiency infection proven by an HIV test within the past 365 days. Patients must have complete results for HBsAg, anti-HBc, anti-HBs, and HBV DNA lab tests as specified in the protocol. Patients must be able to take oral medications.

Patients must be willing to submit specimens for ongoing testing of HBV reactivation. Patients must be offered the opportunity to participate in the translational medicine studies.

Stratification/Descriptive Factors
Patients with chronic HBV infection will be randomized within Cohort 1, with randomization balanced by planned cancer therapy type: any cytotoxic therapy vs immunotherapy alone vs targeted therapy alone vs immunotherapy and targeted therapy.

Patients with past HBV infection will be randomized within Cohort 2 with randomization balanced by the following factors: (1) planned cancer therapy type: any cytotoxic therapy vs immunotherapy alone vs targeted therapy alone vs immunotherapy and targeted therapy; and (2) anti-HBs status: positive vs negative.

Accrual Goals
The accrual goal for this study is 444 patients, 222 patients per cohort to achieve 200 eligible patients per cohort. A single formal interim analysis for efficacy for each cohort will be conducted when one half of patients have reached one year of follow-up.

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

S1815 Phase III

Coordinating Group: SWOG

A Phase III Randomized Trial of Gemcitabine, Cisplatin, and Nab-Paclitaxel versus Gemcitabine and Cisplatin in Newly Diagnosed Advanced Biliary Tract Cancers

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

Date Activated:
12/03/2018

Study Chairs:
R Shroff, A Scott, M Borad (Alliance), L Goff (ECOG-ACRIN), K Matin (NRG)

Statisticians:
K Guthrie, M Duong

Data Coordinator:
S Gurung

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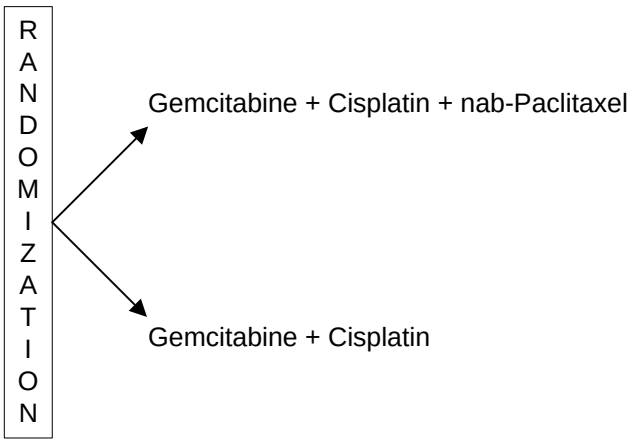


Objectives

To compare overall survival in patients with untreated advanced biliary cancers treated with gemcitabine and cisplatin (GC) versus those treated with gemcitabine, cisplatin, and nab-paclitaxel (GCN).

To compare progression-free survival in patients treated with GC versus GCN.

To compare overall response rate, complete and partial, confirmed and unconfirmed, in the subset of patients with measurable disease treated with GC versus GCN.

To compare disease control rate (confirmed and unconfirmed, complete response + partial response + stable disease) in patients treated with GC versus GCN.

To evaluate the frequency and severity of toxicity associated with GC and GCN in the patient population.

To explore the correlation between change in CA 19-9 levels from baseline to post-treatment (after 3 cycles) and overall response rate, in each treatment arm separately and in the total cohort.

Patient Population

Patients must have histologically or cytologically confirmed intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer. Patients must have documented metastatic or locally advanced unresectable disease on CT or MRI. Patients must not have a current diagnosis of ampullary cancer.

Patients must not have received prior systemic therapy for the current metastatic or locally advanced biliary cancer. Patient must not have received adjuvant therapy within six months prior to registration.

Patients must have a Zubrod performance status of 0 or 1 and have adequate hematologic, hepatic, and renal function. Patients must not have a history of peripheral neuropathy of Grade 2 or greater. Patients must have CA 19-9 and other baseline labs obtained as specified in the protocol. Patients must not have an active infection requiring systemic therapy. Sites must seek additional patient consent for the future use of specimens.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) disease site: gallbladder adenocarcinoma vs intrahepatic cholangio/carcinoma vs extrahepatic cholangio/carcinoma; (2) disease stage: locally advanced vs metastatic; and (3) Zubrod performance status: 0 vs 1.

Accrual Goals

A total of 441 patients will be accrued to achieve 384 eligible patients randomized in a 2:1 ratio (256 in GCN arm and 128 in the GC arm). There are two planned interim analyses to be performed after approximately 40% and 70% of the total expected deaths have occurred.

Summary Statement

Prior to the first interim analysis and 14 months post-activation, 231 patients were enrolled. Given this rapid accrual, it was determined that a more clinically meaningful improvement in median OS could be targeted by increasing the accrual goal from the original plan of 268 patients.

As of June 30, 2020, 272 patients had been enrolled in the study. Seven patients are ineligible due to the following reasons: Laboratory values did not meet the requirement (5 patients); cytology report was insufficient (1) and received prior systemic therapy (1).

Eighteen patients went off protocol treatment with reason coded as "Other - not protocol specified" in the Treatment Summary table due to the following reasons: tumor resection (6 patients), symptomatic deterioration (5), physician's decision (4), fecal transplant (1), intestinal perforation (1), and COVID-19 (1). Major protocol deviations were coded for 11 patients 10 of whom withdrew from the study and one patient never started treatment; this last patient was not assessable for adverse events.

On the gemcitabine + nab-paclitaxel + cisplatin arm, 169 patients have been assessed for adverse events. Three patients died due to the following reasons: sepsis (2 patients) and thromboembolic event (1). Twelve patients have reported Grade 4 events: hematologic events (9 patients), anemia (1), enterocolitis and gastric hemorrhage (1), and sepsis (1).

On the gemcitabine + cisplatin arm, 82 patients have been assessed for adverse events. Five patients experienced Grade 4 toxicities; four patients with hematologic events and one patient with hypomagnesemia.

Registration by Institution

Registrations ending June 30, 2020

Institutions	Total Reg
MD Anderson CC	12
Greenville NCORP	9
Northwestern Univ	9
Yale University	8
Arizona CC, Univ of	7
Hawaii MU-NCORP	7
So Calif, U of	6
Heartland NCORP	5
New Mexico MU-NCORP	5
PCRC NCORP	5
City of Hope Med Ctr	4
Davis, U of CA	4
Columbus NCORP	3
CORA NCORP	3
Gulf South MU-NCORP	3
Michigan, U of	3
Montana NCORP	3
Ozarks NCORP	3
Rochester, Univ of	3
Utah, U of	3
Baylor College	2
CRC West MI NCORP	2
Dayton NCORP	2
Henry Ford Hospital	2
Oregon Hlth Sci Univ	2
Wayne State Univ	2
Arkansas, U of	1
Cincinnati MC, U of	1
Good Samaritan MC/Oregon Hlth Sci Univ	1
San Antonio, U of TX	1
St Luke's Mt State/PCRC NCORP	1
Wichita NCORP	1
ALLIANCE	70
ECOG-ACRIN	55
NRG	24
Total (35 Institutions)	**272**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2020; Data as of July 21, 2020

	TOTAL	Gem+Cisplatin +Nab-paclitaxel	Gemcitabine + Cisplatin
NUMBER REGISTERED	272	179	93
INELIGIBLE	7	4	3
ELIGIBLE	265	175	90
Analyzable, Pend. Elig.	6	3	3
RESPONSE ASSESSMENT			
Determinable	217	144	73
Not Determinable	26	15	11
Too Early	21	15	6
Not Applicable	1	1	0
ADVERSE EVENT ASSESSMENT			
Evaluable	251	169	82
Not Evaluable	1	1	0
Too Early	12	5	7
Not Applicable	1	0	1

Patient Characteristics

All Eligible and Selected Ineligible Patients Included

Registrations ending June 30, 2020; Data as of July 21, 2020

	Gem+Cisplatin+Nab-paclitaxel (n=175)		Gemcitabine + Cisplatin (n=90)	
AGE				
Median	63.5		64.8	
Minimum	24.2		30.8	
Maximum	88.8		83.6	
SEX				
Males	77	44%	43	48%
Females	98	56%	47	52%
HISPANIC				
Yes	17	10%	9	10%
No	156	89%	75	83%
Unknown	2	1%	6	7%
RACE				
White	151	86%	71	79%
Black	10	6%	5	6%
Asian	5	3%	3	3%
Native American	1	1%	1	1%
Multi-Racial	0	0%	1	1%
Unknown	8	5%	9	10%
DISEASE SITE				
Gallbladder adenocarcinoma	21	12%	17	19%
Intrahepatic cholangiocarcinoma	123	70%	56	62%
Extrahepatic cholangiocarcinoma	31	18%	17	19%
DISEASE STAGE				
Locally advanced	52	30%	26	29%
Metastatic	123	70%	64	71%
PERFORMANCE STATUS				
0	95	54%	47	52%
1	80	46%	43	48%

Treatment Summary

All Eligible and Selected Ineligible Patients Included

Registrations ending June 30, 2020; Data as of July 21, 2020

	Total
NUMBER ON PROTOCOL TREATMENT	79
NUMBER OFF PROTOCOL TREATMENT	186
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	44
Refusal unrelated to adverse event	37
Progression/relapse	80
Death	4
Other - not protocol specified	18
Reason under review	3
MAJOR PROTOCOL DEVIATIONS	11

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, 2020; Data as of July 21, 2020

	Gem+Cisplatin+Nab-paclitaxel (n=169) Grade				Gemcitabine + Cisplatin (n=82) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
Abdominal pain	168	1	0	0	82	0	0	0
Acute kidney injury	169	0	0	0	81	1	0	0
Alkaline phosphatase increased	168	1	0	0	82	0	0	0
ALT increased	167	2	0	0	82	0	0	0
Anemia	166	2	1	0	80	2	0	0
Anorexia	168	1	0	0	82	0	0	0
Ataxia	168	1	0	0	82	0	0	0
Blood bilirubin increased	169	0	0	0	81	1	0	0
Cholecystitis	168	1	0	0	82	0	0	0
Colitis	168	1	0	0	82	0	0	0
Dehydration	167	2	0	0	82	0	0	0
Diarrhea	161	8	0	0	82	0	0	0
Edema limbs	168	1	0	0	82	0	0	0
Enterocolitis	168	0	1	0	82	0	0	0
Enterocolitis infectious	168	1	0	0	82	0	0	0
Fatigue	166	3	0	0	82	0	0	0
Febrile neutropenia	166	2	1	0	82	0	0	0
Fever	168	1	0	0	82	0	0	0
Gastric hemorrhage	168	0	1	0	82	0	0	0
Hepatic infection	168	1	0	0	82	0	0	0
Hepatobil disorders-Other	168	1	0	0	82	0	0	0
Hyperkalemia	168	1	0	0	82	0	0	0
Hypokalemia	165	4	0	0	81	1	0	0
Hypomagnesemia	169	0	0	0	81	0	1	0
Hypotension	169	0	0	0	81	1	0	0
Infections/infestations-Other	168	1	0	0	81	1	0	0
Lymphocyte count decreased	164	4	1	0	81	0	1	0
Mucositis oral	168	1	0	0	82	0	0	0
Nausea	167	2	0	0	82	0	0	0
Neutrophil count decreased	148	12	9	0	75	4	3	0
Platelet count decreased	159	6	4	0	80	1	1	0
Sepsis	164	2	1	2	82	0	0	0
Skin infection	169	0	0	0	81	1	0	0
Syncope	169	0	0	0	81	1	0	0
Thromboembolic event	168	0	0	1	82	0	0	0
Urinary tract infection	168	1	0	0	82	0	0	0
Vomiting	168	1	0	0	82	0	0	0
White blood cell decreased	157	8	4	0	80	0	2	0
MAX. GRADE ANY ADVERSE EVENT	114	40	12	3	66	11	5	0

S1820 Pilot

Coordinating Group: SWOG

A Randomized Trial of the Altering Intake, Managing Symptoms Intervention for Bowel Dysfunction in Rectal Cancer Survivors Compared to a Healthy Living Education Control: A Feasibility and Preliminary Efficacy Study (AIMS-RC)

Participants:
SWOG, CTSU

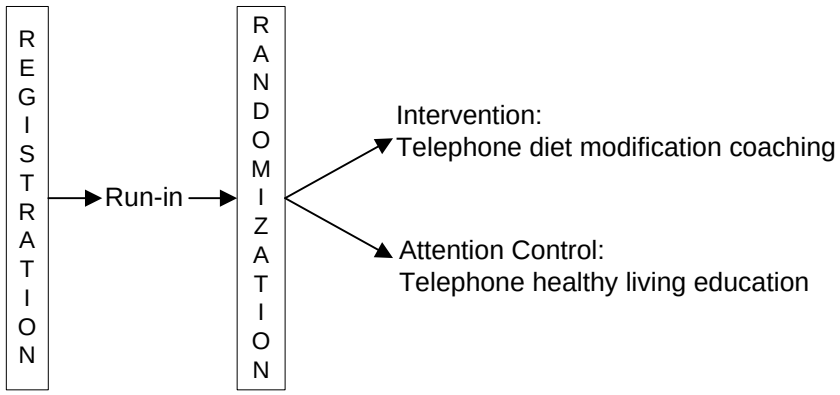
Date Activated:
12/09/2019

Study Chairs:
V Sun, C Thomson

Statisticians:
K Guthrie, K Arnold

Data Coordinator:
R Topacio

SCHEMA



Objectives

To compare total bowel function score, as measured by the Memorial Sloan-Kettering Cancer Center Bowel Function Index (BFI), at 18 weeks post-randomization between the intervention and attention control arms.

To compare total bowel function score at 26 weeks post-randomization between the intervention and attention control arms.

To compare bowel function subscale scores (dietary, urgency, frequency), as measured by the BFI at both 18 and 26 weeks post-randomization between the intervention and attention control arms.

To compare lower anterior resection syndrome (LARS) scores (for anastomosis participants only), quality of life, and dietary quality at both 18 and 26 weeks post-randomization between the intervention and attention control arms.

To compare motivation, self-efficacy, and positive/negative affect at both 18 and 26 weeks post-randomization between the intervention and attention control arms.

To assess study feasibility, adherence, retention, and acceptability at both 18 and 26 weeks post-randomization.

To explore variation in primary and secondary study outcomes according to sex, and to investigate whether intervention effects on the primary outcome differ across subgroups defined by sex.

Patient Population

Patients must have prior history of rectosigmoid colon cancer or rectal cancer. Patients must have a post-surgical permanent ostomy or anastomosis.

Patient's last date of treatment for rectal cancer (any surgery, chemotherapy, radiation therapy) must be at least 6 months prior to registration and not more than 24 months prior to registration.

Anastomosis patients must have LARS score of 21-42 (minor to major symptoms). Patients must be able to read, write and speak English. Patients must be at least 18 years of age. Patients must not be currently undergoing treatment for another cancer. Patients must not have been diagnosed with inflammatory bowel disease.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) sex: female vs male; and (2) ostomy status: permanent ostomy vs anastomosis.

Accrual Goals

The accrual goal is 94 randomized patients to achieve 88 eligible randomized patients, which is anticipated to require 126 patients registered to the run-in.

Summary Statement

For the current status of this study, please refer to the Palliative and End of Life Care chapter.

S1922 Phase II

Coordinating Group: SWOG

Randomized Phase II Selection Study of Ramucirumab and Paclitaxel versus FOLFIRI in Refractory Small Bowel Adenocarcinoma

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Participants:
SWOG, CTSU

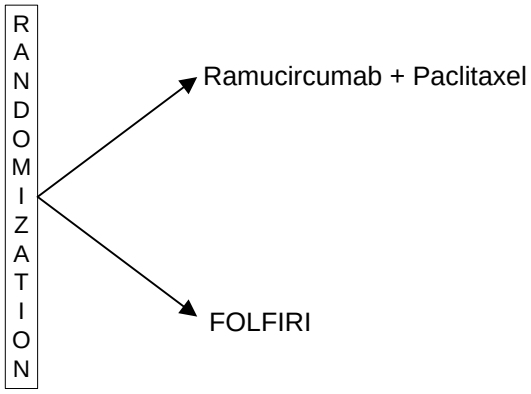
Date Activated:
12/16/2019

Study Chair:
M Overman

Statisticians:
K Guthrie, M Duong

Data Coordinator:
C Magner

SCHEMA



Objectives

To evaluate whether progression-free survival (PFS) meets an efficacy threshold in patients with previously treated advanced small bowel adenocarcinoma who receive treatment with ramucirumab and paclitaxel or FOLFIRI.

If the stated threshold is met in both arms, to choose the better regimen with respect to PFS.

To assess overall response rate (ORR) [complete and partial, confirmed and unconfirmed] in the subset of patients with measurable disease treated with ramucirumab and paclitaxel or FOLFIRI in this patient population.

To assess overall survival (OS) in patients treated with ramucirumab and paclitaxel or FOLFIRI in this patient population.

To evaluate safety and toxicity associated with combination ramucirumab and paclitaxel treatment or FOLFIRI therapy in this patient population.

To explore the correlation of maximum decrease in CEA levels and time to maximum decrease in CEA levels with PFS, OS, and ORR.

Patient Population

Patients must have histologically or cytologically confirmed small bowel adenocarcinoma. Ampullary adenocarcinomas are not eligible. Patients must have metastatic disease or locally advanced unresectable disease. Brain metastases are allowed if they have been adequately treated as described in the protocol.

Patients must have progressed on prior therapy with fluoropyrimidine and/or oxaliplatin, given either for metastatic/locally advanced disease or as adjuvant therapy completed within the previous 12 months. Patients must not have received prior treatment with irinotecan, taxane, or ramucirumab for small bowel adenocarcinoma. Patients must have completed prior chemotherapy, immunotherapy, or radiation therapy at least 14 days prior to registration. Patients must not have had major surgery within 28 days prior to registration, or minor surgery within 7 days prior to registration, and must not be planned for elective major surgery to be performed during protocol treatment. Patients must not be receiving chronic antiplatelet therapy, including dipyridamole or clopidogrel, or similar agents.

Patients must have a Zubrod performance status of 0-1. Patients must have adequate hematologic, hepatic, and renal function. Patients must not have a known bleeding diathesis. Patients must not have uncontrolled or poorly controlled hypertension despite standard medical management. Patient tumors must not have known deficient mismatch repair (dMMR) or microsatellite instability high (MSI-H). Patients must not have known dihydropyrimidine dehydrogenase deficiency. Patients must not have a history of significant thrombotic events as described in the protocol. Patients must not have a prior history of GI perforation/fistula or bleeding as described in the protocol. Patients must not have experienced any serious or non-healing wound, ulcer, or bone fracture within 28 days prior to registration.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) tumor site: duodenum vs non-duodenum; and (2) prior anti-VEGF therapy: yes vs no.

Accrual Goals

A total of 94 patients will be accrued to achieve 84 eligible patients.

Summary Statement

The study was activated on December 16, 2019. As of June 30, 2020, there was one patient registered.

Registration by Institution

Registrations ending June 30, 2020

Institutions	Total Reg
MD Anderson CC	1
Total (1 Institutions)	**1**

S2001 Phase II

Coordinating Group: SWOG

Randomized Phase II Clinical Trial of Olaparib + Pembrolizumab vs. Olaparib Alone as Maintenance Therapy in Metastatic Pancreatic Cancer Patients with Germline BRCA1 or BRCA2 Mutations

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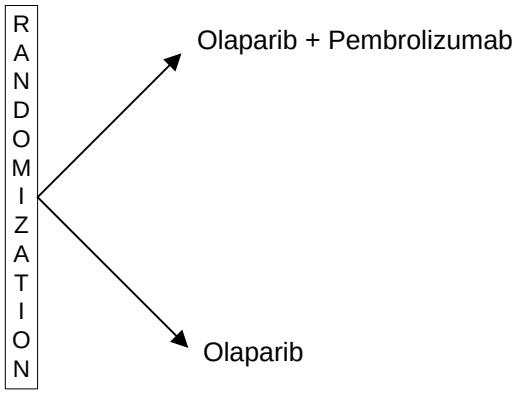
Participants:
SWOG, CTSU

Study Chairs:
V Chung, M Pishvaian

Statisticians:
K Guthrie, M Duong

Data Coordinator:
B Zeller

SCHEMA



Objectives

To evaluate the progression free survival of advanced pancreatic cancer patients with germline BRCA1 or BRCA2 mutations treated with olaparib + pembrolizumab compared to olaparib alone as maintenance therapy.

To evaluate the safety and tolerability associated with the combination of olaparib + pembrolizumab vs. olaparib alone as maintenance therapy.

To evaluate the overall survival of patients treated with olaparib + pembrolizumab compared to olaparib alone as maintenance therapy.

To evaluate overall response rate (ORR) by RECIST 1.1, including confirmed and unconfirmed, complete and partial response, of patients treated with olaparib + pembrolizumab compared to olaparib alone, in the subset of patients with measurable disease.

To evaluate overall response rate (ORR) by immune RECIST, including confirmed and unconfirmed, complete and partial response, of patients treated with olaparib + pembrolizumab compared to olaparib alone, in the subset of patients with measurable disease.

Patient Population

Patients must have a histologic or cytologic diagnosis of pancreatic adenocarcinoma that is metastatic. Patients with neuroendocrine tumors, acinar cell and adenosquamous carcinomas are not eligible. Patients must have positive and/or deleterious germline mutation in BRCA1 or 2 that was tested in a CLIA certified lab. Patients must have had a CT or MRI showing stable or responding disease on first line platinum-based chemotherapy.

Patients must have received at least 16 weeks but no more than 24 weeks of first line platinum-based chemotherapy (i.e. FOLFIRINOX, FOLFOX, or gemcitabine + cisplatin) for metastatic disease. Patients may have received prior investigational drug and/or prior anti-cancer treatment; any toxicities other than neuropathy and alopecia must have resolved to no more than Grade 1. Patients must not have received prior therapy with PARP inhibitors or immune checkpoint inhibitors.

Patients must have Zubrod performance status of 0-2 and must have adequate hematologic, hepatic, and renal function. Patients must not have pneumonitis, active infection, active autoimmune disease as described in protocol. Patients with known HIV, history of chronic HBV, or HCV must meet the restriction described in the protocol. Patients must not be planning to receive CYP3A inhibitors or inducers, nor live vaccines. Patients must be able to swallow and retain oral medications.

Patients must be offered the opportunity to participate in specimen banking and image banking.

Stratification/Descriptive Factors

Patient randomization will be stratified by first line chemotherapy: FOLFIRINOX (or FOLFOX alone) vs gemcitabine + cisplatin.

Accrual Goals

The accrual goal is 88 patients to achieve 78 eligible patients. One interim analysis is planned for when approximately 50% of expected events are observed.