GASTROINTESTINAL COMMITTEE
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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

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## Non-SWOG Studies with SWOG-Credited Registrations

**GASTROINTESTINAL COMMITTEE**

Studies with Accrual from January 2017 - June 2018

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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, and NRG)

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

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

**Stratification/Descriptive Factors**

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

**Accrual Goals**

A total of 420 patients will be enrolled, 210 to each study arm. An additional 71 patients were enrolled to Arms 2 and 3 prior to their closure under Amendment #2 on April 14, 2017.

**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:
R Topacio

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 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 (MO). 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 ≥ 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 ≤ 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:
R Topacio

Date Activated: 11/15/2011
Date Closed: 10/01/2016

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/m² loading dose, 250 mg/m² weekly; (b) cetuximab 500 mg/m² 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 be able to
completed the baseline S1013 FACT-EGFRI 18 within three days prior to initiation of EGFRI therapy.

**Accrual Goals**
Planned accrual for this study is 156 patients in order to achieve 112 evaluable patients.

**Summary Statement**
For the current status of this study, please refer to the Symptom Control and QOL chapter.
S1204 Surveillance

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

Study Chairs: S Ramsey, D Hershman

Statisticians: J Unger, K Arnold

Data Coordinator: M Yee

Date Activated: 08/29/2013

Date Closed: 02/15/2017

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, describe the timing and type of treatments received (if any), both for the viral infections and the cancers.

Describe type adverse events possibly attributable to the patient's viral status in patients with HIV, HBV, and/or HCV infection.

Using simulation modeling that is directly informed by the data obtained from this study, determine the cost-effectiveness (expressed as cost per infection detected and cost per year of life gained) 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.

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

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

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

Summary Statement
For the current status of this study, please refer to the Cancer Care Delivery chapter.
S1316 Pilot

Coordinating Group: SWOG

Prospective Comparative Effectiveness Trial For Malignant Bowel Obstruction

Participants: SWOG, CTSU (Supported by Alliance)
Study Chairs: R Krouse, B Bagwell, A Secord (Alliance)
Statisticians: G Anderson, K Arnold
Data Coordinator: R Topacio

Date Activated: 03/09/2015

SCHEMA

*Consent to randomization

Surgery

Non-surgical management

*NO consent to randomization

Surgery

Non-surgical management

(CLOSED to accrual 4/12/2018)

*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 200 patients will be accrued to achieve 180 eligible patients, with a target of 34 patients in the randomized component.

Summary Statement
For the current status of this study, please refer to the Cancer Survivorship 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

Study Chairs: S Ramsey, D Hershman

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

Project Manager: K Watabayashi (HICOR)

Data Coordinator: K Carvalho

SCHEMA

Randomization is at the NCORP component level. All patients at participating components will be subject to the PP-CSF use care as determined by component assignment (Usual Care, Intervention, or Cohort). Only consented patients registered to the study will participate in the data collection.
Objectives
To compare the use of primary prophylactic colony stimulating factor (PP-CSF) according to recommended clinical practice guidelines among patients registered at Intervention components versus Usual Care components.

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

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

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

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

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

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

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

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

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

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

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

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, 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 Escherichia coli-derived proteins, filgrastim, pegfilgrastim, or tbo-filgrastim.

Patients must be able to understand and provide information for the patient-completed study forms in either English or Spanish. Patients may have had a prior malignancy. Patients 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 6 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.
S1417CD Survey

Coordinating Group: SWOG

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

Participants:
SWOG, CTSU

Date Activated:
05/13/2016

Study Chairs:
V Shankaran, S Ramsey

Statisticians:
J Unger, A Darke

Data Coordinator:
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 components and subcomponents of the NCI Community Oncology Research Program (NCORP).

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

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

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

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

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

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

Patient Population
Patients must have newly diagnosed metastatic colon or rectal cancer (de novo metastatic diagnosis or metastatic recurrence after prior treatment for stage I-III disease), with registration within 120 days of diagnosis. Patients must plan to begin systemic chemotherapy and/or biologic therapy at the registering institution within 30 days after registration or must have initiated treatment no more than 60 days prior to registration.

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.
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

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

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

Statisticians:
K Guthrie, S McDonough

Data Coordinators:
S Gurung

Date Activated: 10/12/2015
Date Closed: 04/20/2018

SCHEMA

*If patient is unable to undergo R0 or R1 surgical resection, he or she must be taken off protocol treatment.
Objectives
To assess two-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 two-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 reviewed by the local interpreting radiologist and then 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 data from the 40th and 80th enrolled patient becomes evaluable.

Summary Statement
This study closed as of April 20, 2018 after meeting the accrual goal with 147 patients registered. Thirty-nine patients have been deemed unresectable by central radiology review and thus are ineligible. One patient withdrew consent for further follow-up immediately after being randomized to mFOLFIRINOX and is not included in analyses.

Four patients have been excluded from adverse event analyses, are coded as ‘Other’ in the Treatment Summary table, and are counted as having major protocol deviations. One patient had disease progression prior to starting protocol treatment. One patient was inadvertently removed from protocol prior to starting treatment due to a misunderstanding regarding eligibility. One patient was unable to begin preoperative chemotherapy due to increased bilirubin and was removed from protocol treatment to go directly to surgery. One patient did not start treatment due to insurance denial. In addition to the four described above, five additional patients are counted as ‘Other’ in the Treatment Summary table: three were found to be unresectable following chemotherapy, one proceeded with a different post-operative chemotherapy plan per physician discretion, and one proceeded to surgery early per physician discretion. None received post-operative chemotherapy per protocol.

On the mFOLFIRINOX arm, 54 patients have been assessed for chemotherapy-related adverse events. There has been one treatment-related death due to sepsis. Five additional patients have experienced Grade 4 hematologic events and 33 additional
patients experienced Grade 3 events, including hepatic macrosteatosis (coded as 'Hepatobil disorders-Other'), skin infection, and bacterial infection (both coded as 'Infection/infestations-Other').

On the gemcitabine + nab-paclitaxel arm, 50 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 and 27 additional patients experienced Grade 3 events, including cellulitis (coded as 'Investigations/infestations-Other').

Of the 54 patients (overall) that have been assessed for surgery-related adverse events, 10 patients have experienced Grade 3/4 events.

Registration by Institution

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<th>Total Reg</th>
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Registration, Eligibility, and Evaluability
Data as of July 24, 2018

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Patient Characteristics
Data as of July 24, 2018

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<tbody>
<tr>
<td></td>
<td>(n=56)</td>
<td>(n=51)</td>
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</table>

| AGE                  | Median 66.3         | Median 63.9       |
|                      | Minimum 43.7         | Minimum 46.3      |
|                      | Maximum 76.0         | Maximum 75.5      |

| SEX                  | Males 36 (64%)        | Males 26 (51%)     |
|                      | Females 20 (36%)      | Females 25 (49%)   |

| HISPANIC             | Yes 3 (5%)            | Yes 4 (8%)         |
|                      | No 52 (93%)           | No 47 (92%)        |
|                      | Unknown 1 (2%)        | Unknown 0 (0%)     |

| RACE                 | White 53 (95%)        | White 44 (86%)     |
|                      | Black 2 (4%)          | Black 5 (10%)      |
|                      | Unknown 1 (2%)        | Unknown 2 (4%)     |

| PERFORMANCE STATUS   | 0 35 (63%)            | 0 33 (65%)         |
|                      | 1 21 (38%)            | 1 18 (35%)         |

Treatment Summary
Data as of July 24, 2018

| NUMBER ON PROTOCOL TREATMENT | 30 |
| NUMBER OFF PROTOCOL TREATMENT | 77 |
| REASON OFF TREATMENT |
| Treatment completed as planned | 23 |
| Adverse Event or side effects | 13 |
| Refusal unrelated to adverse event | 8 |
| Progression/relapse | 13 |
| Death | 3 |
| Other - not protocol specified | 9 |
| Reason under review | 8 |
| MAJOR PROTOCOL DEVIATIONS | 4 |
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 24, 2018

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<th>ADVERSE EVENTS</th>
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Data as of July 24, 2018

S1505/II
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 24, 2018

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</tr>
<tr>
<td>Weight loss</td>
<td>54</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wound infection</td>
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<td>0</td>
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<tr>
<td><strong>MAX. GRADE ANY ADVERSE EVENT</strong></td>
<td>44</td>
<td>9</td>
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</table>
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 McLeod, J Hayward

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 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. Patients who do not qualify for one of the histologic cohorts may be considered for registration in the "Not Otherwise Categorized" (NOC) cohort with confirmation by one of the study chairs. 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 must not have received either prior anti-CTLA4, anti-PD-1, or anti-PD-L1 therapy. Other immunotherapy is permitted, provided that it is completed at least seven days 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 ≥ 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.

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 is 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.

**Accrual Goals**
The accrual goal for this study is 707 patients to achieve 636 eligible 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, and NRG)

Study Chairs: K Raghav, M Fakih (NRG), B Tan, Jr. (Alliance), Y Jia (ECOG-ACRIN)

Statisticians: S McDonough, K Guthrie

Data Coordinator: J Scurlock

Date Activated: 10/09/2017

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 the 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**

The trial opened to accrual on October 9, 2017. As of June 30, 2018, 47 patients had been screened for HER-2 amplification with seven patients randomized to therapy.

**Registration by Institution**

Screening Registration
Registrations ending June 30, 2018

<table>
<thead>
<tr>
<th>Institutions</th>
<th>Total Reg</th>
<th>Institutions</th>
<th>Total Reg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartland NCORP</td>
<td>9</td>
<td>Ozarks NCORP</td>
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<tr>
<td>Hawaii MU-NCORP</td>
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<td>Southeast COR NCORP</td>
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<tr>
<td>MD Anderson CC</td>
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<td>Sutter Cancer RC</td>
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<tr>
<td>Kansas, U of</td>
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<td>ALLIANCE</td>
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<td>Michigan CRC NCORP</td>
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<td>NRG</td>
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<td>CORA NCORP</td>
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<td>ECOG-ACRIN</td>
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<td>Nevada CRF NCORP</td>
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<td>City of Hope Med Ctr</td>
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<td><strong>Total (14 Institutions)</strong></td>
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### Registration by Institution
#### Randomization
Registrations ending June 30, 2018

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<tr>
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<td>MD Anderson CC</td>
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<td><strong>Total (3 Institutions)</strong></td>
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### Registration, Eligibility, and Evaluability
#### Randomization
Registrations ending June 30, 2018; Data as of July 3, 2018

<table>
<thead>
<tr>
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<th>Trastuzumab + Pertuzumab</th>
<th>Cetuximab + Irinotecan</th>
</tr>
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<tr>
<td><strong>TOTAL</strong></td>
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<tr>
<td>Too Early</td>
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<tr>
<td>Too Early</td>
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### Patient Characteristics
#### Randomization
Registrations ending June 30, 2018; Data as of July 3, 2018

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<th>Cetuximab + Irinotecan (n=3)</th>
<th>Trastuzumab + Pertuzumab (n=4)</th>
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<td>Females</td>
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<td><strong>PRIOR USE OF IRINOTECAN</strong></td>
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<td>Yes</td>
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</tr>
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<td>No</td>
<td>2</td>
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<td>3</td>
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<tr>
<td><strong>HER2/CEP17</strong></td>
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<td>&gt; 5</td>
<td>4</td>
<td>100%</td>
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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

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

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

Statisticians:
J Unger, E Mayerson

Data Coordinator:
K Carvalho

SCHEMA

Cohort 1: Chronic HBV

- Prophylactic Antiviral Therapy
- Upon Indication Antiviral Therapy

Cohort 2: Past HBV

- Upon Indication Antiviral Therapy
- Usual Care Antiviral Therapy
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 not be taking antiviral medications active against HBV or 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 HIV test within the past 365 days. Patients must have complete results for HBsAg, anti-HBc, and anti-HBs 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 stratified 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 stratified 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.
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), B Conley (NCI), P O'Dwyer (ECOG-ACRIN), A Chen (NCI), V Villalobos (SWOG)

SCHEMA

Molecular Profiling by Outside Lab → Treatment for Molecular Profile of Interest → Toxicity or Progression

*As of May 1, 2017, patients must be screened via one of the outside laboratories listed in the protocol and only those patients with an applicable rare variant mutation of interest are eligible for subprotocol enrollment.

Objectives

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

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

To evaluate the time until death or disease progression.

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

To assess whether radiomic phenotypes obtained from pre-treatment imaging and changes from pre-through post-therapy imaging can predict Objective Response and Progression Free Survival and to evaluate the association between pre-treatment radiomic phenotypes and targeted gene mutation patterns of tumor biopsy specimens.

Patient Population

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

Patients must not currently be receiving any other investigational agents. Any prior therapy, radiotherapy (except palliative radiation therapy of 30 Gy or less), or major surgery must have been completed at least four weeks prior to treatment on NCI-MATCH and all adverse events due to prior therapy must have resolved to a Grade 1 or better...
(except alopecia and lymphopenia) by start of treatment. Palliative radiation therapy must have been completed at least two weeks prior to start of treatment. Patients with brain metastases or primary brain tumors must have completed treatment, surgery, or radiation therapy at least four weeks prior to start of treatment. Patients must have discontinued steroids at least one week prior to registration and remain off steroids thereafter, except as permitted in the protocol. Patients with glioblastoma must have been on a stable dose of steroids, or be off steroids, for one week prior to registration to treatment step. Patients must not require the use of full dose coumarin-derivative anticoagulants. Low molecular weight heparin is permitted for prophylactic or therapeutic use. Factor X inhibitors are permitted. Patients may receive non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results, but patients may not enroll in another investigational study during this time and the therapy cannot be an arm in this trial.

Patients must be at least 18 years of age, have an ECOG performance status of 0 or 1, must have a life expectancy of at least 3 months, and must be able to swallow tablets. Patients must have adequate hematologic, hepatic, renal, cardiac and marrow function. Patients must not have any uncontrolled intercurrent illness. HIV-positive patients are eligible provided they meet protocol criteria. Each subprotocol will have additional eligibility criteria that will be outlined in Section 2.0 of the agent-specific subprotocol.

Only sites utilizing the CIRB as their IRB of record are able to participate in the trial.

**Accrual Goals**
The target screening accrual for this study is approximately 6,452 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 trial termination. Within any given subprotocol, if rate of enrollment is such that it is unlikely accrual can reach 25 patients by the time the overall study screening accrual goal is met, and if 13 patients have been treated and no responses have been observed, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. After 500 patients are screened, the study design will be reassessed to assure its appropriateness. An interim analysis of the assay results will be performed after biopsies from approximately the first 200 patients are processed.

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