PREVENTION AND EPIDEMIOLOGY COMMITTEE

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Patient Registrations to Studies

By 12 Month Intervals
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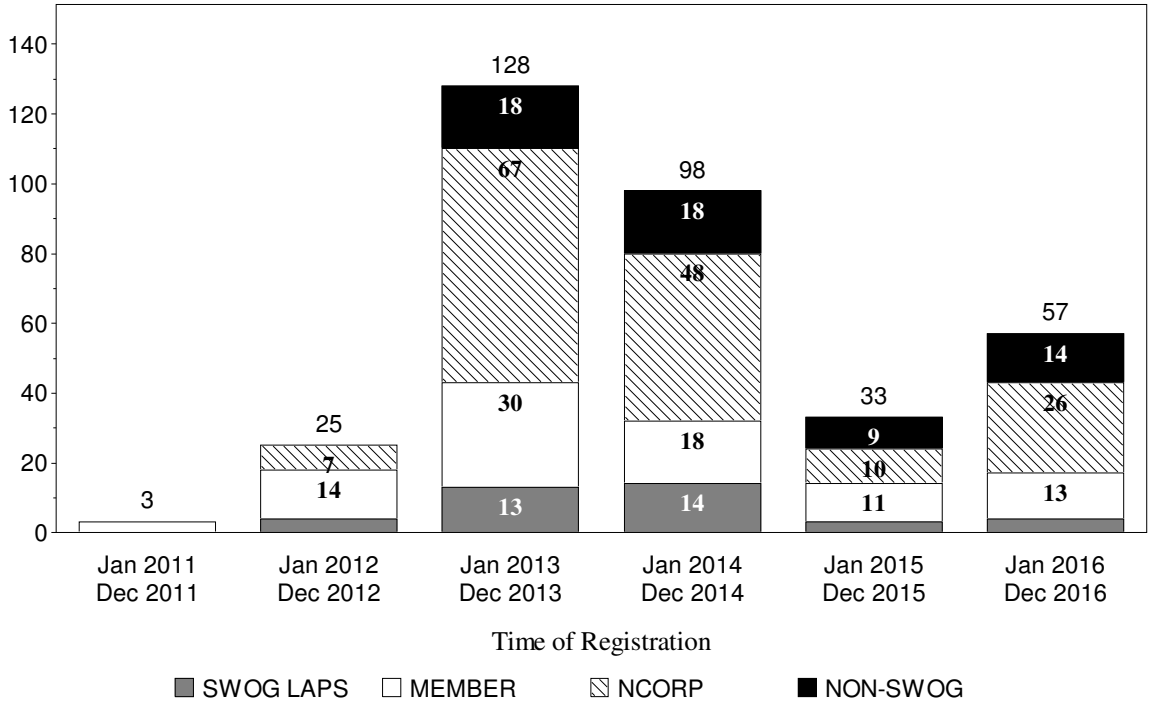

Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

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	Jul 2016 Dec 2016	Jan 2016 Jun 2016	Jul 2015 Dec 2015	All Patients
S0000B SELECT Eye Endpoints (SEE)				
Registration				
Registration	0	0	65	2,774
S0820 PACES: ColrecStg0-3 Blind DFMO/Sulindac				
Pre-Registration				
Pre-Registration	71	162	75	308
Randomization				
Blinded drug	28	24	14	119
A211102 Breast, Atypia via RPFNA, Metformin v Placebo*				
Total Registrations	1	1	0	2
A211201 Breast Density, MA.32 companion*				
Total Registrations	0	2	0	14
NHLBIMDS LEUK, National MDS Study*				
Total Registrations	1	0	0	1

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

Non-SWOG Studies with SWOG-Credited Registrations

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Studies with Accrual from July 2015 – December 2016

	SWOG Champion	Date Activated	Date Closed	Total Accrual
A211102 Breast, Atypia via RPFNA, Metformin v Pl		02/01/15		16
Most Recent Progress Report				
A211201 Breast Density, MA.32 companion		08/22/12		177
Most Recent Progress Report				
NHLBIMDS LEUK, National MDS Study		04/05/16		75
No Progress Report Available				

S0820 Phase III

Coordinating Group: SWOG

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

Participants:
SWOG, CTSU

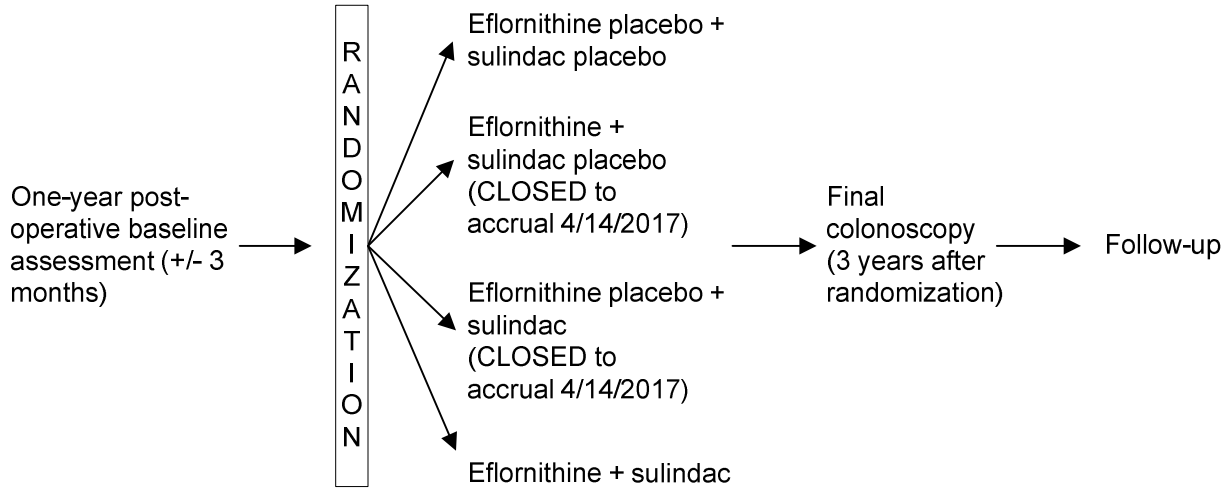
Date Activated:
03/01/2013

Study Chairs:
J Zell, P Brown

Statisticians:
J Unger, G Anderson, K Arnold

Data Coordinator:
M Yee

SCHEMA



Objectives

To assess whether 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 $\geq$ 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 eligible patients will be enrolled, 210 to each study arm. As of December 31, 2016, an additional 58 patients were enrolled to Arms 2 and 3 prior to their closure under Amendment #2.

Summary Statement

This study activated on March 1, 2013. As of December 31, 2016, 119 patients have been randomized.

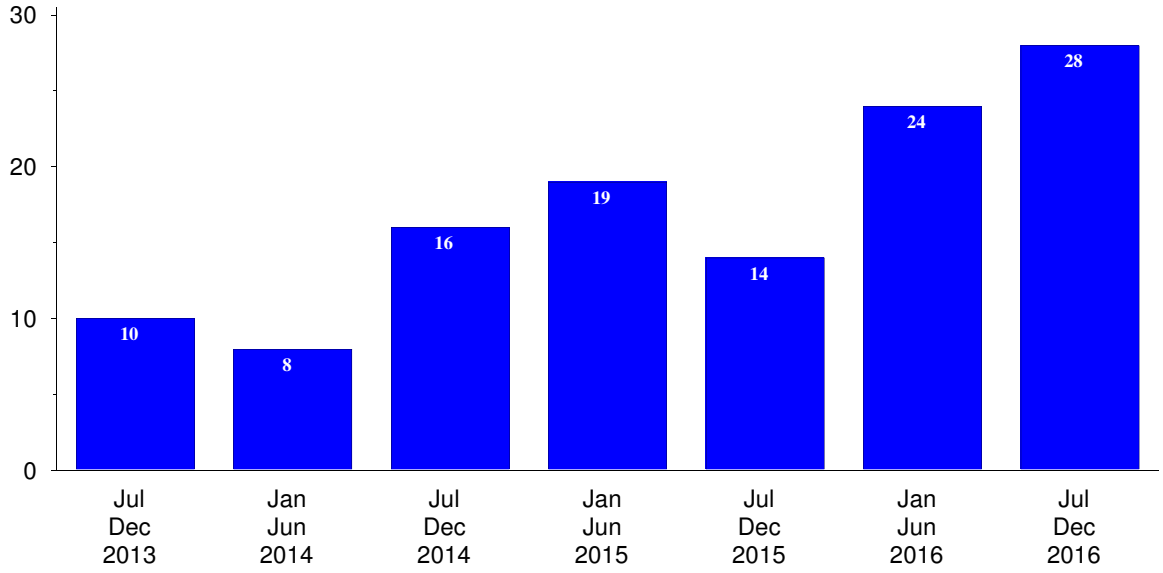
Eight patients are ineligible due to: baseline hearing loss (4), baseline lab values out of range (2), high cardiovascular risk (1), and primary resection done too late (1). One patient is not analyzable due to withdrawal of consent prior to starting treatment. Three patients who never started treatment are coded as major deviations; these patients are also not evaluable for adverse events. Thirty-five patients are off treatment, including six patients coded as "Other – not protocol specified": two did not take study medication for more than 90 days; two the site was unable to contact; one stopped medication; and one the site removed in error.

Among 92 patients who have had adverse events evaluated, six Grade 3 events were reported for four patients: two patients reported hypertension; one patient reported diarrhea; and one patient reported anemia, duodenal ulcer, and upper GI hemorrhage.

In Amendment #2, distributed March 15, 2017, the two single-agent arms of the study (eflornithine + sulindac placebo and eflornithine placebo + sulindac) have been closed effective April 14, 2017. The revised primary objective is to compare the combination of eflornithine + sulindac to eflornithine placebo + sulindac placebo in a 2-arm, phase III trial. The sample size was modified accordingly. The two arms with active drug and placebo combinations (eflornithine plus sulindac placebo and eflornithine placebo plus sulindac) will be closed to further accrual. Patients currently enrolled on those combination arms will continue to be treated and followed per protocol, and sites will continue to order drug per protocol. Surgical eligibility for rectal patients has been modified.

A tool for tracking patients from the time of their initial resection to their registration window was made available in Revision #4. As of December 31, 2016, 308 patients have been entered in the tracking tool, of whom 18 were subsequently randomized.

Initial Registrations By 6 Month Intervals



Registration by Institution

Registrations ending December 31, 2016

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	13	McLaren Cancer Inst/Wayne State Univ	2
Alliance	12	Michigan CRC NCORP	2
Irvine, U of CA	12	Yale University	2
ECOG-ACRIN	8	Baptist MU-NCORP	1
NRG	7	Bridgeport Hospital/Yale University	1
Wichita NCORP	6	Brooke Army Med Ctr	1
San Antonio, U of TX	5	City of Hope Med Ctr	1
Banner MD Anderson/MD Anderson CC	4	Colorado, U of	1
Hawaii MU-NCORP	4	Columbia MU-NCORP	1
MD Anderson CC	4	Eisenhower Army MC/Brooke Army Med Ctr	1
Essentia Hlth NCORP	3	Georgia NCORP	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	Loma Linda Univ	1
Kansas, U of	3	NE Georgia Med Ctr/Georgia NCORP	1
Northwest NCORP	3	Oklahoma, Univ of	1
So Calif, U of	3	Providence Hosp	1
Columbus NCORP	2	Southeast COR NCORP	1
CORA NCORP	2	St Joseph Hospital/Mississippi, Univ of	1
Heartland NCORP	2	Weiss Memorial Hosp/Loyola University	1
MAVERIC	2	**Total (37 Institutions)**	**119**

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2016; Data as of February 14, 2017

	Total
NUMBER REGISTERED	119
INELIGIBLE	8
ELIGIBLE	111
Analyzable, Pend. Elig.	4
Not Analyzable	1
ADVERSE EVENT ASSESSMENT	
Evaluable	92
Not Evaluable	4
Too Early	14

Patient Characteristics

Registrations ending December 31, 2016; Data as of February 14, 2017

	Total (n=110)	
AGE		
Median	52.1	
Minimum	29.2	
Maximum	78.2	
SEX		
Males	44	40%
Females	66	60%
HISPANIC		
Yes	12	11%
No	96	87%
Unknown	2	2%
RACE		
White	80	73%
Black	5	5%
Asian	14	13%
Pacific Islander	2	2%
Native American	1	1%
Multi-Racial	1	1%
Unknown	7	6%
RISK OF RECURRENCE		
Stage 0 or I	19	17%
Stage II with no prior chemotherapy or radiation therapy	20	18%
Stage II with prior chemotherapy or radiation therapy	13	12%
Stage III	58	53%

Treatment Summary

Registrations ending December 31, 2016; Data as of February 14, 2017

	Total
NUMBER ON PROTOCOL TREATMENT	75
NUMBER OFF PROTOCOL TREATMENT	35
REASON OFF TREATMENT	
Treatment completed as planned	4
Adverse Event or side effects	6
Refusal unrelated to adverse event	7
Progression/relapse	6
Death	1
Other - not protocol specified	6
Reason under review	5
MAJOR PROTOCOL DEVIATIONS	3

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2016; Data as of February 14, 2017

	Total (n=92) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	88	4	0	0	0	0
AST increased	91	1	0	0	0	0
Abdominal pain	89	1	2	0	0	0
Alkaline phosphatase increased	91	1	0	0	0	0
Alopecia	91	1	0	0	0	0
Anemia	91	0	0	1	0	0
Anxiety	91	1	0	0	0	0
Arthralgia	90	2	0	0	0	0
Bloating	91	0	1	0	0	0
Blood bilirubin increased	91	1	0	0	0	0
Blurred vision	91	1	0	0	0	0
Cardiac disorder-Other, spec	91	1	0	0	0	0
Chest pain - cardiac	91	1	0	0	0	0
Constipation	83	7	2	0	0	0
Diarrhea	82	5	4	1	0	0
Dizziness	85	7	0	0	0	0
Dry mouth	90	2	0	0	0	0
Duodenal ulcer	91	0	0	1	0	0
Dyspepsia	89	3	0	0	0	0
Dysphagia	91	1	0	0	0	0
Dyspnea	91	1	0	0	0	0
Edema limbs	91	1	0	0	0	0
Fatigue	84	7	1	0	0	0
Flu like symptoms	91	1	0	0	0	0

Number of Patients with a Given Type and Grade of Adverse Event (continued)

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2016; Data as of February 14, 2017

	Total (n=92) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
GERD	91	1	0	0	0	0
GI disorders-Other, specify	91	1	0	0	0	0
Gastritis	91	0	1	0	0	0
Gastrointestinal pain	89	3	0	0	0	0
Headache	86	5	1	0	0	0
Hematuria	90	2	0	0	0	0
Hot flashes	90	2	0	0	0	0
Hyperglycemia	91	0	1	0	0	0
Hypertension	85	3	2	2	0	0
Insomnia	91	0	1	0	0	0
Irregular menstruation	91	1	0	0	0	0
Myalgia	91	1	0	0	0	0
Nausea	83	9	0	0	0	0
Pain	91	1	0	0	0	0
Pain in extremity	91	1	0	0	0	0
Platelet count decreased	91	1	0	0	0	0
Rash maculo-papular	91	1	0	0	0	0
Rectal hemorrhage	91	1	0	0	0	0
Renal/urinary disorders-Other	91	1	0	0	0	0
Skin/subq tissue ds-Other	90	1	1	0	0	0
Somnolence	91	1	0	0	0	0
Stomach pain	91	1	0	0	0	0
Tinnitus	88	3	1	0	0	0
Upper GI hemorrhage	91	0	0	1	0	0
Vaginal dryness	91	1	0	0	0	0
Vomiting	90	2	0	0	0	0
Weight loss	91	1	0	0	0	0
White blood cell decreased	91	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	46	30	12	4	0	0