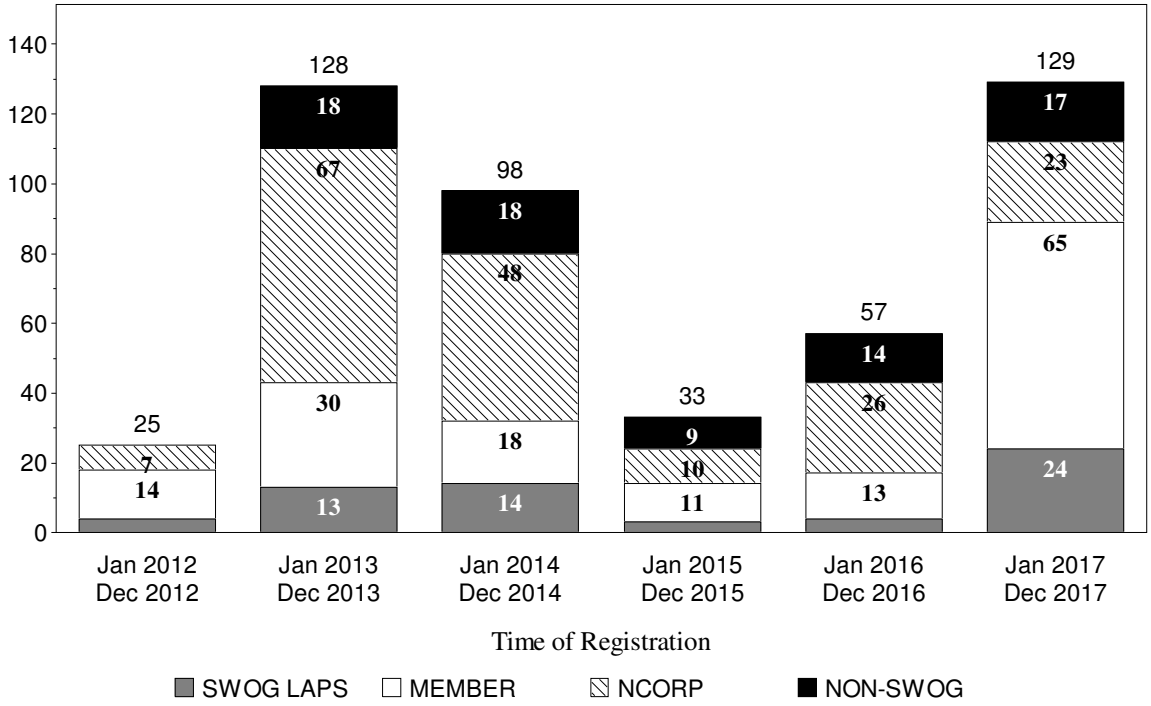
PREVENTION AND EPIDEMIOLOGY COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
PREVENTION AND EPIDEMIOLOGY COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded.

Patient Registrations by Study and Arm

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	Jul 2017 Dec 2017	Jan 2017 Jun 2017	Jul 2016 Dec 2016	All Patients
S0820 PACES: ColrecStg0-3 Blind DFMO/Sulindac				
Pre-Registration				
Pre-Registration	77	52	71	437
Randomization				
Blinded drug	23	34	28	176
A011502 Brst, Adj, Nodal+&HER2-, Aspirin vs. Placebo*				
Total Registrations	17	6	0	23
A211102 Breast, Atypia via RPFNA, Metformin v Placebo*				
Total Registrations	0	1	1	3
EA1141 Breast, Abbrev. MRI vs Digital Tomosynthesis*				
Total Registrations	38	6	0	44
NHLBIMDS LEUK, National MDS Study*				
Total Registrations	1	3	1	5

* 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 2016 - December 2017

	SWOG Champion	Date Activated	Date Closed	Total Accrued
A011502 Brst, Adj, Nodal+&HER2-, Aspirin vs. Placebo *No Progress Report Available*		12/08/16		291
A211102 Breast, Atypia via RPFNA, Metformin v Placebo *Most Recent Progress Report*		02/01/15		41
A211201 Breast Density, MA.32 companion *Most Recent Progress Report*		08/22/12	10/13/17	177
EA1141 Breast, Abbrev. MRI vs Digital Tomosynthesis *Most Recent Progress Report*		09/02/16	11/07/17	1518
NHLBIMDS LEUK, National MDS Study *No Progress Report Available*	B Till	04/05/16		331

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 ECOG-ACRIN, NRG, Alliance)

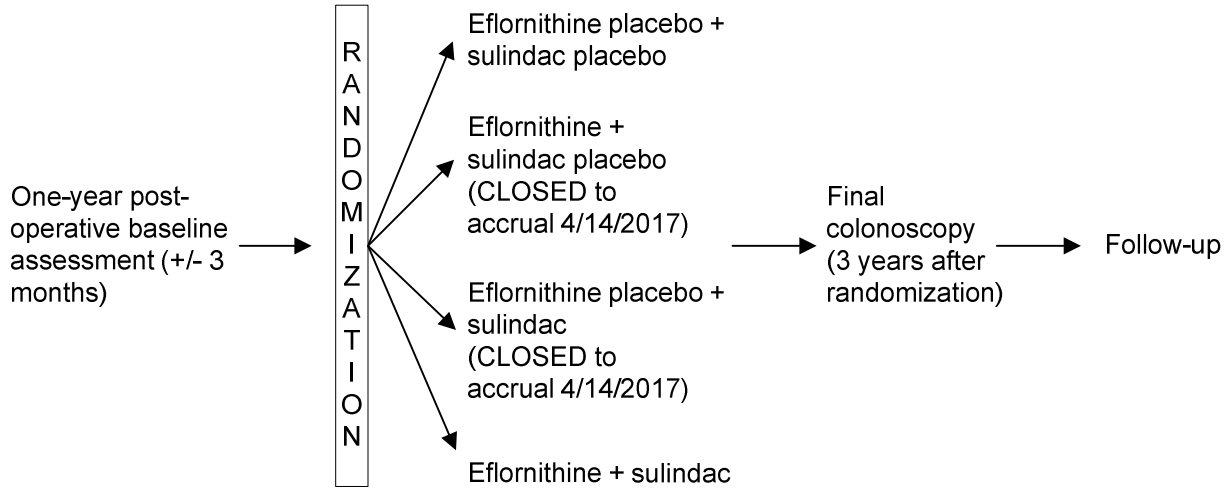
Date Activated:
03/01/2013

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 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

This study activated on March 1, 2013. As of December 31, 2017, 176 patients have been randomized.

In Amendment #2, distributed March 15, 2017, the two single-agent arms of the study (eflornithine + sulindac placebo and eflornithine placebo + sulindac) were closed, effective April 14, 2017. This design change was made because full accrual was determined not be achievable under the original design. The revised primary objective is to compare the combination of eflornithine + sulindac to eflornithine placebo + sulindac placebo in a two-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) were 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 study drugs per protocol. Surgical eligibility for rectal patients has been modified.

This reports presents data only on the two open arms, as these are the arms that contribute to the revised study objectives.

For patients on the currently open arms:

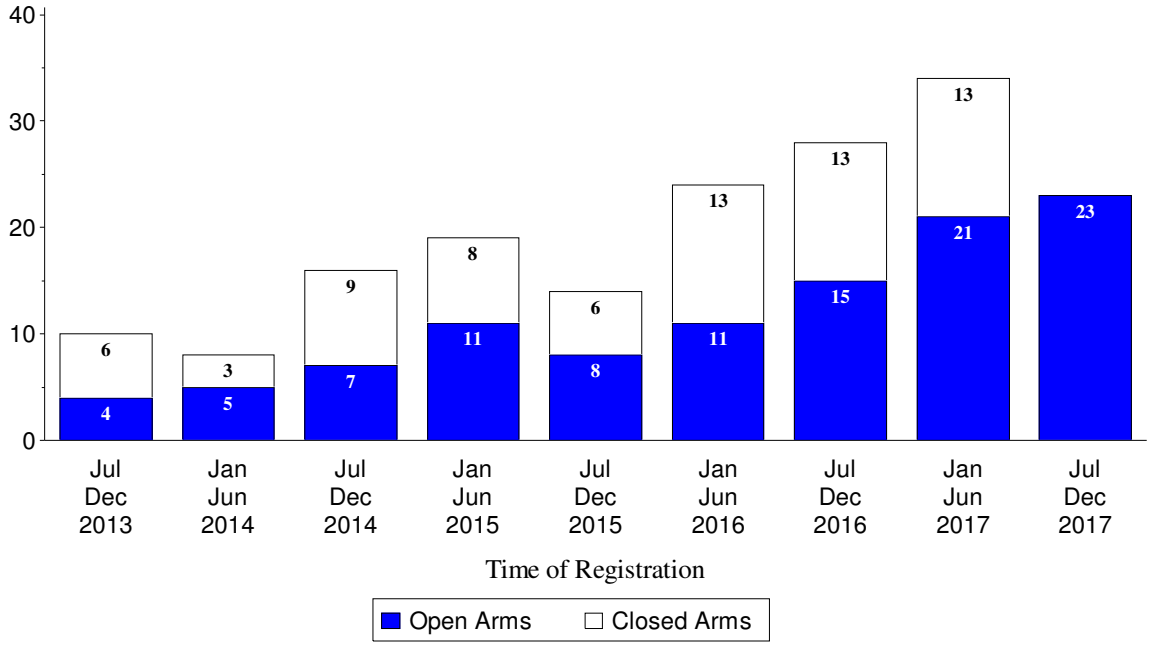
As of December 31, 2017, 105 patients have been randomized to the currently open arms. Eight patients are ineligible due to: baseline hearing loss (4 patients), baseline lab values out of range (1), high cardiovascular risk (1), primary resection done too late (1), and metastatic disease (1). Four patients are coded as major deviations, three of whom never started treatment and one who had had only one day of treatment. Four patients are not evaluable for adverse events due to: never starting treatment (3); and incorrectly removed from treatment (1). Thirty-five patients are off treatment, including six patients coded as "Other – not protocol specified", two of whom did not take study medication for more than 90 days, two due to NSAID use, one of whom the site was unable to contact, and one patient who stopped medication because of incorrectly thinking they had relapsed.

Among 79 patients who have had adverse events evaluated, one patient reported Grade 3 anemia, duodenal ulcer, and upper GI hemorrhage and one patient reported Grade 3 tinnitus.

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, 2017, 437 patients have been logged into the tracking tool, of whom 33 were subsequently randomized, 18 to the open arms and 15 to the closed arms. Two hundred and ninety-seven logged patients have passed the eligibility window and will never be randomized.

Initial Registrations By 6 Month Intervals

Divisions by Study Arm Status



Registration by Institution

All Arms

Registrations ending December 31, 2017

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	20	Baptist MU-NCORP	1
Irvine, U of CA	17	Bridgeport Hospital/Yale University	1
Wichita NCORP	11	Brooke Army Med Ctr	1
Yale University	8	City of Hope Med Ctr	1
Hawaii MU-NCORP	6	Columbia MU-NCORP	1
San Antonio, U of TX	6	Dayton NCORP	1
Banner MD Anderson/MD Anderson CC	5	Eisenhower Army MC/Brooke Army Med Ctr	1
Northwest NCORP	5	Georgia NCORP	1
So Calif, U of	5	Loma Linda Univ	1
Columbus NCORP	4	NE Georgia Med Ctr/Georgia NCORP	1
MD Anderson CC	4	Nevada CRF NCORP	1
Michigan CRC NCORP	4	Oklahoma, Univ of	1
Colorado, U of	3	Providence Hosp	1
Essentia Hlth NCORP	3	Southeast COR NCORP	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	St Joseph Hospital/Mississippi, Univ of	1
Kansas, U of	3	Weiss Memorial Hosp/Loyola University	1
MAVERIC	3	ALLIANCE	17
CORA NCORP	2	NRG	15
Heartland NCORP	2	ECOG-ACRIN	12
McLaren Cancer Inst/Wayne State Univ	2	**Total (39 Institutions)**	**176**

Registration, Eligibility, and Evaluability

Open Arms

Registrations ending December 31, 2017; Data as of February 5, 2018

	Total
NUMBER REGISTERED	105
INELIGIBLE	8
ELIGIBLE	97
Analyzable, Pend. Elig.	13
ADVERSE EVENT ASSESSMENT	
Evaluable	79
Not Evaluable	4
Too Early	14

Patient Characteristics

Open Arms

All eligible and selected ineligible patients included

Registrations ending December 31, 2017; Data as of February 5, 2018

	Total (n=97)	
AGE		
Median	53.0	
Minimum	30.6	
Maximum	79.9	
SEX		
Males	39	40%
Females	58	60%
HISPANIC		
Yes	15	15%
No	79	81%
Unknown	3	3%
RACE		
White	71	73%
Black	5	5%
Asian	11	11%
Pacific Islander	1	1%
Native American	1	1%
Unknown	8	8%
RISK OF RECURRENCE		
Stage 0 or I	17	18%
Stage II with no prior chemotherapy or radiation therapy	18	19%
Stage II with prior chemotherapy or radiation therapy	11	11%
Stage III	51	53%

Treatment Summary

Open Arms

All eligible and selected ineligible patients included

Registrations ending December 31, 2017; Data as of February 5, 2018

	Total
NUMBER ON PROTOCOL TREATMENT	62
NUMBER OFF PROTOCOL TREATMENT	35
REASON OFF TREATMENT	
Treatment completed as planned	7
Adverse Event or side effects	8
Refusal unrelated to adverse event	5
Progression/relapse	4
Death	0
Other - not protocol specified	6
Reason under review	5
MAJOR PROTOCOL DEVIATIONS	4

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

Open Arms

Adverse Events Unlikely or Not Related to Treatment Excluded

All Eligible and Selected Ineligible Patients Included

Registrations ending December 31, 2017; Data as of February 5, 2018

	Total (n=79) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	74	5	0	0	0	0
AST increased	76	3	0	0	0	0
Abdominal pain	76	3	0	0	0	0
Alkaline phosphatase increased	78	1	0	0	0	0
Allergic reaction	78	0	1	0	0	0
Alopecia	78	1	0	0	0	0
Anemia	76	2	0	1	0	0
Anxiety	78	1	0	0	0	0
Arthralgia	78	1	0	0	0	0
Bloating	78	1	0	0	0	0
Blood bilirubin increased	75	3	1	0	0	0
Bruising	77	2	0	0	0	0
Chest pain - cardiac	78	1	0	0	0	0
Constipation	73	6	0	0	0	0
Diarrhea	72	6	1	0	0	0
Dizziness	76	3	0	0	0	0
Dry mouth	78	1	0	0	0	0
Duodenal ulcer	78	0	0	1	0	0
Dysgeusia	78	1	0	0	0	0
Dyspepsia	77	1	1	0	0	0
Dysphagia	78	1	0	0	0	0

	Total (n=79) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Dyspnea	78	1	0	0	0	0
Edema limbs	76	3	0	0	0	0
Fatigue	70	8	1	0	0	0
Flu like symptoms	78	1	0	0	0	0
Flushing	78	0	1	0	0	0
Gastrointestinal pain	78	1	0	0	0	0
Generalized muscle weakness	78	1	0	0	0	0
Headache	74	5	0	0	0	0
Hematuria	77	2	0	0	0	0
Hot flashes	78	1	0	0	0	0
Hyperhidrosis	78	1	0	0	0	0
Hypertension	75	1	3	0	0	0
Hypocalcemia	78	1	0	0	0	0
Insomnia	78	0	1	0	0	0
Investigations-Other, specify	78	1	0	0	0	0
MS/connective tissue disorder	78	1	0	0	0	0
Muscle weakness upper limb	78	1	0	0	0	0
Myalgia	78	1	0	0	0	0
Nausea	73	6	0	0	0	0
Pain	78	1	0	0	0	0
Pain in extremity	77	2	0	0	0	0
Peripheral sensory neuropathy	78	1	0	0	0	0
Platelet count decreased	78	1	0	0	0	0
Pleuritic pain	78	1	0	0	0	0
Postnasal drip	78	1	0	0	0	0
Pruritus	78	0	1	0	0	0
Rash maculo-papular	78	1	0	0	0	0
Renal/urinary disorders-Other	78	1	0	0	0	0
Skin hyperpigmentation	78	1	0	0	0	0
Skin/subq tissue ds-Other	78	1	0	0	0	0
Somnolence	78	1	0	0	0	0
Stroke	78	0	1	0	0	0
Tinnitus	74	3	1	1	0	0
Transient ischemic attacks	78	0	1	0	0	0
Upper GI hemorrhage	78	0	0	1	0	0
Vaginal dryness	78	1	0	0	0	0
Vomiting	77	2	0	0	0	0
White blood cell decreased	78	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	34	32	11	2	0	0