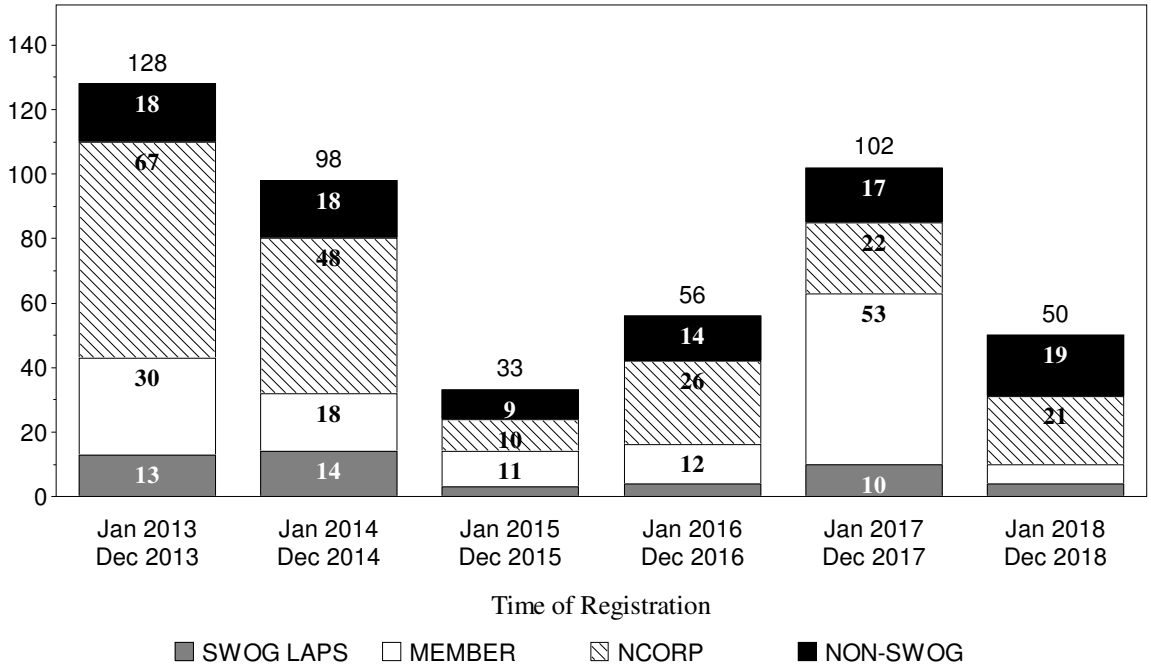
PREVENTION AND EPIDEMIOLOGY COMMITTEE

CONTENTS

Patient Registrations to Studies

by 12 Month Intervals
PREVENTION AND EPIDEMIOLOGY COMMITTEE
As Primary Committee



Screening registrations and registrations to Biologic only studies are excluded.

Patient Registrations by Study and Arm

PREVENTION AND EPIDEMIOLOGY COMMITTEE

	Jul 2018 Dec 2018	Jan 2018 Jun 2018	Jul 2017 Dec 2017	All Patients
S0820 PACES: ColrecStg0-3 Blind DFMO/Sulindac				
Pre-Registration				
Pre-Registration	17	58	77	512
Randomization				
Blinded drug	22	28	23	226

Non-SWOG Studies with SWOG-Credited Registrations

PREVENTION AND EPIDEMIOLOGY COMMITTEE

Studies with Accrual from July 2017 - December 2018

	SWOG Champion	SWOG Accrual Jul 2018 Dec 2018	SWOG Accrual Jan 2018 Jun 2018	SWOG Accrual Jul 2017 Dec 2017	SWOG Total	Total Accrued
A011502 Brst, Adj, Nodal+&HER2-, Aspirin vs. Placebo*	B Symington	18	25	17	66	963
Date Activated: 12/08/16						
Most Recent Progress Report						
A211102 Breast, Atypia via RPFNA, Metformin v Placebo		0	0	0	3	61
Date Activated: 02/01/15						
Most Recent Progress Report						
EA1141 Breast, Abbrev. MRI vs Digital Tomosynthesis		0	0	38	44	1518
Date Activated: 09/02/16 Date Closed: 11/07/17						
Most Recent Progress Report						
NHLBIMDS LEUK, National MDS Study*	D Hill, C Yi	6	8	1	19	610
Date Activated: 04/05/16						
No Progress Report Availalble						

* Studies with Prevention and Epidemiology as a secondary Committee

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)

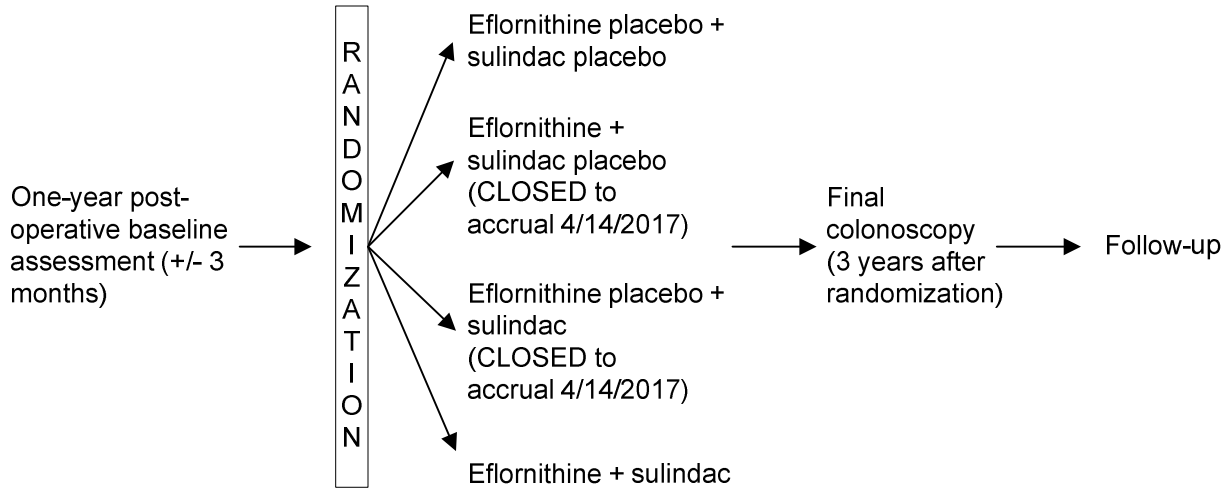
Date Activated:
03/01/2013

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 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 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 of the two open study arms. 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, 2018, 226 patients have been randomized; of these, 155 patients were randomized to the currently open arms. Eleven patients are ineligible due to: baseline hearing loss (5 patients), primary resection done too early (3), baseline lab values out of range (1), high cardiovascular risk (1), and pregnancy (1). Four patients are coded as major deviations, three of whom never started treatment and one who had had only one day of treatment. Sixty-seven patients are off treatment, including 11 patients coded as "Other – not protocol specified" for the following reasons: medication use not allowed on the study (4), intercurrent illness (2), site was unable to contact patient (2), patient moved (2), and patient thought they had relapsed (1). Four patients who are

off treatment for various reasons have withdrawn consent for any further follow-up.

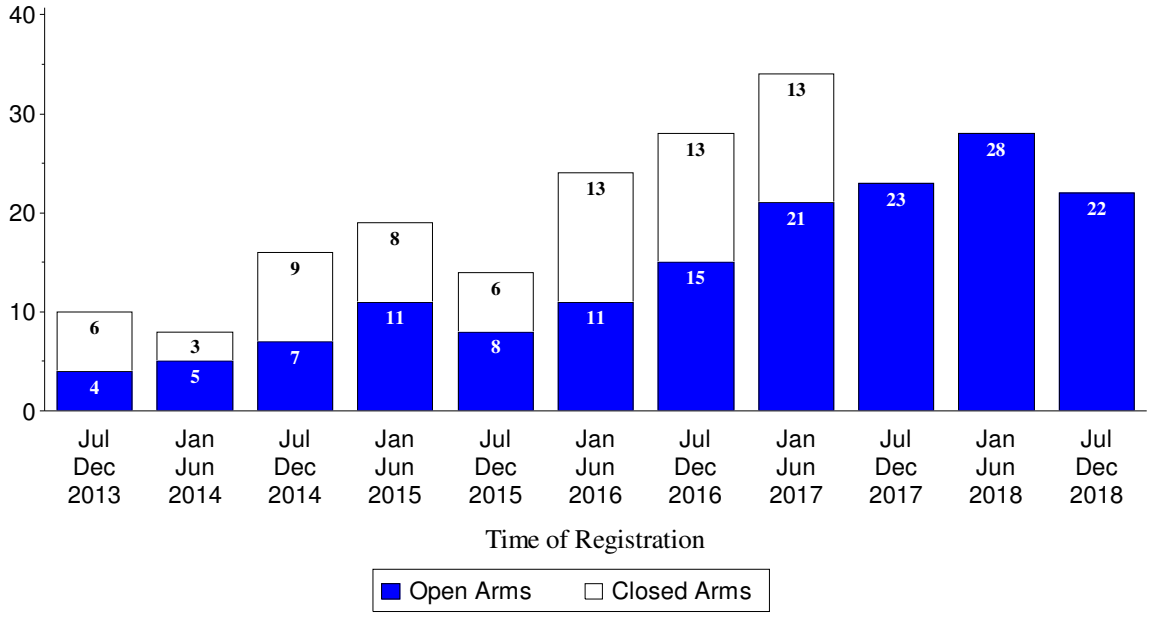
Five patients are not evaluable for adverse events due to never starting treatment (3) and no AE assessment made (2). Among 126 patients who have had adverse events evaluated, three had Grade 3 events: one patient experienced Grade 3 anemia, duodenal ulcer, and upper GI hemorrhage; one patient experienced Grade 3 mucositis oral and rash maculo-papular; and one patient experienced 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, 2018, 512 patients have been logged into the tracking tool, of whom 43 were subsequently randomized, 28 to the open arms and 15 to the closed arms. Four hundred and thirty-two logged patients have passed the eligibility window and will never be randomized. Sites are encouraged to use the tracking tool to facilitate timing of patient randomizations with respect to the prior treatment windows.

Randomization by 6 Month Intervals

Divisions by Study Arm Status

All Arms



Registration by Institution

All Arms

Registrations ending December 31, 2018

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	25	Bay Area NCORP	1
Irvine, U of CA	20	Bridgeport Hospital/Yale University	1
Wichita NCORP	12	Brooke Army Med Ctr	1
Yale University	11	City of Hope Med Ctr	1
Hawaii MU-NCORP	9	Columbia MU-NCORP	1
Northwest NCORP	8	CRC West MI NCORP	1
San Antonio, U of TX	8	Dayton NCORP	1
Banner MD Anderson/MD Anderson CC	5	Eisenhower Army MC/Brooke Army Med Ctr	1
Columbus NCORP	5	Georgia NCORP	1
So Calif, U of	5	NE Georgia Med Ctr/Georgia NCORP	1
Colorado, U of	4	Nevada CRF NCORP	1
Essentia Hlth NCORP	4	New Mexico MU-NCORP	1
MD Anderson CC	4	Oklahoma, Univ of	1
Michigan CRC NCORP	4	PCRC NCORP	1
Baptist MU-NCORP	3	Providence Hosp	1
CORA 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	NRG	24
Heartland NCORP	2	ALLIANCE	23
Loma Linda Univ	2	ECOG-ACRIN	16
McLaren Cancer Inst/Wayne State Univ	2	**Total (43 Institutions)**	**226**

Registration, Eligibility, and Evaluability

Open Arms

Registrations ending December 31, 2018; Data as of February 6, 2019

	Total
NUMBER REGISTERED	155
INELIGIBLE	11
ELIGIBLE	144
Analyzable, Pend. Elig.	17
ADVERSE EVENT ASSESSMENT	
Evaluable	126
Not Evaluable	5
Too Early	13

Patient Characteristics

Open Arms

All eligible and selected ineligible patients included

Registrations ending December 31, 2018; Data as of February 6, 2019

	Total (n=144)	
AGE		
Median	53.3	
Minimum	28.4	
Maximum	78.1	
SEX		
Males	57	40%
Females	87	60%
HISPANIC		
Yes	18	13%
No	123	85%
Unknown	3	2%
RACE		
White	104	72%
Black	9	6%
Asian	18	13%
Pacific Islander	1	1%
Native American	1	1%
Multi-Racial	2	1%
Unknown	9	6%
RISK OF RECURRENCE		
Stage 0 or I	25	17%
Stage II with no prior chemotherapy or radiation therapy	22	15%
Stage II with prior chemotherapy or radiation therapy	21	15%
Stage III	76	53%

Treatment Summary

Open Arms

All eligible and selected ineligible patients included

Registrations ending December 31, 2018; Data as of February 6, 2019

	Total
NUMBER ON PROTOCOL TREATMENT	77
NUMBER OFF PROTOCOL TREATMENT	67
REASON OFF TREATMENT	
Treatment completed as planned	18
Adverse Event or side effects	12
Refusal unrelated to adverse event	12
Progression/relapse	7
Death	0
Other - not protocol specified	11
Reason under review	7
MAJOR PROTOCOL DEVIATIONS	4
LOST TO FOLLOW-UP	1
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	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, 2018; Data as of February 6, 2019

	Total (n=126) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	120	6	0	0	0	0
AST increased	121	5	0	0	0	0
Abdominal pain	123	3	0	0	0	0
Alkaline phosphatase increased	125	1	0	0	0	0
Allergic reaction	125	0	1	0	0	0
Alopecia	123	3	0	0	0	0
Anemia	122	2	1	1	0	0
Anxiety	125	1	0	0	0	0
Arthralgia	125	1	0	0	0	0
Back pain	125	1	0	0	0	0
Bloating	124	2	0	0	0	0
Blood bilirubin increased	122	3	1	0	0	0
Body odor	125	1	0	0	0	0
Bruising	123	3	0	0	0	0
Chest pain - cardiac	125	1	0	0	0	0
Cholesterol high	125	1	0	0	0	0
Constipation	115	11	0	0	0	0
Cough	124	2	0	0	0	0
Diarrhea	116	8	2	0	0	0
Dizziness	119	6	1	0	0	0
Dry mouth	125	1	0	0	0	0
Duodenal ulcer	125	0	0	1	0	0
Dysgeusia	125	1	0	0	0	0
Dyspepsia	122	3	1	0	0	0
Dysphagia	125	1	0	0	0	0
Dyspnea	125	1	0	0	0	0
Edema limbs	122	4	0	0	0	0
Fatigue	117	8	1	0	0	0
Flu like symptoms	125	1	0	0	0	0
Flushing	125	0	1	0	0	0
GERD	125	0	1	0	0	0
GI disorders-Other, specify	124	2	0	0	0	0
Gastrointestinal pain	124	2	0	0	0	0
Generalized muscle weakness	125	1	0	0	0	0
Headache	119	6	1	0	0	0
Hearing impaired	124	2	0	0	0	0
Hematuria	124	2	0	0	0	0
Hot flashes	125	1	0	0	0	0
Hyperhidrosis	125	1	0	0	0	0
Hypertension	118	2	6	0	0	0
Hypocalcemia	125	1	0	0	0	0
Insomnia	124	1	1	0	0	0
Investigations-Other, specify	123	3	0	0	0	0
MS/connective tissue disorder	124	2	0	0	0	0

	Total (n=126) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Mucositis oral	125	0	0	1	0	0
Muscle weakness upper limb	125	1	0	0	0	0
Myalgia	124	2	0	0	0	0
Nausea	118	7	1	0	0	0
Nervous sys disorders-Other	125	1	0	0	0	0
Pain	125	1	0	0	0	0
Pain in extremity	124	2	0	0	0	0
Paresthesia	125	1	0	0	0	0
Peripheral sensory neuropathy	124	1	1	0	0	0
Platelet count decreased	124	2	0	0	0	0
Pleuritic pain	125	1	0	0	0	0
Postnasal drip	125	1	0	0	0	0
Pruritus	124	1	1	0	0	0
Rash acneiform	125	1	0	0	0	0
Rash maculo-papular	124	1	0	1	0	0
Renal/urinary disorders-Other	125	1	0	0	0	0
Skin hyperpigmentation	124	2	0	0	0	0
Skin/subq tissue ds-Other	125	1	0	0	0	0
Somnolence	125	1	0	0	0	0
Stomach pain	125	1	0	0	0	0
Stroke	124	0	2	0	0	0
Tinnitus	118	5	2	1	0	0
Transient ischemic attacks	125	0	1	0	0	0
Upper GI hemorrhage	125	0	0	1	0	0
Vaginal dryness	125	1	0	0	0	0
Vomiting	123	2	1	0	0	0
Weight gain	125	0	1	0	0	0
White blood cell decreased	124	2	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	50	51	22	3	0	0