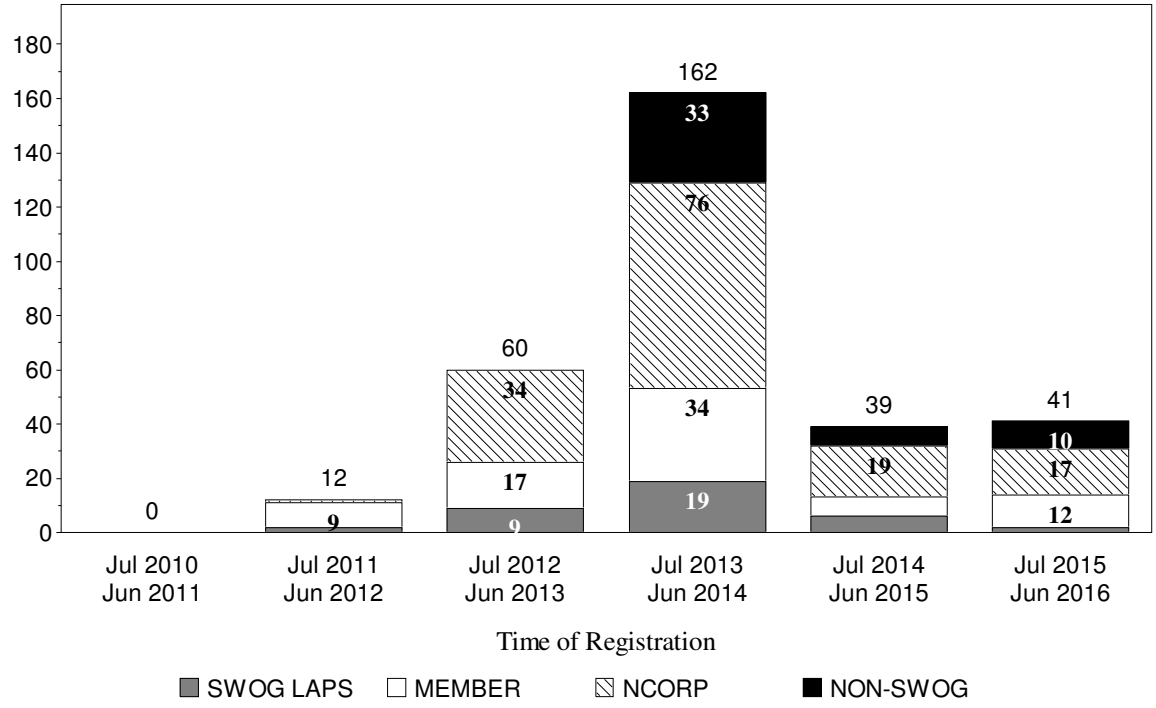
PREVENTION AND EPIDEMIOLOGY COMMITTEE

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

PREVENTION AND EPIDEMIOLOGY COMMITTEE

	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
S0000B SELECT Eye Endpoints (SEE)				
Registration				
Registration	0	65	0	2,774
S0820 PACES: ColrecStg0-3 Blind DFMO/Sulindac				
Pre-Registration				
Tracking Tool	162	75	0	237
Randomization				
Blinded drug	24	14	19	91
A211102 Breast, Atypia via RPFNA, Metformin v Pl*				
Total Registrations	1	0	0	1
A211201 Breast Density, MA.32 companion*				
Total Registrations	2	0	0	14

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

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

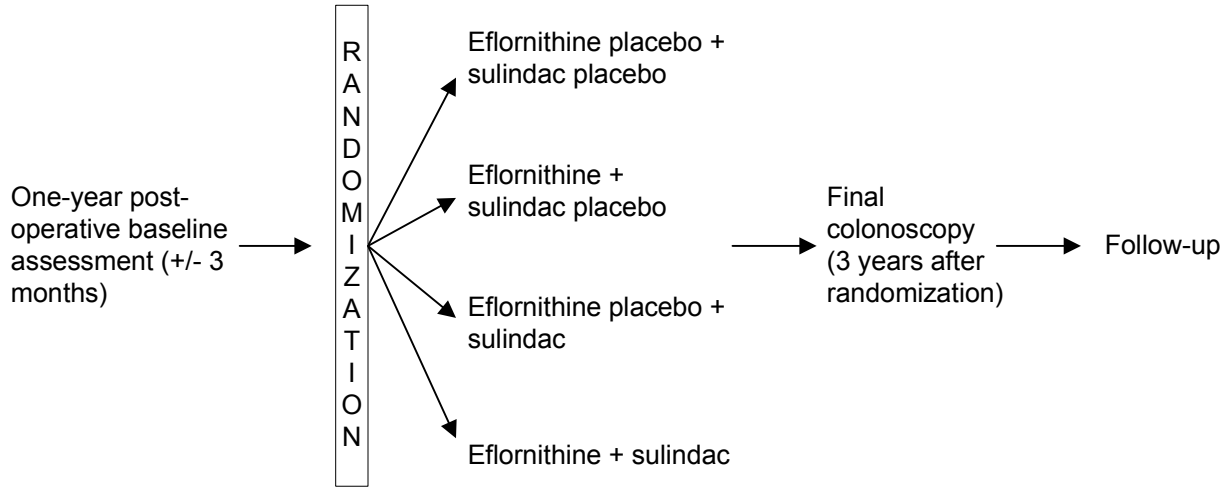
Date Activated:
03/01/2013

Study Chairs:
J Zell, P Brown

Statisticians:
J Unger, G Anderson, K Arnold

Data Coordinator:
M Yee

SCHEMA



Objectives

To assess whether eflornithine (+/- sulindac), sulindac (+/- eflornithine) or the combination are effective in reducing the three-year combined 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 eflornithine, sulindac or the combination 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 eflornithine, sulindac, or the combination compared to placebo.

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 cancer (CRC) risk and adverse events.

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

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

To perform pharmacokinetic (PK) analysis of eflornithine and sulindac in patients with previously treated Stage 0-III colon or rectal cancer.

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 1488 patients will be randomized, 372 to each study arm, to achieve 1,340 eligible patients.

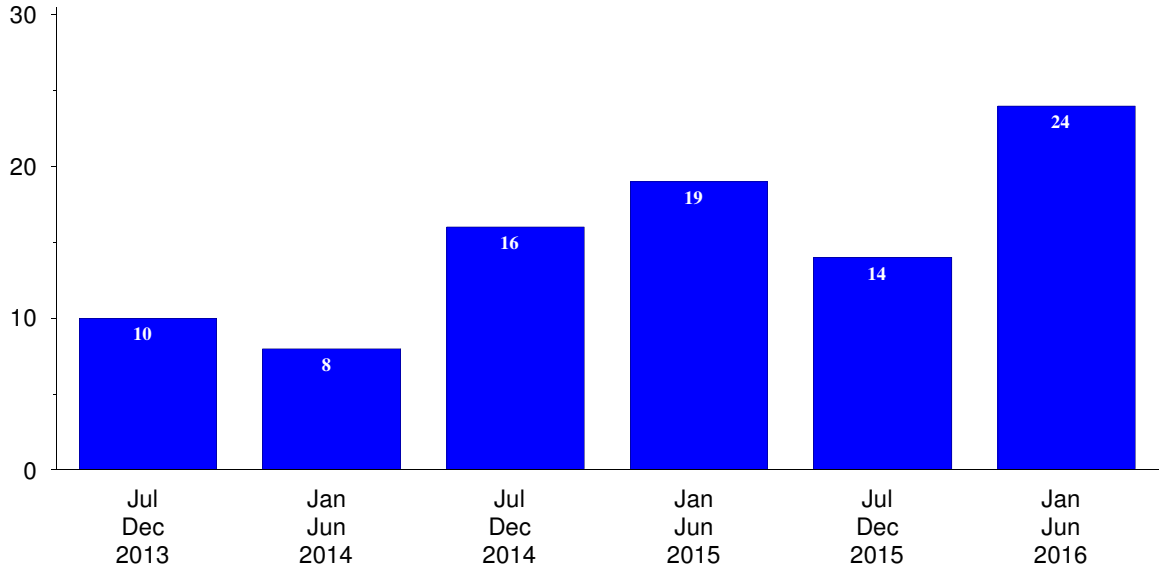
Summary Statement

This study activated on March 1, 2013. As of June 30, 2016, 91 patients have been randomized.

Four patients are ineligible due to: baseline hearing loss (2), high cardiovascular risk (1), and primary resection done too late (1). Three patients who never started treatment are coded as major deviations; these patients are also not evaluable for adverse events. Twenty-two patients are off treatment, including three patients coded as "Other – not protocol specified", two of whom did not take study medication for more than 90 days and one who the site was unable to contact. Among 66 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.

Revision #5 incorporated multiple protocol changes, including clarifying the surgical eligibility requirements, changing the eligibility audiogram threshold from $\geq$ 30 dB to > 40 dB and removing the eligibility restriction on calcium supplementation. A tool for tracking patients from the time of their initial resection to their registration window was made available in Revision #4. As of June 30, 2016, 237 patients have been entered in the tracking tool, of which 15 were subsequently randomized.

Initial Registrations By 6 Month Intervals



Time of Registration

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Irvine, U of CA	12	Michigan CRC NCORP	2
Kaiser Perm NCORP	10	Northwest NCORP	2
Alliance	7	Bridgeport Hospital/Yale University	1
NRG	6	City of Hope Med Ctr	1
ECOG-ACRIN	5	Colorado, U of	1
San Antonio, U of TX	5	Columbia MU-NCORP	1
MD Anderson CC	4	CORA NCORP	1
Hawaii MU-NCORP	3	Eisenhower Army MC/Brooke Army Med Ctr	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	Highline Medical Ctr/Franciscan Res Ctr	1
Kansas, U of	3	MAVERIC	1
So Calif, U of	3	NE Georgia Med Ctr/Georgia NCORP	1
Wichita NCORP	3	Southeast COR NCORP	1
Banner MD Anderson/MD Anderson CC	2	St Joseph Hospital/Mississippi, Univ of	1
Columbus NCORP	2	Weiss Memorial Hosp/Loyola University	1
Essentia Hlth NCORP	2	Yale University	1
Heartland NCORP	2	**Total (32 Institutions)**	**91**
McLaren Cancer Inst/Wayne State Univ	2		

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2016; Data as of July 1, 2016

	Total
NUMBER REGISTERED	91
INELIGIBLE	4
ELIGIBLE	87
Analyzable, Pend. Elig.	2
ADVERSE EVENT ASSESSMENT	
Evaluable	66
Not Evaluable	3
Too Early	18

Patient Characteristics

Registrations ending June 30, 2016; Data as of July 1, 2016

	Total (n=87)	
AGE		
Median	52.1	
Minimum	29.2	
Maximum	78.2	
SEX		
Males	36	41%
Females	51	59%
HISPANIC		
Yes	11	13%
No	74	85%
Unknown	2	2%
RACE		
White	62	71%
Black	5	6%
Asian	14	16%
Pacific Islander	1	1%
Unknown	5	6%
RISK OF RECURRENCE		
Stage 0 or I	16	18%
Stage II with no prior chemotherapy or radiation therapy	17	20%
Stage II with prior chemotherapy or radiation therapy	9	10%
Stage III	45	52%

Treatment Summary

Registrations ending June 30, 2016; Data as of July 1, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	65
NUMBER OFF PROTOCOL TREATMENT	22
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	2
Refusal unrelated to adverse event	5
Progression/relapse	5
Death	1
Other - not protocol specified	3
Reason under review	6
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 June 30, 2016; Data as of July 1, 2016

			Total (n=66) Grade			
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	62	4	0	0	0	0
AST increased	65	1	0	0	0	0
Abdominal pain	65	0	1	0	0	0
Alkaline phosphatase increased	65	1	0	0	0	0
Alopecia	65	1	0	0	0	0
Anemia	65	0	0	1	0	0
Anxiety	65	1	0	0	0	0
Arthralgia	65	1	0	0	0	0
Bloating	65	0	1	0	0	0
Blood bilirubin increased	65	1	0	0	0	0
Chest pain - cardiac	65	1	0	0	0	0
Constipation	57	7	2	0	0	0
Diarrhea	58	4	3	1	0	0
Dizziness	62	4	0	0	0	0
Dry mouth	64	2	0	0	0	0
Duodenal ulcer	65	0	0	1	0	0
Dyspepsia	64	2	0	0	0	0
Dysphagia	65	1	0	0	0	0
Dyspnea	65	1	0	0	0	0
Edema limbs	65	1	0	0	0	0
Fatigue	62	4	0	0	0	0
GERD	65	1	0	0	0	0
Gastrointestinal pain	63	3	0	0	0	0
Headache	63	3	0	0	0	0
Hematuria	64	2	0	0	0	0
Hot flashes	64	2	0	0	0	0
Hyperglycemia	65	0	1	0	0	0
Hypertension	60	0	4	2	0	0
Insomnia	65	0	1	0	0	0
Irregular menstruation	65	1	0	0	0	0
Nausea	60	6	0	0	0	0
Platelet count decreased	65	1	0	0	0	0
Rash maculo-papular	65	1	0	0	0	0
Rectal hemorrhage	65	1	0	0	0	0
Renal/urinary disorders-Other	65	1	0	0	0	0
Skin/subq tissue ds-Other	65	1	0	0	0	0
Somnolence	65	1	0	0	0	0
Stomach pain	65	1	0	0	0	0
Tinnitus	64	1	1	0	0	0
Upper GI hemorrhage	65	0	0	1	0	0
Vomiting	64	2	0	0	0	0
Weight loss	65	1	0	0	0	0
White blood cell decreased	65	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	30	22	10	4	0	0