PREVENTION AND EPIDEMIOLOGY COMMITTEE

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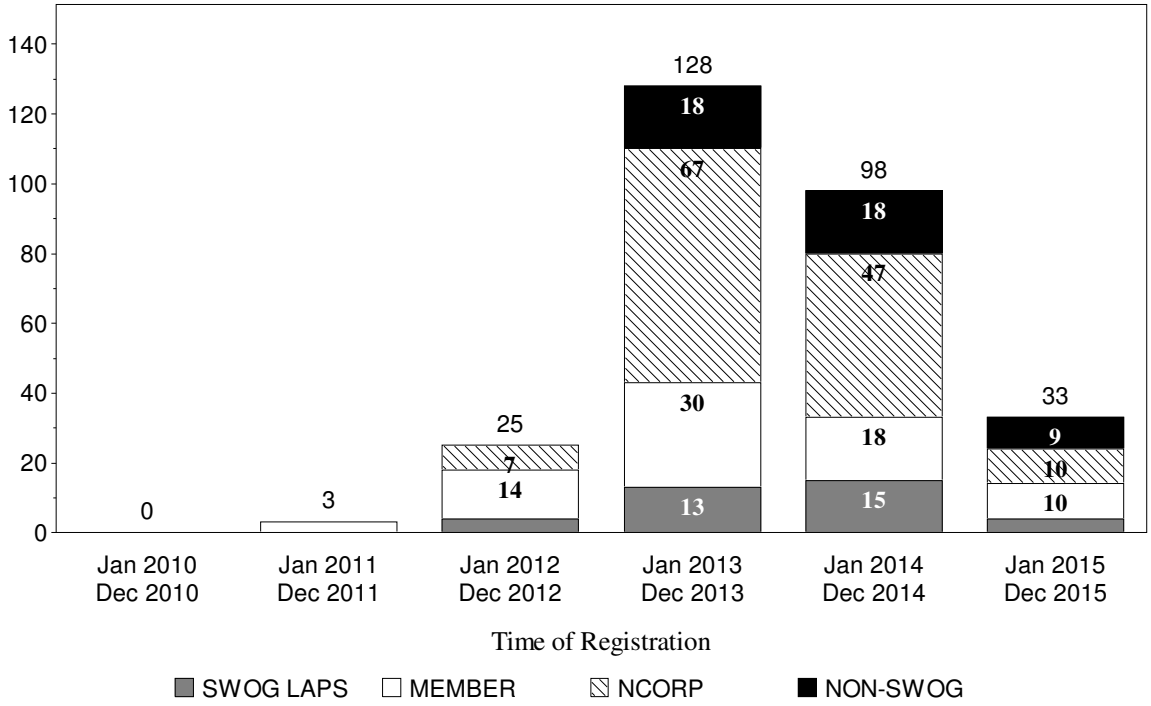
Patient Registrations to Studies

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

	Jul 2015 Dec 2015	Jan 2015 Jun 2015	Jul 2014 Dec 2014	All Patients
S0000B SELECT Eye Endpoints (SEE)				
Registration				
Registration	65	0	0	2,774
S0820 PACES: ColrecStg0-3 Blind DFMO/Sulindac				
Pre-Registration				
Pre-Registration	75	0	0	75
Randomization				
Blinded drug	14	19	16	67
A211201 Breast Density, MA.32 companion*				
Total Registrations	0	0	4	12

* 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

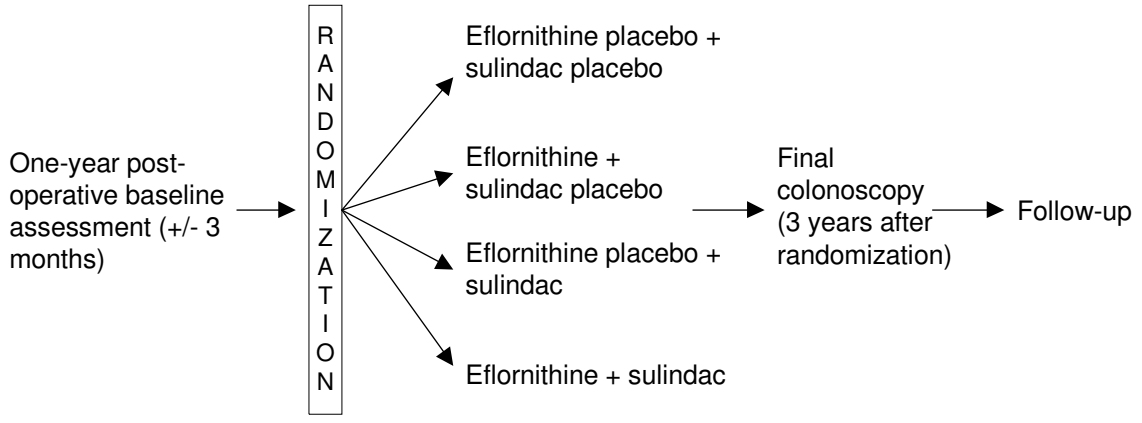
Date Activated:
03/01/2013

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 1,340 eligible patients will be randomized, 335 to each study arm.

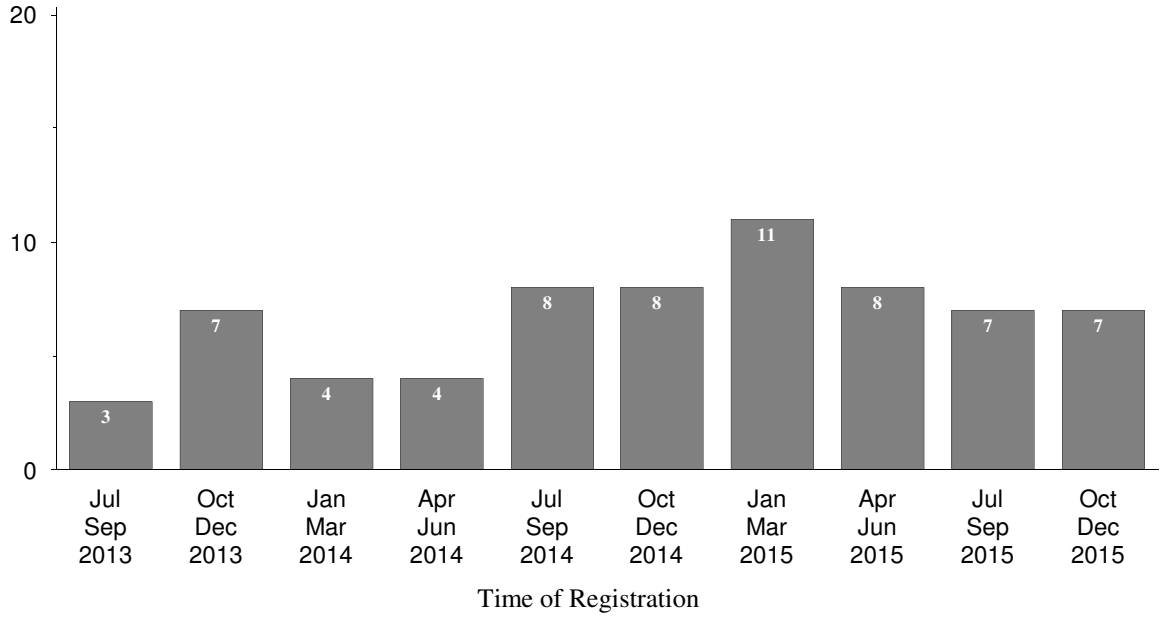
Summary Statement

This study activated on March 1, 2013. As of December 31, 2015, 67 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. Fourteen patients are off treatment, including one patient the site is unable to contact. Multiple grade 3 adverse events were reported for a single patient.

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 February 12, 2016, 98 patients have been entered in the tracking tool.

Initial Registrations By 3 Month Intervals



Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
Irvine, U of CA	11	Bridgeport Hospital/Yale University	1
Alliance	7	City of Hope Med Ctr	1
Kaiser Perm NCORP	7	Colorado, U of	1
MD Anderson CC	4	Columbia MU-NCORP	1
San Antonio, U of TX	4	Columbus NCORP	1
ECOG-ACRIN	3	Eisenhower Army MC/Brooke Army Med Ctr	1
Hawaii MU-NCORP	3	Highline Medical Ctr/Franciscan Res Ctr	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	MAVERIC	1
NRG	3	NE Georgia Med Ctr/Georgia NCORP	1
So Calif, U of	3	St Joseph Hospital/Mississippi, Univ of	1
Heartland NCORP	2	Wichita NCORP	1
Kansas, U of	2	Yale University	1
McLaren Cancer Inst/Wayne State Univ	2	**Total (26 Institutions)**	**67**
Banner MD Anderson/MD Anderson CC	1		

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2015; Data as of February 12, 2016

	Total
NUMBER REGISTERED	67
INELIGIBLE	4
ELIGIBLE	63
ADVERSE EVENT ASSESSMENT	
Evaluable	55
Not Evaluable	3
Too Early	5

Patient Characteristics

Registrations ending December 31, 2015; Data as of February 12, 2016

	Total (n=63)	
AGE		
Median	52.1	
Minimum	29.2	
Maximum	78.2	
SEX		
Males	25	40%
Females	38	60%
HISPANIC		
Yes	6	10%
No	55	87%
Unknown	2	3%
RACE		
White	45	71%
Black	5	8%
Asian	11	17%
Unknown	2	3%
RISK OF RECURRENCE		
Stage 0 or I	12	19%
Stage II with no prior chemotherapy or radiation therapy	11	17%
Stage II with prior chemotherapy or radiation therapy	5	8%
Stage III	35	56%

Treatment Summary

Registrations ending December 31, 2015; Data as of February 12, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	49
NUMBER OFF PROTOCOL TREATMENT	14
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	2
Refusal unrelated to adverse event	4
Progression/relapse	3
Death	0
Other - not protocol specified	1
Reason under review	4
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, 2015; Data as of February 12, 2016

			Total (n=55) Grade			
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	52	3	0	0	0	0
AST increased	54	1	0	0	0	0
Abdominal pain	54	0	1	0	0	0
Alkaline phosphatase increased	54	1	0	0	0	0
Alopecia	54	1	0	0	0	0
Anemia	54	0	0	1	0	0
Anxiety	54	1	0	0	0	0
Bloating	54	0	1	0	0	0
Blood bilirubin increased	53	2	0	0	0	0
Chest pain - cardiac	54	1	0	0	0	0
Constipation	46	7	2	0	0	0
Diarrhea	50	4	1	0	0	0
Dizziness	52	3	0	0	0	0
Dry mouth	54	1	0	0	0	0
Duodenal ulcer	54	0	0	1	0	0
Dysphagia	54	1	0	0	0	0
Dyspnea	54	1	0	0	0	0
Fatigue	52	3	0	0	0	0
GERD	54	1	0	0	0	0
Gastrointestinal pain	53	2	0	0	0	0
Headache	53	2	0	0	0	0
Hematuria	54	1	0	0	0	0
Hot flashes	53	2	0	0	0	0
Hypercalcemia	54	1	0	0	0	0
Hyperglycemia	53	1	1	0	0	0
Hypertension	52	1	2	0	0	0
Insomnia	54	0	1	0	0	0
Irregular menstruation	54	1	0	0	0	0
Nausea	50	5	0	0	0	0
Rash maculo-papular	54	1	0	0	0	0
Rectal hemorrhage	54	1	0	0	0	0
Renal/urinary disorders-Other	54	1	0	0	0	0
Skin/subq tissue ds-Other	54	1	0	0	0	0
Somnolence	54	1	0	0	0	0
Tinnitus	54	1	0	0	0	0
Upper GI hemorrhage	54	0	0	1	0	0
Vomiting	53	2	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	29	18	7	1	0	0