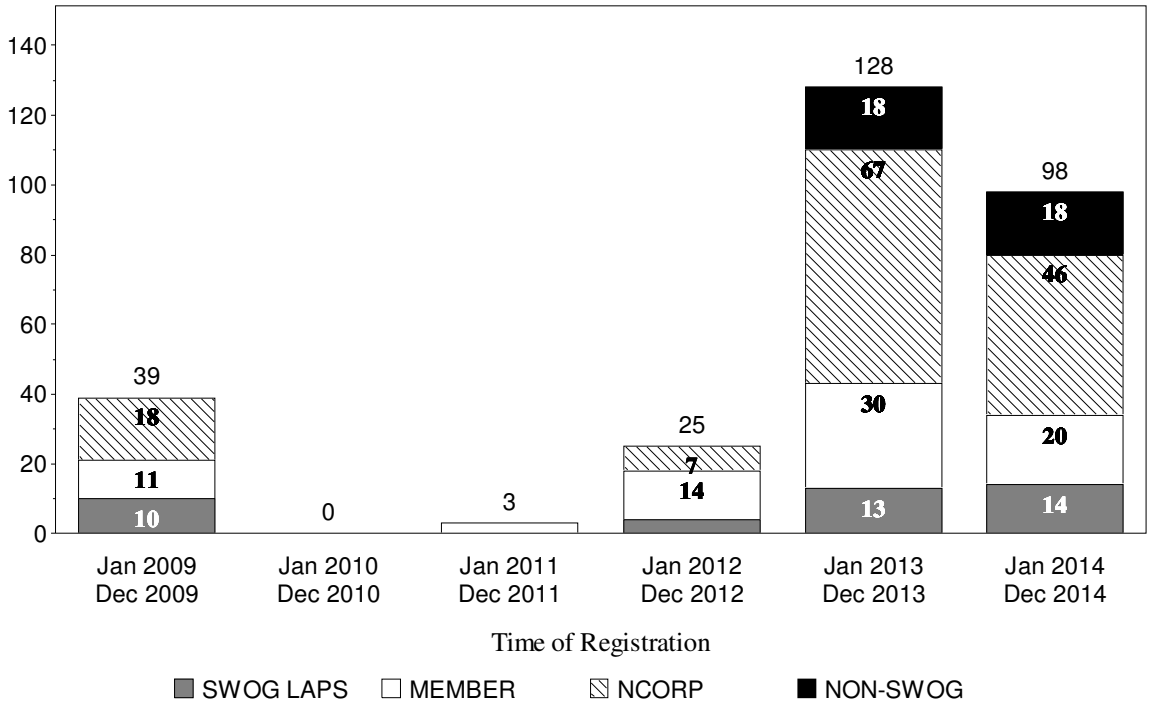
PREVENTION AND EPIDEMIOLOGY COMMITTEE

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

	Jul 2014 Dec 2014	Jan 2014 Jun 2014	Jul 2013 Dec 2013	All Patients
S0000B SELECT Eye Endpoints (SEE)				
Registration				
Registration	0	273	0	2,709
S0812 Breast, Prev, Vit D vs Placebo				
Initial Registration				
Blinded Drug (VitD or Placebo)	0	66	70	208
S0820 Colrec Stg 0-3 Blind DFMO/Sulindac				
Randomization				
Blinded drug	16	8	10	34
S1119 *H. pylori* & Water in Lima, Peru				
Screening Contact - STEP 1				
Total Registrations	0	0	2	192
A211201 Breast Density, MA.32 companion*				
Registration				
Total Registrations	4	4	4	12

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

S0812 Phase IIB

Coordinating Group: SWOG

A Randomized Double-Blind Placebo-Controlled Biomarker Modulation Study of High Dose Vitamin D in Premenopausal Women at High Risk for Breast Cancer, Phase IIB

Participants:
SWOG, CTSU

Study Chairs:
K Crew, D Hershman

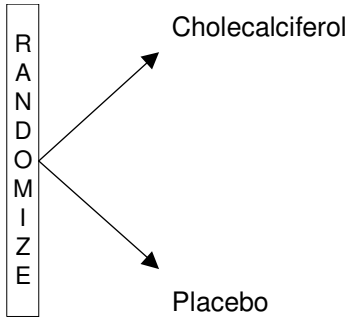
Statisticians:
G Anderson, D Lew

Data Coordinator:
M Yee

Date Activated:
11/01/2011

Date Closed:
08/15/2014

SCHEMA



Objectives

To assess whether mammographic density is reduced in premenopausal women at high risk of breast cancer taking high dose vitamin D3 (cholecalciferol 20,000 IU PO weekly) compared to high risk women taking placebo for one year.

To assess whether proliferation as measured by Ki-67 staining of breast epithelial cells is reduced in premenopausal women at high risk of breast cancer taking high dose vitamin D3 compared to high risk women taking placebo for one year.

To explore the difference in the expression of other biomarkers in breast tissue obtained from women taking high dose vitamin D3 as compared to tissue obtained from women taking placebo for one year. Additional biomarkers to be examined include cleaved caspase-3 (apoptosis marker), ER, vitamin D receptor (VDR), and 1α-hydroxylase expression in breast tissue.

To assess whether parathyroid hormone (PTH), IGF-1, IGFBP-3, 25(OH)D, and 1,25(OH)D serum levels are altered at baseline, 6 months and 12 months in

women at high risk of breast cancer taking high dose vitamin D3 as compared to women taking placebo.

To explore whether a change in mammographic density correlates with polymorphisms in the VDR gene.

To assess other sources of vitamin D (sunlight exposure, diet) in this study population using a validated questionnaire administered at baseline, 12 months and 24 months.

To collect and bank serum, plasma, and breast tissue from premenopausal women at high risk of breast cancer prior to and after a one year intervention with vitamin D for future biomarker analysis.

To assess the toxicity of high dose vitamin D3 compared to placebo in this setting.

Patient Population

Participants must be premenopausal women with an elevated risk of breast cancer as defined by at least one of the following: diagnosis of resected DCIS; ADH, ALH, or LCIS; diagnosis of resected Stage I (T1b-c N0-N1mi) - Stage II breast cancer for which the participant has been disease-free for at least 5 years and has completed all adjuvant treatment; a known deleterious mutation in BRCA1, BRCA2, PTEN or TP53; modified Gail/CARE model risk at 5 years ≥ 1.67% or lifetime risk ≥ 20%; or mammographic breast density ≥ 50% (heterogeneously dense).

Participants must have at least one breast available for imaging and biopsy (not previously irradiated). Participants must have a baseline mammogram performed within 10 days after starting their menstrual period, with a mammographic density > 10%. Participants must not have bilateral breast implants, but prior breast reduction surgery is allowed.

Participants must be between 18 and 50 years of age and have a Zubrod performance status of 0-1. Participants must have adequate renal function and serum 25(OH)D level ≤ 32 ng/mL. Participants must not have a known hypersensitivity to vitamin D or known allergy to soy, and must agree not to take calcium and additional vitamin D supplements.

Stratification/Descriptive Factors

Participant randomization will be dynamically balanced according to the following stratification factors: (1) baseline serum 25(OH)D level: < 20 ng/ml vs 20-32 ng/ml (or < 50 nmol/L vs 50-80 nmol/L); (2) baseline mammographic density: 11-50% vs > 50%; and (3) designated biopsy institution: yes vs no.

Cancer Control Credits

The NCI Division of Cancer Prevention has assigned 1.0 cancer control credit per registration to this study.

Accrual Goals

The accrual goal is 200 eligible participants.

Summary Statement

This study was permanently closed to accrual on August 15, 2014, after accrual of 208 participants. Five participants are ineligible due to insufficient baseline information. An additional six participants with incomplete baseline data are included in the tables with the eligible patients. Major deviations are recorded for seven participants, three who began protocol intervention more than seven weeks late, one who received only half the protocol intervention dose, and three who withdrew from the study without receiving any protocol intervention. These last three participants are not evaluable for adverse events.

Among 199 participants evaluated for adverse events, 11 participants have reported Grade 2 adverse events: abdominal pain (2 participants), bloating, breast pain, bilirubin increase, constipation, flatulence, insomnia, headache, hypertension, increased frequency of bowel movements (listed as "GI disorders - Other, specify"), and urine creatinine/calcium ratio (listed as "Investigations - Other, specify").

Analysis of the primary endpoint is expected to begin this summer, after submission of the one-year mammogram for all participants is complete.

Registration by Institution

Institutions	Total Reg	Institutions	Total Reg
Beaumont NCORP	36	St Luke's Mt State/PCRC NCORP	3
Heartland NCORP	20	Texas Tech Univ/San Antonio, U of TX	3
Upstate Carolina	17	Arizona MC, U of	2
MD Anderson	16	John Muir Med Ctr/Davis, U of CA	2
NRG	14	Michigan CRC NCORP	2
Columbia MU-NCORP	13	Rockwood Clinic, PS/PCRC NCORP	2
City of Hope Med Ctr	11	So Calif, U of	2
Lahey Hosp & Med Ctr	11	Columbia University	1
Alliance	10	Greenville NCORP	1
ECOG-ACRIN	8	Henry Ford Hosp	1
Utah, U of	6	Highlands Onc Group/Arkansas, U of	1
Weissman Cancer Ctr/H Lee Moffitt CC	5	Methodist Hospital	1
Ozarks NCORP	4	Mid Illinois Hem Onc/Cleveland Clinic OH	1
Greenwich Hospital/Yale University	3	Prov Portland MC/PCRC NCORP	1
NE Alabama Reg MC/Mississippi, Univ of	3	St Louis CCOP	1
Southeast CCC NCORP	3	Wayne State Univ	1
St Elizabeth's MC/Davis, U of CA	3	**Total (33 Institutions)**	**208**

Registration, Eligibility, and Evaluability

Data as of March 6, 2015

	Total
NUMBER REGISTERED	208
INELIGIBLE	5
Insufficient Documentation	5
Irreversible	5
ELIGIBLE	203
ADVERSE EVENT ASSESSMENT	
Evaluable	199
Not Evaluable	3
Too Early	1

Patient Characteristics

Data as of March 6, 2015

	Total (n=203)	
AGE		
Median	44.7	
Minimum	21.0	
Maximum	50.7	
HISPANIC		
Yes	16	8%
No	186	92%
Unknown	1	0%
RACE		
White	172	85%
Black	11	5%
Asian	10	5%
Native American	1	0%
Multi-Racial	4	2%
Unknown	5	2%
BASELINE SERUM 25(OH)D LEVEL		
< 20 ng/ml (< 50 nmol/L)	65	32%
20-32 ng/ml (50-80 nmol/L)	138	68%
BASELINE MAMMOGRAPHIC DENSITY		
11-50%	42	21%
> 50%	161	79%
DESIGNATED BIOPSY SITE		
Yes	43	21%
No	160	79%

Intervention Summary

Data as of March 6, 2015

	Total
NUMBER ON PROTOCOL INTERVENTION	46
NUMBER OFF PROTOCOL INTERVENTION	157
REASON OFF INTERVENTION	
Intervention completed as planned	81
Adverse Event or side effects	5
Refusal unrelated to adverse event	15
Progression/relapse	1
Death	0
Other - not protocol specified	9
Reason under review	46
MAJOR PROTOCOL DEVIATIONS	7

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

Adverse Events Unlikely or Not Related to Intervention Excluded

Data as of March 6, 2015

	Total (n=199)	Grade				
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**
Abdominal distension	198	1	0	0	0	0
Abdominal pain	192	5	2	0	0	0
Alkaline phosphatase increased	198	1	0	0	0	0
Bloating	197	1	1	0	0	0
Blood bilirubin increased	198	0	1	0	0	0
Breast pain	197	1	1	0	0	0
Constipation	192	6	1	0	0	0
Dizziness	198	1	0	0	0	0
Dry mouth	198	1	0	0	0	0
Dry skin	198	1	0	0	0	0
Dyspepsia	197	2	0	0	0	0
Fatigue	198	1	0	0	0	0
Flatulence	197	1	1	0	0	0
GI disorders-Other, specify	198	0	1	0	0	0
Headache	198	0	1	0	0	0
Hypercalcemia	198	1	0	0	0	0
Hypertension	197	1	1	0	0	0
Insomnia	198	0	1	0	0	0
Investigations-Other, specify	197	1	1	0	0	0
Metab/nutrition disorders-Oth	198	1	0	0	0	0
Nail ridging	198	1	0	0	0	0
Nausea	193	6	0	0	0	0
Pain in extremity	197	2	0	0	0	0
Palpitations	198	1	0	0	0	0
Vomiting	198	1	0	0	0	0
Weight loss	198	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	160	28	11	0	0	0

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 Cancer, Phase III - Preventing Adenomas of the Colon with Eflornithine and Sulindac (PACES)

Participants:
SWOG, CTSU

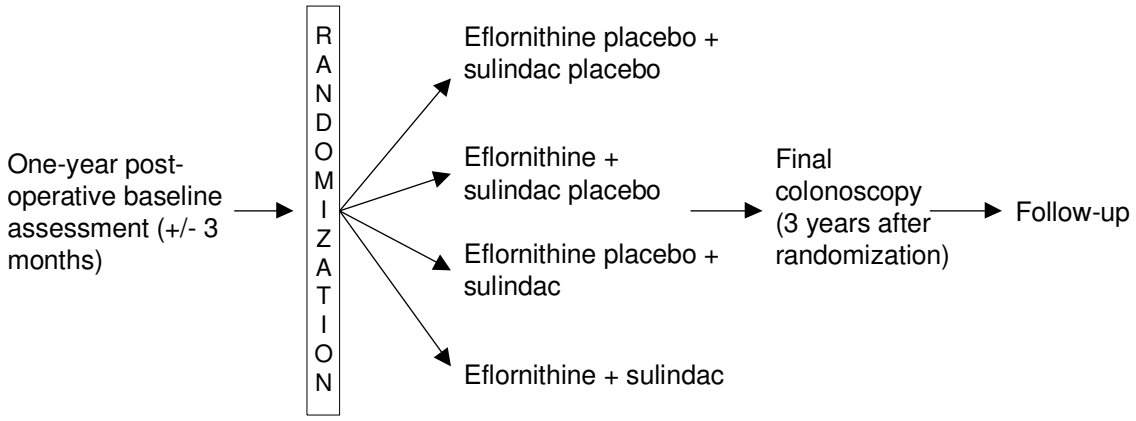
Date Activated:
03/01/2013

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 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 ≥ 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 cancer.

Patient Population

Patients must have a history of Stage 0, I, II or III colon adenocarcinoma that has been treated per standard care with resection alone or in combination with adjuvant chemotherapy. Patients with rectosigmoid cancers are eligible only if their treatment did not involve radiation therapy. Patients with mid-low rectal cancers are not eligible.

Patients must be registered between 274 and 465 days (inclusive) of primary resection. Patients must show no evidence of disease based on post-operative colonoscopy (performed at least 274 days after the resection date and prior to registration) and CT 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 resection date and prior to registration). Patients with adenomas detected at 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 30 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.

Cancer Control Credits

The NCI Division of Cancer Prevention has assigned 1.16 cancer control credits (1.76 credits for High Performance sites) per registration to this study. There are potential additional cancer control credits for specimen submission.

Accrual Goals

A total of 1,340 eligible patients will be enrolled, 335 to each study arm.

Summary Statement

This study activated on March 1, 2013. As of December 31, 2014, 34 patients have been registered to this study.

Two patients are ineligible due to high cardiovascular risk and baseline hearing loss. One patient who never started treatment is not evaluable for toxicity and is also coded as a major deviation. No grade 3 or higher adverse events related to intervention have been reported.

Revision #4, currently being drafted, will incorporate multiple protocol changes, including opening the study to rectal cancer patients and allowing prior radiation therapy.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Irvine, U of CA	6	Columbia MU-NCORP	1
Alliance	4	Heartland NCORP	1
Kaiser Vallejo NCORP	4	Highline Cancer Ctr/PCRC NCORP	1
San Antonio, U of TX	3	McLaren Cancer Inst/Wayne State Univ	1
So Calif, U of	3	NE Georgia Med Ctr/Mississippi, Univ of	1
KaiserPermanenteSCAL/Kaiser Vallejo NCORP	2	Poudre Valley Hosp/Colorado, U of	1
Kansas, U of	2	St Joseph Hospital/Mississippi, Univ of	1
MD Anderson	2	**Total (16 Institutions)**	**34**
City of Hope Med Ctr	1		

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2014; Data as of March 2, 2015

	Total
NUMBER REGISTERED	34
INELIGIBLE	2
ELIGIBLE	32
ADVERSE EVENT ASSESSMENT	
Evaluable	26
Not Evaluable	1
Too Early	5

Patient Characteristics

Registrations ending December 31, 2014; Data as of March 2, 2015

	Total (n=32)	
AGE		
Median	52.3	
Minimum	32.5	
Maximum	71.3	
SEX		
Males	14	44%
Females	18	56%
HISPANIC		
Yes	3	9%
No	28	88%
Unknown	1	3%
RACE		
White	21	66%
Black	3	9%
Asian	6	19%
Unknown	2	6%
RECUR		
Stage 0 or I	6	19%
Stage II with no prior chemotherapy	9	28%
Stage II with prior chemotherapy	3	9%
Stage III	14	44%

Intervention Summary

Registrations ending December 31, 2014; Data as of March 2, 2015

	Total
NUMBER ON PROTOCOL INTERVENTION	28
NUMBER OFF PROTOCOL INTERVENTION	4
REASON OFF INTERVENTION	
Intervention completed as planned	0
Adverse Event or side effects	1
Refusal unrelated to adverse event	2
Progression/relapse	1
Death	0
Other - not protocol specified	0
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	1

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

Adverse Events Unlikely or Not Related to Intervention Excluded

Registrations ending December 31, 2014; Data as of March 2, 2015

	Total (n=26)	Grade				
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**
Abdominal pain	25	0	1	0	0	0
Bloating	25	0	1	0	0	0
Chest pain - cardiac	25	1	0	0	0	0
Constipation	20	5	1	0	0	0
Diarrhea	22	3	1	0	0	0
Dizziness	24	2	0	0	0	0
Dyspnea	25	1	0	0	0	0
Fatigue	25	1	0	0	0	0
Gastrointestinal pain	25	1	0	0	0	0
Headache	25	1	0	0	0	0
Hot flashes	25	1	0	0	0	0
Hyperglycemia	25	0	1	0	0	0
Nausea	23	3	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	16	6	4	0	0	0