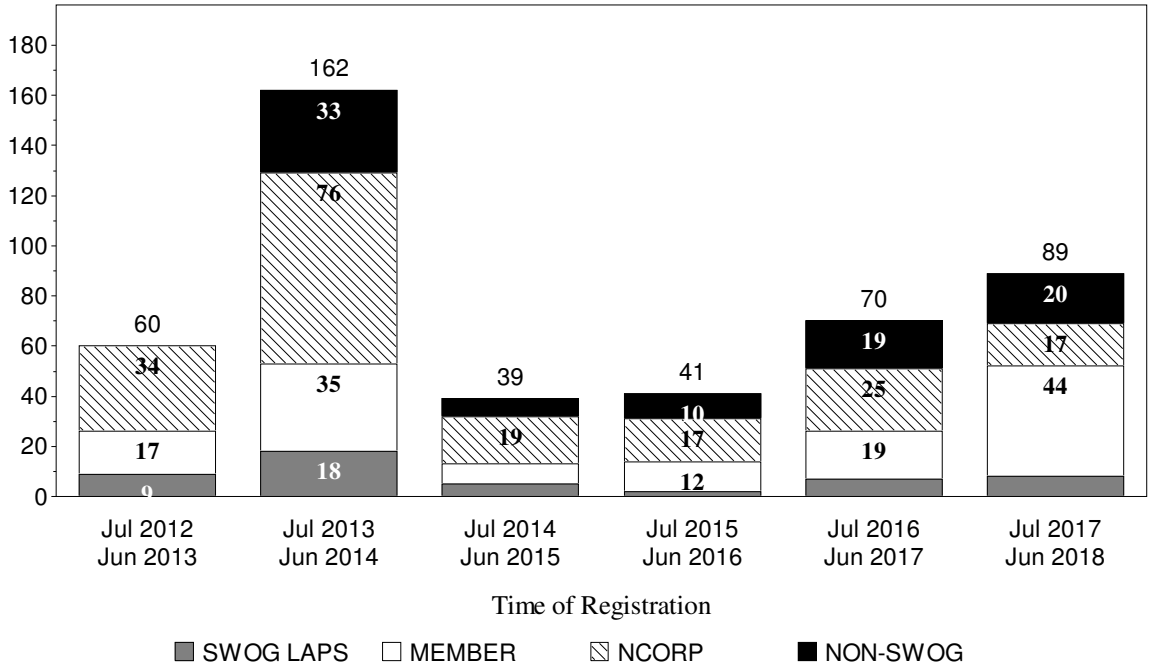
PREVENTION AND EPIDEMIOLOGY COMMITTEE

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

	Jan 2018 Jun 2018	Jul 2017 Dec 2017	Jan 2017 Jun 2017	All Patients
S0820 PACES: ColrecStg0-3 Blind DFMO/Sulindac				
Pre-Registration				
Pre-Registration	58	77	52	495
Randomization				
Blinded drug	28	23	34	204

Non-SWOG Studies with SWOG-Credited Registrations

PREVENTION AND EPIDEMIOLOGY COMMITTEE

Studies with Accrual from January 2017 - June 2018

	SWOG Champion	SWOG Accrual Jan 2018 Jun 2018	SWOG Accrual Jul 2017 Dec 2017	SWOG Total	Total Accrued
A011502 Brst, Adj, Nodal+&HER2-, Aspirin vs. Placebo*		25	17	50	583
Date Activated: 12/08/16					
Most Recent Progress Report					
A211102 Breast, Atypia via RPFNA, Metformin v Placebo		0	0	3	228
Date Activated: 02/01/15					
Most Recent Progress Report					
A211201 Breast Density, MA.32 companion		0	0	14	177
Date Activated: 08/22/12 Date Closed: 10/13/17					
Most Recent Progress Report					
EA1141 Breast, Abbrev. MRI vs Digital Tomosynthesis		0	38	44	1518
Date Activated: 09/02/16 Date Closed: 11/07/17					
Most Recent Progress Report					
NHLBIMDS LEUK, National MDS Study*		8	1	16	469
Date Activated: 04/05/16					
No Progress Report Available					

* Studies with Prevention and Epidemiology as a secondary Committee

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

Date Activated:
11/01/2011

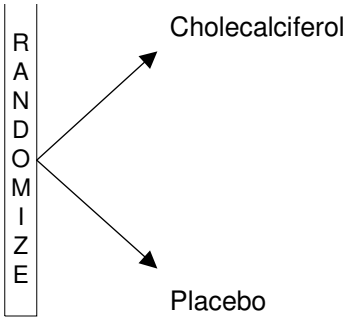
Study Chairs:
K Crew, D Hershman

Date Closed:
08/15/2014

Statisticians:
G Anderson, D Lew

Data Coordinator:
M Yee

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.

Accrual Goals

The accrual goal is 200 eligible participants.

Summary Statement

This study was permanently closed to accrual on August 15, 2014, with 208 women registered. Major deviations were coded for three participants who began taking study intervention several weeks late and four participants who received no study intervention; these four participants are not evaluable for adverse events. Only one Grade 3 adverse event was reported, a Grade 3 headache on the Vitamin D arm. Among the 12 participants who discontinued intervention due to other reasons, the most common reason was noncompliance or loss of contact.

The final analysis for this study was reported as a poster at the 2018 ASCO meeting and the abstract is provided as follows:

Background: Observational studies have reported an inverse association between vitamin D status and breast cancer risk. We examined whether high-dose vitamin D supplementation among high-risk premenopausal women reduces mammographic density (MD), a strong predictor of breast cancer risk.

Methods: We conducted a multicenter randomized double-blind placebo-controlled trial among premenopausal women at high risk for breast cancer [5-year Gail risk score ≥ 1.67%, lobular carcinoma ***in situ***, prior stage 0-II breast cancer, hereditary breast cancer syndrome, or high MD (heterogeneously/extremely dense)] and with a baseline serum 25-hydroxyvitamin D [25(OH)D] ≤32 ng/mL. Subjects were randomized 1:1 to 1 year of vitamin D3 20,000 IU/week or matching placebo. All received standard-dose vitamin D 600 IU/day. The primary endpoint was change in MD from baseline to 1 year as assessed by the Cumulus technique. Secondary endpoints were serial blood biomarkers [25(OH)D, 1,25(OH)D, parathyroid hormone, insulin-like growth factor (IGF)-1, IGF binding protein-3] and MD change at 2 years.

Results: Among 208 subjects registered from December 2011 to April 2014, median age was 44.6 years (range, 21-50); 84% were white; 33% had a baseline serum 25(OH)D < 20 ng/mL; 78% had a

high baseline MD. At 1 year, we observed a significant mean change in serum 25(OH)D in the active vs. placebo group (+18.9 vs. +2.8 ng/mL, $p < .01$), but non-significant change for IGF-1 (-9.8 vs. -1.8 ng/mL, $p = 0.28$). Mean absolute change in MD at 1 year and 2 years after randomization was -0.3% and -1.2%, respectively, in the active arm and +1.5% and +1.6%, respectively, for the placebo arm ($p > 0.05$). At 1 year, MD correlated with serum IGF-1 and IGF-1/IGFBP-3 ($p < .01$). High-dose vitamin D3 was well-tolerated.

Conclusions: Changes in MD at 1-2 years were small and did not significantly differ between high-dose and standard-dose vitamin D. Longer exposure may be required to detect a difference. The relationship between vitamin D, IGF-1, and MD are hypothesis-generating. Understanding the relationship between vitamin D and biomarkers of breast cancer risk may inform future clinical trials.

Registration by Institution

Institutions	Total Reg	Institutions	Total Reg
Beaumont NCORP	36	John Muir Med Ctr/Davis, U of CA	2
Heartland NCORP	20	Michigan CRC NCORP	2
Upstate Carolina	17	Rockwood Clinic, PS/PCRC NCORP	2
MD Anderson CC	16	So Calif, U of	2
Columbia MU-NCORP	13	Columbia University	1
City of Hope Med Ctr	11	Greenville NCORP	1
Lahey Hosp & Med Ctr	11	Henry Ford Hospital	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 COR NCORP	3	Wayne State Univ	1
St Elizabeth's MC/Davis, U of CA	3	NRG	14
St Luke's Mt State/PCRC NCORP	3	ALLIANCE	10
Texas Tech Univ/San Antonio, U of TX	3	ECOG-ACRIN	8
Arizona MC, U of	2	**Total (33 Institutions)**	**208**

Registration, Eligibility, and Evaluability

Classified by Unblinded Arms

Data as of August 29, 2018

	TOTAL	Vitamin D	Placebo
NUMBER REGISTERED	208	103	105
ELIGIBLE	208	103	105
ADVERSE EVENT ASSESSMENT			
Evaluable	204	102	102
Not Evaluable	4	1	3

Patient Characteristics

Classified by Unblinded Arms

Data as of August 29, 2018

	Vitamin D (n=103)		Placebo (n=105)	
AGE				
Median	44.3		44.7	
Minimum	27.7		21.0	
Maximum	49.9		50.6	
HISPANIC				
Yes	11	11%	6	6%
No	92	89%	98	93%
Unknown	0	0%	1	1%
RACE				
White	87	84%	88	84%
Black	6	6%	6	6%
Asian	4	4%	7	7%
Native American	1	1%	0	0%
Multi-Racial	4	4%	0	0%
Unknown	1	1%	4	4%
BASELINE SERUM 25(OH)D LEVEL				
< 20 ng/ml (< 50 nmol/L)	34	33%	34	32%
20-32 ng/ml (50-80 nmol/L)	69	67%	71	68%
BASELINE MAMMOGRAPHIC DENSITY				
11-50%	23	22%	22	21%
> 50%	80	78%	83	79%
DESIGNATED BIOPSY SITE				
Yes	22	21%	23	22%
No	81	79%	82	78%

Treatment Summary

Classified by Unblinded Arms

Data as of August 29, 2018

	TOTAL	Vitamin D	Placebo
NUMBER ON PROTOCOL INTERVENTION	0	0	0
NUMBER OFF PROTOCOL INTERVENTION	208	103	105
REASON OFF INTERVENTION			
Treatment completed as planned	162	79	83
Adverse Event or side effects	6	4	2
Refusal unrelated to adverse event	18	7	11
Progression/relapse	1	1	0
Death	0	0	0
Other - not protocol specified	12	7	5
Reason under review	9	5	4
MAJOR PROTOCOL DEVIATIONS	7	2	5

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

Classified by Unblinded Arms

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of August 29, 2018

	Vitamin D (n=102) Grade						Placebo (n=102) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Abdominal distension	101	1	0	0	0	0	102	0	0	0	0	0
Abdominal pain	97	3	2	0	0	0	99	3	0	0	0	0
Alkaline phosphatase increased	101	1	0	0	0	0	102	0	0	0	0	0
Anorexia	101	1	0	0	0	0	102	0	0	0	0	0
Bloating	102	0	0	0	0	0	100	1	1	0	0	0
Blood bilirubin increased	102	0	0	0	0	0	101	0	1	0	0	0
Breast pain	102	0	0	0	0	0	100	1	1	0	0	0
Constipation	95	6	1	0	0	0	101	1	0	0	0	0
Dizziness	101	1	0	0	0	0	102	0	0	0	0	0
Dry mouth	102	0	0	0	0	0	101	1	0	0	0	0
Dry skin	102	0	0	0	0	0	101	1	0	0	0	0
Dyspepsia	102	0	0	0	0	0	100	2	0	0	0	0
Fatigue	101	1	0	0	0	0	102	0	0	0	0	0
Flatulence	102	0	0	0	0	0	100	1	1	0	0	0
GI disorders-Other, specify	102	0	0	0	0	0	101	0	1	0	0	0
Headache	100	0	1	1	0	0	102	0	0	0	0	0
Hot flashes	102	0	0	0	0	0	101	0	1	0	0	0
Hypercalcemia	101	1	0	0	0	0	102	0	0	0	0	0
Hypertension	102	0	0	0	0	0	100	1	1	0	0	0
Insomnia	101	0	1	0	0	0	102	0	0	0	0	0
Investigations-Other, specify	100	1	1	0	0	0	102	0	0	0	0	0
Metab/nutrition disorders-Oth	102	0	0	0	0	0	101	1	0	0	0	0
Nail ridging	101	1	0	0	0	0	102	0	0	0	0	0
Nausea	99	3	0	0	0	0	98	4	0	0	0	0
Pain in extremity	101	1	0	0	0	0	101	1	0	0	0	0
Palpitations	101	1	0	0	0	0	102	0	0	0	0	0
Vomiting	101	1	0	0	0	0	101	1	0	0	0	0
Weight loss	102	0	0	0	0	0	101	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	76	19	6	1	0	0	84	12	6	0	0	0

Analysis Results

	Vitamin D mean (SD)	Placebo mean (SD)	P-value
MAMMOGRAPHIC DENSITY (%)			
Baseline	36.6 (18.0)	35.0 (19.0)	
Mean change at 12mo	-0.3 (8.0)	1.5 (8.8)	0.22
Mean change at 24mo	-1.2 (8.0)	1.6 (10.3)	0.10
BLOOD BIOMARKERS			
25(OH)D (ng/mL)			
Baseline	23.9 (7.2)	23.7 (8.4)	
Mean change at 12mo	18.9 (8.9)	2.8 (8.0)	<.0001
1,25(OH)D (pg/mL)			
Baseline	51.4 (23.6)	50.8 (22.5)	
Mean change at 12mo	42.7 (26.0)	5.2 (16.7)	<.0001
IGF-1 (ng/mL)			
Baseline	158.8 (67.0)	140.8 (56.6)	
Mean change at 12mo	-9.8 (46.6)	-1.8 (34.3)	0.28
IGFBP-3 (ug/mL)			
Baseline	5.1 (1.0)	5.0 (1.0)	
Mean change at 12mo	-0.2 (0.7)	0.04 (0.8)	0.07
IGF-1/IGFBP-3 (x 10^{-3})			
Baseline	30.9 (11.3)	28.3 (10.5)	
Mean change at 12mo	-0.2 (9.8)	-0.9 (7.6)	0.65

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)

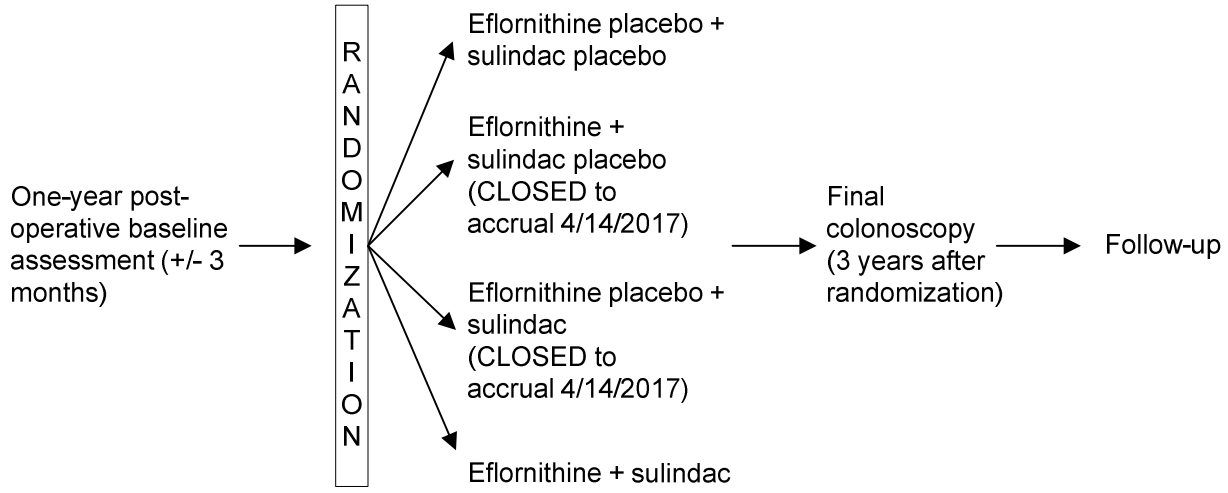
Date Activated:
03/01/2013

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 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 June 30, 2018, 204 patients have been randomized.

As of June 30, 2018, 133 patients have been 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. Fifty-two patients are off treatment, including nine patients coded as "Other – not protocol specified", three 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

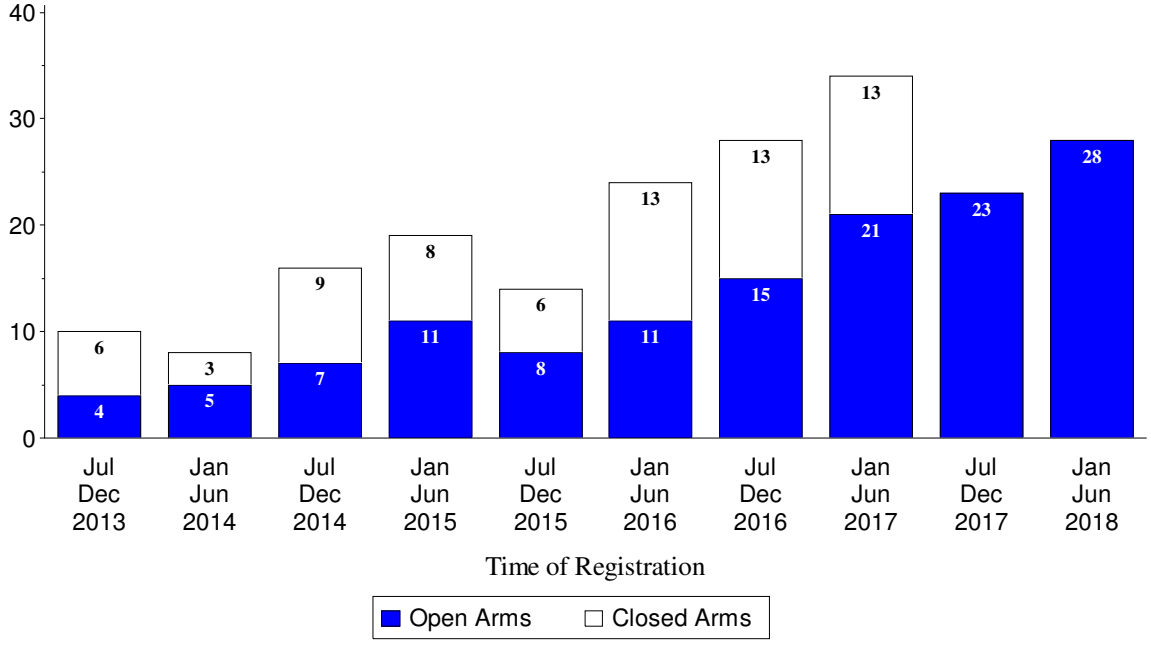
contact, one patient who stopped medication because of incorrectly thinking they had relapsed, one patient who was removed due to a stroke, and one patient who wanted to use arthritis medication not allowed on the study.

Five patients are not evaluable for adverse events due to never starting treatment (3) and no AE assessment made (2). Among 95 patients who have had adverse events evaluated, two had Grade 3 events: one patient experienced Grade 3 anemia, duodenal ulcer, and upper GI hemorrhage; 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 June 30, 2018, 495 patients have been logged into the tracking tool, of whom 40 were subsequently randomized, 25 to the open arms and 15 to the closed arms. Three hundred and sixty-five 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 June 30, 2018

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	21	Brooke Army Med Ctr	1
Irvine, U of CA	19	City of Hope Med Ctr	1
Wichita NCORP	11	Columbia MU-NCORP	1
Yale University	10	CRC West MI NCORP	1
Hawaii MU-NCORP	7	Dayton NCORP	1
San Antonio, U of TX	7	Eisenhower Army MC/Brooke Army Med Ctr	1
Northwest NCORP	6	Georgia NCORP	1
Banner MD Anderson/MD Anderson CC	5	Loma Linda Univ	1
So Calif, U of	5	NE Georgia Med Ctr/Georgia NCORP	1
Colorado, U of	4	Nevada CRF NCORP	1
Columbus NCORP	4	New Mexico MU-NCORP	1
Essentia Hlth NCORP	4	Oklahoma, Univ of	1
MD Anderson CC	4	PCRC NCORP	1
Michigan CRC NCORP	4	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	22
Baptist MU-NCORP	2	ALLIANCE	20
Heartland NCORP	2	ECOG-ACRIN	15
McLaren Cancer Inst/Wayne State Univ	2	**Total (42 Institutions)**	**204**
Bridgeport Hospital/Yale University	1		

Registration, Eligibility, and Evaluability

Open Arms

Registrations ending June 30, 2018; Data as of July 10, 2018

	Total
NUMBER REGISTERED	133
INELIGIBLE	11
ELIGIBLE	122
Analyzable, Pend. Elig.	17
ADVERSE EVENT ASSESSMENT	
Evaluable	95
Not Evaluable	5
Too Early	22

Patient Characteristics

Open Arms

All eligible and selected ineligible patients included

Registrations ending June 30, 2018; Data as of July 10, 2018

	Total (n=122)	
AGE		
Median	52.9	
Minimum	30.6	
Maximum	78.1	
SEX		
Males	50	41%
Females	72	59%
HISPANIC		
Yes	17	14%
No	102	84%
Unknown	3	2%
RACE		
White	90	74%
Black	8	7%
Asian	12	10%
Pacific Islander	1	1%
Native American	1	1%
Multi-Racial	2	2%
Unknown	8	7%
RISK OF RECURRENCE		
Stage 0 or I	21	17%
Stage II with no prior chemotherapy or radiation therapy	19	16%
Stage II with prior chemotherapy or radiation therapy	18	15%
Stage III	64	52%

Treatment Summary

Open Arms

All eligible and selected ineligible patients included

Registrations ending June 30, 2018; Data as of July 10, 2018

	Total
NUMBER ON PROTOCOL TREATMENT	70
NUMBER OFF PROTOCOL TREATMENT	52
REASON OFF TREATMENT	
Treatment completed as planned	14
Adverse Event or side effects	10
Refusal unrelated to adverse event	7
Progression/relapse	6
Death	0
Other - not protocol specified	9
Reason under review	6
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 June 30, 2018; Data as of July 10, 2018

	Total (n=95) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	89	6	0	0	0	0
AST increased	91	4	0	0	0	0
Abdominal pain	92	3	0	0	0	0
Alkaline phosphatase increased	94	1	0	0	0	0
Allergic reaction	94	0	1	0	0	0
Alopecia	93	2	0	0	0	0
Anemia	91	2	1	1	0	0
Anxiety	94	1	0	0	0	0
Arthralgia	94	1	0	0	0	0
Back pain	94	1	0	0	0	0
Bloating	94	1	0	0	0	0
Blood bilirubin increased	91	3	1	0	0	0
Bruising	93	2	0	0	0	0
Chest pain - cardiac	94	1	0	0	0	0
Constipation	88	7	0	0	0	0
Cough	94	1	0	0	0	0
Diarrhea	87	7	1	0	0	0
Dizziness	92	3	0	0	0	0
Dry mouth	94	1	0	0	0	0
Duodenal ulcer	94	0	0	1	0	0
Dysgeusia	94	1	0	0	0	0

	Total (n=95) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Dyspepsia	92	2	1	0	0	0
Dysphagia	94	1	0	0	0	0
Dyspnea	94	1	0	0	0	0
Edema limbs	91	4	0	0	0	0
Fatigue	86	8	1	0	0	0
Flu like symptoms	94	1	0	0	0	0
Flushing	94	0	1	0	0	0
GI disorders-Other, specify	94	1	0	0	0	0
Gastrointestinal pain	94	1	0	0	0	0
Generalized muscle weakness	94	1	0	0	0	0
Headache	89	5	1	0	0	0
Hematuria	93	2	0	0	0	0
Hot flashes	94	1	0	0	0	0
Hyperhidrosis	94	1	0	0	0	0
Hypertension	90	1	4	0	0	0
Hypocalcemia	94	1	0	0	0	0
Insomnia	94	0	1	0	0	0
Investigations-Other, specify	93	2	0	0	0	0
MS/connective tissue disorder	93	2	0	0	0	0
Muscle weakness upper limb	94	1	0	0	0	0
Myalgia	93	2	0	0	0	0
Nausea	87	7	1	0	0	0
Nervous sys disorders-Other	94	1	0	0	0	0
Pain	94	1	0	0	0	0
Pain in extremity	93	2	0	0	0	0
Peripheral sensory neuropathy	94	1	0	0	0	0
Platelet count decreased	93	2	0	0	0	0
Pleuritic pain	94	1	0	0	0	0
Pruritus	94	0	1	0	0	0
Rash maculo-papular	94	1	0	0	0	0
Renal/urinary disorders-Other	94	1	0	0	0	0
Skin hyperpigmentation	93	2	0	0	0	0
Skin/subq tissue ds-Other	94	1	0	0	0	0
Somnolence	94	1	0	0	0	0
Stroke	94	0	1	0	0	0
Tinnitus	90	3	1	1	0	0
Transient ischemic attacks	94	0	1	0	0	0
Upper GI hemorrhage	94	0	0	1	0	0
Vaginal dryness	94	1	0	0	0	0
Vomiting	92	2	1	0	0	0
White blood cell decreased	93	2	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	39	40	14	2	0	0