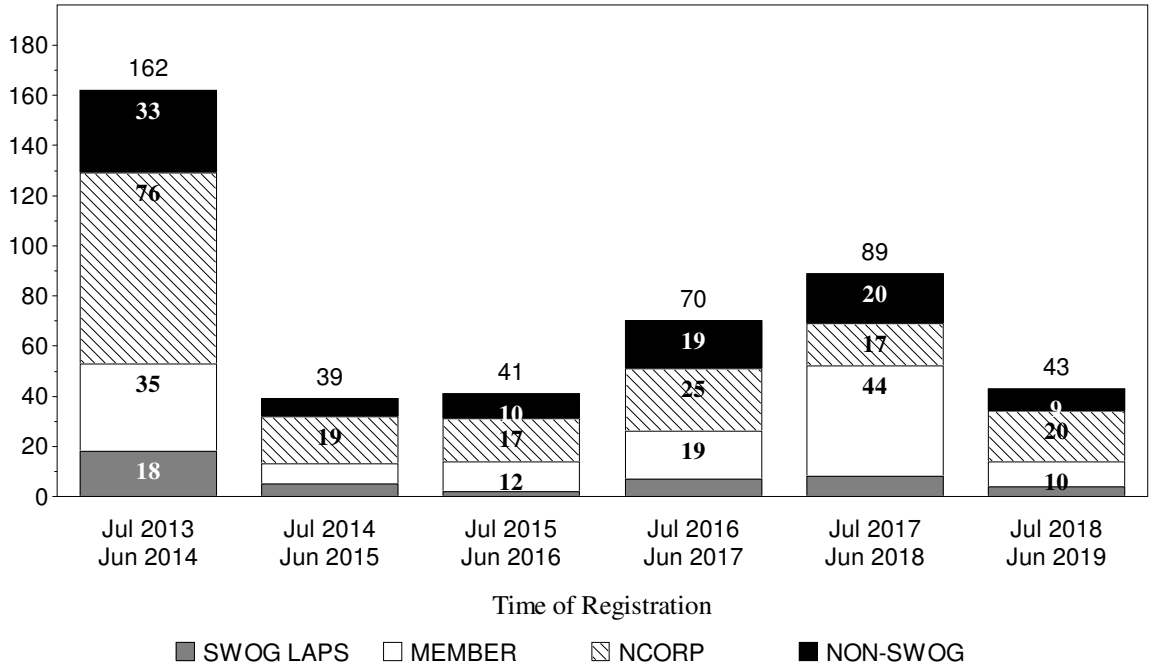
PREVENTION AND EPIDEMIOLOGY COMMITTEE

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 2019 Jun 2019	Jul 2018 Dec 2018	Jan 2018 Jun 2018	All Patients
S0820 PACES: ColrecStg0-3 Blind DFMO/Sulindac				
Pre-Registration				
Pre-Registration	62	17	58	574
Randomization				
Blinded drug	18	22	28	244

Non-SWOG Studies with SWOG-Credited Registrations

PREVENTION AND EPIDEMIOLOGY COMMITTEE

Studies with Accrual from January 2018 - June 2019

	SWOG Champion	SWOG Accrual Jan 2019 Jun 2019	SWOG Accrual Jul 2018 Dec 2018	SWOG Accrual Jan 2018 Jun 2018	SWOG Total	Total Accrued
A011502 Brst, Adj, Nodal+&HER2-, Aspirin vs. Placebo*	Symington, B	45	18	25	111	1605
Date Activated: 12/08/16						
Most Recent Progress Report						
A211102 Breast, Atypia via RPFNA, Metformin v Placebo		0	0	0	3	66
Date Activated: 02/01/15						
Most Recent Progress Report						
A211401 Lung, Varenic v Placebo, Surg Complications		2	0	0	2	12
Date Activated: 09/29/17						
No Progress Report Available						
A211601 Breast, Stg II-III, Aspirin		1	0	0	1	3
Date Activated: 08/01/18						
No Progress Report Available						

* 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)

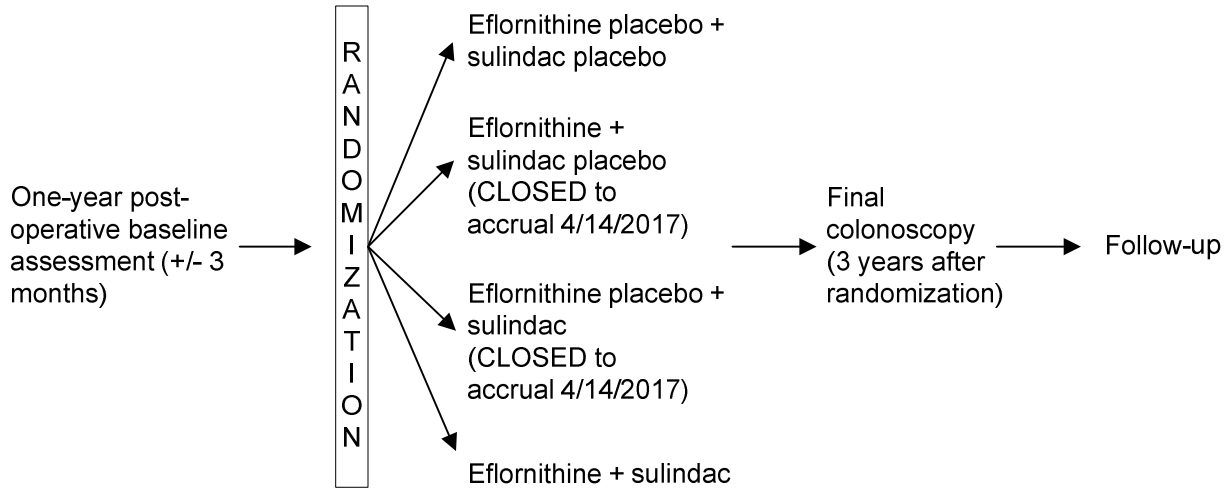
Date Activated:
03/01/2013

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 June 30, 2019, 244 patients have been randomized; of these, 173 patients were randomized to the currently open arms. Ten patients are ineligible due to: baseline hearing loss (5 patients), primary resection done too early (2), baseline lab values out of range (1), high cardiovascular risk (1), and pregnancy (1). Six patients are coded as major deviations, five of whom never started treatment and one who had only one day of treatment. Eighty-five patients are off treatment, including 14 patients coded as "Other – not protocol specified" for the following reasons: medication use not allowed on the study (4), intercurrent illness (3), site was unable to contact patient (2), patient moved (2), patient thought they had relapsed or progressed (2), and treatment delay greater than 90 days (1). Eight patients who are off

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

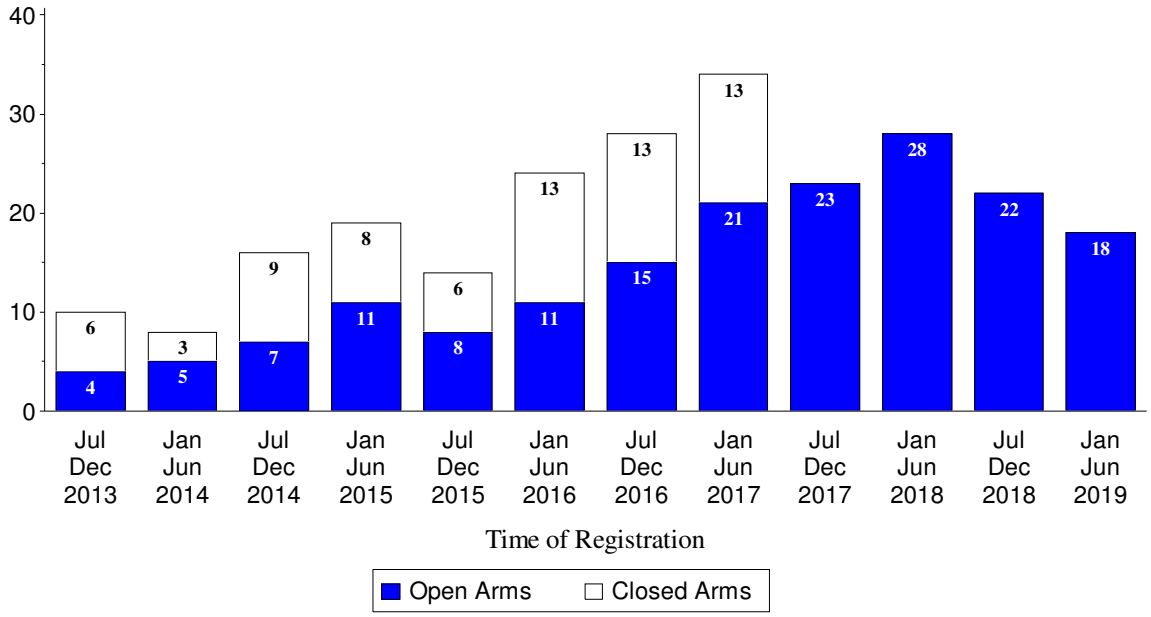
Seven patients are not evaluable for adverse events due to never starting treatment (5) and no AE assessment made (2). Among 145 patients who have had adverse events evaluated, one had a Grade 4 event of colonic perforation.

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, 2019, 574 patients have been logged into the tracking tool, of whom 47 were subsequently randomized, 32 to the open arms and 15 to the closed arms. Four hundred and fifty-eight 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 June 30, 2019

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	27	Southeast COR NCORP	2
Irvine, U of CA	21	Bay Area NCORP	1
Wichita NCORP	13	Bridgeport Hospital/Yale University	1
Yale University	13	Brooke Army Med Ctr	1
Hawaii MU-NCORP	9	City of Hope Med Ctr	1
Northwest NCORP	9	Columbia MU-NCORP	1
San Antonio, U of TX	8	CRC West MI NCORP	1
Banner MD Anderson/MD Anderson CC	6	Dayton NCORP	1
Michigan CRC NCORP	6	Georgia NCORP	1
Colorado, U of	5	NE Georgia Med Ctr/Georgia NCORP	1
Columbus NCORP	5	Nevada CRF NCORP	1
So Calif, U of	5	New Mexico MU-NCORP	1
Essentia Hlth NCORP	4	Oklahoma, Univ of	1
MD Anderson CC	4	PCRC NCORP	1
Baptist MU-NCORP	3	Providence Hosp	1
CORA NCORP	3	St Joseph Hospital/Mississippi, Univ of	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	Weiss Memorial Hosp/Loyola University	1
Kansas, U of	3	West Suburban MC/Loyola University	1
MAVERIC	3	Wisconsin NCORP	1
Eisenhower Army MC/Brooke Army Med Ctr	2	NRG	25
Heartland NCORP	2	ALLIANCE	24
Loma Linda Univ	2	ECOG-ACRIN	17
McLaren Cancer Inst/Wayne State Univ	2	**Total (45 Institutions)**	**244**

Registration, Eligibility, and Evaluability

Open Arms

Registrations ending June 30, 2019; Data as of July 18, 2019

	Total
NUMBER REGISTERED	173
INELIGIBLE	10
ELIGIBLE	163
Analyzable, Pend. Elig.	8
ADVERSE EVENT ASSESSMENT	
Evaluable	145
Not Evaluable	7
Too Early	11

Patient Characteristics

Open Arms

All eligible and selected ineligible patients included

Registrations ending June 30, 2019; Data as of July 18, 2019

	Total (n=163)	
AGE		
Median	53.0	
Minimum	28.4	
Maximum	78.1	
SEX		
Males	64	39%
Females	99	61%
HISPANIC		
Yes	20	12%
No	140	86%
Unknown	3	2%
RACE		
White	120	74%
Black	10	6%
Asian	20	12%
Pacific Islander	1	1%
Native American	1	1%
Multi-Racial	2	1%
Unknown	9	6%
RISK OF RECURRENCE		
Stage 0 or I	29	18%
Stage II with no prior chemotherapy or radiation therapy	24	15%
Stage II with prior chemotherapy or radiation therapy	25	15%
Stage III	85	52%

Treatment Summary

Open Arms

All eligible and selected ineligible patients included

Registrations ending June 30, 2019; Data as of July 18, 2019

	Total
NUMBER ON PROTOCOL TREATMENT	78
NUMBER OFF PROTOCOL TREATMENT	85
REASON OFF TREATMENT	
Treatment completed as planned	24
Adverse Event or side effects	16
Refusal unrelated to adverse event	16
Progression/relapse	11
Death	0
Other - not protocol specified	14
Reason under review	4
MAJOR PROTOCOL DEVIATIONS	6
LOST TO FOLLOW-UP	1
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	8

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, 2019; Data as of July 18, 2019

	Total (n=145) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	139	6	0	0	0	0
AST increased	138	7	0	0	0	0
Abdominal pain	136	9	0	0	0	0
Alkaline phosphatase increased	143	2	0	0	0	0
Allergic reaction	144	0	1	0	0	0
Alopecia	142	3	0	0	0	0
Anemia	141	2	1	1	0	0
Anxiety	144	1	0	0	0	0
Arthralgia	143	2	0	0	0	0
Back pain	144	1	0	0	0	0
Bloating	143	2	0	0	0	0
Blood bilirubin increased	141	3	1	0	0	0
Blurred vision	144	0	1	0	0	0
Body odor	144	1	0	0	0	0
Bruising	142	3	0	0	0	0
Chest pain - cardiac	144	1	0	0	0	0
Cholesterol high	144	1	0	0	0	0
Colonic perforation	144	0	0	0	1	0
Constipation	131	12	2	0	0	0
Cough	143	2	0	0	0	0
Diarrhea	132	9	3	1	0	0
Dizziness	138	6	1	0	0	0
Dry mouth	143	2	0	0	0	0
Duodenal ulcer	144	0	0	1	0	0
Dysgeusia	144	1	0	0	0	0
Dyspepsia	141	3	1	0	0	0
Dysphagia	144	1	0	0	0	0
Dyspnea	143	2	0	0	0	0
Ear/labyrinth disorders-Other	144	1	0	0	0	0
Edema limbs	140	5	0	0	0	0
Fatigue	134	10	1	0	0	0
Flu like symptoms	144	1	0	0	0	0
Flushing	144	0	1	0	0	0
GERD	144	0	1	0	0	0
GI disorders-Other, specify	142	3	0	0	0	0
Gastrointestinal pain	143	2	0	0	0	0
Generalized muscle weakness	144	1	0	0	0	0
Headache	137	7	1	0	0	0
Hearing impaired	144	1	0	0	0	0
Hematuria	143	2	0	0	0	0
Hot flashes	144	1	0	0	0	0
Hyperglycemia	144	0	1	0	0	0
Hyperhidrosis	144	1	0	0	0	0

	Total (n=145) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Hypertension	137	2	6	0	0	0
Hypocalcemia	144	1	0	0	0	0
Insomnia	143	1	1	0	0	0
Investigations-Other, specify	142	3	0	0	0	0
MS/connective tissue disorder	143	2	0	0	0	0
Mucositis oral	143	1	0	1	0	0
Muscle weakness upper limb	144	1	0	0	0	0
Myalgia	143	2	0	0	0	0
Nausea	136	8	1	0	0	0
Neoplasms, all	144	1	0	0	0	0
Nervous sys disorders-Other	144	1	0	0	0	0
Pain	144	1	0	0	0	0
Pain in extremity	143	2	0	0	0	0
Paresthesia	144	1	0	0	0	0
Peripheral sensory neuropathy	143	1	1	0	0	0
Platelet count decreased	143	2	0	0	0	0
Pleuritic pain	144	1	0	0	0	0
Postnasal drip	144	1	0	0	0	0
Pruritus	143	1	1	0	0	0
Rash acneiform	144	1	0	0	0	0
Rash maculo-papular	143	1	0	1	0	0
Renal/urinary disorders-Other	144	1	0	0	0	0
Skin hyperpigmentation	143	2	0	0	0	0
Skin/subq tissue ds-Other	143	2	0	0	0	0
Somnolence	144	1	0	0	0	0
Stomach pain	143	1	1	0	0	0
Stroke	143	0	2	0	0	0
Tinnitus	134	7	3	1	0	0
Transient ischemic attacks	144	0	1	0	0	0
Upper GI hemorrhage	144	0	0	1	0	0
Vaginal dryness	144	1	0	0	0	0
Vomiting	142	2	1	0	0	0
Weight gain	144	0	1	0	0	0
White blood cell decreased	143	2	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	56	56	28	4	1	0

S1904 Pilot

Coordinating Group: SWOG

Cluster Randomized Controlled Trial of Patient and Provider Decision Support to Increase Chemoprevention Informed Choice among Women with Atypical Hyperplasia or Lobular Carcinoma *In Situ* - Making Informed Choices On Incorporating Chemoprevention into Care (MiCHOICE)

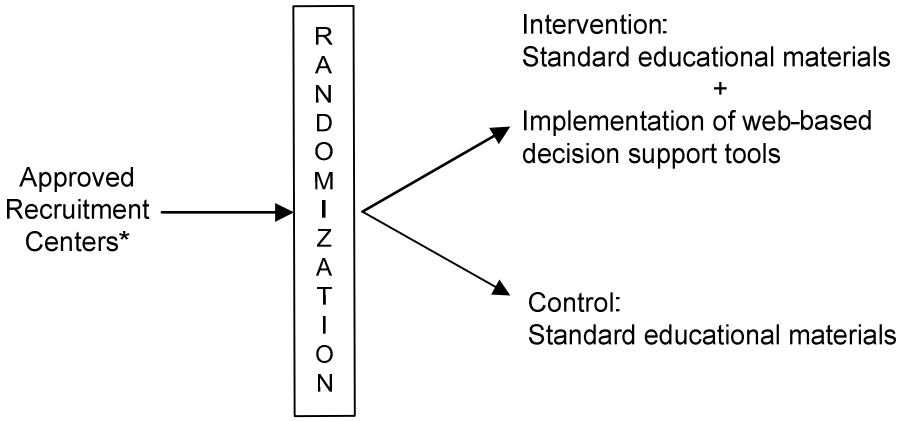
Participants:
SWOG, CTSU

Study Chairs:
K Crew, R Kukafka

Statisticians:
G Anderson, K Arnold

Data Coordinator:
M Yee

SCHEMA



*Recruitment Center is defined as a site that has an active electronic health record and patient portal used in the outpatient clinics which is common and accessible across all sites belonging to the Recruitment Center. An **S1904** Recruitment Center Application must be completed and approved for participation.

Objectives

To compare the frequency of chemoprevention informed choice at 6 months after registration among women with atypical hyperplasia (AH) or lobular carcinoma *in situ* (LCIS) between the intervention (*RealRisks* decision aid/*BNAV* + standard educational materials) and control (standard educational materials alone) arms.

To assess patient chemoprevention knowledge, chemoprevention intention/decision, perceived breast cancer risk and worry, accuracy of breast cancer risk perception, decision conflict and decision regret at baseline, 6 months, and 12 months in the intervention and control arms.

To compare patient chemoprevention usage, adherence, and reasons for discontinuation of a selective estrogen receptor modulator (SERM) or aromatase inhibitor (AI) annually for up to 5 years between the intervention and control arms.

To assess shared decision-making about chemoprevention among patients and healthcare providers after their 6-month clinic visit in the intervention and control arms.

To assess the implementation of the decision support tools, *RealRisks* and *BNAV*, into clinic workflow, and to better understand barriers and facilitators to chemoprevention usage by conducting telephone/video-conference interviews of healthcare providers and high-risk women with AH or LCIS assigned to the active intervention.

Patient Population

Patients must have histologically confirmed AH or LCIS documented by breast pathology report at any time in the past. Patients with borderline breast lesions and pleomorphic LCIS are also eligible. Patients must not have a history of invasive breast cancer or ductal carcinoma *in situ*.

Patients must not have prior or current use of SERMs or AIs. Patients must not be currently taking hormone replacement therapy.

Patients must be women 35 to 74 years of age. Patients must not have a history of bilateral mastectomies or breast implants. Both pre/perimenopausal and postmenopausal women are eligible. Patients must not be pregnant or lactating. Premenopausal patients must not have a history of thromboembolism.

Patients must be able to read and write in English or Spanish. Patients must be able to access the internet and receive email or text messages. Patient must be able to access the patient portal for their Recruitment Center.

Stratification/Descriptive Factors

Recruitment Centers will be randomly assigned to control or intervention with stratification by the following: (1) eligible patient volume: ≤ 100 vs > 100 patients with a diagnosis of AH or LCIS per year; and (2) type of component: Minority/Underserved-NCORP vs. non-Minority/Underserved-NCORP or NCTN).

Accrual Goals

A total of 415 patients will be accrued to achieve 374 eligible patients.