BREAST COMMITTEE

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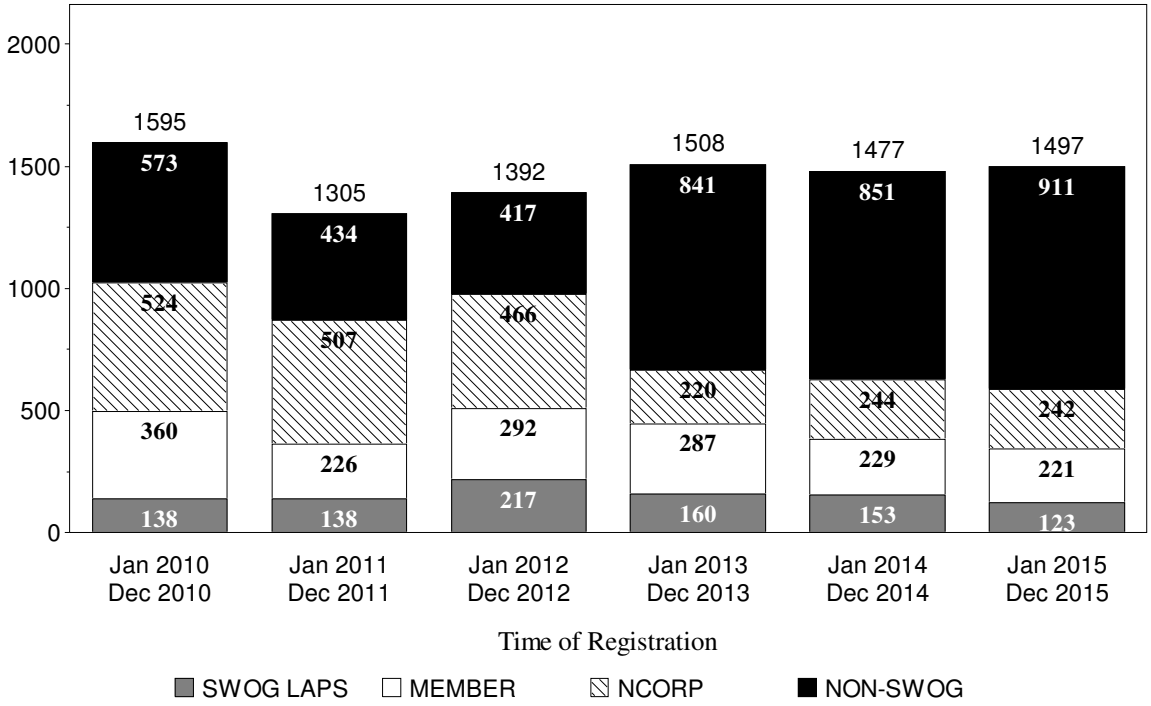
Patient Registrations to Studies

By 12 Month Intervals
BREAST COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

BREAST COMMITTEE

	Jul 2015 Dec 2015	Jan 2015 Jun 2015	Jul 2014 Dec 2014	All Patients
S1007 Breast, Adj, N1, Endocrine+/-Chemo				
Initial Registration				
Recurrence Score testing	764	1,048	950	8,059
Randomization				
Chemo and Endocrine Therapy	239	284	245	2,093
Endocrine Therapy Alone	236	279	243	2,081
	475	563	488	4,174
S1207 Breast, Adj, Endocrine+/-Everolimus				
Randomization				
Blinded drug + Endocrine	181	156	134	563
S1222 Breast, Fulvestrant +/- Everolimus +/- Anastrozole				
Randomization				
Blinded treatment	0	7	24	37
A011106 Breast, Neoadj, ALTERNATE Study*				
Total Registrations	3	6	3	13
A011202 Breast, Nodal XRT +/- ALND*				
Total Registrations	5	10	4	21
A011203 Breast, Adv, Tam vs Endoxifen*				
Total Registrations	3	0	0	3
B43 Breast, DCIS, HER2+, RT +/- Tras*				
Total Registrations	0	0	5	66
B47 Chemo vs Chemo + Trastuzumab*				
Total Registrations	0	5	18	155
B51 Breast, Regional Nodal XRT*				
Total Registrations	4	0	1	6
B52 Breast, Neoadj TCHP +/- AI*				
Total Registrations	2	3	1	6
B55 Breast, Adj Olaparib for BRCA,TNBC*				
Total Registrations	3	2	0	5
E1Z11 Breast, Genetic Predictors of AIMSS*				
Total Registrations	5	23	11	125
E2108 Breast, Early Local Tx for Intact Primary Tumor*				
Total Registrations	1	9	8	52
E2112 Breast, Adv, Exemestane +/- Entinostat*				
Total Registrations	7	1	0	8

	Jul 2015 Dec 2015	Jan 2015 Jun 2015	Jul 2014 Dec 2014	All Patients
E4112 Breast, MRI + DCIS Score*				
Total Registrations	12	0	0	12
NRGBR003 Breast, Adj, TNBC, AC -> WP +/- Carbo*				
Total Registrations	4	0	0	4
Z11102 Breast Conserv. Surgery for MIBC*				
Total Registrations	3	4	0	9

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

S1007 Phase III

Coordinating Group: SWOG

A Phase III Randomized Clinical Trial of Standard Adjuvant Endocrine Therapy +/- Chemotherapy in Patients with 1-3 Positive Nodes, Hormone Receptor-Positive and HER2-Negative Breast Cancer with Recurrence Score (RS) of 25 or Less. RxPONDER: A Clinical Trial Rx for Positive Node, Endocrine Responsive Breast Cancer

---

Participants:
SWOG, CTSU (endorsed by NRG, Alliance, ECOG-ACRIN, CCTG, GEICAM, and UNICANCER)

Study Chairs:
K Kalinsky, J Gralow, G Hortobagyi, K Albain

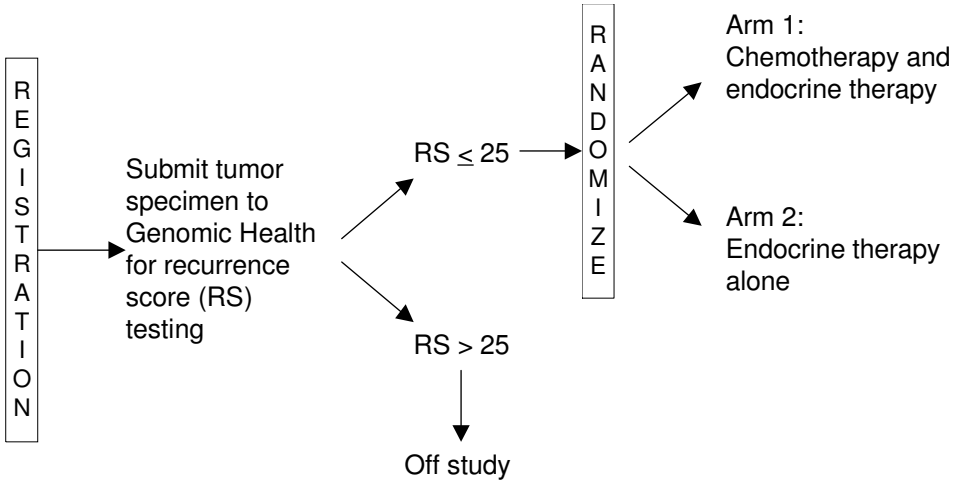
Statisticians:
W Barlow, D Lew

Data Coordinators:
L Kaye, J Scurlock

Date Activated:
01/15/2011

Date Closed:
10/01/2015

SCHEMA



Objectives

To determine the effect of chemotherapy in patients with node-positive breast cancer who do not have high Recurrence Scores (RS) by Oncotype DX®. In patients with 1-3 positive nodes, and hormone receptor (HR)-positive, HER2-negative breast cancer with RS ≤ 25 treated with endocrine therapy we will test whether the difference in disease-free survival for

patients treated with chemotherapy compared to no chemotherapy depends directly on the magnitude of RS. If benefit depends on the RS score, the trial will determine the optimal cutpoint for recommending chemotherapy or not.

To compare overall survival (OS), distant disease-free survival (DDFS) and local disease-free interval (LDFI) by receipt of chemotherapy or not and its interaction with RS.

To compare the toxicity across the treatment arms.

To perform other assays or tests (in particular the PAM50 risk of relapse score), as they are developed and validated, that measure potential benefit of chemotherapy and compare them to Oncotype DX®.

To determine the impact of management with Oncotype DX® on patient-reported anxiety (co-primary Health-Related Quality of Life [HRQL] outcome) prior to screening, after disclosure of test results, and during the randomized trial.

To determine the impact of Oncotype DX® on the initial management cost of node-positive, HR-positive, HER2-negative breast cancer.

To compare patient-reported utilities (e.g. QOL) for those randomized to chemotherapy versus no chemotherapy.

Using modeling and DFS information from the trial, to estimate the cost-effectiveness of management with Oncotype DX® versus usual care.

To determine the role of other assays (e.g. PAM50) as predictors of DFS, DDFS and LDFI for patients randomized to chemotherapy versus no chemotherapy.

To determine the impact of treatment with chemotherapy versus no chemotherapy on patient-reported fatigue and cognitive concerns (secondary HRQL outcomes).

To determine the impact of management with Oncotype DX® on patient-reported decision conflict, perceptions regarding Oncotype DX® testing, and survivor concerns prior to screening, after disclosure of test results, and during the randomized trial (secondary HRQL outcomes).

Patient Population

Patients must be women with a histologically confirmed diagnosis of node-positive (1-3 nodes) invasive breast carcinoma with positive estrogen and/or progesterone receptor status, and negative HER-2 status. HER-2 test result negativity must be assessed as per ASCO/CAP 2013 guidelines using IHC, ISH or both. If HER-2 IHC is 2+, evaluation for gene amplification (ISH) must be performed and the ISH must be negative; ISH is not required if IHC is 0 or 1+. Patients with equivocal HER-2 are not eligible. Patients with multifocal, multicentric, and synchronous bilateral breast cancers are allowed. Patients must not have inflammatory breast cancer and must not have metastatic disease.

Patients must have had either breast-conserving surgery with planned radiation therapy or total mastectomy (with or without planned postmastectomy radiation). Patients must have clear margins from both invasive cancer and DCIS; LCIS at the margins is allowed. Patients must have undergone axillary staging by sentinel node biopsy or axillary lymph node dissection. Patients with positive sentinel node are not required to undergo full axillary lymph node dissection; this is at the discretion of the treating physician. Patients with micrometastases as the only nodal involvement (pN1mi) are not eligible. Patients must not have begun chemotherapy or endocrine therapy for their breast cancer prior to registration. Patients must be able to receive taxane and/or anthracycline based chemotherapy. Patients must not have received an aromatase inhibitor (AI) or a selective estrogen receptor modulator (SERM) such as tamoxifen or raloxifene within five years prior to registration. Partial breast irradiation (including brachytherapy) is not allowed. Radiation in the opposite breast is acceptable. Patients with a prior diagnosis of contralateral DCIS are eligible if they underwent a mastectomy or lumpectomy with whole breast radiation. Patients with a prior diagnosis of ipsilateral DCIS or invasive breast cancer who received radiation to that breast are not eligible.

Registration of patients who have not yet undergone Oncotype DX® screening must occur no later than 56 days after definitive surgery. For all patients, randomization (Step 2 Registration) must occur within 84 days after definitive surgery. If the Oncotype DX® Breast Cancer Assay has not been performed, patients must be willing to submit tissue samples directly to Genomic Health for testing to determine Recurrence Score value. If the Oncotype DX® Recurrence Score is already known and is 25 or less, the patient must be randomized (registered to

Step 2) immediately following initial registration. If the Oncotype DX® Recurrence Score is already known and is greater than 25, the patient is ineligible.

Patients must have a Zubrod performance status of 0-2 and must not require chronic treatment with systemic steroids (inhaled steroids are allowed) or other immunosuppressive agents.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) Recurrence Score: 0-13 vs 14-25; (2) menopausal status: pre vs post; and (3) type of nodal dissection: axillary lymph node dissection (with or without sentinel node mapping) vs sentinel node biopsy without axillary lymph node dissection.

Accrual Goals

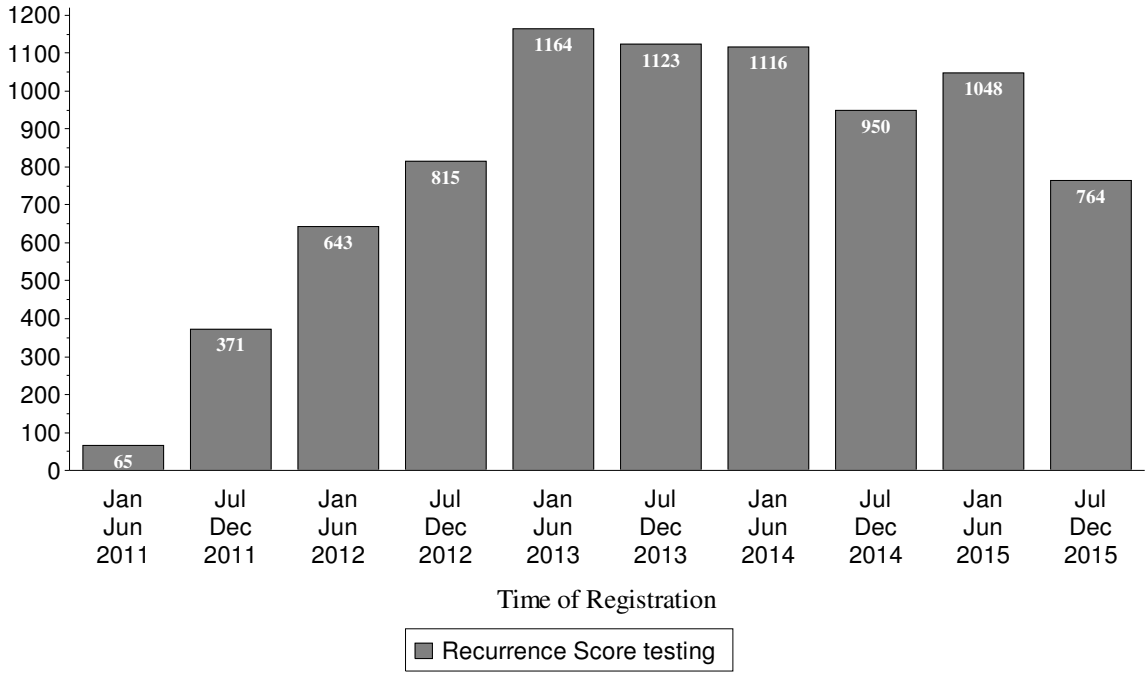
The accrual goal for the randomized trial is 4,000 eligible patients, which will require approximately 9,400 women to be screened for inclusion. An additional 1,000 eligible patients from UNICANCER in France will be randomized. Annual interim analyses are planned beginning when 24% of the events have been observed, approximately 6.6 years after initiation of the study.

Summary Statement

This study was activated on January 15, 2011, and closed on October 1, 2015, after meeting the accrual goal of 4,000 eligible patients. The study remains open to continued accrual of the additional 1,000 patients from UNICANCER sites only. As of December 31, 2015, there had been 8,058 registrations to the screening step and 4,173 patients with Oncotype DX® Recurrence Score $\leq$ 25 randomized. Sixty-nine patients are currently ineligible, the most common reason being margins not clear. One patient who refused randomization and withdrew consent for all follow-up is not analyzable for any endpoint. Major deviations are coded for 409 additional patients (10%) who refused their randomized treatment assignment, did not receive any protocol treatment, or received a non-approved chemotherapy regimen. These 409 patients are not evaluable for adverse events. The most common reason off treatment among the 45 patients coded as “Other - not protocol specified” is secondary cancer.

There have been four treatment-related deaths reported among 3,292 patients evaluated for adverse events: one due to small bowel, colon, and liver necrosis (listed as "GI disorders - Other, specify"), one due to stroke, one due to typhlitis, and one due to sepsis. An additional 97 patients reported Grade 4 adverse events as maximum degree, primarily hematologic, including one more case of neutropenia currently coded as "Blood/lymph disorder-Other." The Grade 4 "Infections/infestations-Other" was infection at port-a-cath. Toxicities are reviewed by treatment group by the Data Safety and Monitoring Committee, the SWOG Breast Committee leadership, and the Study Chair.

Initial Registrations By 6 Month Intervals



Registration by Institution

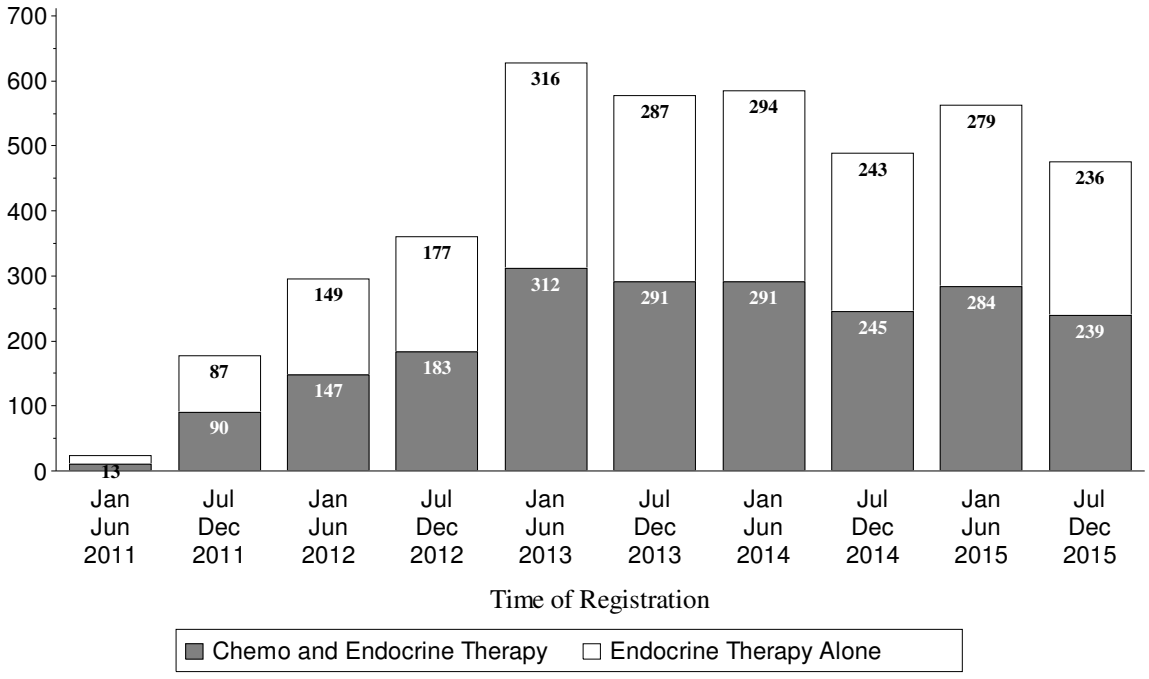
Screening Registration

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
ECOG-ACRIN	1448	U of Tennessee MC/Tennessee, U of	25
GEICAM	1252	Virginia Mason MC/Northwest NCORP	24
Alliance	1074	Kentucky, U of	23
NCIC-CTG	734	S Georgia Med Ctr/Brooke Army Med Ctr	22
NRG	602	Henry Ford Hosp	20
MD Anderson CC	269	CRC West MI NCORP	19
UNICANCER	196	McLaren Cancer Inst/Wayne State Univ	19
National Cancer Ctr	175	PCRC NCORP	19
Michigan CRC NCORP	134	Sacred Heart Hosp/Arkansas, U of	19
INCan	132	San Diego, U of CA	18
Michigan, U of	100	Dayton NCORP	17
City of Hope Med Ctr	91	Good Samaritan Hosp/CORA NCORP	17
Cleveland Clinic OH	83	INC, Bogota	16
Kaiser Perm NCORP	80	Montana NCORP	16
Wichita NCORP	78	SW Cancer & Res Ctr/San Antonio, U of TX	16
Southeast COR NCORP	57	Long Beach Mem MC/Irvine, U of CA	15
Kansas, U of	50	Colorado, U of	14
Utah, U of	50	St Joseph Med Ctr/PCRC NCORP	14
KaiserPermanenteSCAL/Kaiser Perm NCORP	49	Atlanta Reg CCOP	13
Columbus NCORP	48	Cookeville Reg MC	13
Loyola University	48	Rochester, Univ of	13

Institutions	Total Reg	Institutions	Total Reg
New Mexico MU-NCORP	47	Singing River Hosp/Mississippi, Univ of	13
Beaumont NCORP	44	Mem Hosp, Co Springs/Colorado, U of	12
Yale University	44	Univ of Louisville	12
Wayne State Univ	40	Harrison Bremerton/Harrison Medical Ctr	11
Columbia MU-NCORP	39	San Antonio, U of TX	11
So Calif, U of	34	Davis, U of CA	10
St Charles Hlth Sys/PCRC NCORP	34	Oklahoma, Univ of	10
St Luke's Mt State/PCRC NCORP	34	UF Cancer Center/Arkansas, U of	10
Methodist Hospital	31	Bridgeport Hospital/Yale University	9
Northwest NCORP	31	Cedars-Sinai Med Ctr	9
Poudre Valley Hosp/Colorado, U of	31	Providence Hosp	9
Heartland NCORP	29	Carolinas Med Ctr/San Antonio, U of TX	8
Hawaii MU-NCORP	28	Northwestern Univ	8
MUSC MU-NCORP	28	Upstate Carolina	8
Kansas City NCORP	27	Utah Valley Reg MC/Intermountain MC	8
Ozarks NCORP	27	All Other Institutions	215
Lahey Hosp & Med Ctr	26	**Total (142 Institutions)**	**8059**

Randomization By 6 Month Intervals



Registration by Institution

Randomization

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
GEICAM	792	Columbia MU-NCORP	16
ECOG-ACRIN	713	Wayne State Univ	16
Alliance	526	So Calif, U of	15
NCIC-CTG	328	Virginia Mason MC/Northwest NCORP	14
NRG	265	Northwest NCORP	13
MD Anderson CC	147	Hawaii MU-NCORP	12
National Cancer Ctr	143	Heartland NCORP	12
UNICANCER	113	Atlanta Reg CCOP	11
INCan	96	Colorado, U of	11
Wichita NCORP	57	Henry Ford Hosp	11
City of Hope Med Ctr	45	INC, Bogota	11
Michigan CRC NCORP	44	Kansas City NCORP	11
Kaiser Perm NCORP	43	Long Beach Mem MC/Irvine, U of CA	11
KaiserPermanenteSCAL/Kaiser Perm NCORP	42	PCRC NCORP	11
Kansas, U of	32	Poudre Valley Hosp/Colorado, U of	11
Southeast COR NCORP	31	San Antonio, U of TX	10
Beaumont NCORP	30	St Luke's Mt State/PCRC NCORP	10
New Mexico MU-NCORP	27	Harrison Bremerton/Harrison Medical Ctr	9
Cleveland Clinic OH	26	Montana NCORP	9
Loyola University	23	Ozarks NCORP	9
Michigan, U of	23	Cedars-Sinai Med Ctr	8
Kentucky, U of	21	Good Samaritan Hosp/CORA NCORP	8
Yale University	21	Oklahoma, Univ of	8
MUSC MU-NCORP	19	Providence Hosp	8
Columbus NCORP	18	Univ of Louisville	8
Lahey Hosp & Med Ctr	18	All Other Institutions	223
Utah, U of	18	**Total (124 Institutions)**	**4174**
Sacred Heart Hosp/Arkansas, U of	17		

Registration, Eligibility, and Evaluability

Randomization

Registrations ending December 31, 2015; Data as of February 23, 2016

	TOTAL	Chemo and Endocrine Therapy	Endocrine Therapy Alone
NUMBER REGISTERED	4174	2093	2081
INELIGIBLE	68	39	29
ELIGIBLE	4106	2054	2052
Analyzable, Pend. Elig.	7	4	3
Not Analyzable	1	1	0
ADVERSE EVENT ASSESSMENT			
Evaluable	3292	1568	1724
Not Evaluable	409	285	124
Too Early	404	200	204

Patient Characteristics

Randomization

Registrations ending December 31, 2015; Data as of February 23, 2016

	Total (n=4105)	
AGE		
Median	57.6	
Minimum	18.4	
Maximum	87.7	
HISPANIC		
Yes	623	15%
No	3284	80%
Unknown	198	5%
RACE		
White	3157	77%
Black	248	6%
Asian	323	8%
Pacific Islander	12	0%
Native American	24	1%
Multi-Racial	7	0%
Unknown	334	8%
RECURRENCE SCORE		
0-13	1726	42%
14-25	2379	58%
MENOPAUSAL STATUS		
Pre-menopausal	1319	32%
Post-menopausal	2786	68%
NODAL DISSECTION		
Axillary lymph node dissection (with or without sentinel node mapping)	2371	58%
Sentinel node biopsy without axillary lymph node dissection	1734	42%

Treatment Summary

Registrations ending December 31, 2015; Data as of February 23, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	3769
NUMBER OFF PROTOCOL TREATMENT	336
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	7
Refusal unrelated to adverse event	200
Progression/relapse	53
Death	15
Other - not protocol specified	45
Reason under review	16
MAJOR PROTOCOL DEVIATIONS	409

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Adverse Events with No Entries for Grades 3 to 5 Have Been Suppressed

Registrations ending December 31, 2015; Data as of February 23, 2016

	Total (n=3292) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
ALT increased	3289	3	0	0
AST increased	3291	1	0	0
Abdominal pain	3285	7	0	0
Acute kidney injury	3291	1	0	0
Alkaline phosphatase increased	3291	1	0	0
Allergic reaction	3286	6	0	0
Anemia	3273	17	2	0
Anorexia	3291	1	0	0
Anxiety	3291	1	0	0
Arthralgia	3238	54	0	0
Atrial fibrillation	3290	2	0	0
Back pain	3290	2	0	0
Blood/lymph disorder-Other	3290	1	1	0
Bone marrow hypocellular	3291	1	0	0
Bone pain	3279	13	0	0
Breast infection	3290	2	0	0
CD4 lymphocytes decreased	3291	1	0	0
Cataract	3291	1	0	0
Catheter related infection	3290	1	1	0
Chest pain - cardiac	3291	1	0	0
Chest wall pain	3291	1	0	0
Colitis	3288	4	0	0
Constipation	3289	3	0	0
Dehydration	3281	11	0	0
Depression	3289	3	0	0

	Total (n=3292) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
Dermatitis radiation	3288	4	0	0
Device related infection	3288	3	1	0
Diarrhea	3261	31	0	0
Dizziness	3289	3	0	0
Dry skin	3291	1	0	0
Dyspareunia	3290	2	0	0
Dyspepsia	3291	1	0	0
Dyspnea	3290	2	0	0
Ear pain	3290	2	0	0
Edema limbs	3291	1	0	0
Ejection fraction decreased	3291	0	1	0
Erythema multiforme	3291	1	0	0
Erythroderma	3290	2	0	0
Esophagitis	3290	2	0	0
Fatigue	3250	42	0	0
Febrile neutropenia	3232	51	9	0
Fever	3290	1	1	0
Flank pain	3291	1	0	0
Flu like symptoms	3291	1	0	0
GI disorders-Other, specify	3291	0	0	1
Gastric hemorrhage	3291	1	0	0
Gastric ulcer	3291	1	0	0
Gastrointestinal pain	3291	1	0	0
Gen disorders/admin site cond	3290	2	0	0
Generalized muscle weakness	3288	4	0	0
Hand-Foot syndrome	3288	4	0	0
Headache	3286	6	0	0
Heart failure	3291	1	0	0
Hot flashes	3277	15	0	0
Hyperglycemia	3278	14	0	0
Hypertension	3282	10	0	0
Hypokalemia	3287	5	0	0
Hyponatremia	3290	2	0	0
Hypotension	3288	4	0	0
INR increased	3291	1	0	0
Infections/infestations-Other	3288	3	1	0
Injection site reaction	3291	1	0	0
Insomnia	3286	6	0	0
Irregular menstruation	3291	1	0	0
Kidney infection	3291	1	0	0
LV systolic dysfunction	3291	1	0	0
Leukocytosis	3288	3	1	0
Lipase increased	3291	1	0	0
Localized edema	3290	2	0	0
Lung infection	3287	4	1	0
Lymphedema	3290	2	0	0
Lymphocyte count decreased	3275	16	1	0
Mucositis oral	3274	18	0	0
Myalgia	3268	24	0	0
Myelitis	3291	1	0	0
Myocardial infarction	3291	1	0	0

	Total (n=3292) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
Nausea	3277	15	0	0
Neck pain	3290	2	0	0
Neoplasms, all	3291	1	0	0
Nervous sys disorders-Other	3291	1	0	0
Neutrophil count decreased	3174	43	75	0
Pain	3290	2	0	0
Pain in extremity	3289	3	0	0
Paresthesia	3290	2	0	0
Peripheral ischemia	3291	1	0	0
Peripheral motor neuropathy	3289	2	1	0
Peripheral sensory neuropathy	3273	18	1	0
Platelet count decreased	3291	1	0	0
Pleuritic pain	3291	1	0	0
Pneumonitis	3285	7	0	0
Premature menopause	3291	1	0	0
Pruritus	3288	4	0	0
ROM decreased	3291	1	0	0
RT recall reaction, derm	3291	1	0	0
Rash acneiform	3291	1	0	0
Rash maculo-papular	3287	5	0	0
Renal/urinary disorders-Other	3291	1	0	0
Resp/thoracic/mediastinal ds	3291	1	0	0
Sepsis	3287	0	4	1
Sinus tachycardia	3291	1	0	0
Skin infection	3286	6	0	0
Skin/subq tissue ds-Other	3290	2	0	0
Stroke	3289	1	1	1
Suicidal ideation	3291	1	0	0
Supraventricular tachycardia	3291	1	0	0
Syncope	3290	2	0	0
Thromboembolic event	3283	7	2	0
Tinnitus	3291	1	0	0
Typhlitis	3291	0	0	1
Upper GI hemorrhage	3291	0	1	0
Urinary tract infection	3289	3	0	0
Urticaria	3289	3	0	0
Uterine hemorrhage	3291	1	0	0
Vaginal dryness	3289	3	0	0
Vascular access complication	3291	1	0	0
Vomiting	3277	15	0	0
Watering eyes	3288	4	0	0
Weight gain	3291	1	0	0
Weight loss	3290	2	0	0
White blood cell decreased	3234	41	17	0
Wound dehiscence	3291	1	0	0
MAX. GRADE ANY ADVERSE EVENT	2850	341	97	4

S1200 Phase III

Randomized Blinded Sham- and Waitlist-Controlled Trial of Acupuncture for Joint Symptoms Related to Aromatase Inhibitors in Women with Early Stage Breast Cancer

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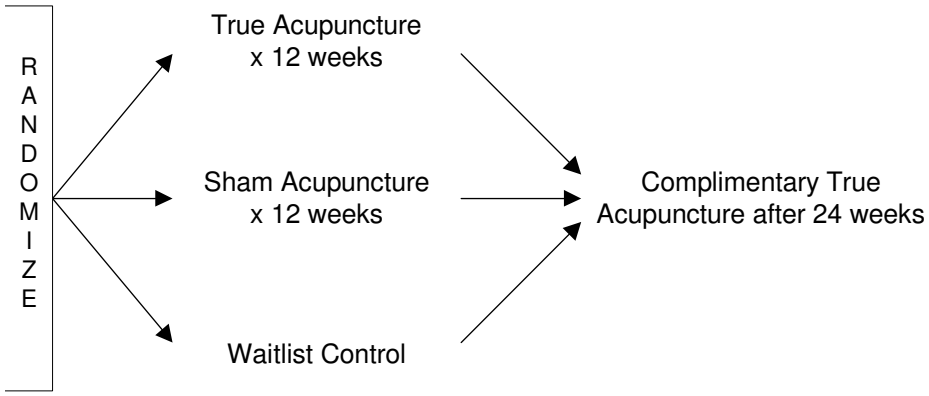
Study Chairs:
D Hershman, K Crew

Date Activated:
03/27/2012

Statisticians:
J Unger, D Lew

Data Coordinators:
D Marrah, R Topacio

SCHEMA



Objectives

To determine whether true acupuncture administered twice weekly for six weeks compared to sham acupuncture and waitlist control causes a significant reduction in joint pain related to aromatase inhibitors (AIs) in women with early stage breast cancer as measured by the Brief Pain Inventory-Short Form (BPI-SF) worst pain score at six weeks.

To evaluate the effects of acupuncture on the Brief Pain Inventory-Short Form (BPI-SF) worst pain, worst stiffness, pain severity, and pain-related interference scores.

To evaluate the effects of acupuncture on Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index (pain, stiffness, and function) for the hips and knees.

To evaluate the effects of acupuncture on Modified-Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands (M-SACRAH) (pain, stiffness, and function).

To evaluate the effects of acupuncture on the PROMIS Pain Impact-Short Form (PROMIS PI-SF).

To evaluate the effects of acupuncture on quality of life (QOL) as assessed by the Functional Assessment of Cancer Therapy-Endocrine Subscales (FACT-ES).

To evaluate the effects of acupuncture on functional testing with grip strength and "Timed Get Up and Go" (TGUG) test.

To evaluate the effects of acupuncture on analgesic and opioid use.

To evaluate the effects of acupuncture on self-reported AI adherence.

To assess AI adherence via urine AI metabolites.

To evaluate the effects of acupuncture on serum hormones (estradiol, FSH, LH) and inflammatory biomarkers (serum TNFα, IL-6, IL-12, CRP and urine CTX-II).

To evaluate whether polymorphisms in CYP19A1 aromatase gene predict severity of AI-related joint symptoms.

To assess the safety and tolerability of acupuncture in this study population.

Patient Population

Patients must be women with histologically confirmed primary invasive carcinoma of the breast (Stage I, II, or III) with no evidence of metastatic disease (M0), or with histologically confirmed DCIS. Patients must have ER and/or PgR positive disease.

If patient has undergone breast cancer surgery, she must have recovered from all side-effects of the surgery. Patients must currently be taking a third-generation aromatase inhibitor (anastrazole, letrozole, or exemestane) for at least the previous 30 days prior to registration, with plans to continue for at least an additional one year. Patients may have switched AIs provided that they have been on a stable dose for at least 30 days. Concurrent trastuzumab (Herceptin) is allowed.

Patients must have had two or fewer acupuncture treatments within the past 12 months for any reason except for joint symptoms. Patients must not have had prior acupuncture treatment for joint symptoms at any time. Patients must not be on narcotics or have received topical analgesics to the study joint or any other analgesics with the exception of NSAIDS and acetaminophen within 14 days prior to registration. Patients must not have received oral corticosteroids, intramuscular corticosteroids, or intra-articular steroids for joint symptoms within 28 days prior to registrations. Patients must not have received or implemented any other medical therapy, alternative therapy, or physical therapy for the treatment of joint pain/stiffness within 28 days prior to registration. Therapeutic massage is allowed. Patients must not have a history of bone fracture or surgery of the afflicted knees and/or hands within six months prior to registration.

Patients must be post-menopausal as defined in the protocol and have a Zubrod performance status of 0-1. Patients must have completed the S1200 Brief Pain Inventory - Short Form within 14 days prior to registration and have a worst pain score of at least 3 that has started or increased since starting AI therapy. Patients must not have a severe bleeding disorder, an allergy to latex, or concurrent medical/arthritic disease that could confound or interfere with evaluation of pain or efficacy. Patients must be willing to submit blood and urine for correlative analyses as specified in the protocol. Patients must be able to complete study questionnaires in English or Spanish.

Stratification/Descriptive Factors

Patients will be randomized using a 2:1:1 ratio to true acupuncture vs. sham acupuncture vs. waitlist control. Patient randomization will be dynamically balanced according to study site at time of registration.

Accrual Goals

A total of 228 patients will be enrolled to achieve 208 eligible patients.

Summary Statement

For the current status of this study, please refer to the Symptom Control and QOL chapter.

S1202 Phase III

A Randomized Placebo-Controlled Phase III Study of Duloxetine for Treatment of Aromatase Inhibitor-Associated Musculoskeletal Symptoms in Women with Early Stage Breast Cancer

---

Study Chairs:
N Henry, A Schott

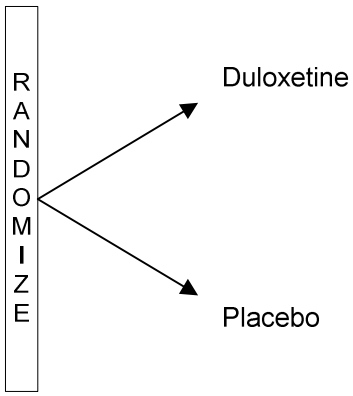
Statisticians:
J Unger, D Lew

Data Coordinator:
R Topacio

Date Activated:
05/15/2013

Date Closed:
10/01/2015

SCHEMA



Objectives

To assess whether daily duloxetine decreases average joint pain in women with aromatase inhibitor-associated musculoskeletal syndrome (AIMSS), as measured at 12 weeks by the modified Brief Pain Inventory Short Form (BPISF).

To assess whether daily duloxetine decreases worst joint pain in women with AIMSS, as measured at 12 weeks by the modified BPI-SF.

To assess whether daily duloxetine decreases pain interference in women with AIMSS, as measured at 12 weeks by the modified BPI-SF.

To investigate whether daily duloxetine improves functioning, pain, and stiffness in the knees/hips according to the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) scale.

To investigate whether daily duloxetine improves function, pain and stiffness in the hands according to the Modified Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands (M-SACRAH).

To investigate whether daily duloxetine improves functional quality of life as measured by the Functional Assessment of Cancer Therapy-Endocrine Scale (FACT-ES).

To investigate whether daily duloxetine improves the proportion of patients reporting changes for the better versus worst as measured by the Global Rating of Change Scale.

To investigate whether daily duloxetine improves/decreases analgesic use.

To investigate whether daily duloxetine improves/increases adherence to, and reduces the discontinuation rate for, aromatase inhibitor (AI) therapy.

To assess whether patients receiving duloxetine as compared to placebo have improved depression as measured by the Patient Health Questionnaire (PHQ-9) at Weeks 6 and 12 (for patients experiencing depression at baseline).

To explore the relationship between inherited variants in genes responsible for duloxetine metabolism and activity (COMT, HTR3A, SLC6A2, SLC6A4, CYP1A2, CYP2D6) and aromatase (CYP19A1) and change in pain with 12 weeks of treatment.

To explore the impact of treatment on serum inflammatory cytokine levels with 12 weeks of treatment at baseline and 12 weeks.

To bank blood samples for future correlative analyses.

Patient Population

Patients must be women with histologically confirmed ER and/or PgR positive invasive carcinoma of the breast with no evidence of metastatic disease (M0).

Patients must have completed mastectomy or breast sparing surgery and have recovered from all side-effects of the surgery. Any chemotherapy and/or radiation therapy must be completed at least 28 days prior to registration, and patients must have recovered from all Grade 2 or higher side effects with the exception of alopecia and peripheral neuropathy. Concurrent bisphosphonate and trastuzumab therapies are allowed. Patients must currently be taking one of the following aromatase inhibitor (AI) doses for at least 21 days with plans to continue for at least an additional 180 days after registration: anastrozole 1 mg daily, letrozole 2.5 mg daily, or exemestane 25 mg daily. Patients may have received any number of prior AI therapies, but the first AI therapy must have started no more than 36 months prior to registration. Patients must not have previously taken the serotonin norepinephrine reuptake inhibitors (SNRI) duloxetine or milnacipran. Patients must not require selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants during study participation. Prior venlafaxine is allowed as long as it was not taken for treatment of pain (e.g., prior treatment for hot flashes is permitted). Patients must not take MAO-inhibitors for 14 days before registration or any time during study treatment. Concommitant therapy with heparin and warfarin is also not permitted at registration or while on protocol treatment. Aspirin is permitted.

Patients must be post-menopausal as defined in the protocol and have adequate renal and hepatic function and a Zubrod performance status of 0-2. Patients must have AI associated musculoskeletal symptoms that began or increased after starting AI therapy. New musculoskeletal pain must not be due specifically to fracture or traumatic injury. Patients must have completed the S1202 Brief Pain Inventory - Short Form within 7 days prior to registration and have an average pain score of at least 4 (BPI-SF item #4). Patients must have no known allergy or hypersensitivity to duloxetine or any of the inactive ingredients in the matching placebo. Patients must not have any contraindicated concurrent illnesses or be taking any contraindicated medications listed on the duloxetine package insert including anticoagulation medicine. Patients must not have concurrent medical/arthritic disease that could confound or interfere with evaluation of pain or efficacy. Patients who are receiving treatment with narcotics, tramadol, gabapentin, and/or pregabalin must have been taking a stable dose for at least 30 days prior to registration. Patients must be willing to submit blood samples for correlative analyses as specified in the protocol. Patients must be able to complete study questionnaires in English or Spanish.

Stratification/Descriptive Factors

Patient randomization will be dynamically balanced according to the following stratification factors: (1) baseline pain score (BPI-SF item #4): 4-6 vs 7-10; and (2) prior taxane use: yes vs no.

Accrual Goals

A total of 294 patients will be enrolled to achieve 270 eligible patients.

Summary Statement

For the current status of this study, please refer to the Symptom Control and QOL chapter.

S1204 Surveillance

A Sero-Epidemiologic Survey and Cost-Effectiveness Study of Screening for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Among Newly Diagnosed Cancer Patients

Study Chairs:
S Ramsey, R Loomba, R Chugh, D Hershman, J Hwang

Date Activated:
08/29/2013

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Objectives

Among newly diagnosed cancer patients presenting to SWOG-affiliated community and academic oncology clinics, estimate the prevalence of human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) infection.

Evaluate known sociodemographic, clinical, and behavioral factors that are significantly associated with previously undiagnosed HIV, HBV, and/or HCV infection in a population of people with newly diagnosed cancer.

Among patients who are identified as having HIV, HBV, and/or HCV, evaluate the timing and type of treatments received, both for the viral infections and the cancers.

Evaluate type and rate of cancer treatment-related adverse events in patients with HIV, HBV, and/or HCV infection.

Determine the cost-effectiveness of (1) routine, universal screening and (2) risk factor-directed screening of newly diagnosed cancer patients for HIV, HBV and/or HCV versus current care.

Create a biorepository of stored serum for future translational medicine studies that may include identifying genomic and viral factors that increase the risk of serious adverse effects among participants infected with HIV, HBV, and/or HCV being treated for invasive cancers.

Patient Population

Patients must be presenting for evaluation or treatment for the first diagnosis of a new solid or hematologic cancer malignancy. Confirmed diagnosis date must be within 120 days prior to first clinic visit as a newly diagnosed cancer patient at the registering clinic. Patients presenting for "second opinions" of confirmed malignancies are eligible, including those who have started cancer treatment at other facilities. Patients must be registered within 90 days after their first clinic visit. Patients must not have been diagnosed with a malignancy other than the current malignancy within the past five years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer. Patients must have no evidence of disease for a prior malignancy for at least five years prior to randomization except as noted above.

Patients must be 18 years of age or older. Patients must have had their blood drawn for viral status testing for HIV, HBV and HCV or provide acceptable viral status documentation prior to registration, as defined in the protocol. Note that patients must have blood drawn for testing prior to registration for any of the three viruses not covered by the documentation. Patients are allowed to participate in other clinical trials.

Accrual Goals

A total of 3,061 patients will be accrued to achieve 3,000 eligible patients.

Summary Statement

For the current status of this study, please refer to the Cancer Care Delivery chapter.

S1207 Phase III

Coordinating Group: SWOG and NRG

Phase III Randomized, Placebo-Controlled Clinical Trial Evaluating the Use of Adjuvant Endocrine Therapy +/- One Year of Everolimus in Patients with High-Risk, Hormone Receptor-Positive and Her2/neu Negative Breast Cancer

e3 Breast Cancer Study - evaluating everolimus with endocrine therapy

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Participants:
SWOG, CTSU, NRG

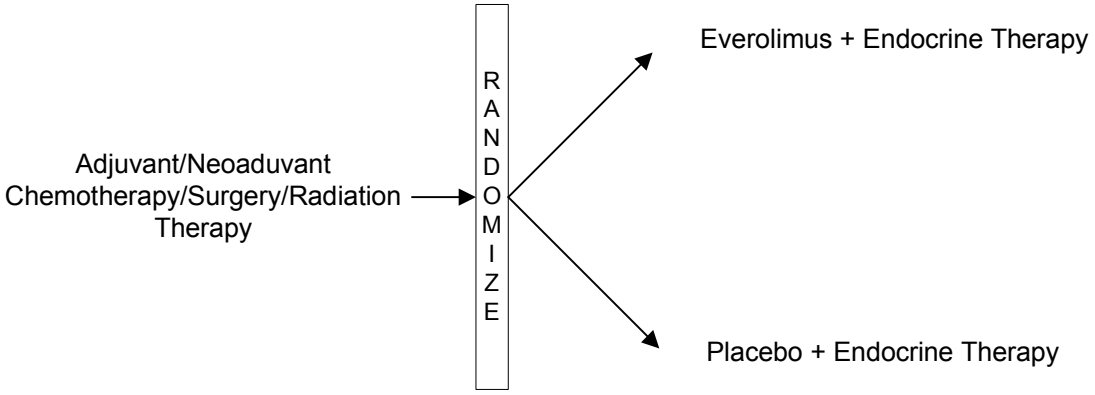
Date Activated:
09/03/2013

Study Chairs:
M Chavez MacGregor, P Ganz (NRG), L Pusztai, P Rastogi (NRG)

Statisticians:
W Barlow, J Miao, D Lew

Data Coordinator:
I Syquia

SCHEMA



Objectives

To compare whether the addition of one year of everolimus (10 mg daily) to standard adjuvant endocrine therapy improves invasive disease-free survival (IDFS) in patients with high-risk, hormone-receptor (HR) positive and HER2-negative breast cancer.

To compare whether the addition of one year of everolimus to standard adjuvant endocrine therapy improves overall survival (OS) and distant recurrence-free survival (DRFS) in this patient population.

To evaluate the safety, toxicities, and tolerability of one year of everolimus in combination with standard adjuvant endocrine therapy and compare it with

standard adjuvant endocrine therapy plus placebo in this patient population.

To determine whether the benefit of one year of everolimus use in addition to standard adjuvant endocrine therapy varies by recurrence score (RS), nodal status, or other commonly used prognostic factors.

To evaluate adherence to 1-year treatment of everolimus in comparison to placebo in addition to standard adjuvant endocrine therapy in this patient population.

To collect specimens in order to evaluate biomarkers of therapeutic efficacy.

Patient Population

Patients must have histologically confirmed invasive breast carcinoma with positive ER and/or PgR status and negative HER-2, for whom standard adjuvant endocrine therapy is planned. Patients must not have metastatic breast cancer. Patients with multifocal, multicentric, synchronous bilateral, and primary inflammatory breast cancers are allowed. Patients must be high risk as defined in the protocol, based on Recurrence Score and grade, number of positive nodes, and prior therapy. Patients with micrometastases as the only nodal involvement (pN1mi) are eligible, and will be categorized as node-negative.

Patients must have completed either breast-conserving surgery or total mastectomy with negative margins and appropriate axillary staging. Patients must have completed appropriate radiation therapy as described in the protocol. Patients must have completed standard neoadjuvant or adjuvant taxane and/or anthracycline based chemotherapy prior to randomization. Patients may have started endocrine therapy at any time after the diagnosis of the current breast cancer. Patients must not be receiving or planning to receive trastuzumab. Concurrent bisphosphonate therapy is allowed. Patients must not have prior exposure to mTOR inhibitors.

Patients must have a Zubrod performance status of 0-2 and adequate hematologic, hepatic, renal, and cardiac function. Patients must not have received immunization with an attenuated live vaccine within seven days prior to registration. Patients must be able to take oral medications. Patients at NCORP institutions must be offered the opportunity to participate in the Behavioral and Health Outcomes (BAHO) substudy.

Stratification/Descriptive Factors

Patient randomization will be stratified by risk level as described in the protocol based on Recurrence Score and grade, number of positive nodes, and prior therapy.

Accrual Goals

The accrual goal is 1,900 patients. Interim analyses are planned for after approximately 40%, 60%, and 80% of the events in the control arm have been observed.

Summary Statement

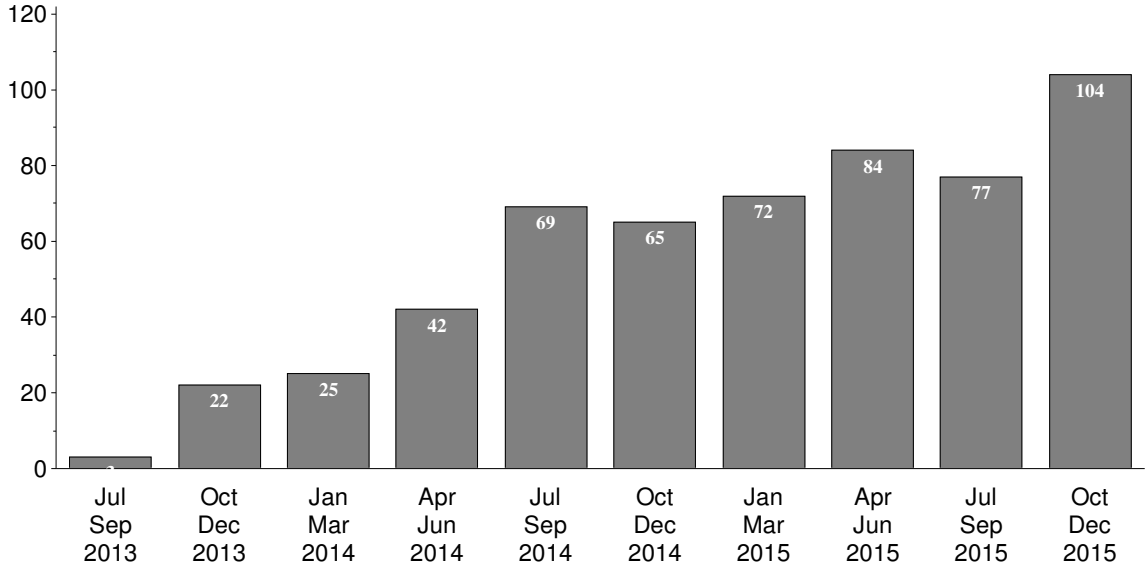
This study was activated on September 3, 2013. As of December 31, 2015, there had been 563 patients randomized. Thirty-four patients are currently ineligible, the most common reasons being registration on study too soon after completion of radiation therapy or too late after completion of chemotherapy. Major deviations are coded for 14 patients who received no protocol treatment; these 14 patients are not evaluable for adverse events, along with an additional patient who discontinued protocol treatment without being assessed for adverse events. Eight patients were removed from protocol treatment for other non-protocol specified reasons. These including patients never received treatment (3), treatment delay that exceeded protocol guidelines (3), non-compliance (1), physician discretion (1).

There have been seven patients with Grade 4 toxicities reported among 490 patients evaluated for adverse events, including three with Grade 4 hypertriglyceridemia. Eighy-three patients experienced Grade 3 adverse events as maximum degree, including 18 cases of oral mucositis. The Grade 3 "Investigations-Other, specify" was decreased neutrophils, the Grade 3 "Eye disorders - Other, specify" was herpes simplex keratoconjunctivitis, the Grade 3 "GI disorders - Other, specify" was enteritis requiring two hospitalizations, and the four cases of Grade 3 "Infections/infestations-Other" were abscess, cellulitis, continued soft tissue infection, and pending review. Toxicities are reviewed by treatment group by the Data Safety and Monitoring Committee, the SWOG Breast Committee leadership, and the Study Chair.

Revision #4 distributed October 15, 2015, reduced the accrual goal from 3,800 to 1,900 patients and expanded eligibility to allow registration up to 42 weeks following chemotherapy and micrometastases (pN1mi) as the only nodal involvement (categorized as node negative). Additionally, patients who have

already started endocine therapy are now eligible for the BAHO substudy.

Initial Registrations By 3 Month Intervals



Time of Registration

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	112	Cincinnati MC, U of	5
ECOG-ACRIN	99	Good Samaritan Hosp/Oregon Hlth Sci Univ	5
NRG	84	H Lee Moffitt CC	5
MD Anderson CC	19	Michigan CRC NCORP	5
Wichita NCORP	12	MUSC MU-NCORP	5
Michigan, U of	11	Oklahoma, Univ of	5
Yale University	11	CORA NCORP	4
City of Hope Med Ctr	9	Northwestern Univ	4
PCRC NCORP	9	Rochester, Univ of	4
Gulf South MU-NCORP	8	San Antonio, U of TX	4
Kansas, U of	8	Thompson Ca Surv Ctr/San Antonio, U of TX	4
Cedars-Sinai Med Ctr	7	Wayne State Univ	4
Heartland NCORP	7	Beaumont NCORP	3
New Mexico MU-NCORP	7	Colorado, U of	3
Southeast COR NCORP	7	Columbia MU-NCORP	3
Cleveland Clinic OH	6	CRC West MI NCORP	3
Columbus NCORP	6	Davis, U of CA	3
Fred Hutchinson CRC	6	Hawaii MU-NCORP	3
Kaiser Perm NCORP	6	So Calif, U of	3
Ozarks NCORP	6	All Other Institutions	37
Sutter Cancer RC	6	**Total (69 Institutions)**	**563**
Arizona MC, U of	5		

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2015; Data as of February 24, 2016

	Total
NUMBER REGISTERED	563
INELIGIBLE	34
ELIGIBLE	529
Analyzable, Pend. Elig.	15
ADVERSE EVENT ASSESSMENT	
Evaluable	490
Not Evaluable	15
Too Early	24

Patient Characteristics

Registrations ending December 31, 2015; Data as of February 24, 2016

	Total (n=529)	
AGE		
Median	54.6	
Minimum	26.5	
Maximum	79.3	
SEX		
Males	2	0%
Females	527	100%
HISPANIC		
Yes	36	7%
No	479	91%
Unknown	14	3%
RACE		
White	455	86%
Black	32	6%
Asian	20	4%
Pacific Islander	1	0%
Native American	3	1%
Multi-Racial	2	0%
Unknown	16	3%
RISK GROUP		
Node-negative and RS > 25 treated with adjuvant chemotherapy	48	9%
1-3 positive lymph nodes and RS > 25 or Grade III disease treated with adjuvant therapy	53	10%
≥ 4 positive lymph nodes (any RS value) treated with adjuvant chemotherapy	300	57%
≥1 positive lymph node (any RS value) with neoadjuvant chemotherapy	128	24%

Treatment Summary

Registrations ending December 31, 2015; Data as of February 24, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	254
NUMBER OFF PROTOCOL TREATMENT	275
REASON OFF TREATMENT	
Treatment completed as planned	106
Adverse Event or side effects	84
Refusal unrelated to adverse event	53
Progression/relapse	12
Death	0
Other - not protocol specified	8
Reason under review	12
MAJOR PROTOCOL DEVIATIONS	14

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Adverse Events with No Entries for Grades 3 to 5 or Unknown Have Been Suppressed

Registrations ending December 31, 2015; Data as of February 24, 2016

	Total (n=490) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	455	30	3	2	0	0
AST increased	447	39	2	2	0	0
Abdominal pain	478	8	2	2	0	0
Anemia	439	36	13	2	0	0
Appendicitis	488	0	0	2	0	0
Arthralgia	425	43	21	1	0	0
Breast infection	487	0	1	2	0	0
Cardiac arrest	489	0	0	0	1	0
Cholesterol high	377	95	17	1	0	0
Diarrhea	427	50	10	3	0	0
Dyspnea	465	18	6	1	0	0
Eye disorders - Other, specify	482	6	1	1	0	0
Fatigue	337	107	41	5	0	0
GI disorders-Other, specify	467	19	3	1	0	0
Headache	439	40	10	1	0	0
Hot flashes	444	36	9	1	0	0
Hyperglycemia	428	46	9	7	0	0
Hyperhidrosis	487	2	0	1	0	0
Hypertension	472	10	6	2	0	0
Hypertriglyceridemia	411	54	15	7	3	0
Hypokalemia	478	7	3	2	0	0
Hypoxia	489	0	0	1	0	0
Infections/infestations-Other	483	2	1	4	0	0
Insomnia	456	28	5	1	0	0
Lipase increased	489	0	0	0	1	0
Lung infection	485	0	3	2	0	0
Lymphedema	483	3	3	1	0	0
Lymphocyte count decreased	434	23	25	7	1	0
Mucositis oral	319	91	62	18	0	0
Nausea	420	58	10	2	0	0
Neuralgia	488	1	0	1	0	0
Neutrophil count decreased	446	19	17	8	0	0
Peripheral sensory neuropathy	474	12	2	2	0	0

	Total (n=490) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Platelet count decreased	454	30	5	1	0	0
Pneumonitis	480	1	7	2	0	0
Productive cough	488	0	1	1	0	0
Rash acneiform	464	21	4	1	0	0
Rash pustular	489	0	0	1	0	0
Respiratory failure	489	0	0	0	1	0
Sepsis	489	0	0	0	1	0
Skin infection	479	0	7	4	0	0
Skin ulceration	489	0	0	1	0	0
Thromboembolic event	487	0	1	2	0	0
Urinary tract infection	487	0	2	1	0	0
Vascular access complication	489	0	0	1	0	0
Weight loss	471	15	3	1	0	0
White blood cell decreased	410	46	31	3	0	0
Wound complication	487	1	1	1	0	0
Wound dehiscence	489	0	0	1	0	0
Wound infection	487	0	2	1	0	0
MAX. GRADE ANY ADVERSE EVENT	102	119	179	83	7	0

S1415CD Pragmatic Trial

Pragmatic Trial to Evaluate a Guideline-Based Colony Stimulating Factor Standing Order Intervention and to Determine the Effectiveness of Colony Stimulating Factor Use as Prophylaxis for Patients Receiving Chemotherapy with Intermediate Risk for Febrile Neutropenia – Pragmatic Trial Assessing CSF Prescribing Effectiveness and Risk (TrACER)

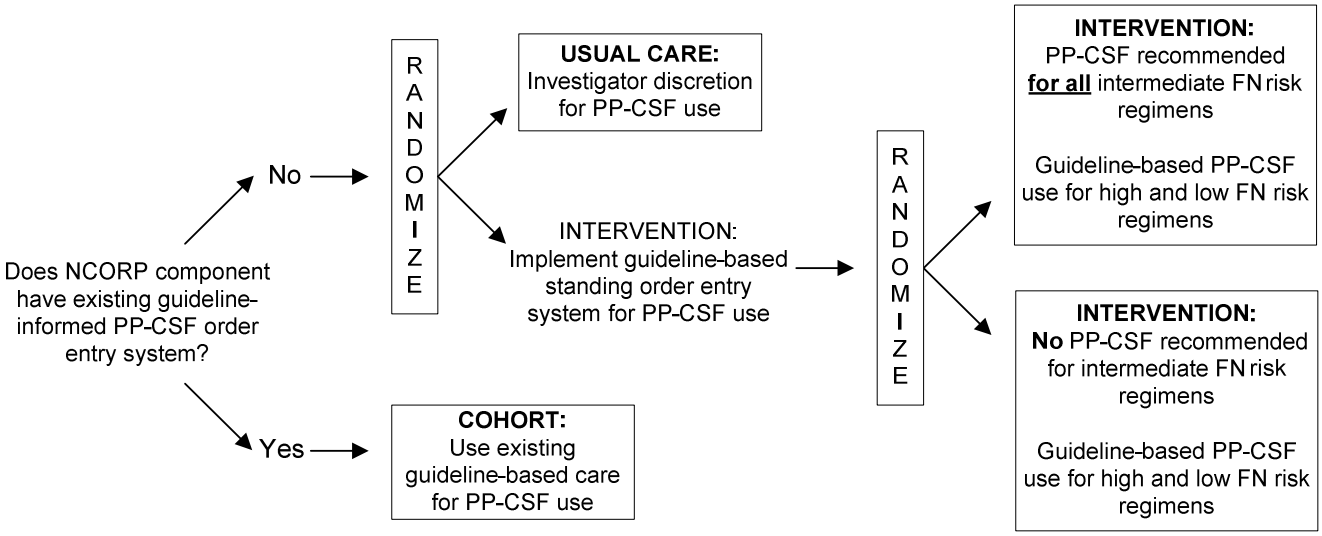
Study Chairs:
S Ramsey, D Hershman, G Lyman, S Sullivan

Statisticians:
A Bansal, W Barlow, K Arnold

Project Manager:
K Watabayashi

Data Coordinator:
M Yee

SCHEMA



Randomization is at the NCORP component level. All patients at participating components will be subject to the PP-CSF use care as determined by component assignment (Usual Care, Intervention, or Cohort). Only consented patients registered to the study will participate in the data collection.

Objectives

To compare the use of primary prophylactic colony stimulating factor (PP-CSF) according to recommended clinical practice guidelines among patients registered at Intervention components versus Usual Care components.

To compare the rate of febrile neutropenia (FN) among patients registered at Intervention components versus Usual Care components.

To compare the rate of FN among intermediate risk patients registered at Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare the rate of FN among low-risk patients registered at Intervention components versus Usual Care components.

To compare the FN-related health-related quality of life (HRQOL) among low-risk patients registered at Intervention components versus Usual Care components.

To compare patient adherence to PP-CSF prescribing among patients registered at Intervention components versus Usual Care components.

To compare patient knowledge of the indications for, efficacy of, and side effects associated with PP-CSF between the initiation and conclusion of the first cycle of myelosuppressive systemic therapy among patients registered at Intervention components versus Usual Care components.

To compare the proportion of patients completing the initial systemic therapy regimen at planned duration and at planned dose intensity among patients registered at Intervention components versus Usual Care components.

To compare antibiotic use both as prophylaxis and as treatment for FN among patients registered at Intervention components versus Usual Care components.

To compare the rate of FN-related emergency department visits and hospitalizations among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare the FN-related health-related quality of life (HRQOL) among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare overall survival among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To characterize and descriptively report the differences among Cohort components and the Intervention and Usual Care components, according to the endpoints outlined in Section 10.0.

Patient Population

Patients must have a current diagnosis of breast cancer, non-small cell lung cancer, or colorectal cancer. Cancer may be metastatic or non-metastatic.

Patients must be planning to receive one of the study-allowed regimens as their initial treatment for their current diagnosis. Patients must be registered prior to their first cycle of systemic therapy (chemotherapy, immunotherapy, biologic therapy, or combination regimens). Prior systemic therapy must have been completed at least 180 days prior to registration. Patients must not have any known contraindication to CSFs, including prior hypersensitivity to Escherichia coli-derived proteins, filgrastim, pegfilgrastim, or tbo-filgrastim.

Patients must be able to understand and provide information for the patient-completed study forms in either English or Spanish. Patients may have had a prior malignancy. Patients must not be participating or plan to participate in other clinical trials that involve investigational systemic cancer treatments or investigational uses of CSF.

Stratification/Descriptive Factors

NCORP components eligible for randomization will be randomly assigned to Usual Care or Intervention with stratification by component size (number of patients at that component) and type of NCORP component (minority/underserved vs not).

Accrual Goals

A total of 3,960 patients will be accrued to achieve 3,600 eligible patients. The Intervention components will accrue 2,376 patients, the Usual Care components will accrue 792 patients and the Cohort components will accrue 792 patients.

One interim analysis will be conducted when 360 patients in the intermediate risk group at Intervention components have complete outcome information. A second interim analysis will be conducted when 650 patients in the intermediate risk group at Intervention components have complete outcome information.

Summary Statement

For the current status of this study, please refer to the Cancer Care Delivery chapter.

S1416 Phase II

Phase II Randomized Placebo-Controlled Trial of Cisplatin with or without ABT-888 (Veliparib) in Metastatic Triple-Negative Breast Cancer and/or BRCA Mutation-Associated Breast Cancer

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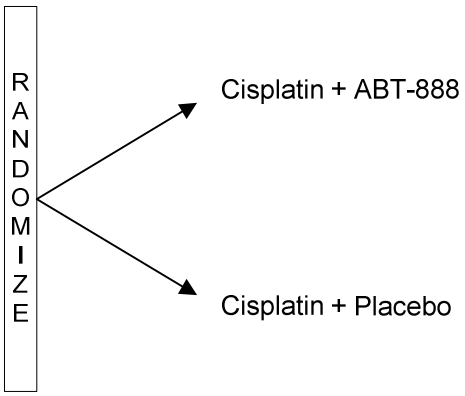
Study Chairs:
E Rodler, P Sharma

Statisticians:
W Barlow, D Lew, J Miao

Data Coordinator:
S O'Bryan

SCHEMA



Objectives

To compare the efficacy of cisplatin with or without ABT-888 (veliparib) on progression-free survival (PFS) in each of the following groups:

1. Patients with germline *BRCA* (*gBRCA*) mutation-associated breast cancer
2. Patients with germline *BRCA* wild-type breast cancer who have evidence of BRCAness phenotype
3. Patients with germline *BRCA* wild-type breast cancer who do not have evidence of BRCAness phenotype.

Brain Metastases Cohort: To compare the efficacy of cisplatin with or without ABT-888 on PFS in patients with triple negative and/or *gBRCA* mutation-associated breast cancer and brain metastases.

For patients with *gBRCA* mutation associated breast cancer (group 1 above) or TNBC with (group 2) or without (group 3) BRCAness phenotype, to compare the efficacy of cisplatin with or without ABT-888 on overall survival (OS), response rate (RR), and clinical benefit rate.

To compare the differential benefit of ABT-888 across the three groups using both PFS and OS as outcomes.

For patients in the brain metastases cohort, to compare the efficacy of cisplatin with or without ABT-888 on OS.

For patients in the brain metastases cohort, to compare the efficacy of cisplatin with or without ABT-888 on intracranial and extracranial response rates (intracranial by RANO and extracranial by RECIST 1.1).

To compare toxicities of ABT-888 to placebo in each of the four groups separately.

To evaluate the impact of Homologous Recombination Deficiency score (independent of other BRCAness markers) on RR and PFS in patients treated with chemotherapy versus chemotherapy plus ABT-888.

To evaluate the overlap among various markers utilized to define the BRCAness phenotype.

To evaluate the impact of PAM50 basal subtype and BRCAness phenotype on RR and PFS in patients treated with chemotherapy versus chemotherapy plus ABT-888.

To evaluate the impact of BRCA1 mRNA expression (independent of other BRCAness markers) on RR and PFS in patients treated with chemotherapy versus chemotherapy plus ABT-888.

Application of somatic BRCAness phenotype markers on metastatic tumor tissue to identify patients likely to benefit from platinum-based therapy and ABT-888.

To test molecular determinants of response to PARPi therapy in circulating tumor cells: CTC enumeration using the HC-CTC assay; and CTC-Next Generation Sequencing Analysis (CTC-NGS) of single cells captured on the HD-CTC® platform.

Patient Population

Patients must have metastatic breast cancer (Stage IV disease) and be HER2 non-over expressing per 2013 ASCO-CAP HER testing guidelines, and must also meet at least one of the following criteria: histologically confirmed primary and/or metastatic site that is ER- and PR-negative (≤ 1%) and HER2-negative, or previously confirmed deleterious or suspected deleterious *BRCA1* or *BRCA2* germline mutation. Patients must have measurable or non-measurable disease with a chest/abdominal CT scan and bone scan prior to registration. Patients with known brain metastases must either meet additional criteria as outlined in the protocol and enroll as part of the Brain Metastases Cohort, or else have clinically controlled neurologic symptoms, defined as surgical excision and/or radiation therapy followed by 14 days of stable neurologic function prior to registration. Patients with previously treated progressive brain metastases are not eligible for the Standard Cohort, but may be considered for the Brain Metastases Cohort.

Patients must have had no more than one prior cytotoxic regimen for metastatic disease. Patients must not have received any prior chemotherapy, radiation therapy, and hormonal therapy at least 14 days prior to registration; any immunotherapy, biologic, or any investigational drug within 28 days prior to registration; or any bevacizumab within 42 days prior to registration. Patients must not have received prior cisplatin or PARP inhibitors. Prior carboplatin in the adjuvant/neoadjuvant setting is allowed, if completed more than 12 months prior to study entry. Patients may receive bisphosphonates or denosumab concurrently with study treatment provided it has been started at least seven days prior to registration. Patients must have recovered to ≤ Grade 2 following a significant adverse event or toxicity attributed to previous anti-cancer treatment except neurotoxicity which must be ≤ Grade 1.

Patients must be at least 18 years of age and have a Zubrod performance status of 0-2. Patients must have adequate hematologic, hepatic, and renal function. Patients must not have a clinically relevant hearing impairment ≥ Grade 2 or baseline neuropathy that exceeds Grade 1 and must be able to swallow whole capsules. Patients must have a complete history and physical examination within 28 days prior to registration, have adequate tissue available, and agree to have specimens submitted for germline DNA sequencing and other correlative studies.

Stratification/Descriptive Factors

Patient randomization will be stratified by number of prior cytotoxic regimens for metastatic disease: 0 vs 1. Additionally, patients within the brain metastases cohort will be stratified by Modified Breast Graded Prognostic Assessment Index (modified breast-GPA): ≤ 1 vs >1.

Accrual Goals

The accrual goal is 235 patients in the standard cohort and 98 patients in the brain metastases cohort.

A011106 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

Alternate Approaches for Clinical Stage II or III Estrogen Receptor Positive Breast Cancer Neoadjuvant Treatment (ALTERNATE) in Postmenopausal Women: A Phase III Study

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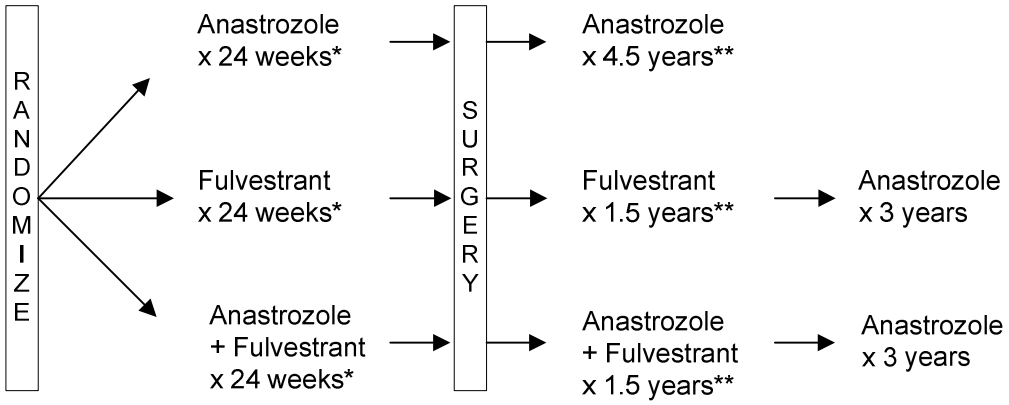
Participants:
Alliance, CTSU

Date Activated:
02/15/2014

Study Chairs:
C Ma (Alliance), A Forero (SWOG)

SCHEMA



*Patients who have an endocrine resistant tumor at week 4 or week 12 will discontinue endocrine protocol therapy, with recommended switch to neoadjuvant chemotherapy.

**Patients with modified PEPI score of 0 will continue assigned endocrine treatment. Those with modified PEPI >0 after completion of surgery will receive adjuvant chemotherapy +/- endocrine therapy of physician's choice.

Objectives

To determine whether fulvestrant administered for 24 weeks as neoadjuvant endocrine treatment decreases the proportion of endocrine resistant tumors (as defined in the protocol) relative to patients treated with anastrozole.

To determine whether fulvestrant in combination with anastrozole, administered for 24 weeks as neoadjuvant endocrine treatment, decreases the proportion of endocrine resistant tumors (as defined in the protocol) relative to patients treated with anastrozole.

To assess whether the 5-year RFS rate among women with a modified preoperative endocrine prognostic index (PEPI) score of 0 following 24 weeks of neoadjuvant anastrozole treatment is at least 95%.

To assess whether the 5-year RFS rate among women with a modified PEPI score of 0 following 24 weeks of neoadjuvant fulvestrant, or fulvestrant in combination with anastrozole, is at least 95%. Note that this objective will only be tested if the selected fulvestrant arm was shown to be superior to anastrozole in objective 1 or 2.

To assess whether the 5-year RFS rate among women with a preoperative endocrine prognostic index (PEPI) score of 0 following 24 weeks of neoadjuvant anastrozole treatment is at least 95%.

To examine the differences in surgical outcome, clinical and radiological response rates, and safety profile between the fulvestrant arm and the anastrozole arm.

To examine the differences in surgical outcome, clinical and radiological response rates, and safety profile between patients randomized to fulvestrant in combination with anastrozole and those randomized to anastrozole.

To examine the rate of pathologic complete response (pCR) of 12 weeks of neoadjuvant paclitaxel in patients with endocrine resistant disease following 4 weeks or 12 weeks of neoadjuvant endocrine therapy (with either fulvestrant or anastrozole or the combination of fulvestrant and anastrozole).

To examine the rate of pathologic complete response (pCR) among those patients with endocrine resistant disease, following 4 weeks or 12 weeks of neoadjuvant endocrine therapy (with either fulvestrant or anastrozole or the combination of fulvestrant and anastrozole), who choose not to receive neoadjuvant paclitaxel, but another standard neoadjuvant taxane and /or anthracycline containing regimen or CMF.

To summarize the frequency of severe (NCI CTCAE grade > 3) adverse events encountered with administration of paclitaxel in the neoadjuvant setting.

To assess RFS for patients with endocrine resistant tumors defined by tumor 1) Ki67 >10% at week 4, 2) Ki67 >10% at week 12 and 3) modified PEPI score of non-zero on neoadjuvant endocrine therapy, with all three groups combined or separated.

To assess whether the degree of tumor Ki67 suppression at week 4 differs between patients randomized to fulvestrant and those randomized to anastrozole.

To assess whether the degree of tumor Ki67 suppression at week 4 differs between patients randomized to fulvestrant in combination with anastrozole and those randomized to anastrozole.

To examine the impact of tumor ER expression level post-neoadjuvant endocrine therapy on RFS in each treatment arm separately.

To examine whether RFS differs with respect to pathologic tumor stage (T1 vs. T2) post-neoadjuvant endocrine therapy in the subgroup of women with a modified PEPI score of 0.

To examine whether rate of endocrine resistant tumors or RFS differs with respect to the degree of week 4 Ki67 suppression.

To examine whether the rate of week 4 Ki67 level > 10%, the rate of endocrine resistant tumors or RFS differs with respect to pre-treatment gene expression profile.

To examine whether gene expression profiles at week 4 can further refine the patient population who have modified PEPI score non-0 or shorter RFS.

To assess the pCR/RCB-1 rate in each of the following cohorts: a) Those who chose to switch to paclitaxel afterfinding their week 4 Ki67 was > 10%. b) Those who chose to switch to paclitaxel after finding their week 12 Ki67 was > 10%. c) Those patients who chose to switch to a standard neoadjuvant taxane and/or anthracycline containing regimen or CMF (rather than paclitaxel) after finding their week 4 Ki67 was > 10%. d) Those patients who chose to switch to a standard neoadjuvant taxane and/or anthracycline containing regimen or CMF (rather than paclitaxel) after finding their week 12 Ki67 was > 10%.

To evaluate Cycle 1, day 2 tumor biopsy following the initiation of paclitaxel to develop early molecular markers of tumor response to paclitaxel.

To evaluate tumor tissue, serum, and plasma specimens collected at baseline, on-therapy, and at surgery for biomarker discovery (through methods such as gene expression profiling, patterns of gains or losses of DNA, tumor whole genome and targeted DNA and RNA sequencing and proteomics) studies

that aim to understand signaling pathways associated with endocrine therapy and taxane therapy sensitivity and resistance.

Patient Population

Patients must be postmenopausal women with pathologic confirmation of invasive breast cancer diagnosed by core needle biopsy, clinical T2-T4c, any N, M0 by AJCC 7th edition clinical staging, with the goal being surgery to complete excision of the tumor in the breast and the lymph nodes. Patients must not have inflammatory breast cancer, contralateral invasive breast cancer and/or DCIS, or multifocal/multi-lesional breast cancer if more than one lesion is invasive cancer in the same breast. Invasive breast cancer must be estrogen receptor positive with an Allred score of 6, 7 or 8 by local institution standard protocol and HER2 negative defined as 0 or 1+ by IHC or with a FISH ratio < 2 if IHC 2+ by local institution standard protocol. If an Allred Score is not reported on the diagnostic pathology report, ER positivity in > 66% cells is eligible. If ER positivity is ≤ 66%, the staining intensity (weak, intermediate, strong) is needed to calculate the Allred Score to determine eligibility.

Patients must have documentation of mammogram and ultrasound (including DCIS and invasive cancer) of the diseased breast performed within 42 days prior to registration, with mammogram of the unaffected contralateral breast within 12 months prior to registration. Patients must not have received treatment for this cancer including surgery, radiation therapy, chemotherapy, biotherapy, hormonal therapy or investigational agent prior to study entry. Patients must not have hormone replacement therapy of any type within one week prior to registration.

Patients must be at least 18 years of age and have an ECOG performance status of 0-2. Patients must have adequate hematologic, renal, and hepatic function and agree to provide the required research biopsies at baseline, week 4 and at surgery for biomarker and correlative studies.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) clinical tumor stage: T2 vs T3 vs T4a-c; (2) clinical lymph node status: positive vs negative; and (3) performance status: 0 or 1 vs 2.

Accrual Goals

A maximum of 2,820 eligible patients will be enrolled on the study.

Summary Statement

CTSU reports that 317 patients had been registered to this study as of December 31, 2015, including 13 SWOG registrations. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg
Arizona MC, U of	6
Baptist MU-NCORP	5
CORA NCORP	1
New Mexico MU-NCORP	1
Total (4 Institutions)	**13**

B55 Phase III SWOG Supported CTSU Study

Coordinating Group: NRG

A Randomised, Double-Blind, Parallel Group, Placebo-Controlled Multi-Centre Phase III Study to Assess the Efficacy and Safety of Olaparib Versus Placebo as Adjuvant Treatment in Patients with Germline *BRCA1/2* Mutations and High Risk HER2 Negative Primary Breast Cancer Who Have Completed Definitive Local Treatment and Neoadjuvant or Adjuvant Chemotherapy

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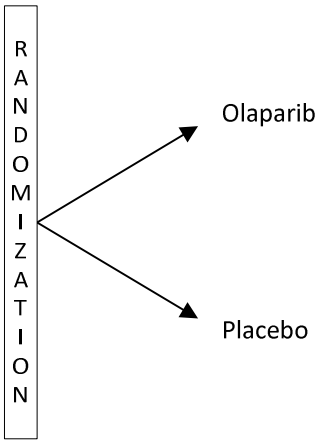
Participants:
NRG, CTSU

Date Activated:
07/03/2014

Study Chairs:
C Geyer (NRG), P Sharma (SWOG)

SCHEMA



Objectives

The primary objective is to assess the effect of adjuvant treatment with olaparib on Invasive Disease Free Survival (IDFS).

To assess the safety and tolerability of adjuvant treatment with olaparib.

To assess the effect of adjuvant treatment with olaparib on overall survival (OS).

To assess the effect of adjuvant treatment with olaparib on Distant Disease Free Survival (DDFS).

To assess the effect of adjuvant treatment with olaparib on the incidence of new primary contralateral breast cancers (invasive and non-invasive), new primary ovarian cancer, new primary fallopian tube cancer and new primary peritoneal cancer.

To assess the effect of olaparib on patient reported outcomes using the FACIT-Fatigue and EORTC QLQ-C30 QOL questionnaires.

To assess efficacy of olaparib in patients identified as having a deleterious or suspected deleterious variant in either of the *BRCA* genes using variants identified with current and future germline *BRCA* mutation assays (gene sequencing and large rearrangement analysis).

To determine the exposure to olaparib (in plasma) in patients receiving olaparib as adjuvant therapy.

Patient Population

Patients must have histologically confirmed non-metastatic primary invasive adenocarcinoma of the breast that is high risk as described in the protocol, with documented mutation in *BRCA1* or *BRCA2* that is predicted to be deleterious or suspected deleterious.

Patients must have completed adequate breast and axilla surgery with clear margins as defined in the protocol. Patients must have completed at least six cycles of neoadjuvant or adjuvant chemotherapy containing anthracyclines, taxanes, or the combination of both. Prior platinum as potentially curative treatment for prior cancer (e.g. ovarian) or as adjuvant or neoadjuvant treatment for breast cancer is allowed. Patients must not have received systemic chemotherapy within three weeks prior to start of study treatment, adjuvant radiotherapy within two weeks prior to start of study treatment, exposure to an investigational product within 30 days or five half lives (whichever is longer) prior to randomization, or any previous treatment with a PARP inhibitor.

Patients must be at least 18 years of age and have ECOG performance status 0-1 and adequate hematologic, hepatic, cardiac, and renal function. Female patients must be postmenopausal or evidence of non-childbearing status as defined in the protocol. Patients must not have known active Hepatitis B or C, HIV, previous allogeneic bone marrow transplant, or whole blood tranfusions in the 120 days prior to study entry which may interfere with *gBRCA* testing. FFPE tumor sample from the primary tumor is required unless waived by Study Team if tumor is not available.

Stratification/Descriptive Factors

Patients will be stratified at randomization by the following baseline factors: (1) hormone receptor status: ER/PgR positive/HER2 negative vs TNBC; (2) prior therapy: neoadjuvant vs adjuvant; and (3) prior platinum therapy for current breast cancer: yes vs no.

Accrual Goals

Approximately 1,500 patients will be randomized into the study. An interim analysis will be performed once a minimum of 165 IDFS events have been observed from the first 750 patients recruited, estimated to be approximately 4.5 years after the first patient is randomized.

Summary Statement

CTSU reports that 37 patients had been registered to this study as of December 31, 2015, including 5 from SWOG institutions.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg
Wayne State Univ	2
Cedars-Sinai Med Ctr	1
Intermountain MC/Northwest NCORP	1
Michigan, U of	1
Total (4 Institutions)	**5**

E1Z11 SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Cohort Study to Evaluate Genetic Predictors of Aromatase Inhibitor Musculoskeletal Symptoms (AIMSS)

Participants:
ECOG-ACRIN, CTSU

Date Activated:
05/31/2013

Study Chairs:
V Stearns (ECOG-ACRIN), N Henry (SWOG)

Objectives

To validate previously identified associations between 10 specific single nucleotide polymorphisms (SNPs) and discontinuation of treatment with aromatase inhibitors (AIs) due to the development of musculoskeletal symptoms (MSS) among women with breast cancer.

To determine whether other SNPs in CYP, UGT, Vitamin D, serotonin and other receptors are associated with discontinuation of treatment due to the development of severe AIMSS.

To determine whether other SNPs in CYP, UGT, Vitamin D, serotonin and other receptors are associated with the development of other potential complications of AI therapy.

To develop a gene signature that can identify patients at risk for developing severe anastrozole-related AIMSS and other potential complications of AI therapy.

To determine the epidemiology and predictors of severe AIMSS and of AI discontinuation.

To describe patient reported outcomes for minority patients with breast cancer treated with AIs.

To assess the utility of the PROMIS system to collect patient reported outcomes in a cooperative group study, and validate the PROMIS Physical Function 20a form in patients with AIMSS.

To develop a model that incorporates patient ratings of treatment burden, fear of recurrence and adherence behaviors to describe patient decisions to continue or discontinue anastrozole.

To collect serum samples for future testing for biomarkers of AIMSS.

Patient Population

Patients must be female and post-menopausal as defined in the protocol, with estrogen and/or progesterone receptor positive histologically confirmed Stage I-III adenocarcinoma of the breast. Patients must not have prior history of ovarian, endometrial, or fallopian tube carcinoma, and/or primary peritoneal carcinomatosis.

Patients must have completed planned local therapy (i.e., definitive surgery and radiation therapy) and adjuvant chemotherapy for breast cancer, with plans to treat with anastrozole for at least 12 months. Concomitant treatment with ongoing trastuzumab (Herceptin®) or other targeted/biologic agents is allowed. Concomitant treatment with any other type of chemotherapy or hormonal therapy is not allowed. Patients must not have received prior AI therapy with exemestane, letrozole, or anastrozole as preoperative/adjuvant therapy or for prevention of breast cancer. Prior tamoxifen is allowed.

Patients must have adequate hepatic, hematologic and renal functioning to be able to be administered anastrozole at the discretion of the treating physician. Patients must have worst pain rated as no worse than 3 out of 10 on the following question (i.e., a pain score of 0, 1, 2, or 3): "In the past week, how much pain have you had on a scale of 0 to 10, where 0 equals no pain and 10 means the worst pain you can imagine." NOTE: This question regarding patient's pain should be completed within one week prior to registration. This pain item may be completed orally prior to consent up to seven days prior to registration. Patients must not be currently taking (or have taken in the past six months) medication for active, chronic conditions, including rheumatoid arthritis, carpal tunnel syndrome, tenosynovitis, systemic lupus erythematosus, gout, fibromyalgia, or severe osteoarthritis involving the hands, wrists, hips, knees, feet or ankles. This includes analgesic medications or medications being taken with the purpose of treating pain or that may have an effect on pain (e.g. anti-depressants for help with pain or neuropathy, corticosteroid shots for arthritis). Patients taking daily low dose aspirin are allowed to participate in this trial.

Patients must be at least 18 years old, have an ECOG performance status of 0-2, and must not have a prior history of deep vein thrombosis (DVT) or pulmonary embolism in the past five years.

Accrual Goals

The accrual goal is 1000 patients, including 200 Asian and 200 African American.

Summary Statement

CTSU reports that as of December 31, 2015, there had been 925 registrations to this study, including 125 SWOG registrations. The Caucasian/Other Races cohort was closed to accrual on February 24, 2014, and the African American cohort was closed to accrual on July 20, 2015. The Asian and Native Hawaiian/Pacific Islanders cohort remains open to accrual. The complete Fall 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
KaiserPermanenteSCAL/Kaiser Perm NCORP	20	Beaumont NCORP	3
Columbia MU-NCORP	16	Columbus NCORP	2
Greenville NCORP	12	CRC West MI NCORP	2
Michigan, U of	11	Dayton NCORP	2
Ozarks NCORP	9	Greenwich Hospital/Yale University	2
Hawaii MU-NCORP	8	Providence Hosp	2
St Joseph's/Candler/Georgia NCORP	8	Cincinnati MC, U of	1
Prov Portland MC/PCRC NCORP	6	Fowler Family Center/Baptist MU-NCORP	1
LSU-Shreveport/Gulf South MU-NCORP	5	Good Samaritan Hosp/CORA NCORP	1
MUSC MU-NCORP	5	NorthBay Med Ctr/Davis, U of CA	1
Montana NCORP	4	Poudre Valley Hosp/Colorado, U of	1
Baptist Health/Cincinnati MC, U of	3	**Total (23 Institutions)**	**125**

E2112 SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Randomized Phase III Trial of Endocrine Therapy plus Entinostat/Placebo in Patients with Hormone Receptor-Positive Advanced Breast Cancer

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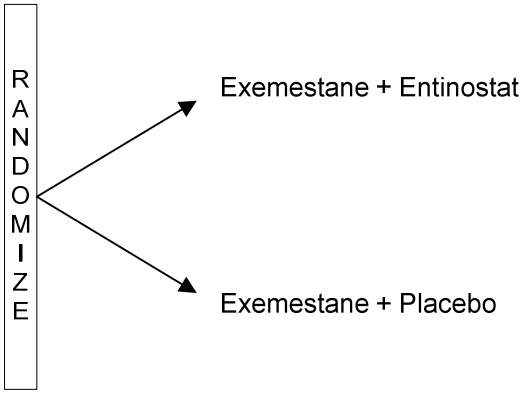
Participants:
ECOG-ACRIN, CTSU

Date Activated:
03/29/2104

Study Chairs:
R Connolly (ECOG-ACRIN), M Royce (SWOG)

SCHEMA



Objectives

To evaluate whether the addition of entinostat to endocrine therapy (exemestane) improves progression-free survival (PFS) and/or overall survival (OS) in patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer who have previously progressed on a non-steroidal aromatase inhibitor (AI).

To evaluate the safety and tolerability of entinostat in combination with exemestane, and to compare the safety profile to that of endocrine therapy with placebo.

To evaluate the objective response rate of exemestane in combination with entinostat or placebo.

To evaluate whether the efficacy of exemestane with entinostat varies with changes in acetylation status in peripheral blood mononuclear cells (PBMCs).

To evaluate the time to treatment deterioration (as defined by decrease in HRQL, progression, death) of exemestane + entinostat versus exemestane + placebo arms.

To evaluate the differences in overall health-related quality of life (HRQL) between the exemestane + entinostat versus exemestane + placebo arms.

To evaluate the difference with respect to specific symptoms that are associated with entinostat, i.e., fatigue, nausea, anorexia and diarrhea, between the exemestane + entinostat versus exemestane + placebo arms.

To measure adherence to protocol therapy.

To collect archival tumor samples and germline DNA to explore other potential biomarkers of therapeutic efficacy.

To collect patient ratings of AEs using select PRO-CTCAE items to evaluate the psychometric properties of PRO-CTCAE items and explore the incorporation of PRO-CTCAE items into a phase III double-blind placebo-controlled trial.

Patient Population

Patients must have ER and/or PR positive histologically confirmed adenocarcinoma of the breast which is HER2 negative as defined in the protocol. Patients must have measurable or non-measurable Stage II/locally advanced or metastatic disease where local therapy with curative intent is not possible. Patients must not have known CNS metastasis, history of CNS metastases, or leptomeningeal disease. Patients must have had disease progression any time after non-steroidal AI use in the advanced disease setting, or relapse while on or within 12 months of end of adjuvant non-steroidal AI therapy with no prior endocrine therapy for advanced disease.

Patients may have received on prior chemotherapy regimen for metastatic disease provided treatment was completed at least three weeks prior to randomization. Treatment with any prior endocrine therapy must be completed at least two weeks prior to randomization, with the exception of exemestane, which is allowed in the advanced disease setting for up to four weeks immediately prior to study enrollment. Prior adjuvant exemestane is allowed if the disease free interval is greater than 12 months from the discontinuation of exemestane. Prior radiotherapy, everolimus therapy, prior palbociclib or other CDK inhibitor, and prior fulvestrant are allowed and must have been completed at least two weeks prior to randomization. Patients must not be receiving valproic acid or have previously received any HDAC inhibitor. Patients may be treated with bone modifying agents such as bisphosphonates or denosumab.

Patients must have adequate hematologic, hepatic, and renal function and an ECOG performance status of 0-1. Patients must be at least 18 years of age, have a life expectancy of at least 12 weeks, and be able to swallow tablets. Pre/perimenopausal women and all men must agree to receive concomitant LHRH agonist.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) setting in which patient developed resistance to prior non steroidal AI treatment: adjuvant vs metastatic; (2) geographic region: USA vs other; (3) visceral disease defined as lung and/or liver involvement: yes vs no; and (4) prior fulvestrant use: yes vs no.

Accrual Goals

The accrual goal is 600 patients.

Summary Statement

CTSU reports that as of December 31, 2015, there had been 170 registrations to this study, including 8 SWOG registrations. The complete Fall 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg
CORA NCORP	2
Kansas, U of	2
Columbia MU-NCORP	1
Good Samaritan Hosp/CORA NCORP	1
Henry Ford Hosp	1
Northwestern Univ	1
Total (6 Institutions)	**8**

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

NCI-MATCH: Molecular Analysis for Therapy Choice

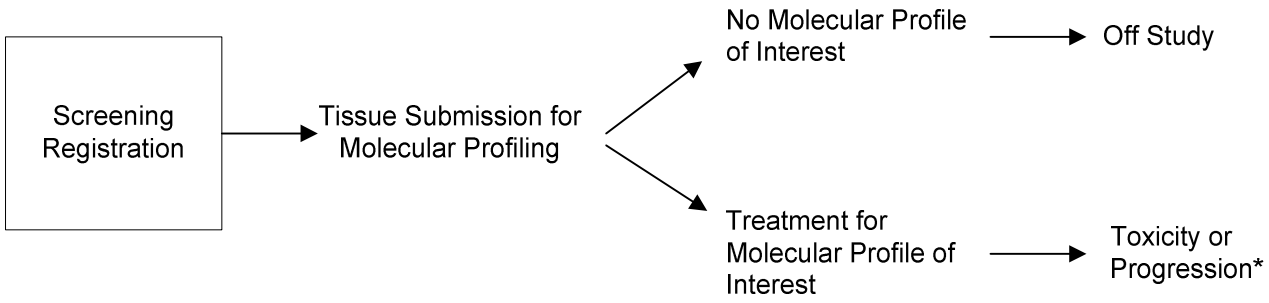
Participants:
ECOG-ACRIN, CTSU

Study Chairs:
K Flaherty (ECOG-ACRIN), A Chen (NCI),
P O'Dwyer (ECOG-ACRIN), B Conley (NCI)

Date Activated:
08/12/2015

Date Closed:
11/11/2015

SCHEMA



*Upon progression or inability to tolerate protocol treatment, patients may be re-screened for additional molecular profiles of interest and corresponding protocol treatment.

Objectives

To evaluate the proportion of patients with objective response (OR) to targeted study agent(s) in patients with advanced refractory cancers/lymphomas.

To evaluate the proportion of patients alive and progression free at six months of treatment with targeted study agent in patients with advanced refractory cancers/lymphomas.

To evaluate the time until death or disease progression.

To identify potential predictive biomarkers beyond the genomic alteration by which treatment is assigned or resistance mechanisms using additional genomic, RNA and protein-based assessment platforms.

Patient Population

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma that has progressed following at least one line of standard systemic therapy and/or for whose disease no standard treatment exists that has been shown to prolong survival. Patients must have measurable disease, have tumor amenable to image guided or direct vision biopsy, and be willing and able to undergo biopsy for molecular profiling.

Patients must not currently be receiving any other investigational agents. Any prior therapy,

radiotherapy (except palliative radiation therapy of 30 Gy or less), or major surgery must have been completed at least four weeks prior to treatment on NCI-MATCH and patient must be recovered from adverse events due to prior therapy (except alopecia and lymphopenia). Palliative radiation therapy must have been completed at least two weeks prior to enrollment on a NCI-MATCH treatment subprotocol, and patient must have recovered from any adverse events of this therapy. Patients with brain metastases or primary brain tumors must have completed treatment , surgery, or radiation therapy at least four weeks prior to initial registration. Patients must not require the use of full dose coumarin-derivative anticoagulants such as warfarin. Low molecular weight heparin is permitted for prophylactic or therapeutic use.

Patients must be at least 18 years of age, have an ECOG performance status of 0 or 1 and must be able to swallow tablets. Patients must have adequate hematologic, hepatic, renal, cardiac and marrow function. HIV-positive patients are eligible provided they meet protocol criteria. Each subprotocol will have additional eligibility criteria that will be outlined in Section 2.0 of the agent-specific subprotocol.

Accrual Goals

The target screening accrual for this study is approximately 3,000 patients, with the goal of accruing 35 patients in each treatment subprotocol. If after screening 500 patients, the total number of patients with actionable tumor alteration (therefore qualifying for treatment) is below 50, results will be presented to the steering committee for consideration of terminating the trial. Within any given subprotocol, if rate of enrollment is such that it is unlikely accrual can be completed in 7.5 years, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. An interim analysis of the assay results will be performed after biopsies from approximately the first 200 patients are processed.

Summary Statement

This study activated on August 12, 2015, with 10 subprotocols included in the activation. Only sites utilizing the CIRB as their IRB of record are able to participate in the trial. The study was temporarily closed to accrual on November 11, 2015, after rapid accrual of 795 patients to the screening step in only three months, including 119 SWOG registrations. This pause in patient enrollment for interim analysis and review is expected to lift by May 2016, when an additional 12 to 14 new subprotocols are expected to be open.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	25	Southeast COR NCORP	4
Henry Ford Hosp	17	KaiserPermanenteSCAL/Kaiser Perm NCORP	3
Wayne State Univ	15	Ozarks NCORP	3
Cleveland Clinic OH	9	S Georgia Med Ctr/Brooke Army Med Ctr	3
Intermountain MC/Northwest NCORP	8	Beaumont NCORP	2
Michigan, U of	6	Cedars-Sinai Med Ctr	1
Sutter Cancer RC	6	Poudre Valley Hosp/Colorado, U of	1
Sutter General Hosp/Sutter Cancer RC	6	Providence Hosp	1
Colorado, U of	5	**Total (18 Institutions)**	**119**
KaiserPermanenteCOL/Kaiser Perm NCORP	4		