BREAST COMMITTEE

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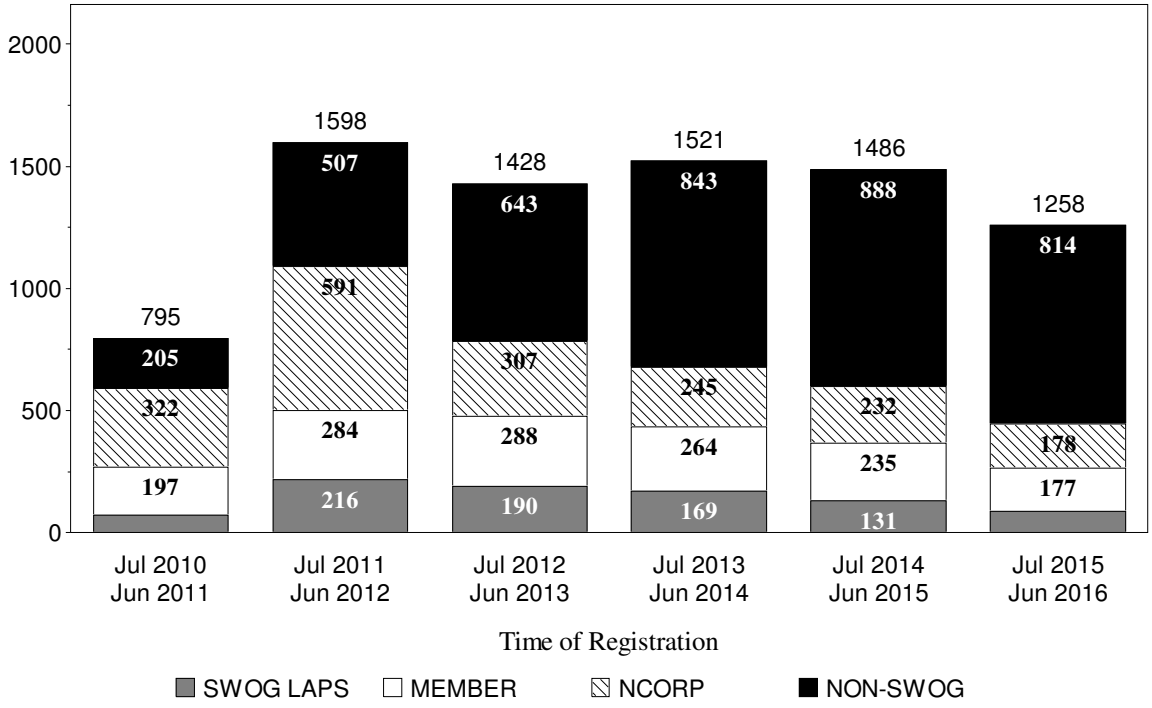
Patient Registrations to Studies

By 12 Month Intervals
BREAST COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

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	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
S1007 Breast, Adj, N1, Endocrine+/-Chemo				
Initial Registration				
Recurrence Score testing	346	764	1,048	8,405
Randomization				
Chemo and Endocrine Therapy	116	239	284	2,209
Endocrine Therapy Alone	108	236	279	2,189
	224	475	563	4,398
S1207 Breast, Adj, Endocrine+/-Everolimus				
Randomization				
Blinded drug + Endocrine	261	181	156	824
S1222 Breast, Fulvestrant +/- Everolimus +/- Anastrozole				
Randomization				
Blinded treatment	0	0	7	37
A011106 Breast, Neoadj, ALTERNATE Study*				
Total Registrations	6	3	6	19
A011202 Breast, Nodal XRT +/- ALND*				
Total Registrations	10	5	10	31
A011203 Breast, Adv, Tam vs Endoxifen*				
Total Registrations	3	3	0	6
B47 Breast, Chemo vs Chemo + Trastuzumab*				
Total Registrations	0	0	5	155
B51 Breast, Regional Nodal XRT*				
Total Registrations	2	4	0	8
B52 Breast, Neoadj TCHP +/- AI*				
Total Registrations	3	2	3	9
B55 Breast, Adj Olaparib for BRCA, TNBC*				
Total Registrations	4	3	2	9
E1Z11 Breast,Genetic Predictors of AIMSS*				
Total Registrations	7	5	23	132
E2108 Breast, Early Local Tx for Intact Primary Tumor*				
Total Registrations	0	1	9	52
E2112 Breast, Adv, Exemestane +/- Entinostat*				
Total Registrations	8	7	1	16
E4112 Breast, MRI + DCIS Score*				
Total Registrations	8	12	0	20

	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
NRGBR003 Breast, Adj, TNBC, AC -> WP +/- Carbo*				
Total Registrations	10	4	0	14
Z11102 Breast Conserv. Surgery for MIBC*				
Total Registrations	4	3	4	13

* 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

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

Study Chairs:
K Kalinsky, J Gralow

Statisticians:
W Barlow, D Lew, J Miao

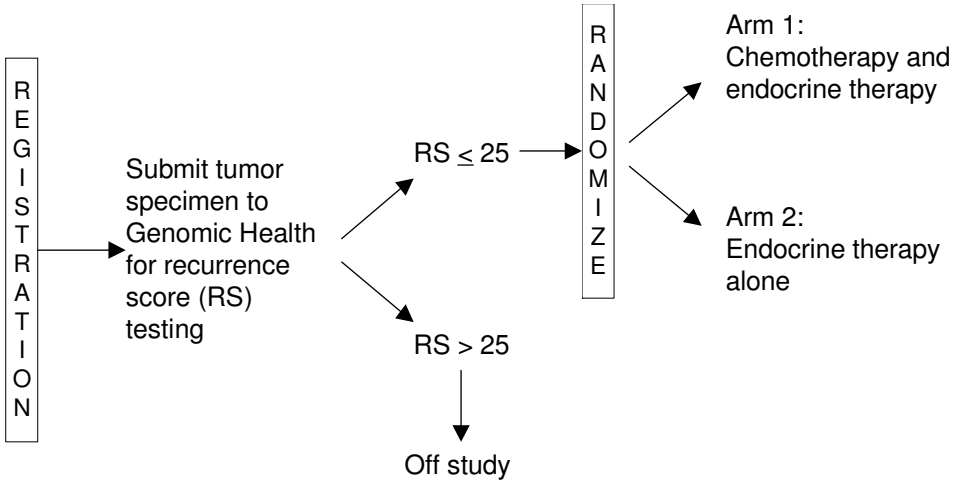
Data Coordinators:
L Kaye, J Scurlock

Date Activated:
01/15/2011

Date Closed*:
10/01/2015

*Open to UNICANCER sites only

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 June 30, 2016, there had been 8,405 registrations to the screening step and 4,398 patients with Oncotype DX® Recurrence Score $\leq$ 25 randomized. Seventy-four 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 441 additional patients (10%) who refused their randomized treatment assignment, did not receive any protocol treatment, or received a non-approved chemotherapy regimen. These 441 patients are not evaluable for adverse events. The most common reason off treatment among the 43 patients coded as "Other - not protocol specified" is secondary cancer.

There have been four treatment-related deaths reported among 3,575 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 105 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.

Registration by Institution

Screening Registration

Registrations ending June 30, 2016

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
CCTG	734	S Georgia Med Ctr/Brooke Army Med Ctr	22
NRG	602	Henry Ford Hosp	20
UNICANCER	542	PCRC NCORP	20
MD Anderson CC	269	CRC West MI NCORP	19
National Cancer Ctr	175	McLaren Cancer Inst/Wayne State Univ	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
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	214
Lahey Hosp & Med Ctr	26	**Total (143 Institutions)**	**8405**

Registration by Institution

Randomization

Registrations ending June 30, 2016

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
UNICANCER	337	Virginia Mason MC/Northwest NCORP	14
CCTG	328	Northwest NCORP	13
NRG	265	Hawaii MU-NCORP	12
MD Anderson CC	147	Heartland NCORP	12
National Cancer Ctr	143	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 (125 Institutions)**	**4398**
Sacred Heart Hosp/Arkansas, U of	17		

Registration, Eligibility, and Evaluability

Randomization

Registrations ending June 30, 2016; Data as of July 14, 2016

	TOTAL	Chemo and Endocrine Therapy	Endocrine Therapy Alone
NUMBER REGISTERED	4398	2209	2189
INELIGIBLE	74	43	31
ELIGIBLE	4324	2166	2158
Analyzable, Pend. Elig.	81	43	38
Not Analyzable	1	1	0
ADVERSE EVENT ASSESSMENT			
Evaluable	3575	1699	1876
Not Evaluable	441	313	128
Too Early	307	153	154

Patient Characteristics

Randomization

Registrations ending June 30, 2016; Data as of July 14, 2016

	Chemo and Endocrine Therapy (n=2165)		Endocrine Therapy Alone (n=2158)	
AGE				
Median	58.0		57.1	
Minimum	28.0		18.4	
Maximum	87.7		86.0	
HISPANIC				
Yes	296	14%	325	15%
No	1664	77%	1647	76%
Unknown	205	9%	186	9%
RACE				
White	1606	74%	1579	73%
Black	127	6%	120	6%
Asian	153	7%	170	8%
Pacific Islander	4	0%	8	0%
Native American	11	1%	13	1%
Multi-Racial	3	0%	4	0%
Unknown	261	12%	264	12%
RECURRENCE SCORE				
0-13	915	42%	911	42%
14-25	1250	58%	1247	58%

MENOPAUSAL STATUS				
Pre-menopausal	705	33%	702	33%
Post-menopausal	1460	67%	1456	67%
NODAL DISSECTION				
Axillary lymph node dissection (with or without sentinel node mapping)	1282	59%	1272	59%
Sentinel node biopsy without axillary lymph node dissection	883	41%	886	41%

Treatment Summary

Registrations ending June 30, 2016; Data as of July 14, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	3966
NUMBER OFF PROTOCOL TREATMENT	357
REASON OFF TREATMENT	
Treatment completed as planned	2
Adverse Event or side effects	7
Refusal unrelated to adverse event	217
Progression/relapse	66
Death	15
Other - not protocol specified	43
Reason under review	7
MAJOR PROTOCOL DEVIATIONS	441

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 June 30, 2016; Data as of July 14, 2016

	Total (n=3575) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
ALT increased	3570	5	0	0
AST increased	3574	1	0	0
Abdominal pain	3568	7	0	0
Acute kidney injury	3574	1	0	0
Alkaline phosphatase increased	3574	1	0	0
Allergic reaction	3569	6	0	0
Anemia	3555	18	2	0
Anorexia	3574	1	0	0
Anxiety	3573	2	0	0
Arthralgia	3517	58	0	0
Atrial fibrillation	3572	3	0	0
Back pain	3573	2	0	0
Blood/lymph disorder-Other	3572	2	1	0
Bone marrow hypocellular	3574	1	0	0
Bone pain	3559	16	0	0
Breast infection	3573	2	0	0
CD4 lymphocytes decreased	3573	2	0	0
Cataract	3574	1	0	0
Catheter related infection	3572	2	1	0
Chest pain - cardiac	3574	1	0	0
Chest wall pain	3574	1	0	0
Colitis	3571	4	0	0
Constipation	3572	3	0	0
Dehydration	3564	11	0	0
Depression	3571	4	0	0
Dermatitis radiation	3569	6	0	0
Device related infection	3571	3	1	0
Diarrhea	3543	32	0	0
Dizziness	3572	3	0	0
Dry skin	3574	1	0	0
Dyspareunia	3573	2	0	0
Dyspepsia	3574	1	0	0
Dyspnea	3573	2	0	0
Ear pain	3573	2	0	0
Edema limbs	3574	1	0	0
Ejection fraction decreased	3574	0	1	0
Erythema multiforme	3574	1	0	0
Erythroderma	3573	2	0	0
Esophagitis	3573	2	0	0
Fatigue	3528	47	0	0
Febrile neutropenia	3503	62	10	0
Fever	3573	1	1	0
Flank pain	3574	1	0	0
Flu like symptoms	3574	1	0	0

	Total (n=3575) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
GGT increased	3574	1	0	0
GI disorders-Other, specify	3574	0	0	1
Gastric hemorrhage	3574	1	0	0
Gastric ulcer	3574	1	0	0
Gastrointestinal pain	3574	1	0	0
Gen disorders/admin site cond	3573	2	0	0
Generalized muscle weakness	3571	4	0	0
Hand-Foot syndrome	3569	6	0	0
Headache	3569	6	0	0
Heart failure	3574	1	0	0
Hematuria	3574	1	0	0
Hot flashes	3558	17	0	0
Hyperglycemia	3559	16	0	0
Hypertension	3564	11	0	0
Hypokalemia	3570	5	0	0
Hyponatremia	3573	2	0	0
Hypotension	3571	4	0	0
INR increased	3574	1	0	0
Infections/infestations-Other	3571	3	1	0
Injection site reaction	3574	1	0	0
Insomnia	3566	9	0	0
Irregular menstruation	3573	2	0	0
Kidney infection	3574	1	0	0
LV systolic dysfunction	3574	1	0	0
Leukocytosis	3571	3	1	0
Lipase increased	3574	1	0	0
Localized edema	3573	2	0	0
Lung infection	3570	4	1	0
Lymphedema	3573	2	0	0
Lymphocyte count decreased	3558	16	1	0
Mucositis oral	3555	20	0	0
Muscle weakness lower limb	3574	1	0	0
Myalgia	3547	28	0	0
Myelitis	3574	1	0	0
Myocardial infarction	3574	1	0	0
Nausea	3559	16	0	0
Neck pain	3573	2	0	0
Neoplasms, all	3574	1	0	0
Nervous sys disorders-Other	3574	1	0	0
Neutrophil count decreased	3447	48	80	0
Pain	3573	2	0	0
Pain in extremity	3572	3	0	0
Paresthesia	3573	2	0	0
Peripheral ischemia	3574	1	0	0
Peripheral motor neuropathy	3571	3	1	0
Peripheral sensory neuropathy	3555	19	1	0
Platelet count decreased	3573	2	0	0
Pleuritic pain	3574	1	0	0
Pneumonitis	3568	7	0	0
Premature menopause	3574	1	0	0
Pruritus	3570	5	0	0

	Total (n=3575) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
ROM decreased	3574	1	0	0
RT recall reaction, derm	3574	1	0	0
Rash acneiform	3574	1	0	0
Rash maculo-papular	3569	6	0	0
Renal/urinary disorders-Other	3574	1	0	0
Resp/thoracic/mediastinal ds	3574	1	0	0
Sepsis	3570	0	4	1
Sinus tachycardia	3574	1	0	0
Skin infection	3568	7	0	0
Skin/subq tissue ds-Other	3572	3	0	0
Stroke	3572	1	1	1
Suicidal ideation	3574	1	0	0
Supraventricular tachycardia	3574	1	0	0
Surg/medical procedures-Oth	3570	5	0	0
Syncope	3572	3	0	0
Thromboembolic event	3566	7	2	0
Tinnitus	3574	1	0	0
Typhlitis	3574	0	0	1
Upper GI hemorrhage	3574	0	1	0
Urinary tract infection	3572	3	0	0
Urticaria	3571	4	0	0
Uterine hemorrhage	3574	1	0	0
Vaginal dryness	3572	3	0	0
Vascular access complication	3574	1	0	0
Vomiting	3560	15	0	0
Watering eyes	3571	4	0	0
Weight gain	3574	1	0	0
Weight loss	3573	2	0	0
White blood cell decreased	3512	43	20	0
Wound dehiscence	3574	1	0	0
MAX. GRADE ANY ADVERSE EVENT	3074	392	105	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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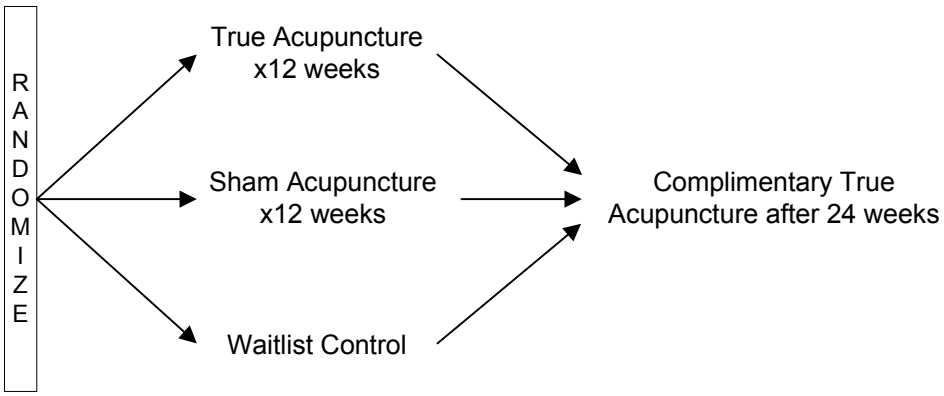
Study Chairs:
D Hershman, K Crew

Date Activated:
03/27/2012

Statisticians:
J Unger, D Lew

Data Coordinator:
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

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Study Chairs:
N Henry, A Schott

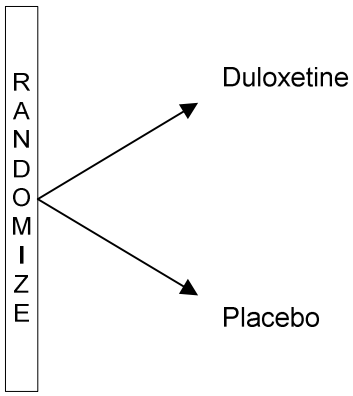
Statisticians:
J Unger, D Lew, A Moseley

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 (BPI-SF).

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.

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, D Hershman

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Date Activated:
08/29/2013

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.

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, NRG, CTSU (Supported by Alliance)

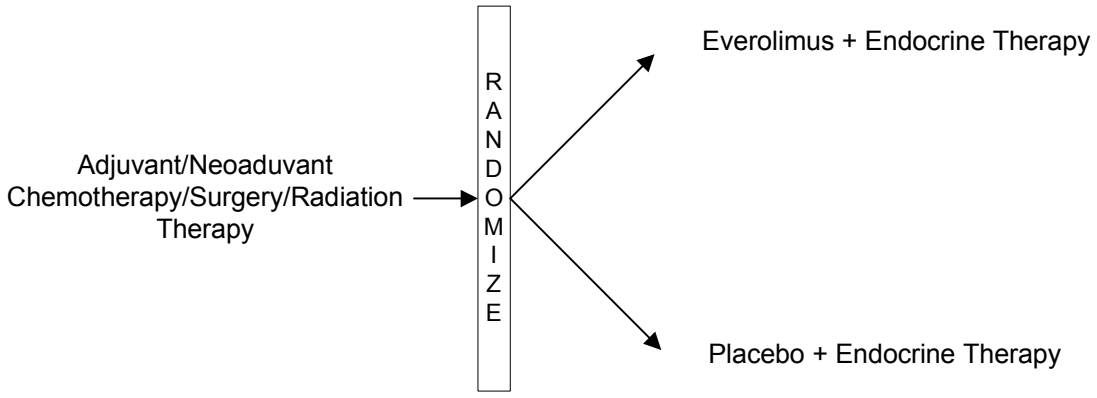
Date Activated:
09/03/2013

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

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.

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

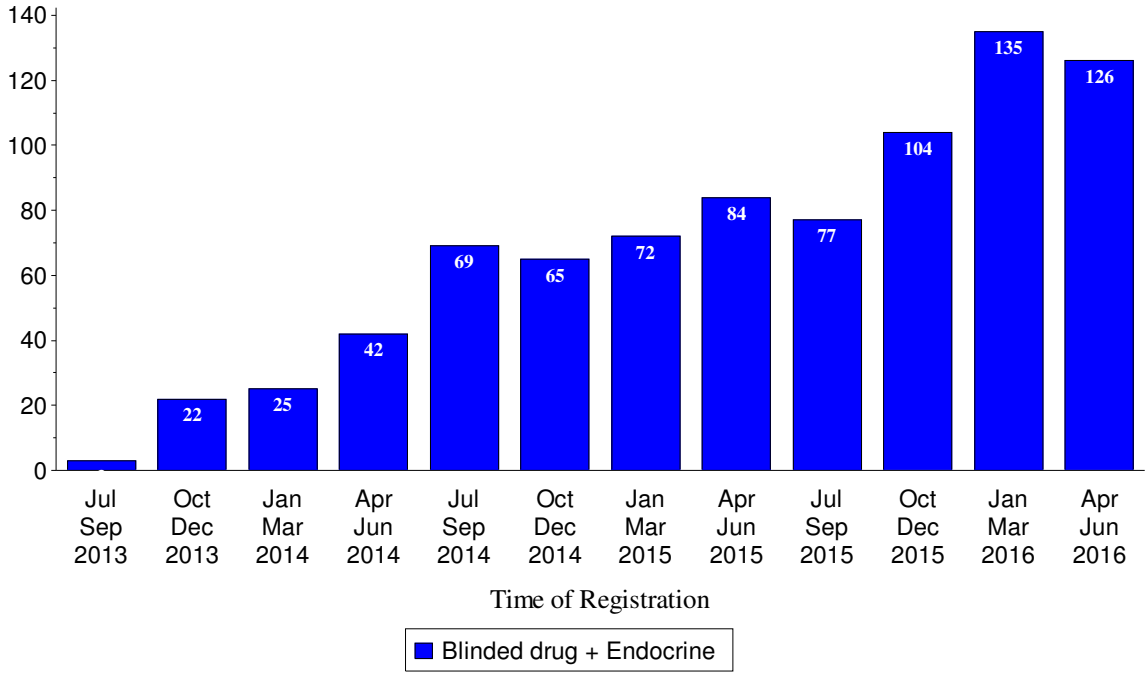
The accrual goal is 1,900 patients. Interim analyses are planned for after approximately 40%, 60%, and 80% of the events in the control arm have been observed.

Summary Statement

This study was activated on September 3, 2013. As of June 30, 2016, there had been 824 patients enrolled. Fifty-six 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 19 patients who received no protocol treatment; these 19 patients are not evaluable for adverse events, along with two additional patients who discontinued protocol treatment without being assessed for adverse events. Fifteen patients were removed from protocol treatment for other non-protocol specified reasons. These including treatment delay that exceeded protocol guidelines (8), non-compliance (3), physician discretion (2), receiving other treatment (1), off due to other complicating disease(1).

There have been 10 patients with Grade 4 toxicities reported among 665 patients evaluated for adverse events, including three with Grade 4 hypertriglyceridemia. One hundred seventeen patients experienced Grade 3 adverse events as maximum degree, including 26 cases of mucositis oral. Grade 3 adverse events not fully specified include herpes simplex keratoconjunctivitis, enteritis, tinnitus, right sided weakness, facial droop, abscess, cellulitis, continued soft tissue infection, and left breast infection. 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 3 Month Intervals



Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Alliance	152	Oklahoma, Univ of	8
NRG	148	San Antonio, U of TX	8
ECOG-ACRIN	147	Arizona MC, U of	7
MD Anderson CC	25	Cedars-Sinai Med Ctr	7
Kansas, U of	16	Cincinnati MC, U of	7
Wichita NCORP	16	Columbus NCORP	7
Yale University	15	Good Samaritan Hosp/Oregon Hlth Sci Univ	6
Kaiser Perm NCORP	13	Northwestern Univ	6
Michigan, U of	12	Sutter Cancer RC	6
Fred Hutchinson CRC	11	Thompson Ca Surv Ctr/San Antonio, U of TX	6
Southeast COR NCORP	11	Colorado, U of	5
City of Hope Med Ctr	10	H Lee Moffitt CC	5
Gulf South MU-NCORP	10	MUSC MU-NCORP	5
Ozarks NCORP	10	Wayne State Univ	5
PCRC NCORP	10	Columbia MU-NCORP	4
CORA NCORP	9	Rochester, Univ of	4
Heartland NCORP	9	Sacred Heart Hosp/Arkansas, U of	4
Michigan CRC NCORP	9	Tennessee, U of	4
Cleveland Clinic OH	8	All Other Institutions	71
New Mexico MU-NCORP	8	**Total (77 Institutions)**	**824**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2016; Data as of July 14, 2016

	Total
NUMBER REGISTERED	824
INELIGIBLE	56
ELIGIBLE	768
Analyzable, Pend. Elig.	70
ADVERSE EVENT ASSESSMENT	
Evaluable	665
Not Evaluable	21
Too Early	82

Patient Characteristics

Registrations ending June 30, 2016; Data as of July 14, 2016

	Total (n=768)	
AGE		
Median	54.6	
Minimum	22.3	
Maximum	79.3	
SEX		
Males	4	1%
Females	764	99%
HISPANIC		
Yes	60	8%
No	688	90%
Unknown	20	3%
RACE		
White	662	86%
Black	48	6%
Asian	28	4%
Pacific Islander	1	0%
Native American	5	1%
Multi-Racial	2	0%
Unknown	22	3%
RISK GROUP		
Node-negative and RS > 25 treated with adjuvant chemotherapy	62	8%
1-3 positive lymph nodes and RS > 25 or Grade III disease treated with adjuvant therapy	78	10%
≥ 4 positive lymph nodes (any RS value) treated with adjuvant chemotherapy	407	53%
≥ 1 positive lymph node (any RS value) wit h neoadjuvant chemotherapy	221	29%

Treatment Summary

Registrations ending June 30, 2016; Data as of July 14, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	367
NUMBER OFF PROTOCOL TREATMENT	401
REASON OFF TREATMENT	
Treatment completed as planned	162
Adverse Event or side effects	127
Refusal unrelated to adverse event	67
Progression/relapse	18
Death	0
Other - not protocol specified	15
Reason under review	12
MAJOR PROTOCOL DEVIATIONS	19

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 June 30, 2016; Data as of July 14, 2016

	Total (n=665) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	621	38	4	2	0	0
AST increased	611	48	3	3	0	0
Abdominal pain	652	9	2	2	0	0
Anemia	599	50	13	3	0	0
Appendicitis	662	0	0	3	0	0
Arthralgia	575	59	30	1	0	0
Back pain	649	11	4	1	0	0
Breast infection	660	0	2	2	1	0
Cardiac arrest	664	0	0	0	1	0
Cholesterol high	515	128	21	1	0	0
Depression	653	10	1	0	1	0
Diarrhea	572	72	16	5	0	0
Dyspnea	634	23	7	1	0	0
Ear/labyrinth disorders-Other	664	0	0	1	0	0
Eye disorders - Other, specify	658	5	1	1	0	0
Fatigue	454	145	58	8	0	0
GI disorders-Other, specify	640	21	3	1	0	0
Headache	589	56	19	1	0	0
Hot flashes	595	53	16	1	0	0
Hyperglycemia	577	65	13	10	0	0
Hyperhidrosis	661	3	0	1	0	0
Hypertension	639	13	9	4	0	0
Hypertriglyceridemia	554	78	20	10	3	0

	Total (n=665) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Hypokalemia	651	8	4	2	0	0
Hyponatremia	661	3	0	1	0	0
Hypoxia	664	0	0	1	0	0
Infections/infestations-Other	651	4	4	6	0	0
Insomnia	622	34	8	1	0	0
Irregular menstruation	664	0	0	1	0	0
Kidney infection	664	0	0	1	0	0
Lipase increased	664	0	0	0	1	0
Lung infection	660	0	3	2	0	0
Lymphedema	657	4	3	1	0	0
Lymphocyte count decreased	597	24	33	10	1	0
Menorrhagia	664	0	0	1	0	0
Mucositis oral	423	128	88	26	0	0
Nausea	566	82	15	2	0	0
Nervous sys disorders-Other	662	1	1	1	0	0
Neuralgia	663	1	0	1	0	0
Neutrophil count decreased	606	25	21	12	1	0
Paroxysmal atrial tachycardia	664	0	0	1	0	0
Peripheral sensory neuropathy	640	19	4	2	0	0
Platelet count decreased	614	44	6	1	0	0
Pneumonitis	652	2	9	2	0	0
Productive cough	662	0	2	1	0	0
Pruritus	635	23	6	1	0	0
Rash acneiform	627	31	6	1	0	0
Rash pustular	664	0	0	1	0	0
Respiratory failure	664	0	0	0	1	0
Sepsis	664	0	0	0	1	0
Skin infection	653	1	7	4	0	0
Skin ulceration	663	0	0	2	0	0
Suicidal ideation	664	0	0	0	1	0
Thromboembolic event	662	0	1	2	0	0
Urinary tract infection	661	0	3	1	0	0
Vascular access complication	664	0	0	1	0	0
Weight loss	645	16	3	1	0	0
White blood cell decreased	559	60	39	6	1	0
Wound complication	662	1	1	1	0	0
Wound dehiscence	663	0	0	2	0	0
Wound infection	662	0	2	1	0	0
MAX. GRADE ANY ADVERSE EVENT	131	156	251	117	10	0

S1415CD Phase III

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 –Trial Assessing CSF Prescribing Effectiveness and Risk (TrACER)

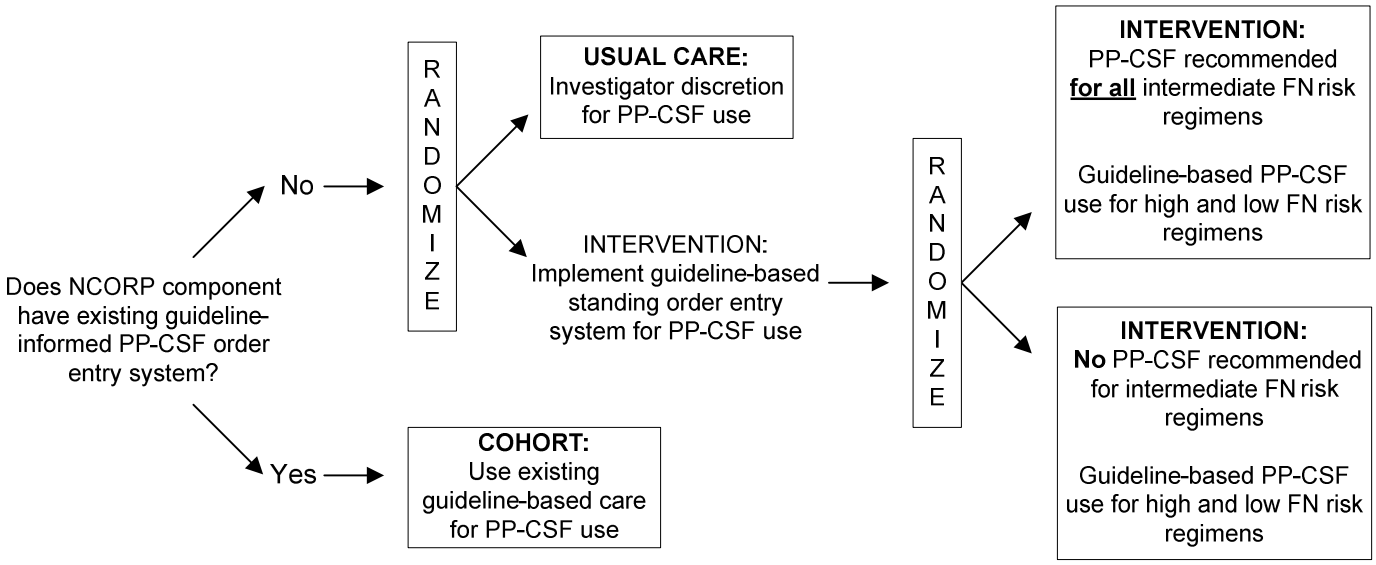
Study Chairs:
S Ramsey, D Hershman

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 (HRQL) 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 (HRQL) 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).

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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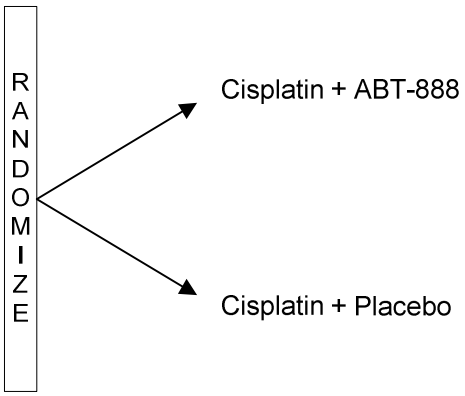
Study Chairs:
E Rodler, P Sharma

Date Activated:
07/07/2016

Statisticians:
W Barlow, D Lew, J Miao

Data Coordinator:
L Kaye

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.

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.

S1418 Phase III

Coordinating Group: SWOG and NRG

A Randomized, Phase III Trial to Evaluate the Efficacy and Safety of MK-3475 (Pembrolizumab) as Adjuvant Therapy for Triple Receptor-Negative Breast Cancer with ≥ 1 cm Residual Invasive Cancer or Positive Lymph Nodes (ypN+) after Neoadjuvant Chemotherapy

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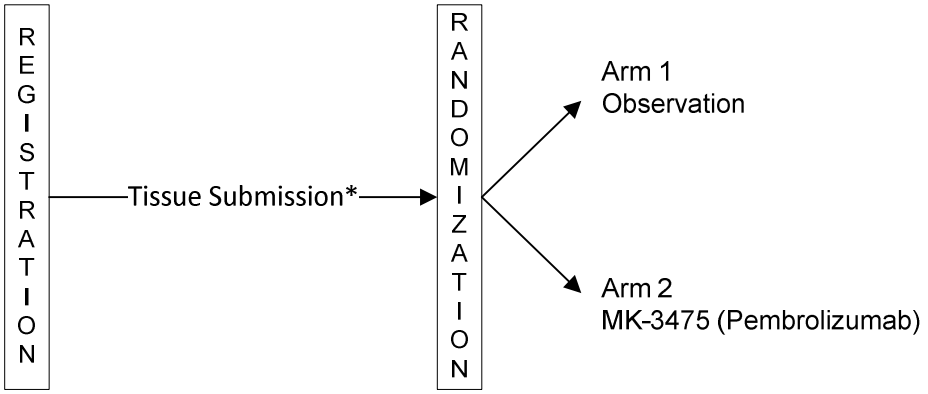
Participants:
SWOG, NRG, CTSU

Study Chairs:
L Pusztai, J Mammen, P Ganz (NRG)

Statisticians:
W Barlow, D Lew, J Miao

Data Coordinator:
I Syquia

SCHEMA



*PD-L1 status determined by central laboratory

Objectives

To compare invasive disease-free survival (IDFS) of patients with triple-negative breast cancer (TNBC) who have either ≥1 cm residual invasive breast cancer and/or positive lymph nodes (>ypN+) after neoadjuvant chemotherapy randomized to 1 year of MK-3475 (pembrolizumab) adjuvant therapy compared to no MK-3475 (pembrolizumab), in both the entire study population and also in the PD-L1 positive subset.

To compare the effects of MK-3475 (pembrolizumab) on overall survival (OS) and distant recurrence-free survival (DRFS) between the two randomized arms for the PD-L1 positive patients and then all patients.

To assess the toxicity and tolerability of MK-3475 (pembrolizumab) in this patient population with or without radiation therapy.

To examine the association between biomarkers of inflammation and quality of life and patient reported outcomes between the two groups during and shortly after the end of therapy.

To examine the long-term and late effects of treatment on patient-reported outcomes.

Patient Population

Patients must have histologically confirmed ER-, PR- and HER2-negative breast cancer (triple-negative, TNBC) with residual invasive disease after completion of neoadjuvant chemotherapy. Residual disease must be ≥ 1 cm in greatest dimension, and/or have positive lymph nodes (ypN+) determined as described in the protocol. Patients must not have metastatic disease. Patients must have adequate tumor tissue for PD-L1 testing.

Patients must have received neoadjuvant chemotherapy which should include 12 to 24 weeks of a third generation chemotherapy regimen as recommended by NCCN guidelines for TNBC. Patients may receive post-operative (adjuvant) chemotherapy for up to 24 weeks, which must be given prior to any radiation and must have been completed within 35 days prior to registration. Patients must have completed their final breast surgery with clear resection margins for invasive cancer and DCIS within 210 days or 90 days (if no adjuvant chemotherapy) prior to registration. Patients may receive concomitant radiation therapy (XRT) or XRT prior to registration; the intention to use XRT and the extent of intended XRT must be specified at registration if it has not been initiated. Patients must not have had prior immunotherapy with anti PD-L1 or anti-CTLA4 or similar drugs.

Patients must be at least 18 years of age, have a Zubrod performance status of 0-2, and must not have received live vaccines within 30 days prior to registration. Patients must not be HIV positive or have known active hepatitis B or C. Patients must not have active autoimmune disease that has required systemic treatment in the past 2 years, non-infectious pneumonitis, or an active infection requiring systemic therapy. Patients who speak/read English or Spanish must agree to participate in the BAHO substudy.

Patients must be registered to Step 2 for randomization within seven days of receiving e-mail notification that the patient's tissue specimen was adequate for PD-L1 testing. Patients must have adequate hematologic, hepatic, renal and thyroid function prior to randomization.

Stratification/Descriptive Factors

Randomization will be stratified by the following factors: (1) nodal stage: ypN0 vs ypN+; (2) residual tumor size: ≤ 20 mm vs > 20 mm; (3) PD-L1 status: positive vs negative; and (4) prior use of post-operative (adjuvant) chemotherapy: yes vs no.

Accrual Goals

The accrual goal is 1,000 patients to achieve 910 eligible patients. Two interim analyses will be performed when approximately 50% and 75% of the IDFS events in the PD-L1 positive population have been observed.

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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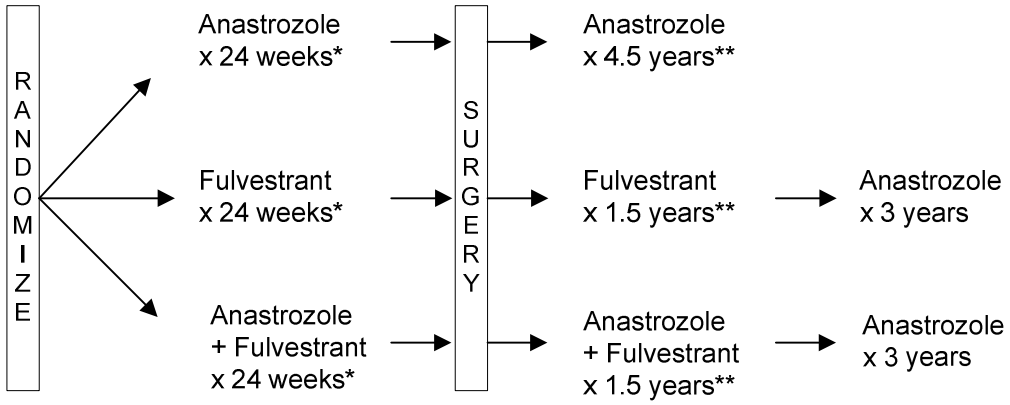
Participants:
Alliance, CTSU

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.

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 478 patients had been registered to this study as of June 30, 2016, including 19 SWOG registrations. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg
Arizona MC, U of	8
Baptist MU-NCORP	8
CORA NCORP	1
New Mexico MU-NCORP	1
St Jude Medical Ctr/Irvine, U of CA	1
Total (5 Institutions)	**19**

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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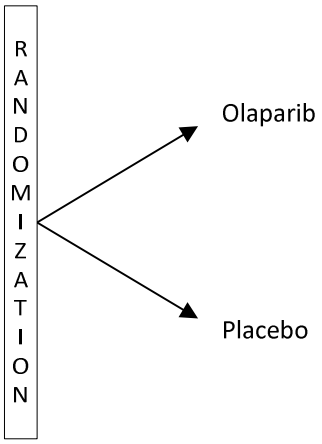
Participants:
NRG, CTSU

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 the 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 *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 when 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 63 patients had been registered to this study as of June 30, 2016, including 9 from SWOG institutions.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg
Cedars-Sinai Med Ctr	3
Wayne State Univ	2
Intermountain MC/Northwest NCORP	1
Kansas, U of	1
Michigan, U of	1
Shaw Reg Cancer Ctr/Colorado, U of	1
Total (6 Institutions)	**9**

E1Z11 Cohort 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 June 30, 2016, there had been 948 registrations to this study, including 132 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 March 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
KaiserPermanenteSCAL/Kaiser Perm NCORP	25	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
Hawaii MU-NCORP	9	Greenwich Hospital/Yale University	2
Ozarks NCORP	9	Poudre Valley Hosp/Colorado, U of	2
St Joseph's/Candler/Georgia NCORP	8	Providence Hosp	2
Prov Portland MC/PCRC NCORP	6	Cincinnati MC, U of	1
LSU-Shreveport/Gulf South MU-NCORP	5	Fowler Family Center/Baptist MU-NCORP	1
MUSC MU-NCORP	5	Good Samaritan Hosp/CORA NCORP	1
Montana NCORP	4	NorthBay Med Ctr/Davis, U of CA	1
Baptist Health/Cincinnati MC, U of	3	**Total (23 Institutions)**	**132**

E2112 Phase III 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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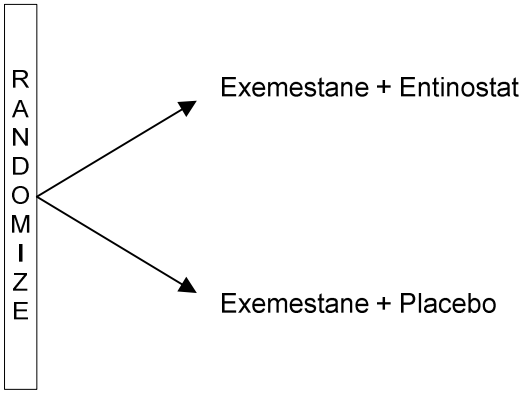
Participants:
ECOG-ACRIN, CTSU

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 June 30, 2016, there had been 285 registrations to this study, including 16 SWOG registrations. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Kansas, U of	3	Wayne State Univ	2
Cleveland Clinic OH	2	Good Samaritan Hosp/CORA NCORP	1
Columbia MU-NCORP	2	Henry Ford Hosp	1
CORA NCORP	2	Texas Tech Univ HSC/San Antonio, U of TX	1
Northwestern Univ	2	**Total (9 Institutions)**	**16**

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

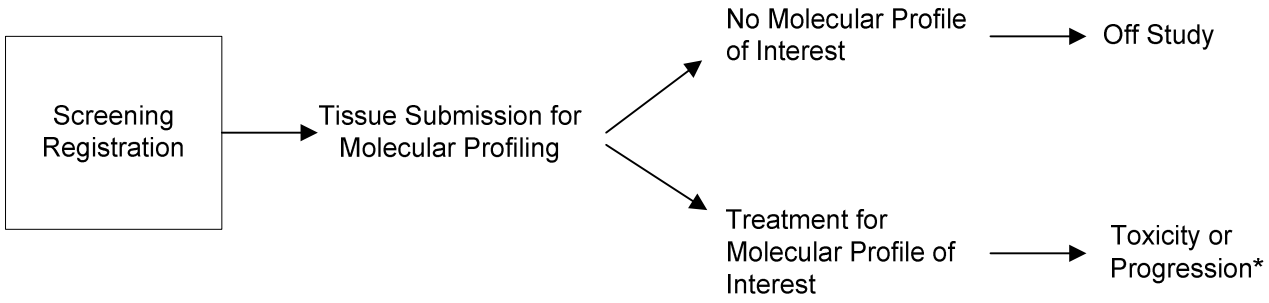
NCI-MATCH: Molecular Analysis for Therapy Choice

Participants:
ECOG-ACRIN, CTSU

Date Activated:
08/12/2015

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

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/multiple myeloma.

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/multiple myeloma.

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 protein and imaging-based assessment platforms.

To assess whether radiomic phenotypes obtained from pre-treatment imaging and changes from pre- through post-therapy imaging can predict objective response and progression-free survival and to evaluate the association between pre-treatment radiomic phenotypes and targeted gene mutation patterns of tumor biopsy specimens.

Patient Population

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma or multiple myeloma 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 and meet one of the criteria in the protocol regarding tissue procurement.

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 start of treatment. Patients must not require the use of full dose coumarin-derivative anticoagulants. Factor X inhibitors are permitted. Patients may receive non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results, but patients may not enroll in another investigational study during this time and the therapy cannot be an arm in this trial.

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. Patients must not have any uncontrolled intercurrent illness. 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 reach 25 patients by the time the overall study screening accrual goal is met, and if 13 patients have been treated and no responses have been observed, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. After 500 patients are screened, the study design will be reassessed to assure its appropriateness. 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 January 26, 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 assessment of study design appropriateness was lifted on May 31, 2016, when this study reopened to enrollment with an additional 14 new subprotocols.

Patients with multiple myeloma will be allowed to enroll in the MATCH protocol at a future amendment. The screening sample collection, processing and assay are currently being validated for the marrow specimens for patients with myeloma. Once this is completed, an amendment allowing these patients to enroll will be submitted. Patients with myeloma cannot be entered on the trial until that is completed.

ECOG-ACRIN reported a total of 1,013 screened patients and 29 molecularly matched patients as of June 30, 2016. This includes 139 screened and two molecularly matched SWOG registrations. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.