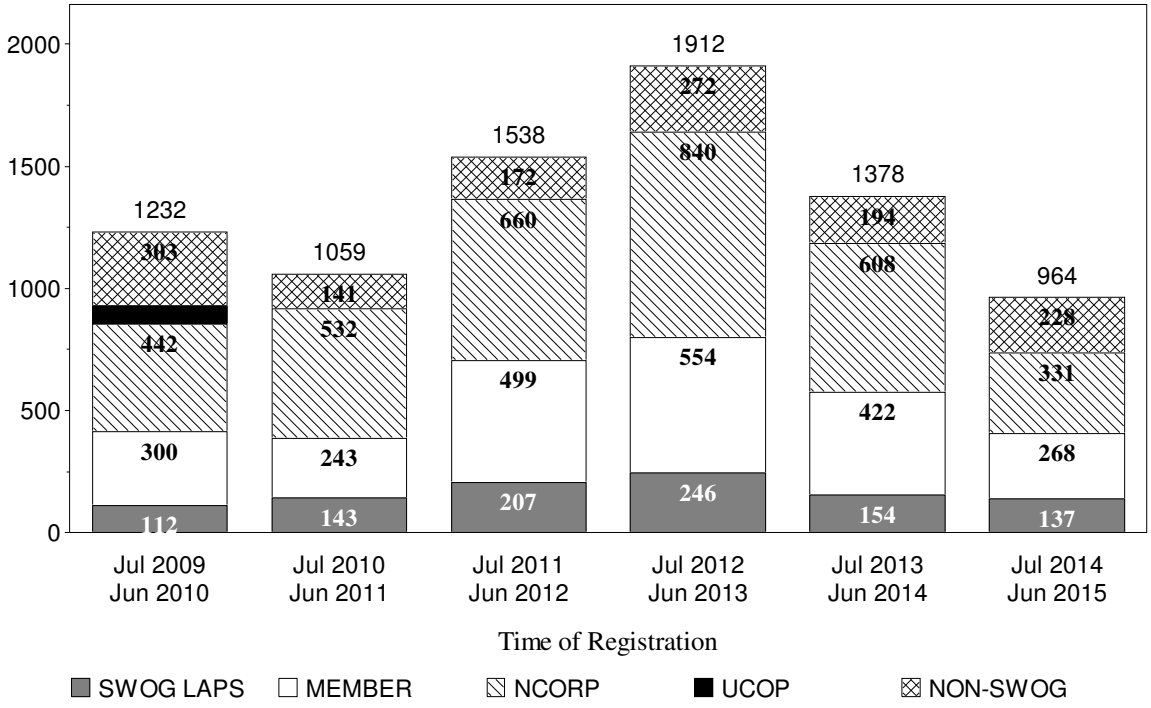
SYMPTOM CONTROL AND QOL COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
SYMPTOM CONTROL AND QOL COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

SYMPTOM CONTROL AND QOL COMMITTEE

	Jan 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
S1013 Validation Study of FACT-EGFRI				
Initial registration				
EGFRI-induced skin-related tox	21	21	12	110
S1200 Breast, AI Joint Pain, Acupuncture				
Randomization				
Waitlist Control	8	10	6	38
Blinded Treatment	22	22	25	115
	30	32	31	153
S1202 Duloxetine AI Joint Pain				
Randomization				
Blinded Drug	90	76	63	238
S1207 Brst, Adj, Endocrine+/-Everolimus				
Randomization				
Blinded drug + Endocrine	156	134	67	382
A011104 Preoperative Breast MRI*				
Total Registrations	0	1	1	2
A021202 Carcinoid, Pazopanib vs Placebo*				
Total Registrations	10	8	5	23
A041202 CLL, 65+, Ben+Rtx vs Ibrut±Rtx*				
Total Registrations	30	29	6	65
A091105 Desmoid, Sorafenib vs Placebo*				
Total Registrations	4	2	0	6
A221101 Glioma, Nuvigil/Placebo Fatigue*				
Total Registrations	1	1	3	7
A221102 Brst,AI Arthralgia,Testosterone*				
Total Registrations	1	0	0	1

Patient Registrations by Study and Arm

SYMPTOM CONTROL AND QOL COMMITTEE

	Jan 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
B43 Breast, DCIS, HER2+, RT +/- Tras*				
Total Registrations	0	5	15	66
B51 Breast, Regional Nodal XRT*				
Total Registrations	0	1	1	2
B52 Breast, Neoadj TCHP +/- AI*				
Total Registrations	3	1	0	4
B55 Brst, Adj Olaparib for BRCA,TNBC*				
Total Registrations	2	0	0	2
C30610 SCLC, Thoracic RT*				
Total Registrations	1	1	2	49
C51101 CNS, myelo/non-myelo chemo, PhII*				
Total Registrations	2	0	3	5
C80803 Esoph, PET-directed combined Tx*				
Total Registrations	0	1	3	5
C90203 Pros, Surgery +/- Neoadj Chemo*				
Total Registrations	7	7	3	152
E1411 MCL, RB+R, RBV+R, RB+LR, RBV+LR*				
Total Registrations	17	10	14	55
E1609 Mel, Adj Ipil vsInterferon*				
Total Registrations	0	36	96	500
E1912 CLL, age 18-70, Ibrutinib vs FCR*				
Total Registrations	31	19	16	66
E1A11 MM, frontline, BLD vs CLD*				
Total Registrations	6	13	6	25
E1Z11 Brst,Genetic Predictors of AIMSS*				
Total Registrations	23	11	54	120

Patient Registrations by Study and Arm

SYMPTOM CONTROL AND QOL COMMITTEE

	Jan 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
E2108 Early Local Tx for Int Prim Tum*				
Total Registrations	9	8	6	51
E2112 Brst,Adv,Exemestane+/-Entinostat*				
Total Registrations	1	0	0	1
E2810 Renal, Pazopanib vs Placebo*				
Total Registrations	5	1	9	28
E2906 AML, age 60+, Clo vs Dauno+Cy*				
Total Registrations	0	16	9	75
E3311 Oroph, Srg + Low or Std IMRT *				
Total Registrations	7	3	0	10
E3A06 AMM, Lenalidomide vs Observation*				
Total Registrations	5	4	5	22
G0258 Endo, Adv, CDDP+RT->CP vs CP*				
Total Registrations	0	0	1	2
G0286B Adv Endometrial, Metformin/Chemo*				
Total Registrations	1	0	0	1
N1048 Rectal, Local Adv, Chemo RT+/-FOLFOX*				
Total Registrations	15	19	17	61
N1174 Bev +/- TRC105 in Bev Naïve GBM*				
Total Registrations	0	1	0	1
NRGCC002 GYN, Pre/Post Op Eval in Elderly*				
Total Registrations	1	0	0	1
R0534 Pros, PBRT +/- NC-STAD +/- PLNRT*				
Total Registrations	0	3	0	3

Patient Registrations by Study and Arm

SYMPTOM CONTROL AND QOL COMMITTEE

	Jan 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
R0815 Pros, dose-esca. RT +/- ADT*				
Total Registrations	3	2	3	9
R0920 HN, Adv, Postop IMRT ± Cetuximab*				
Total Registrations	2	1	0	5
R0924 Pros, NADT+WPRT vs. NADT+P&SV RT*				
Total Registrations	1	2	0	4
R1010 Esoph, HER2, Trimodal Tx+/-Trastu*				
Total Registrations	0	0	1	5
R1016 Orophx, p16+, RT+Cis v RT+Cetuxmab*				
Total Registrations	0	5	3	8
R1115 Pros, (ADT + RT) +/- TAK-700*				
Total Registrations	0	0	1	2
SCUSF806 Breast, Adj, Cardiotoxicity*				
Total Registrations	0	1	7	19
Z11102 Breast Conserv. Surgery for MIBC*				
Total Registrations	4	0	2	6

* 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, NCIC CTG, GEICAM, and UNICANCER)

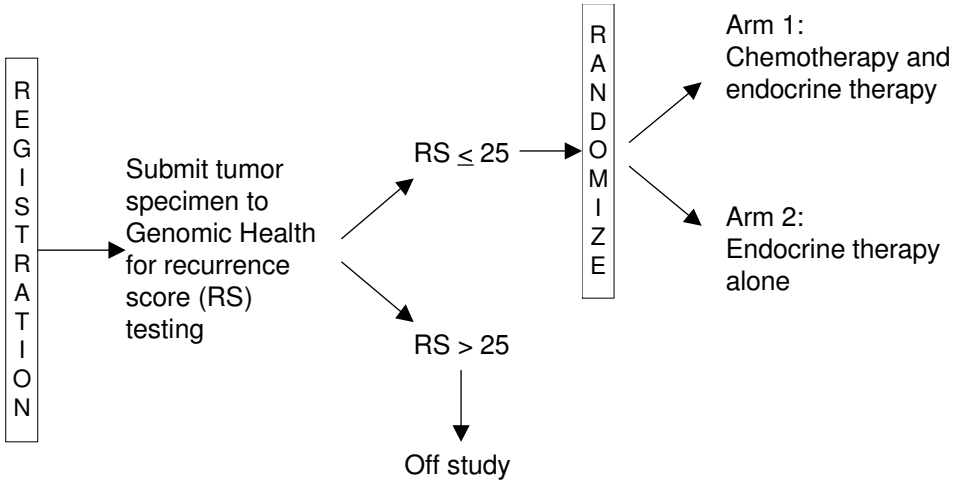
Date Activated:
01/15/2011

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

Statisticians:
W Barlow, D Lew

Data Coordinators:
L Kaye, J Barce

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

For the current status of this study, please refer to the Breast chapter.

S1013 Validation

A Prospective Study of Epidermal Growth Factor Receptor (HER-1/EGFR) Inhibitor-Induced Dermatologic Toxicity: Validation of the Functional Assessment of Cancer Therapy-EGFRI 18 (FACT-EGFRI 18) Questionnaire for EGFRI-Induced Skin Toxicities

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Study Chairs:
S Wong, C Moinpour, J Wade

Statisticians:
J Unger, K Arnold

Data Coordinator:
D Marrah

Date Activated:
11/15/2011

Objectives

To establish psychometric properties for the Functional Assessment of Cancer Therapy Epidermal Growth Factor Receptor Inhibitor (FACT-EGFRI 18) module (based on criterion validity, known group's validity, internal consistency reliability, and responsiveness to change) as a patient-reported outcome (PRO) measure of EGFRI-induced skin-related toxicity.

To document minimally important differences over time for the FACT-EGFRI 18 by comparing mean changes in this PRO measure to the patient's direct assessment of change using two anchor items (change in skin condition severity and impact).

To examine the association between toxicity profiles (severity and time to onset), and treatment profiles (e.g., delays and discontinuation) and the FACT-EGFRI 18 scores.

To assess degree of concordance between FACT-EGFRI 18 ratings and study site physician CTCAE Version 4.0 EGFRI-Induced Dermatologic Toxicity Grading Assessment ratings.

To evaluate feasibility outcomes.

Patient Population

Patients must have a diagnosis of colorectal or lung cancer and be planning to receive one of the following HER1/EGFR inhibitor therapies listed below for at least 6 weeks: (a) cetuximab 400 mg/m^2 loading dose, 250 mg/m^2 weekly; (b) cetuximab 500 mg/m^2 every 2 weeks; (c) panitumumab 6 mg/kg every 2 weeks; (d) erlotinib 100-150 mg daily. Other HER1/EGFR inhibitor therapies, schedules, or doses of the above listed agents are not allowed.

Concurrent chemotherapy and other anti-cancer therapies (such as carboplatin, paclitaxel, and bevacizumab) are allowed EXCEPT for the following chemotherapeutic agents which are known to cause skin rash that could interfere with EGFRI-induced skin toxicity assessment: gemcitabine, capecitabine, and topical fluorouracil. Patients may have had prior HER1/EGFR inhibitor therapy but must have fully recovered from any skin toxicities prior to registration. Patients must not have any of the serious concomitant skin disorders specified in the protocol that, in the investigator's opinion, could interfere with assessment of EGFRI induced skin toxicity. Patients must not be planning to receive any of the concomitant medications specified in the protocol that can cause skin rash or other dermatologic reactions that could interfere with the EGFRI-induced skin toxicity assessments, for the duration of

the study. Patients must not be planning to receive concurrent external beam radiation therapy, including prophylactic cranial radiation.

Patients must have a Zubrod performance status of 0-2. Patients must be able to complete questionnaires in English. Patients may concurrently participate in other therapeutic clinical trials. Patients must have completed the baseline S1013 FACT-EGFRI 18 within seven days prior to registration.

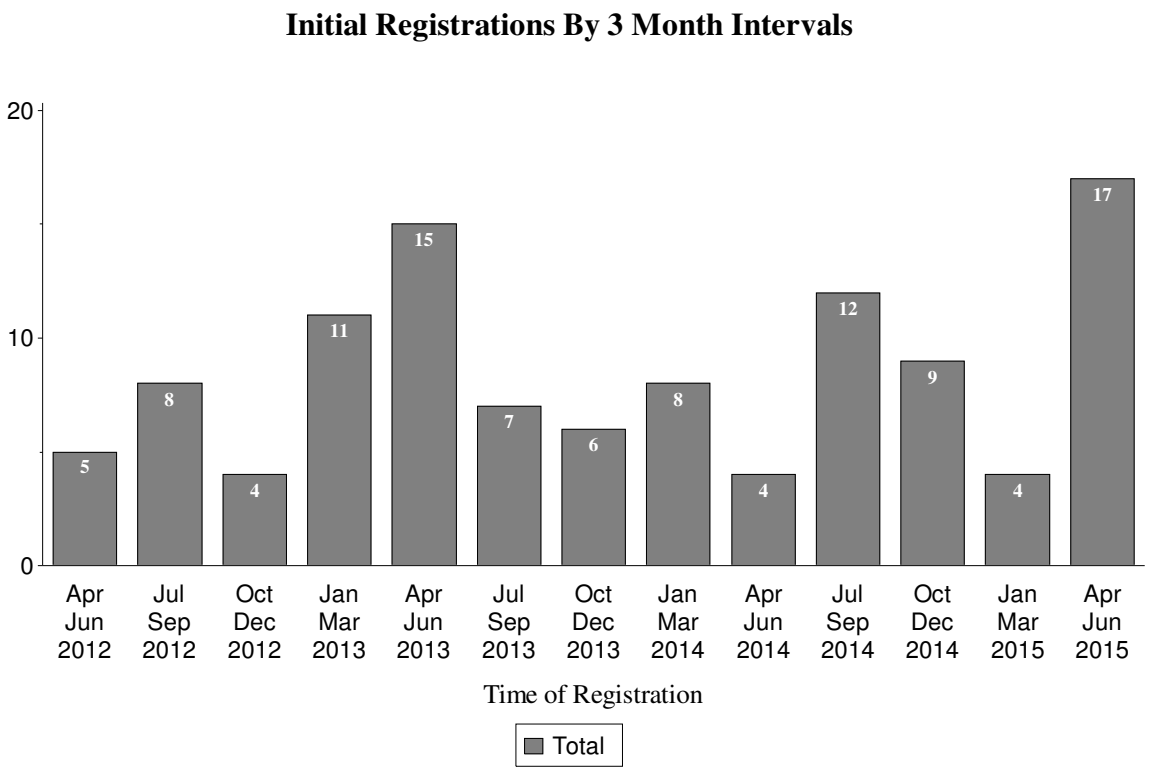
Accrual Goals

This study will enroll 112 analyzable patients.

This study activated on November 15, 2011, to limited institutions. As of June 30, 2015, 110 participants have been registered.

Eighty-three patients are off protocol. One patient who received treatment prior to the baseline assessment, two patients who never received EGFRI treatment, and ten patients who did not have a rash by six weeks are not analyzable. Ten patients refused further follow-up: four withdrew consent, one could not maintain the examination schedule at the site, two refused to complete further questionnaires, and three declined all further participation. One patient who is coded as off protocol due to "Other – not protocol specified" received off-protocol radiation treatment.

Summary Statement



Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Heartland NCORP	42	Columbia MU-NCORP	3
So Calif, U of	24	Gulf South MU-NCORP	3
City of Hope Med Ctr	17	McLaren Cancer Inst/Wayne State Univ	3
Wichita NCORP	8	Loma Linda Univ	1
Southeast COR NCORP	5	**Total (10 Institutions)**	**110**
LSU-Shreveport/Gulf South MU-NCORP	4		

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 21, 2015

	Total
NUMBER REGISTERED	110
INELIGIBLE	1
Insufficient Documentation	1
Irreversible	1
ELIGIBLE	109
Analyzable, Pend. Elig.	1
Not Analyzable	13

Patient Characteristics

Registrations ending June 30, 2015; Data as of August 21, 2015

	Total (n=96)	
AGE		
Median	64.3	
Minimum	36.7	
Maximum	87.3	
SEX		
Males	50	52%
Females	46	48%
HISPANIC		
Yes	12	13%
No	84	88%
RACE		
White	82	85%
Black	2	2%
Asian	11	11%
Native American	1	1%

Treatment Summary

Registrations ending June 30, 2015; Data as of August 21, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	13
NUMBER OFF PROTOCOL TREATMENT	83
REASON OFF TREATMENT	
Treatment completed as planned	46
Adverse Event or side effects	3
Refusal unrelated to adverse event	10
Progression/relapse	11
Death	7
Other - not protocol specified	1
Reason under review	5
MAJOR PROTOCOL DEVIATIONS	0

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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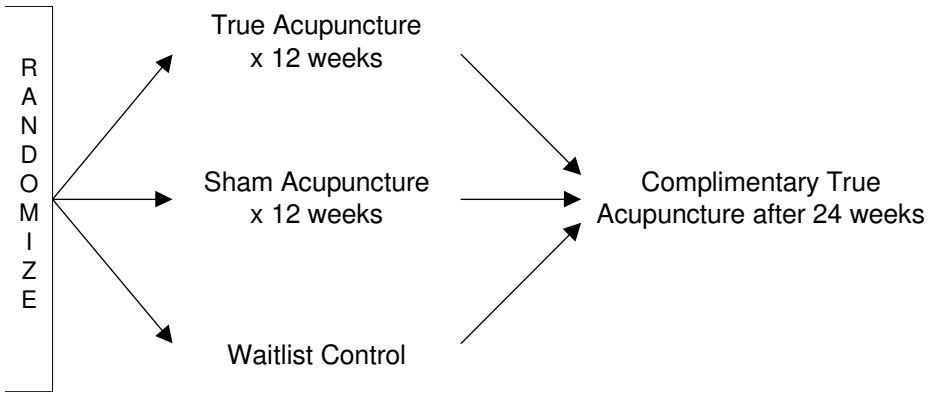
Study Chairs:
D Hershman, K Crew

Date Activated:
03/27/2012

Statisticians:
J Unger, D Lew

Data Coordinator:
D Marrah

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

This study opened to accrual on March 27, 2012, and is open to limited institutions. As of June 30, 2015, there had been 153 registrations. One patient who was not post-menopausal and four patients who did not complete the Brief Pain Inventory within 14 days prior to registration are ineligible. An additional 29 patients who are currently ineligible due to incomplete baseline information but who may become eligible if documentation is received are included in the tables with the eligible patients. Major deviations are coded for one patient who received the incorrect acupuncture treatment for two sessions when a different acupuncturist was covering her appointments, two patients who were randomized to acupuncture but received no treatment, and one patient who was randomized to waitlist but was in too much pain to wait for treatment.

No Grade 3 or higher adverse events have been reported.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Kaiser Vallejo NCORP	40	Fred Hutchinson CRC	7
CRC West MI NCORP	35	Good Samaritan Hosp/Oregon Hlth Sci Univ	7
Columbia MU-NCORP	21	So Calif, U of	3
St Luke's Mt State/PCRC NCORP	14	Utah, U of	3
Greenville NCORP	13	PCRC NCORP	2
Lahey Hosp & Med Ctr	8	**Total (11 Institutions)**	**153**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total
NUMBER REGISTERED	153
INELIGIBLE	5
Insufficient Documentation	4
Irreversible	4
ELIGIBLE	148
Analyzable, Pend. Elig.	8
ADVERSE EVENT ASSESSMENT	
Evaluable	106
Not Evaluable	3
Too Early	2
Not Applicable	37

Patient Characteristics

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total (n=148)	
AGE		
Median	60.6	
Minimum	27.1	
Maximum	79.3	
HISPANIC		
Yes	11	7%
No	137	93%
RACE		
White	130	88%
Black	7	5%
Asian	9	6%
Native American	1	1%
Unknown	1	1%
STUDY SITE		
Columbia U	21	14%
FHCRC	6	4%
West Michigan NCORP	35	24%
Kaiser NCORP	38	26%
Good Samaritan/Oregon HSU	7	5%
USC	3	2%
St. Luke's Mountain States	13	9%
Greenville NCORP	13	9%
Lahey Hospital	8	5%
University of Utah	3	2%
PCRC NCORP	1	1%

Treatment Summary

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	52
NUMBER OFF PROTOCOL TREATMENT	96
REASON OFF TREATMENT	
Treatment completed as planned	73
Adverse Event or side effects	0
Refusal unrelated to adverse event	13
Progression/relapse	2
Death	0
Other - not protocol specified	3
Reason under review	5
MAJOR PROTOCOL DEVIATIONS	4

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total (n=106) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Arthralgia	55	34	17	0	0	0
Back pain	105	1	0	0	0	0
Bruising	67	39	0	0	0	0
Dizziness	104	2	0	0	0	0
Ear pain	105	1	0	0	0	0
Edema limbs	104	2	0	0	0	0
Hematoma	105	1	0	0	0	0
Hot flashes	105	0	1	0	0	0
Inj/poisoning/proced comp-Oth	102	4	0	0	0	0
Myalgia	104	2	0	0	0	0
Pain	102	4	0	0	0	0
Pain in extremity	105	1	0	0	0	0
Peripheral sensory neuropathy	105	1	0	0	0	0
ROM decreased	100	5	1	0	0	0
MAX. GRADE ANY ADVERSE EVENT	36	53	17	0	0	0

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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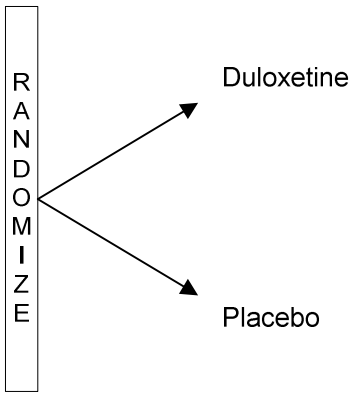
Study Chairs:
N Henry, A Schott

Date Activated:
05/15/2013

Statisticians:
J Unger, D Lew

Data Coordinator:
R Topacio

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

This study was activated on May 15, 2013. As of June 30, 2015, 238 patients had been enrolled. Three patients are ineligible, two due to AI therapy started more than 36 months prior to registration, and one due to FSH not measured to confirm post-menopausal status. A major deviation is recorded for nine other patients: three who received only one day of intervention, five who did not receive any protocol intervention, and one who did not begin protocol intervention until over a month after registration.

Thirteen patients have experienced Grade 3 toxicities among 225 patients assessed for adverse events, including five cases of Grade 3 insomnia. There have been no Grade 4 or 5 toxicities reported.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	37	Michigan, U of	2
Kaiser Vallejo NCORP	31	MUSC MU-NCORP	2
NRG	31	PCRC NCORP	2
ECOG-ACRIN	19	Porter Memorial Hosp/Loyola University	2
Southeast COR NCORP	14	Schumpert St Mary/San Antonio, U of TX	2
Wichita NCORP	12	Texas Tech Univ HSC/San Antonio, U of TX	2
Sacred Heart Hosp/Arkansas, U of	9	Baptist MU-NCORP	1
Michigan CRC NCORP	7	Columbia MU-NCORP	1
Heartland NCORP	6	Columbus NCORP	1
Dayton NCORP	5	Greenville NCORP	1
Gulf South MU-NCORP	5	Highline Medical Ctr/Franciscan Res Ctr	1
Montana NCORP	5	Loyola University	1
Tulane University	5	McLaren Cancer Inst/Wayne State Univ	1
Prov Portland MC/PCRC NCORP	4	Nevada CRF NCORP	1
Cedars-Sinai Med Ctr	3	New Mexico MU-NCORP	1
Hawaii MU-NCORP	3	Northwest NCORP	1
LSU-Shreveport/Gulf South MU-NCORP	3	Ozarks NCORP	1
Presbyterian Hosp/Irvine, U of CA	3	S Georgia Med Ctr/Brooke Army Med Ctr	1
Sutter Cancer RC	3	Tulane Univ MBCCOP	1
Wayne State Univ	3	Watson Clinic Center/H Lee Moffitt CC	1
Beaumont NCORP	2	**Total (42 Institutions)**	**238**
Kansas City NCORP	2		

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total
NUMBER REGISTERED	238
INELIGIBLE	3
Insufficient Documentation	1
Irreversible	1
ELIGIBLE	235
Analyzable, Pend. Elig.	1
ADVERSE EVENT ASSESSMENT	
Evaluable	225
Not Evaluable	6
Too Early	4

Patient Characteristics

All eligible and selected ineligible patients included

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total (n=235)	
AGE		
Median	61.0	
Minimum	27.4	
Maximum	83.4	
HISPANIC		
Yes	10	4%
No	225	96%
RACE		
White	196	83%
Black	26	11%
Asian	7	3%
Pacific Islander	1	0%
Native American	2	1%
Multi-Racial	2	1%
Unknown	1	0%
BASELINE PAIN SCORE		
4-6	181	77%
7-10	54	23%
PRIOR TAXANE USE		
Yes	124	53%
No	111	47%

Treatment Summary

All eligible and selected ineligible patients included

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	67
NUMBER OFF PROTOCOL TREATMENT	168
REASON OFF TREATMENT	
Treatment completed as planned	108
Adverse Event or side effects	28
Refusal unrelated to adverse event	12
Progression/relapse	2
Death	0
Other - not protocol specified	7
Reason under review	11
MAJOR PROTOCOL DEVIATIONS	9

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

Adverse Events Unlikely or Not Related to Treatment Excluded

All Eligible and Selected Ineligible Patients Included

Registrations ending June 30, 2015; Data as of August 26, 2015

	Total (n=225) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Abdominal pain	214	8	2	1	0	0
Agitation	217	7	1	0	0	0
Akathisia	224	1	0	0	0	0
Anorectal infection	224	1	0	0	0	0
Anorexia	212	10	3	0	0	0
Anorgasmia	224	1	0	0	0	0
Anxiety	222	3	0	0	0	0
Arthralgia	207	9	7	2	0	0
Back pain	222	2	1	0	0	0
Bloating	224	1	0	0	0	0
Blurred vision	219	6	0	0	0	0
Bone pain	224	0	1	0	0	0
Chills	223	2	0	0	0	0
Concentration impairment	222	1	2	0	0	0
Constipation	208	14	3	0	0	0
Cough	218	7	0	0	0	0
DLOC	224	0	1	0	0	0
Delayed orgasm	224	1	0	0	0	0
Depression	221	1	3	0	0	0
Diarrhea	206	16	2	1	0	0
Dizziness	208	13	4	0	0	0
Dry eye	224	1	0	0	0	0

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

Adverse Events Unlikely or Not Related to Treatment Excluded
All Eligible and Selected Ineligible Patients Included
Registrations ending June 30, 2015; Data as of August 26, 2015

	Total (n=225)	Grade				
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Dry mouth	186	38	1	0	0	0
Dysgeusia	223	2	0	0	0	0
Dyspepsia	219	5	1	0	0	0
Dyspnea	224	1	0	0	0	0
Eye disorders - Other, specify	224	1	0	0	0	0
Fatigue	175	35	15	0	0	0
Flashing lights	224	1	0	0	0	0
Flatulence	219	5	1	0	0	0
Floaters	224	1	0	0	0	0
Flu like symptoms	219	5	1	0	0	0
Headache	190	30	5	0	0	0
Hot flashes	198	20	7	0	0	0
Hyperhidrosis	213	8	4	0	0	0
Insomnia	205	10	5	5	0	0
Lethargy	218	2	5	0	0	0
Libido decreased	219	6	0	0	0	0
MS/connective tissue disorder	223	0	2	0	0	0
Memory impairment	224	1	0	0	0	0
Muscle weakness upper limb	223	2	0	0	0	0
Myalgia	198	12	14	1	0	0
Nasal congestion	220	5	0	0	0	0
Nausea	183	37	4	1	0	0
Neck pain	224	1	0	0	0	0
Nervous sys disorders-Other	223	1	1	0	0	0
Pain	210	5	9	1	0	0
Pain in extremity	220	2	3	0	0	0
Paresthesia	219	5	1	0	0	0
Psych disorders-Other, spec	222	3	0	0	0	0
ROM decreased	216	6	2	1	0	0
Rash acneiform	223	1	1	0	0	0
Rash maculo-papular	223	2	0	0	0	0
Restlessness	223	2	0	0	0	0
Somnolence	212	8	5	0	0	0
Spasticity	223	1	1	0	0	0
Tremor	220	5	0	0	0	0
Vertigo	214	8	3	0	0	0
Vomiting	222	1	1	1	0	0
Weight gain	223	2	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	91	68	53	13	0	0

S1207 Phase III

Coordinating Group: SWOG

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

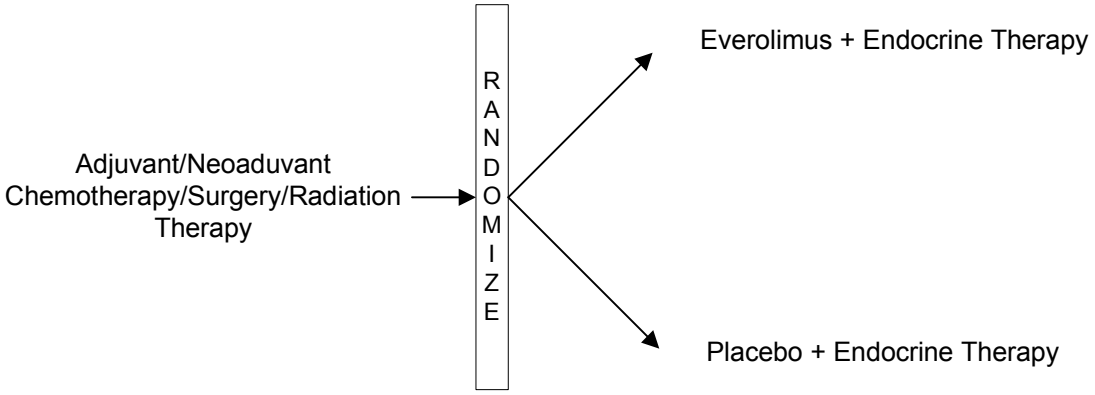
Date Activated:
09/03/2013

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

Statisticians:
W Barlow, D Lew

Data Coordinators:
J Barrett, 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 not eligible.

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 who have not already started endocrine therapy 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 3,500 eligible patients. Interim analyses are planned for after approximately 39%, 60%, and 81% of the events in the control arm have been observed.

Summary Statement

For the current status of this study, please refer to the Breast chapter.

A021202 Phase II SWOG Supported CTSU Study

Coordinating Group: Alliance

Prospective Randomized Phase II Trial of Pazopanib (NSC #737754, IND #75648) Versus Placebo in Patients with Progressive Carcinoid Tumors

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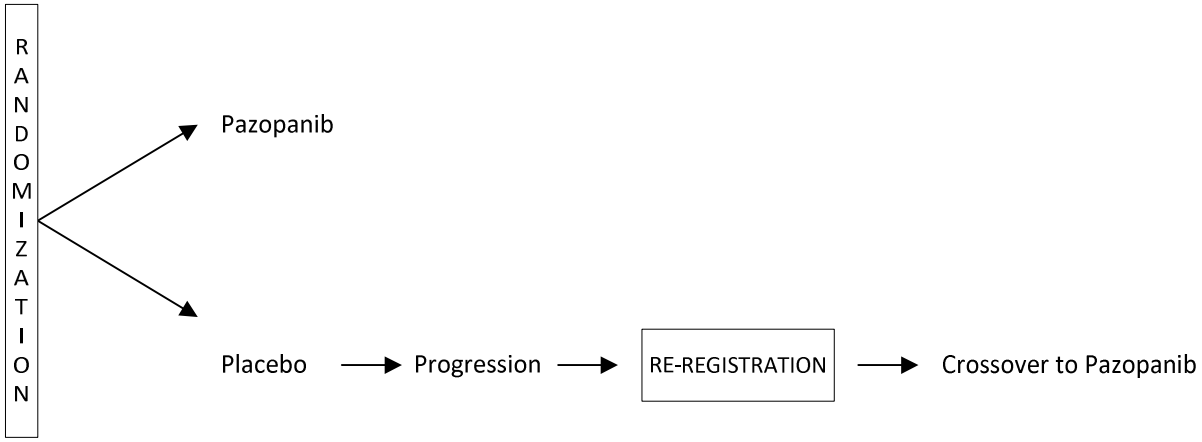
Participants:
Alliance, SWOG, CTSU

Date Activated:
05/08/2013

Study Chairs:
E Bergsland (Alliance), A Phan (SWOG)

SCHEMA



Objectives

To compare centrally reviewed progression-free survival (PFS) between patients with progressive carcinoid tumors randomized to treatment with pazopanib versus placebo.

To compare overall survival between treatment arms.

To compare objective response rate, duration of response, and time to treatment failure between treatment arms.

To compare PFS as assessed by central radiology review and local radiology review overall and within treatment arms.

To estimate PFS at 6 months and 12 months within each treatment arm.

To evaluate safety and tolerability of treatment with pazopanib/placebo.

To compare biochemical response between treatment arms among patients with elevated baseline levels of CGA and 5-HIAA.

To estimate PFS and other indicators of efficacy in patients who crossover to pazopanib from placebo.

To estimate average time to submission of scans to the Alliance Imaging Core Laboratory (ICL) and average ICL "turn-around" time.

To estimate discordance between the local and central radiology review in assessment of progression.

To characterize the rates and quality of radiographic progression.

To assess differences in QOL-related domains between the two treatment groups.

To determine if the more brief measures of QOL-related domains provide comparable information to that which is provided by the longer assessments.

To provide validation data for the EORTC NET21 module in terms of responsiveness over time and differences across arms.

Patient Population

Patients must have low- or intermediate-grade neuroendocrine carcinoma, including the following subtypes: carcinoid tumor, low- to intermediate-grade or well- to moderately-differentiated neuroendocrine carcinoma or tumor, or atypical carcinoid tumor. Patients must have locally unresectable or metastatic carcinoid tumors arising in the foregut, midgut, hindgut, or other non-pancreatic site. Patients must have radiological evidence for progressive disease within 12 months prior to registration. Patients must have measurable disease per RECIST 1.1. Patients with tumors arising in the midgut must have progressed on octreotide. Patients must not have known endobronchial lesions and/or lesions infiltrating major pulmonary vessels that increase the risk of pulmonary hemorrhage. Patients must not have clinical evidence of brain metastases or carcinomatous meningitis.

Patients must not have received prior treatment with an inhibitor of VEGF or VEGFR. Treatment with strong inhibitors of CYP3A4 must be discontinued 14 days prior to start of study treatment. Other prior treatment must be completed at least four weeks prior to registration, and any treatment-related toxicities must have improved to Grade 1 or lower. Prior treatment with embolization or ablative therapies is allowed if measurable disease remains outside of the treated area or there is documented disease progression in a treated site. Patients should have completed any major surgery at least four weeks prior to registration and must have completed any minor surgery at least two weeks prior to registration.

Patients must be at least 18 years of age and have ECOG performance status of 0-1. Patients must have adequate cardiac, hematologic, hepatic, renal, immunologic, and clotting function. Patients with symptomatic peripheral vascular disease are not eligible.

Stratification/Descriptive Factors

Patients are stratified by (1) site of primary: small bowel (defined as tumors arising in the small bowel, cecum, appendix, or unknown primary site) vs other; and (2) concurrent somatostatin analog: yes vs no.

Accrual Goals

The accrual goal for this study is 150 patients. Interim analyses for futility will be conducted when 38% and 75% of the expected number of events have been observed.

Summary Statement

For the current status of this study, please refer to the Gastrointestinal chapter.

A041202 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

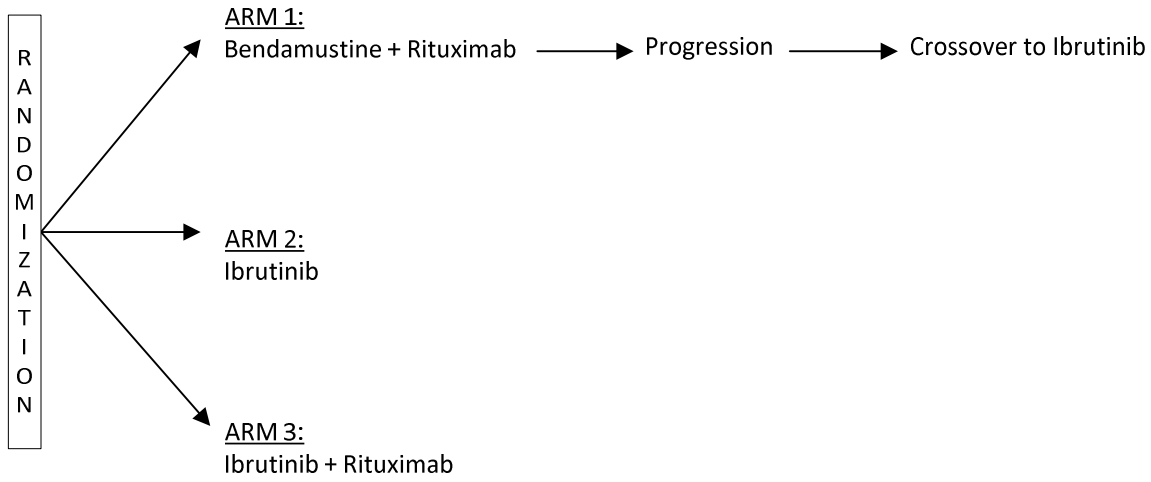
A Randomized Phase III Study of Bendamustine plus Rituximab Versus Ibrutinib plus Rituximab Versus Ibrutinib Alone In Untreated Older Patients (≥ 65 Years of Age) With Chronic Lymphocytic Leukemia (CLL)

Participants:
Alliance, SWOG, CTSU

Date Activated:
12/10/2013

Study Chairs:
J Woyach (Alliance), S Coutre (SWOG)

SCHEMA



Objectives

To determine whether progression free survival (PFS) is superior after therapy with bendamustine in combination with rituximab, ibrutinib alone, or ibrutinib in combination with rituximab in patients age 65 or older with previously untreated CLL.

To determine 2-year PFS in each of the three treatment arms.

To determine which treatment arm produces superior overall survival (OS).

To determine the complete response (CR) rate, complete and nodular partial response (CR/nPR) rate, and overall response (PR+nPR+CR) rate (ORR) among the three treatment arms and compare these arms.

To determine the impact of MRD-negative disease at time of CR documentation and at 2 years on PFS and OS in each of the treatment arms.

To determine duration of response after each of the three treatments and compare these treatment arms.

To determine toxicity and tolerability of the three treatment regimens.

To determine response and PFS of patients initially on the bendamustine in combination with rituximab arm who cross over to ibrutinib.

To determine whether baseline cytogenetic markers, Zap-70 methylation, IgVH mutational status, or select DNA mutations predict outcomes or time to response in these three arms.

To determine whether local FISH results for del(11q22.3) and del(17p13.1) are consistent with central analysis.

To determine whether baseline microRNA and gene expression markers are correlated with clinical outcomes of interest (e.g. progression-free and alive at 2 years versus not), as well as to explore changes in microRNA expression from baseline to post-treatment time points, with a focus on those with persistent lymphocytosis and relapse.

To determine whether eradication of MRD predicts longer duration of response with standard therapy and ibrutinib-based regimens.

To describe the baseline functional status, comorbid medical conditions, and number of medications of older CLL patients who meet criteria for therapy.

To determine how functional status changes with therapy using baseline to 3-month evaluation and end-of-study/2-year evaluation; to determine whether this change is different among the treatment groups.

To determine whether geriatric assessment variables known to be associated with chemotherapy toxicity in other disease groups can also predict therapy-associated toxicity in the CLL population.

To assess whether the FCGR3A polymorphism (rs396991) is correlated with depth of response (MRD status) to ibrutinib plus rituximab after six cycles, with secondary endpoints CR rate, rapidity of response, and progression-free survival (PFS).

To assess whether C1QA polymorphism (rs172378) is correlated with MRD status, CR rate, rapidity of response, and PFS.

Patient Population

Patients must be diagnosed with CLL in accordance with IWCLL 2008 criteria as defined in the protocol. Patients must have intermediate or high-risk Rai stage CLL. Patients must not have any prior history of Richter's transformation or prolymphocytic leukemia.

Patients must not have had prior therapy for CLL (except palliative steroids or treatment of autoimmune complications of CLL with rituximab or steroids). Treatment with rituximab and/or high dose corticosteroids for autoimmune complications of CLL must be completed at least four weeks prior to enrollment. Palliative steroids must be at a dose not higher than 20 mg/day of prednisone or equivalent corticosteroid at the time of registration. Patients must not be receiving active systemic anticoagulation with heparin or warfarin. Patients must be off warfarin therapy for at least 30 days prior to enrollment. Patients must not have had major surgery within ten days or minor surgery within seven days of enrollment.

Patients must be at least 65 years of age and have ECOG performance status of 0-2. Patients with active hepatitis B are not eligible. Patients with a positive hepatitis B core antibody but with negative hepatitis B DNA may participate, but must have hepatitis serologies and hepatitis B DNA monitored periodically. Patients must not have uncontrolled active systemic infection requiring intravenous antibiotics. Patients must have adequate hematologic, renal, cardiac and hepatic function. Patients with HIV are eligible if their CD4 count is ≥ 350 cells/mm^3 and if they are not taking prohibited CYP-interacting medications. Patients must not have a known allergy to mannitol or prior significant hypersensitivity to rituximab.

Stratification/Descriptive Factors

Patients are stratified by (1) Rai stage: intermediate vs high; (2) presence or absence of del(11q22.3) or del(17p13.1) on FISH; and (3) methylation of CpG 3 on Zap-70: $< 20\%$ vs $\geq 20\%$. In the event that a sample dose not yield a Zap-70 methylation status, data will be input based on IgVH mutation status: $>$ 20 if IgVH mutated or $<$ 20 for unmutated.

Accrual Goals

A total of 498 evaluable patients will be accrued to this study. The study will conduct three interim analyses taking place after approximately 33%, 50% and 75% of events have occurred.

Summary Statement

For the current status of this study, please refer to the Leukemia chapter.

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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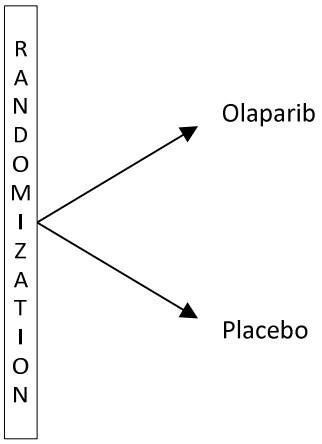
Participants:
NRG, SWOG, CTSU

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 invasive breast primary cancer and/or new epithelial ovarian cancer.

To assess the effect of olaparib on patient reported outcomes using the FACIT fatigue scale and EORTC QLQ-C30 QoL scale.

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).

Patient Population

Patients must have histologically confirmed non-metastatic primary triple negative 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) prior therapy: neoadjuvant vs adjuvant; and (2) prior platinum therapy for current breast cancer: yes vs no.

Accrual Goals

Approximately 1,320 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 660 patients recruited, estimated to be approximately 4.5 years after the first patient is randomized.

Summary Statement

For the current status of this study, please refer to the Breast chapter.

C30610 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer Also Receiving Cisplatin and Etoposide

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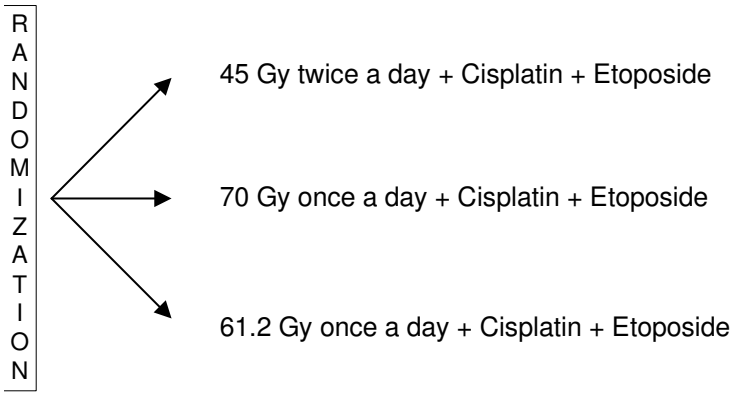
Participants:
Alliance, SWOG, CTSU

Date Activated:
03/21/2008

Study Chairs:
J Bogart (Alliance), L Gaspar (SWOG)

SCHEMA



Objectives

To determine whether administering high dose thoracic radiotherapy, 70 Gy or 61.2 Gy, will improve median and two-year survival compared with 45 Gy in patients with limited stage small cell lung cancer.

To compare response rates, failure-free survival, and toxicity between these thoracic radiotherapy regimens.

To compare rates of local relapse, distant metastases, and brain metastases.

To compare patients' quality of life between these treatment regimens in terms of their physical symptoms, physical functioning, and psychological state.

To describe the patterns of use of thoracic intensity modulated radiation therapy (IMRT) in patients with limited stage small cell lung cancer.

To examine blood-based biomarkers of response and resistance to cisplatin and etoposide.

Patient Population

Patients must have histologically or cytologically documented limited stage small cell lung cancer. Patients must not have had prior radiotherapy or chemotherapy for limited stage small cell lung cancer. Patients with complete surgical resection of disease are not eligible.

Patients must have adequate hematologic, hepatic, and renal function with an ECOG performance status of 0-2. Patients must be offered participation in the

substudies for correlative science (C150712) and quality of life (C7072).

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following factors: (1) gender: male vs female; (2) weight loss during the six months prior to study entry: ≤ 5% vs > 5%; (3) performance status: 0 vs 1 vs 2; (4) radiotherapy technique: IMRT vs 3D.

Accrual Goals

The implementation of the study will be divided into two stages (see protocol for details) and will enroll 670-712 patients.

Summary Statement

For the current status of this study, please refer to the Lung chapter.

C51101 Phase II SWOG Supported CTSU Study

Coordinating Group: Alliance

A Randomized Phase II Trial of Myeloablative versus Non-myeloablative Consolidation Chemotherapy for Newly Diagnosed Primary CNS-B-cell Lymphoma

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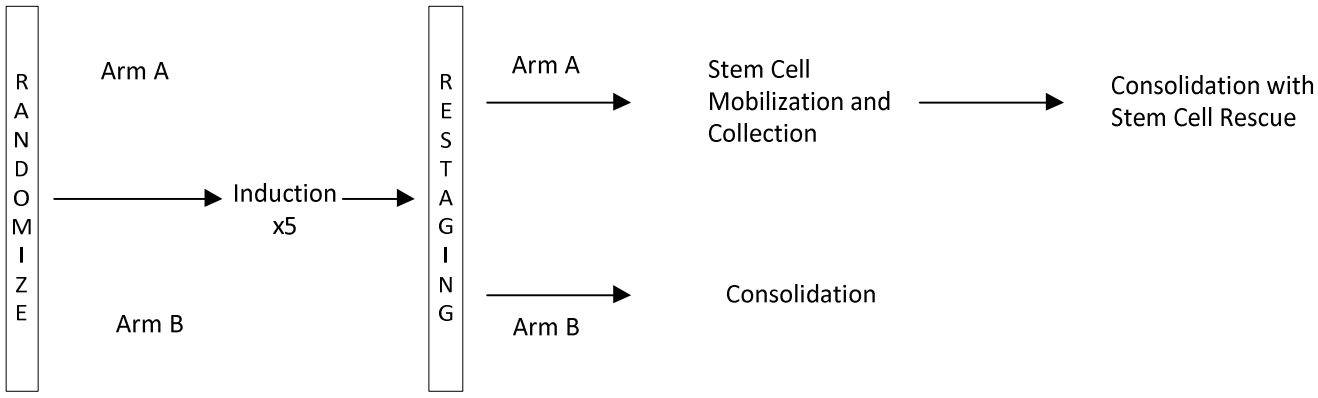
Participants:
Alliance, SWOG, CTSU

Date Activated:
07/01/2012

Study Chairs:
T Batchelor (Alliance), N Mohile (SWOG)

SCHEMA



Objectives

To compare the two-year progression-free survival (PFS) of patients treated with the myeloablative consolidation treatment strategy of HDT/ASCT versus those treated with non-myeloablative consolidation chemotherapy with cytarabine and etoposide.

To compare the two-year event-free survival (EFS) and the overall survival (OS) of patients treated with consolidation HDT/ASCT versus those treated with consolidation chemotherapy consisting of etoposide and cytarabine.

To assess the toxicities associated with consolidation HDT/ASCT versus consolidation consisting of etoposide and cytarabine.

To determine diffusion MRI metrics (ADCmini, ADC25%, and ADCmean) prior to induction chemotherapy, after one full induction chemotherapy cycle, and at the end of induction chemotherapy as a predictor of response and outcome.

To determine brain FDG-PET metrics (tumor SUV and tumor versus background SUV) prior to induction chemotherapy, after one full induction chemotherapy cycle, and at the end of induction chemotherapy as a predictor of response and outcome.

To determine whether low baseline ADC measurements are associated with shorter PFS and OS.

To determine whether reduction in tumor SUV by > 25% on brain FDGPET/CT after one cycle of induction therapy is associated with improved PFS and OS.

To determine which IHC-based biomarkers are predictive of an adverse prognosis.

To determine which IHC-based biomarkers are predictive of a favorable prognosis for BCL6 (B-cell CLL/lymphoma 6), and STAT 6 (signal transducer and activator of transcription 6, interleukin-4 induced).

To analyze tumor tissue for gene expression profiles, and to correlate these profiles with treatment outcomes.

To determine whether CSF proteome is a predictor of outcomes (prognostic marker) irrespective of treatment arm for IL-10 (interleukin 10) and C3 (complement component 3).

To assess the neurocognitive function of patients treated with consolidation HDT/ASCT versus those treated with consolidation chemotherapy (etoposide and cytarabine) as measured by serial administration of the International PCNSL Collaborative Group (IPCG) neurocognitive battery and evaluate the long-term survivorship differences between the two arms.

To assess the quality of life of patients treated with consolidation HDT/ASCT versus those treated with consolidation etoposide and cytarabine as measured by the EORTC Quality of Life Questionnaire-Core 30/Brain Cancer Module-20 (EORTC-QLQ30/BCM20), and to evaluate the long-term survivorship differences between the two arms.

Patient Population

Patients must have confirmed central nervous system (CNS) diffuse large B-cell lymphoma. Patients must have no evidence or history of non-Hodgkin lymphoma (NHL) outside of CNS. Patients must not have isolated ocular lymphoma.

Patient must not have received any prior chemotherapy or radiation therapy for lymphoma. Patients must have no history of organ transplantation or ongoing immunosuppressant therapy.

Patients must be between 18 to 75 years old and have Karnofsky Performance Scale (KPS) ≥ 30 (≥ 50 for patients ages 60-70). Patients must have adequate cardiac, pulmonary, hematologic, renal, and hepatic function. Patients must be HIV negative and HCV negative (unless HBsAb positive patients has recently received HBV vaccine, in this case HBcAb should be negative).

Stratification/Descriptive Factors

Patient randomization will be stratified by age and KPS score: age < 51 years vs age ≥ 51 years and KPS ≥ 70 vs age ≥ 51 years and KPS < 70.

Accrual Goals

A total of 160 patients will be accrued to this study (80 per arm).

Summary Statement

For the current status of this study, please refer to the Lymphoma chapter.

C90203 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Randomized Phase III Study of Neo-Adjuvant Docetaxel and Androgen Deprivation Prior to Radical Prostatectomy Versus Immediate Radical Prostatectomy in Patients with High-Risk, Clinically Localized Prostate Cancer

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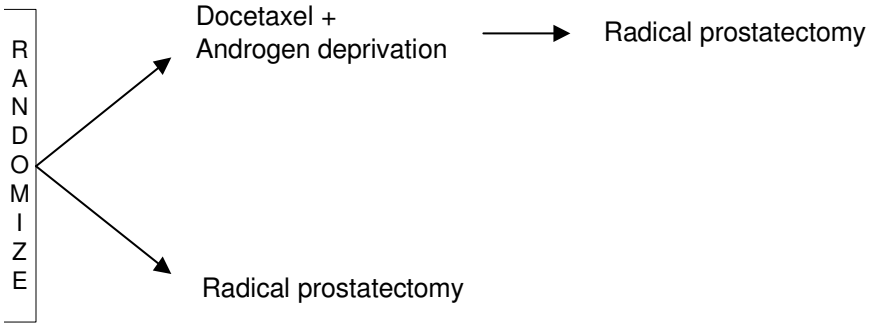
Participants:
Alliance, SWOG

Date Activated:
07/01/2007

Study Chairs:
J Eastham (Alliance), D Lin (SWOG)

SCHEMA



Objectives

To determine whether treatment with neoadjuvant docetaxel and androgen deprivation therapy prior to radical prostatectomy will increase the rate of three-year biochemical progression-free survival (bPFS) compared to treatment with immediate radical prostatectomy alone for high-risk prostate cancer patients.

To compare the five-year bPFS rate, bPFS, disease progression, disease-free survival, and overall survival of patients randomized to the two arms of this trial.

To determine the safety and tolerability of neoadjuvant docetaxel and androgen deprivation therapy prior to surgery for high-risk patients undergoing radical prostatectomy.

To compare the impact of neoadjuvant docetaxel and androgen deprivation therapy on time to clinically apparent local disease recurrence and metastatic disease in high-risk patients undergoing radical prostatectomy for clinically localized prostate cancer.

To compare the impact of neoadjuvant docetaxel and androgen deprivation therapy relative to radical prostatectomy on pathologic tumor stage, frequency of lymph node metastases, and positive margin rates for high-risk patients undergoing radical prostatectomy for clinically localized prostate cancer.

To determine if changes in serum testosterone levels will predict bPFS.

To determine prospectively whether PSA doubling time (PSADT) is a surrogate endpoint for time to clinical metastases and overall survival.

To evaluate associations between post-diagnosis diet and lifestyle, change in food group intake, and risk of prostate cancer recurrence, independent of treatment.

To identify novel protein expression patterns in serum that predict three-year and five-year bPFS rates in high-risk, clinically localized prostate cancer patients.

To identify novel protein expression patterns in serum that predict biochemical response to neoadjuvant chemotherapy and androgen deprivation therapy.

To determine if immunohistochemical staining profiles of primary tumors can predict three-year and five-year bPFS rates in high-risk, clinically localized prostate cancer.

To determine whether immunohistochemical staining profiles of primary tumors can predict biochemical response to neoadjuvant chemotherapy and androgen deprivation therapy.

To determine if genes identified during RNA expression analysis as being correlated with recurrence have protein expression that correlates with outcome.

Patient Population

Patients must have histologic documentation of stage T1-T3a prostatic adenocarcinoma. Patients must not have small cell, neuroendocrine, or transitional cell carcinoma. Patients must not have metastatic disease as demonstrated by negative biopsy in pelvic lymph nodes > 1.5 cm and negative bone scan. The Kattan nomogram predicted probability of being free from biochemical progression at five years after surgery must be ≥ 8.

Patients must not have any prior treatment for prostate cancer including surgery (excluding TURP), pelvic lymph node dissection, radiation therapy, or chemotherapy. Patients may have received up to four months of androgen deprivation therapy (LHRH agonists, antiandrogens, or both) prior to being enrolled on this study.

Patients must have an ECOG performance status of 0-2 and have adequate renal, hepatic, and hematologic function. Prestudy PSA must be ≤ 100 ng/mL.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) nomogram-predicted biochemical progression-free survival at five years: 0%-20.9% vs 21%-39.9% vs 40%-59.9% vs ≥ 60%; and (2) androgen deprivation therapy prior to randomization (≤ 4 months): yes vs no.

Accrual Goals

The accrual goal for this study is 750 patients (375 per arm). Interim analyses will be performed when the percentage of men with at least three years of follow-up reaches the following points: 30%, 40%, 50%, 60%, 70%, 80%, 90%, and 100%.

Summary Statement

For the current status of this study, please refer to the Genitourinary chapter.

E1411 Phase II SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

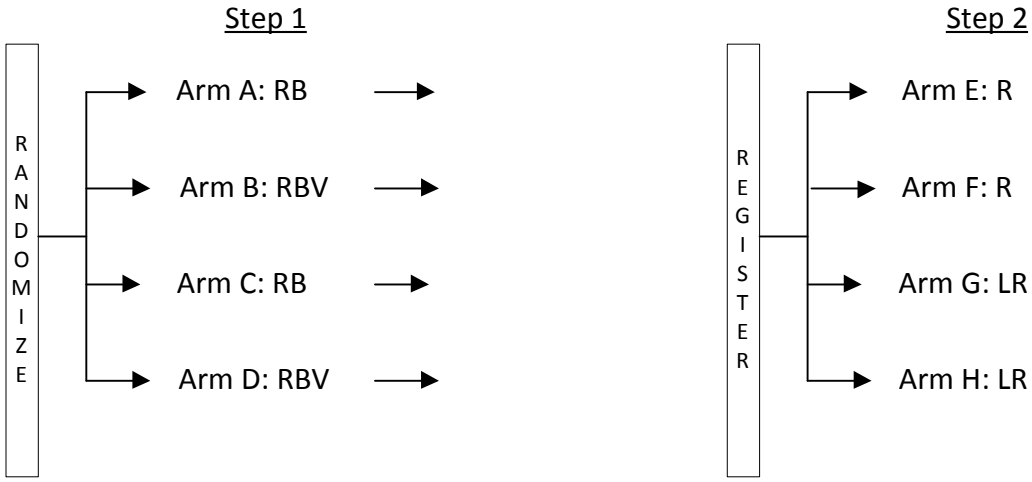
Intergroup Randomized Phase II Four Arm Study in Patients with Previously Untreated Mantle Cell Lymphoma of Therapy with: Arm A = Rituximab + Bendamustine Followed by Rituximab Consolidation (RB → R), Arm B = Rituximab + Bendamustine + Bortezomib Followed by Rituximab Consolidation (RBV → R), Arm C = Rituximab + Bendamustine Followed by Lenalidomide + Rituximab Consolidation (RB → LR) or Arm D = Rituximab + Bendamustine + Bortezomib Followed by Lenalidomide + Rituximab Consolidation (RBV→ LR)

Participants:
ECOG-ACRIN, SWOG, CTSU

Date Activated:
06/15/2012

Study Chairs:
M Smith (ECOG-ACRIN), B Till (SWOG)

SCHEMA



RB: Rituximab + Bendamustine
RBV: Rituximab + Bendamustine + Bortezomib

R: Rituximab
LR: Lenalidomide + Rituximab

Objectives

To determine whether the addition of bortezomib (RBV) to an induction regimen of rituximab bendamustine (RB) improves progression-free survival (PFS) compared to RB alone in patients > 60 years of age with previously untreated mantle cell lymphoma.

To determine whether the addition of lenalidomide to a consolidation regimen of rituximab following an induction regimen of RB or RBV improves PFS compared to consolidation rituximab alone in this patient population.

To determine whether the addition of bortezomib to induction therapy improves the PET-documented complete response rate compared to RB alone.

To determine whether the addition of lenalidomide to consolidation therapy improves CR and ORR compared with rituximab alone among patients who do not have PET-documented CR at the end of induction.

To determine overall survival (OS) in the treatment arms.

To determine safety, with attention to the addition of bortezomib in the induction regimen and lenalidomide-rituximab as consolidation therapy.

To determine the extent and severity of neuropathy associated with the addition of bortezomib to induction treatment using patient-reported outcomes data.

To determine the extent of severity of fatigue associated with the addition of lenalidomide to consolidation treatment using patient-reported outcomes data.

To evaluate the effects of the addition of bortezomib and lenalidomide and the effect of bortezomib-related neuropathy on patient-reported health-related quality of life.

To evaluate the response of lymphoma-specific symptoms to treatment.

To describe the trajectory of lymphoma symptoms, neuropathy, fatigue and overall health-related quality of life prior to, during and following treatment among older adults with MCL using longitudinal patient-reported outcomes data.

See protocol for objectives for laboratory correlative studies, imaging correlative studies, and residual disease assessment by molecular and flow cytometric techniques.

Patient Population

Patients must have histologically confirmed untreated mantle cell lymphoma (MCL). Patients must have at least one objective measurable disease parameter. Patients must have no known CNS involvement.

Patients must not have received prior therapy for MCL, except less than two week of steroid therapy for symptom control. Patients must not be participating in any other clinical trial or taking any other experimental medications within 14 days prior to registration.

Patients must have ECOG performance status 0-2 and adequate cardiac, hematologic, renal, and hepatic function. Patients must not have Grade 2 or greater peripheral neuropathy. HIV positive patients are not excluded, but may enroll with restrictions. Patients must have no hypersensitivity to bortezomib, boron or mannitol. Patients must agree that if randomized to Arms C or D, and proceed onto Arms G and H, they must register into the mandatory RevAssist program. Patients must have no medical contra-indications to DVT prophylaxis.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) mantle cell lymphoma IPI (MIPI) risk status: low risk vs intermediate risk vs high risk; and (2) age: < 60 vs ≥ 60.

Accrual Goals

A total of 332 patients will be accrued to this study.

Summary Statement

For the current status of this study, please refer to the Lymphoma chapter.

E1609 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Phase III Randomized Study of Adjuvant Ipilimumab Anti-CTLA4 Therapies Versus High-Dose Interferon Alfa-2b for Resected High-Risk Melanoma

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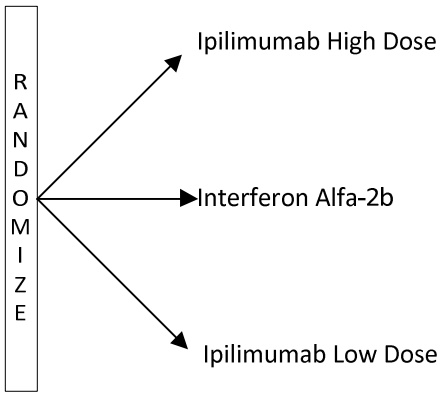
Participants:
ECOG-ACRIN, SWOG, CTSU

Date Activated:
06/08/2011

Study Chairs:
A Tarhini (ECOG-ACRIN), L Flaherty (SWOG)

SCHEMA



Objectives

First co-primary endpoint:

To evaluate recurrence-free survival (RFS) between patients randomized to receive post-operative adjuvant ipilimumab given at either 10 mg/kg (high dose ipilimumab; HIP) or 3 mg/kg (low dose ipilimumab; LIP) versus those randomized to receive high dose interferon alfa-2b (HDI) utilizing a heirarchical design assessing HIP versus HDI first and LIP versus HDI second (if the first comparison is significant).

Second co-primary endpoint:

To evaluate overall survival (OS) between patients randomized receive post-operative adjuvant HIP or LIP versus those randomized to receive HDI utilizing a heirarchical design assessing HIP versus HDI first and LIP versus HDI second (if the first comparison is significant).

Secondary endpoints:

To evaluate safety and tolerability of post-operative adjuvant ipilimumab therapy given at either 10 mg/kg or 3 mg/kg.

Among patients enrolled by CCOPs, to compare the global QOL between the ipilimumab arms versus HDI using FACT-G form and to evaluate the effect of treatment-related side effects that may have an impact on the health-related domains of QOL using FACITD and FACT-BRM.

Patient Population

Patients must have one of the following: selected Stage III (IIIB/IIIC) or selected Stage IV (M1a/M1b) melanoma of cutaneous origin; unknown primary melanoma presenting with cutaneous, subcutaneous, nodal and/or lung metastases with LDH within the institutional upper limit of normal; recurrence in a regional lymph node basin following resection of an original cutaneous primary; recurrence in the form of satellite/in-transit, distant skin/subcutaneous, nodal or lung metastases following resection of an original cutaneous primary or unknown primary melanoma; recurrence in a regional lymph node basin following a prior complete lymph node dissection and resection of an original cutaneous primary or unknown primary melanoma. All disease must be completely resected with free margins. Patients rendered free of disease by non-surgical means are not eligible. Patients with disease recurrence are eligible provided all relapsed disease has been completely resected with free margins. Patients must be randomized within 12 weeks of their most recent surgical procedure required to render the patient disease-free.

Patients must not have received any adjuvant treatment (chemotherapy, biotherapy, or limb perfusion). Previous radiation is allowed, including radiation following complete resection of disease. Patients must not have received any prior treatment with anti-CTLA4 monoclonal antibodies, CTLA-4 inhibitors/agonists, CD137 agonists, or interferon-alpha. Other forms of prior treatment for melanoma (e.g. IL-2, anti-tumor vaccine, chemotherapy) are allowed if completed prior to the resection(s) performed to render the patient free of disease.

Patients must have adequate hematologic, renal, and hepatic function and an ECOG performance status of 0-1. All females of childbearing potential must have a blood test or urine study to rule out pregnancy. Patients must not have any active infections requiring current treatment with parental antibiotics, autoimmmune disorders or conditions that require ongoing treatment with systemic corticosteroids, or a documented history of inflammatory bowel disease (including ulcerative colitis and Crohn's disease) or diverticulitis. Patients must not have had any infectious disease vaccination (e.g. standard influenza, H1N1 influenza, pneumococcal, meningococcal, tetanus toxoid) within four weeks prior to randomization. Patients must not have active or chronic infection with HIV, hepatitis B, or Hepatitis C. All patients must have negative testing for HIV, HBV, and HCV within four weeks prior to randomization.

Patients must submit tissue samples for central pathology review.

Stratification/Descriptive Factors

Treatment randomization will be stratified by AJCC Stage: IIIB vs IIIC vs M1a vs M1b.

Accrual Goals

A total of 1,500 patients will be enrolled.

Summary Statement

For the current status of this study, please refer to the Melanoma chapter.

E1912 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

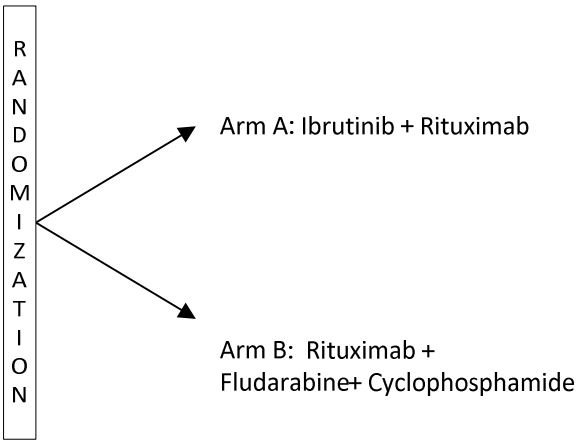
A Randomized Phase III Study of Ibrutinib (PCI-32765)-based Therapy vs Standard Fludarabine, Cyclophosphamide, and Rituximab (FCR) Chemoimmunotherapy in Untreated Younger Patients with Chronic Lymphocytic Leukemia (CLL)

Participants:
ECOG-ACRIN, SWOG

Date Activated:
02/07/2014

Study Chairs:
T Shanafelt (ECOG-ACRIN), S O'Brien (SWOG)

SCHEMA



Objectives

The primary objective for the trial is to evaluate the ability of ibrutinib-based induction therapy to prolong progression free survival (PFS) compared to standard FCR chemoimmunotherapy for younger patients with CLL.

To evaluate overall survival (OS) of patients based on treatment arm.

To monitor and assess toxicity of treatment with ibrutinib-based induction relative to standard FCR chemotherapy.

To compare quality of life (QOL) in CLL patients during the first six months of treatment among patients receiving ibrutinib-based induction therapy relative to standard FCR chemoimmunotherapy.

To compare QOL over the long-term in CLL patients receiving continuous therapy using ibrutinib to that of CLL patients who completed FCR therapy.

To determine the effect of pretreatment clinical and biological characteristics on clinical outcomes of the different arms.

To determine if the minimal residual disease (MRD) status as assessed by flow cytometry at different time points during and after treatment is an effective surrogate marker for prolonged PFS and overall survival.

To compare the genetic abnormalities and dynamics of intra-clonal architecture of CLL patients before and after treatment with CIT and non-CIT approaches and explore relationships with treatment resistance.

To explore the effects of FCR and ibrutinib-based therapy on T-cell immune function.

To conduct confirmatory validation genotyping of single nucleotide polymorphisms (SNPs) associated with the efficacy and toxicity of fludarabine-based therapy as in a prior ECOG GWAS analysis in the E2997 trial.

To evaluate the ability of a prognostic model that incorporates clinical and biologic characters to predict a response to therapy and clinical outcome (PFS, OS).

To evaluate signaling networks downstream of the B-cell receptor in patients receiving ibrutinib-based therapy.

To collect relapse samples to study mechanisms of resistance to both FCR and ibrutinib-based therapy.

Patient Population

Patients must have a diagnosis of CLL according to the NCI/WCLLL criteria or SLL according to the WHO criteria. Patients must meet at least one of the indications for treatment of CLL or small lymphocytic leukemia (SLL) listed in the protocol. Patients must not have deletion of 17p13 on cytogenetic analysis by FISH.

Patients must not have had prior chemotherapy or monoclonal anti-body therapy for treatment of CLL or SLL. Patients must not have had previous use of corticosteroids for autoimmune complications that have developed since the intial diagnosis of CLL. Patients must not have had major surgery within the last 28 days prior to registration or minor surgery within the last five days. Patients must not have had radiation therapy within four weeks prior to registration. Patients must not have received warfarin or another vitamin K antagonist in the preceding 30 days.

Patients must be between 18 and 70 years of age, life expectancy of at least 12 months, and have an ECOG performance status of 0-2. Patients must have adequate renal, hepatic and cardiac function. Patients must not have active hemolytic anemia requiring immunosuppressive therapy or other pharmacologic treatment. Patients with HIV infection may be eligible provided they meet the criteria listed in the protocol. Patients must not have uncontrolled infection or infection with known chronic, active hepatitis C, or positive serology for hepatitis B. Patients must not have had a cerebral vascular accident or intracranial bleed within the last six months.

Stratification/Descriptive Factors

At randomization, patients will be stratified as follows: (1) age at registration: < 60 years vs ≥ 60 years; (2) ECOG performance status: 0 or 1 vs 2; (3) disease stage: 3 or 4 vs 1 or 2; (4) baseline cytogenetic abnormalities on FISH: deletion 11q22.3(ATM) vs other.

Accrual Goals

The accrual goal of this study is 519 patients: 346 in arm A (Ibrutinib) and 173 patients in arm B (FCR). The first interim analysis will be performed when follow-up is available through the later of five years after the start of accrual or two years after accrual is completed. If this study is not at full information at this time, then interim analyses will be performed annually until full information is reached.

Summary Statement

For the current status of this study, please refer to the Leukemia chapter.

E1A11 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

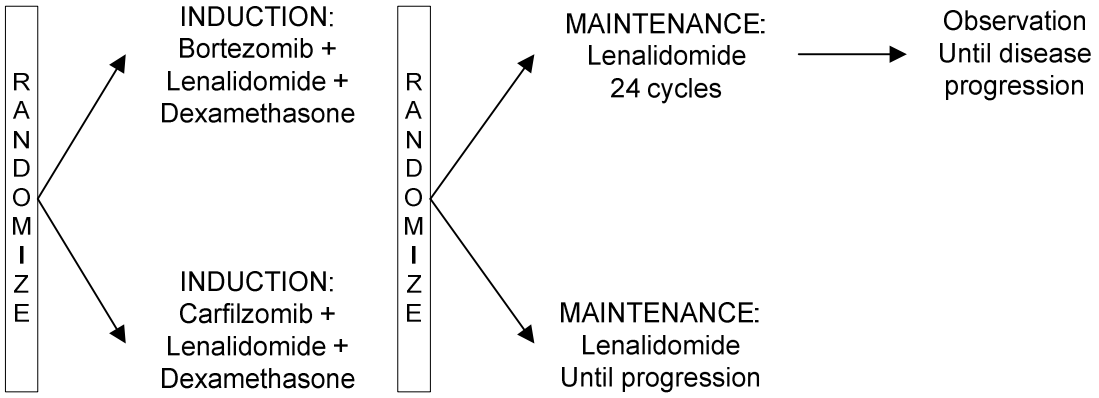
Randomized Phase III Trial of Bortezomib, LENalidomide and Dexamethasone (VRd) Versus Carfilzomib, Lenalidomide and Dexamethasone (CRd) Followed by Limited or Indefinite DURation Lenalidomide MaintenANCE in Patients with Newly Diagnosed Symptomatic Multiple Myeloma (ENDURANCE)

Participants:
ECOG-ACRIN, SWOG, CTSU

Date Activated:
11/22/2013

Study Chairs:
S Kumar (ECOG-ACRIN), A Cohen, J Zonder (SWOG)

SCHEMA



Objectives

To compare overall survival with the two different lenalidomide maintenance strategies

To compare the progression-free survival and safety of each lenalidomide maintenance approach

To compare the progression-free survival between induction treatments

To compare rates of response, duration of response, time to progression, overall survival, and safety of the induction therapies.

Patient Population

Patients must have been diagnosed with symptomatic standard-risk multiple myeloma within the last 90 days and have measurable or evaluable disease.

Patients must not have received lenalidomide, bortezomib, or carfilzomib for the treatment of symptomatic myeloma.

Patients must be at least 18 years of age with an ECOG performance status of 0-2, although 3 is allowed if it is secondary to pain. Patients must have adequate hepatic, renal and hematologic function. Prior malignancies are allowed if treated with curative intent that does not require active therapy. Gluticorticoid use is restricted following registration. Patients must use effective contraception.

Stratification/Descriptive Factors

At registration to induction therapy, patient randomization will be stratified by intent to stem cell transplant at progression: yes vs no. At registration to maintenance therapy, patient randomization will be stratified by induction treatment: Arm A vs Arm B.

Accrual Goals

Seven hundred fifty-six patients will be accrued to this study.

Summary Statement

For the current status of this study, please refer to the Myeloma chapter.

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, SWOG, 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

For the current status of this study, please refer to the Breast chapter.

E2108 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Randomized Phase III Trial of the Value of Early Local Therapy for the Intact Primary Tumor in Patients with Metastatic Breast Cancer

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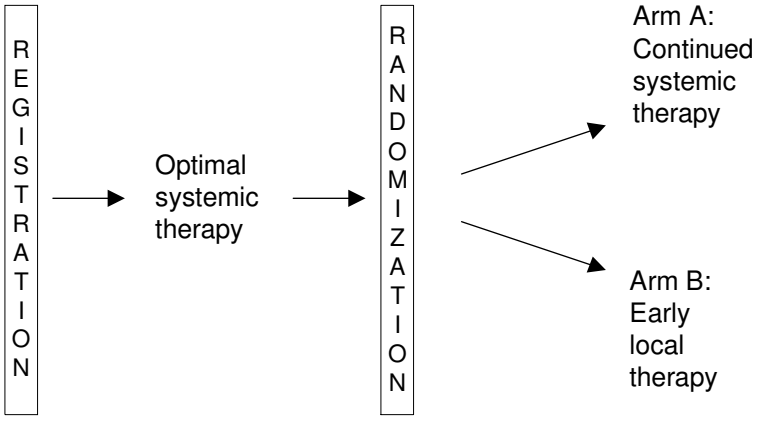
Participants:
ECOG-ACRIN, SWOG, CTSU

Study Chairs:
S Khan (ECOG-ACRIN), C Lee (SWOG)

Date Activated:
02/28/2011

Date Closed:
07/23/2015

SCHEMA



Objectives

To evaluate whether early local therapy of intact primary disease in women with Stage IV breast cancer whose disease does not progress during initial optimal systemic therapy, will result in prolonged survival, compared to women who receive local therapy for palliation only.

To compare the time to uncontrolled chest wall disease between patients who receive early local therapy versus patients who receive palliative local therapy.

To determine whether there is a difference in HRQOL between patients who receive early local therapy and those who receive palliative local therapy.

To determine whether the absolute value of the CTC burden at six months following randomization will be lower in Arm B than Arm A and whether this value is inversely related to survival.

To collect tumor and blood specimens for future exploration of the biological interactions between the primary tumor and metastatic lesions and the effect of primary tumor resection.

Patient Population

Patients must have an intact biopsy-proven primary (not recurrent) invasive carcinoma of the breast. Patients must not have bilateral disease. Patients should have at least one site of distant metastatic disease; if only a single metastatic lesion, this must be proven by biopsy. Radiology reports documenting status of disease must be available. Patients must not

have experienced distant disease progression since the start of systemic therapy.

Patients must have completed at least 16 weeks of optimal systemic therapy (appropriate to the tumor biological profile and patient's age and menopausal status). Patients must be randomized between 16 and 32 weeks of initiation of optimal systemic therapy and must not have experienced disease progression. Patients must be judged to be candidates for complete resection with free margins followed by radiation therapy. Local disease at the primary site must be asymptomatic.

Patients must have adequate organ function to undergo local therapy.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) marker status and treatment plan: ER+ or PR+, HER2-, and plan to treat with endocrine therapy alone vs ER+ or PR+, HER2-, and plan to treat with chemotherapy (with or without endocrine therapy) vs ER- or PR-, HER2- vs HER2+; and (2) number of organ systems with metastatic involvement: 1 vs >1.

Accrual Goals

Target accrual is 368 patients to accrue 258 responders to the randomized trial.

Summary Statement

For the current status of this study, please refer to the Breast chapter.

E2810 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

Randomized, Double-Blind Phase III Study of Pazopanib vs. Placebo in Patients with Metastatic Renal Cell Carcinoma Who Have No Evidence of Disease Following Metastatectomy

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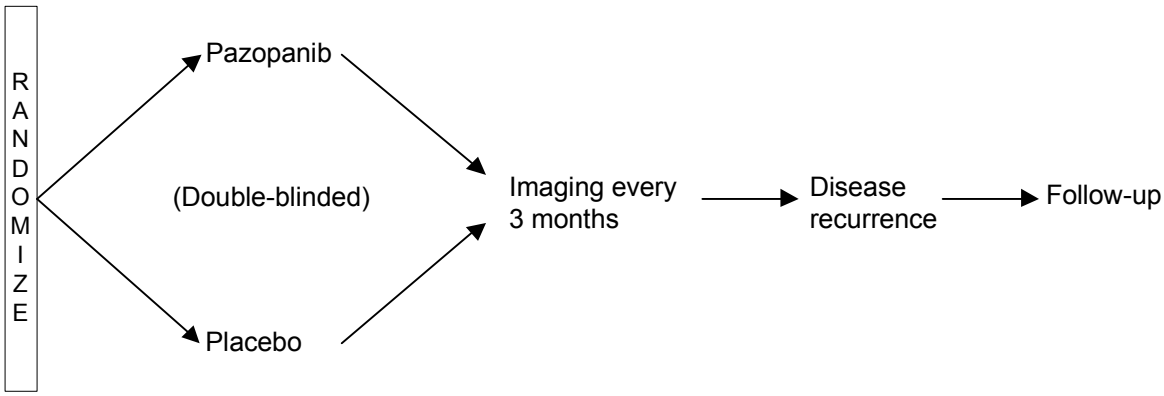
Participants:
ECOG-ACRIN, SWOG, CTSU

Date Activated:
04/17/2012

Study Chairs:
L Appleman (ECOG-ACRIN), S Pal (SWOG)

SCHEMA



Objectives

To evaluate disease-free survival of patient with renal cell carcinoma (RCC) treated with pazopanib as compared to placebo.

To describe the overall survival of patients with advanced RCC randomly assigned to receive placebo or pazopanib for one year following metastatectomy to NED.

To describe treatment- and (at recurrence) disease-related adverse events in the two treatment arms.

To analyze quality-adjusted time without symptoms of disease or treatment (Q-TWiST) for subjects in the two treatment arms.

To characterize changes in patient-reported fatigue and (at recurrence) kidney cancer-related symptoms during and following treatment with pazopanib compared to placebo.

To explore the association between plasma trough levels of pazopanib and disease-free and overall survival.

To prospectively bank preserved tissue from primary tumors and associated metastatic sites in patients with RCC.

Patient Population

Patients must have pathologically confirmed renal cell carcinoma with a clear cell component. Pure papillary and chromophobe histologies are excluded.

Patients must have undergone nephrectomy or partial nephrectomy to remove primary renal cell carcinoma. Patients must have undergone surgical resection to remove one or more sites of metastatic disease, with successful removal of all known sites two to twelve weeks prior to randomization. Eligible patients must have no evidence of disease on post-operative imaging. Patients must not have received any prior or concurrent systemic therapy for RCC; prior adjuvant placebo administration is permitted. Patients cannot be taking strong CYP3A4 inhibitors. Patients must not be taking drugs known to prolong the QTc interval; such drugs should be discontinued at least one week prior to randomization.

Patients must have ECOG performance status of 0 or 1 and adequate hematologic, renal, hepatic, and cardiac function. Patients must have no uncontrolled intercurrent illness. Patients must have no history of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess, myocardial infarction, cerebrovascular accident (CVA), hospital admission for unstable angina, cardiac angioplasty, or stenting, venous thrombosis, or hemoptysis in excess of 2.5 mL.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) disease-free interval: ≤ 1 year vs > 1 year; and (2) number of sites of metastatic disease resected at metastatectomy: 1 vs >1.

Accrual Goals

The accrual goal for this study is 128 patients (64 per arm). Interim analyses will be performed after 31% information is attained and then every six months until full information.

Summary Statement

For the current status of this study, please refer to the Genitourinary chapter.

E2906 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

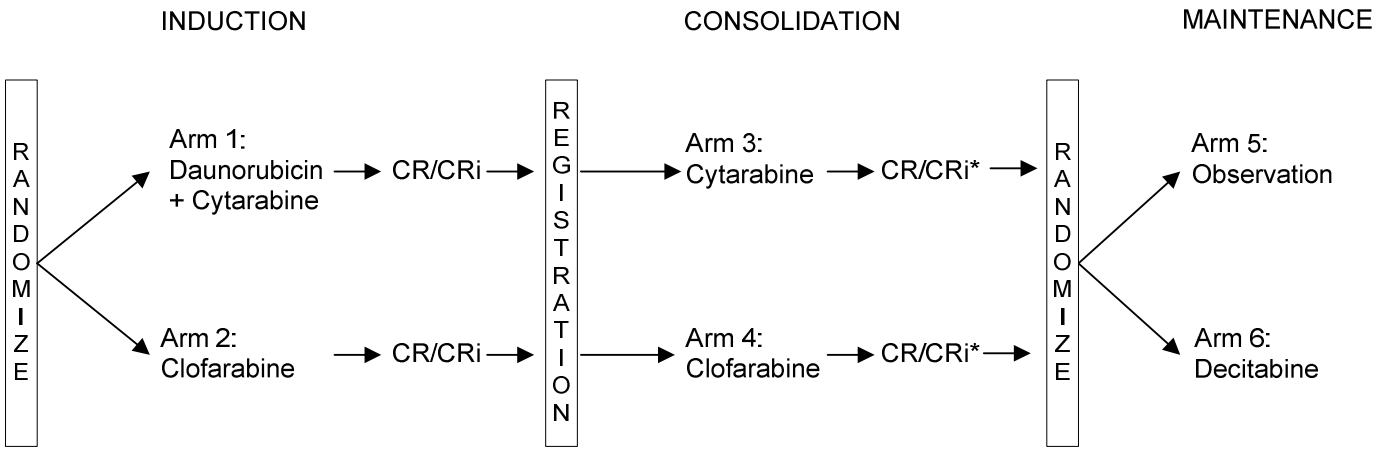
Phase III Randomized Trial of Clofarabine as Induction and Post-Remission Therapy vs. Standard Daunorubicin & Cytarabine Induction and Intermediate Dose Cytarabine Post-Remission Therapy, Followed by Decitabine Maintenance vs. Observation in Newly-Diagnosed Acute Myeloid Leukemia in Older Adults (Age ≥ 60 Years)

Participants:
ECOG-ACRIN, SWOG, CTSU

Date Activated:
02/24/2011

Study Chairs:
J Foran (ECOG-ACRIN), J Godwin (SWOG)

SCHEMA



*Note: Patients with an HLA matched donor who achieve CR/CRi or morphologic leukemia-free state will proceed to allogeneic Hematopoietic Stem Cell Transplantation after consolidation.

Objectives

To evaluate the effect of clofarabine induction and consolidation therapy on overall survival in comparison with standard therapy (daunorubicin + cytarabine) in newly-diagnosed AML patients age 60 years and older.

To evaluate complete remission (CR) rates, duration of remission, and toxicity/treatment-related mortality of clofarabine in comparison with standard therapy (daunorubicin + cytarabine) in newly-diagnosed AML patients age 60 years and older.

To evaluate the feasibility of consolidation with reduced-intensity conditioning and allogeneic hematopoietic stem cell transplantation from HLA-

identical donors in patients who achieve a response to induction therapy, including the incidence of successful engraftment, acute and chronic graft-versus-host disease, transplant-related mortality, and its impact on overall survival in comparison to patients receiving chemotherapy.

To evaluate the duration of remission and disease-free survival of patients in complete remission following completion of consolidation therapy who are subsequently randomized to receive scheduled low-dose decitabine maintenance in comparison with observation.

To perform expression and methylation profiling on all patients receiving decitabine and to correlate their integrated epigenetic signatures with response to decitabine.

To examine the epigenetic profiles of remission marrow in patients randomized to observation vs. decitabine to determine whether epigenetic signature of apparently morphologically normal bone marrow is predictive of relapse or response to decitabine maintenance.

To explore the possible association of response to clofarabine with nucleoside transporters hENT1, hCNT3, and ABC-transporter P-glycoprotein (Pgp).

To assess the expression of CXCR4 and to correlate its expression with other established prognostic factors in patients receiving induction treatments.

To compare health-related QOL (physical, functional, leukemia-specific well-being) and fatigue in elderly AML patients receiving standard induction therapy with those receiving clofarabine.

To measure the change in health-related QOL that occurs over time (within treatment groups).

To comprehensively assess patient function at the time of study enrollment.

To determine if components of a comprehensive geriatric assessment of QOL scales predict ability to complete AML treatment.

To describe the impact of transplant on QOL in AML patients above age 60.

Patient Population

Patients must have newly-diagnosed AML according to WHO classification and be considered candidates for intensive chemotherapy based upon examination of peripheral blood, bone marrow aspirate specimens, or touch preparations of the bone marrow biopsy. Patients must not have blastic transformation of chronic myelogenous leukemia. Patients with secondary AML are eligible. Patients with documented CNS involvement are not eligible.

Patients must not have received prior chemotherapy for AML with the exception of hydroxurea for increased blast count or leukapheresis for leukocytosis. Patients who have received a limited and short-term exposure of ATRA (all trans retinoic acid) while AML-M3 (Acute Promyelocytic Leukemia) was being ruled out, and which has been discontinued, will be eligible. Patients who have received previous treatment for antecedent hematologic disorder (AHD) with 5-azacitidine, decitabine, or low dose cytarabine are not eligible.

Patients must have an ECOG performance status 0-3 and reached their 60th birthday. Patients must have adequate cardiac, hepatic, and renal function. Patients must not have a concurrent active malignancy for which they are receiving treatment (other than MDS). Patients with known HIV infection are not eligible.

Stratification/Descriptive Factors

At initial randomization patients will be stratified by (1) age: 60-69 vs $\geq$ 70 years; (2) therapy-related AML: yes vs no; and (3) presence of AHD at the time of diagnosis of AML: yes vs no.

For the randomization to maintenance, treatment randomization will be stratified by (1) age: 60-69 vs $\geq$ 70 years; (2) cytogenetics: unfavorable vs other; and (3) induction treatment: arm 1 vs arm 2.

Accrual Goals

The accrual goal for this study is 747 patients. Up to nine interim analyses will be performed beginning when approximately 25% of planned full information has occurred. Interim analyses will include both futility and efficacy analyses.

Summary Statement

For the current status of this study, please refer to the Leukemia chapter.

E3A06 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

Randomized Phase III Trial of Lenalidomide versus Observation Alone in Patients with Asymptomatic Smoldering Multiple Myeloma

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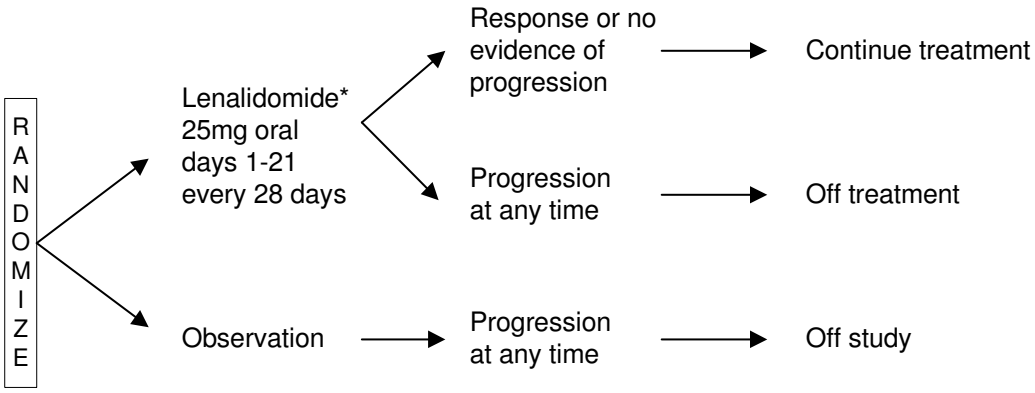
Participants:
ECOG-ACRIN, SWOG, CTSU

Date Activated:
02/01/2011

Study Chairs:
S Lonial (ECOG-ACRIN), M Dhodapkar (SWOG)

SCHEMA



*Mobilize stem cells following 4 cycles of therapy

Objectives

To compare progression-free survival (where failure is defined as death or the development of symptomatic multiple myeloma (MM) requiring therapy) between patients treated with lenalidomide versus observation alone in asymptomatic, smoldering/indolent multiple myeloma.

To compare the response rate, time to progression, one-year progression-free survival rate, duration of response, and overall survival between patients randomized to receive lenalidomide therapy versus observation alone for early-stage multiple myeloma.

To study the effects of lenalidomide on laboratory markers of immune function, evaluate the effect of IgH translocations, and gene expression profiling as predictors of response and risk of progression, and to study the prognostic value of MRI-detected asymptomatic bone disease on outcome.

To evaluate immune function as measured by SOX-2 and correlate to progression-free survival.

Patient Population

Patients must have previously untreated asymptomatic MM diagnosed within one year prior to registration. Patients with smoldering multiple

myeloma (SMM) are eligible. Patients with MGUS are not eligible.

Patients must have received no prior therapy for myeloma or SMM. Prior radiation therapy for the treatment of solitary plasmacytoma is permitted, but more than three months must have elapsed from the last day of radiation.

Patients must be 18 years of age or older. Patients must have an ECOG performance status between 0 and 2 and must not have Grade 2 or higher peripheral neuropathy or active, uncontrolled infection. Patients must not have baseline bone lesions or plasmacytomas.

Accrual Goals

Three hundred thirty-six patients will be randomized with equal allocation to lenalidomide versus observation.

Summary Statement

For the current status of this study, please refer to the Myeloma chapter.

N1048 Phase II/III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Phase II/III Trial of Neoadjuvant FOLFOX with Selective Use of Combined Modality Chemoradiation versus Preoperative Combined Modality Chemoradiation for Locally Advanced Rectal Cancer Patients Undergoing Low Anterior Resection with Total Mesorectal Excision

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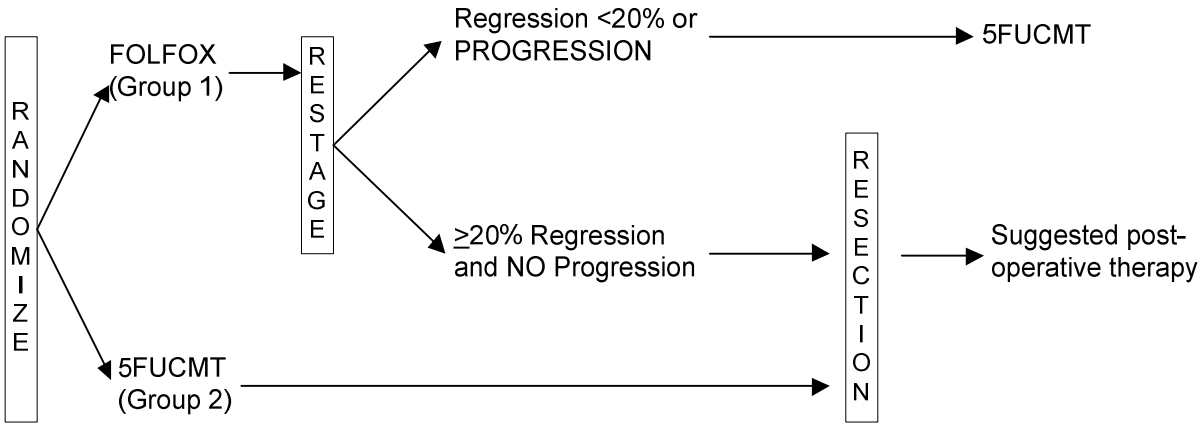
Participants:
Alliance, SWOG, CTSU

Date Activated:
01/13/2012

Study Chairs:
D Schrag (Alliance), C Eng (SWOG)

SCHEMA



Objectives

Phase II component primary objective:

To assure that neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) maintains the current high rate of pelvic R0 resection and is consistent with non-inferiority for time to local recurrence (TLR).

Phase III component primary objective:

To compare neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) to standard 5FUCMT (Group 2) with respect to the co-primary endpoints of the Time to Local Recurrence (TLR) and Disease-free Survival (DFS).

Secondary Objectives:

To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-inferior to the standard group 5FUCMT (Group 2) with respect to the proportion of patients who achieve a pathologic complete response (pCR) at the time of surgical resection.

To determine if the neoadjuvant FOLFOX followed by selective use of 5FUCMT (Group 1) is non-

inferior to the standard 5FUCMT (Group 2) with respect to overall survival.

To evaluate and compare the adverse event profile and surgery complications between two groups.

To estimate the proportion of patients in the selective group (Group 1) who receive: 1) pre-operative 5FUCMT; 2) post-operative 5FUCMT; 3) either pre- or post-operative 5FUCMT.

Patient Population

Patients must have rectal adenocarcinoma of clinical stage T2N1, T3N0 or T3N1. Patients must have radiologically measurable or clinically evaluable disease with tumor tissue evident between 5 and 12 cm from the anal verge. Tumor must not be adjacent to (within 3 mm of) the mesorectal fascia. Patients must not need abdominaloperineal (APR) at baseline.

Patients must not have had chemotherapy within five years prior to registration. Hormonal therapy is allowable if the disease free interval is five years or longer. Patients must not have had any prior pelvic radiation.

Patients must have an ECOG performance status 0-2 and be at least 18 years of age. Patients must have adequate hematologic, hepatic and renal function.

Stratification/Descriptive Factors

Patients will be stratified by ECOG performance status: 0 or 1 vs 2.

Accrual Goals

There will be total of 500 patients randomized to each group of this study (total of 1000 patients) if the trial completes the full phase III accrual. The phase II portion is defined as the first 366 randomized patients.

Summary Statement

For the current status of this study, please refer to the Gastrointestinal chapter.

N107C Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Phase III Trial of Post-Surgical Stereotactic Radiosurgery (SRS) Compared with Whole Brain Radiotherapy (WBRT) on Resected Metastatic Brain Disease

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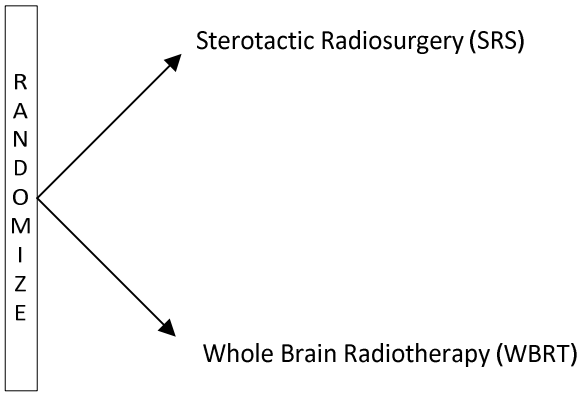
Participants:
Alliance, SWOG, CTSU

Date Activated:
07/08/2011

Study Chairs:
P Brown (Alliance), L Gaspar (SWOG)

SCHEMA



Objectives
Co-Primary Endpoints:

To ascertain in patients with one to four brain metastases whether there is improved overall survival in patients who receive stereotactic radiosurgery (SRS) to the surgical bed compared to patients who receive whole brain radiotherapy (WBRT).

To ascertain in patients with one to four brain metastases whether there is less neurocognitive progression at six months post-randomization in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

Secondary:

To ascertain whether there is improved QOL in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To ascertain whether there is improved time to central nervous system failure in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To ascertain whether there is longer duration of functional independence in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To ascertain in patients with one to four brain metastases whether there is better long-term neurocognitive status in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To tabulate and descriptively compare the post-treatment adverse events associated with the interventions.

To evaluate local tumor bed recurrence at six months with post-surgical SRS to the surgical bed in comparison to WBRT.

To evaluate time to local recurrence with post-surgical SRS to the surgical bed in comparison to WBRT.

To evaluate if there is any difference in CNS failure patterns (local, distant, leptomeningeal) in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

Correlative:

To evaluate radiation changes in the limbic system that may correlate with neurotoxicity using brain MRI scans.

To determine if Apo E (i.e. Apo E2, Apo E3, and Apo E4) genotyping may prove to be a predictor of radiation induced neurocognitive decline (or neuroprotection).

To determine if inflammatory markers (i.e. IL-2, IL-6, and TNF-alpha) may prove to be predictors of radiation induced neurocognitive decline.

To determine if oxidative stress biomarkers (i.e. protein carbonyl content, lipid hydroperoxides, and isoprostane levels) may prove to be predictors of radiation induced neurocognitive decline.

To determine if hormone and growth factors [i.e. glucocortcoids (e.g. cortisol), gonal steroids (e.g. estradiol, testosterone, progesterone), growth hormone, human chorionic gonadotropin (hCG), insulin-like growth factor-1 (IGF-1), and neuronal growth factor (NGF)] may prove to be a predictor of radiation induced neurocognitive decline.

Patient Population

Patients must have one to four brain metastases,as defined on a pre-operative brain MRI, with one brain lesion resected. Pathology from the resected brain lesion must be consistent with a non-central nervous system primary site. The resection cavity must measure < 5.0 cm in maximal extent on the post-operative brain MRI (or CT). Any unresected lesions must measure ≤ 3.0 cm in maximal extent on the contrasted pre-operative brain MRI. Patients may have active disease outside of the nervous sytem. Patients must be an appropriate candidate to be treated with either a gamma knife or a linear accelerator-based radiosurgery system. Patients must not have a brain metastasis that is located ≤ 5 mm of the optic chiasma or within the brainstem. Patients must not have widespread definitive leptomeningeal metastases, primary germ cell tumor, small cell carcinoma, or lymphoma.

Patients must not have received any prior cranial radiation therapy.

Patients must have an ECOG performance status of 0-2 and must be able to complete a neurocognitive examination without assistance. Patients must be willing and able to complete quality of life questionairres with or without assistance. Patients must be able to complete a MRI with contrast of the head and must not have a known allergy to gadolinium. Patients must be willing to provide mandatory blood and urine samples for correlative research purposes.

The SRS facility must be Radiological Physics Center (RPC) approved and the Neurocognitive Testing examiner must have credentialing confirming completion of the neurocognitive testing training.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) age: < 60 vs ≥ 60; (2) number of months extracranial disease controlled: ≤ 3 vs > 3; (3) number of pre-operative brain-metastases: 1 vs 2-4; (4) histology: lung vs radioresistant (brain metastases from a sarcoma, melanoma, or renal cell carcinoma histology) vs other; (5) resection cavity maximal diameter: ≤ 3cm vs > 3 cm.

Accrual Goals

A total of 192 patients, including an extra 18 to accomodate losses due to cancellations, ineligibility, or major protocol deviations.

Summary Statement

For the current status of this study, please refer to the Lung chapter.

R0848 Phase III SWOG Supported CTSU Study

Coordinating Groups: NRG and SWOG

A Phase III Trial Evaluating Both Erlotinib and Chemoradiation as Adjuvant Treatment for Patients with Resected Head of Pancreas Adenocarcinoma

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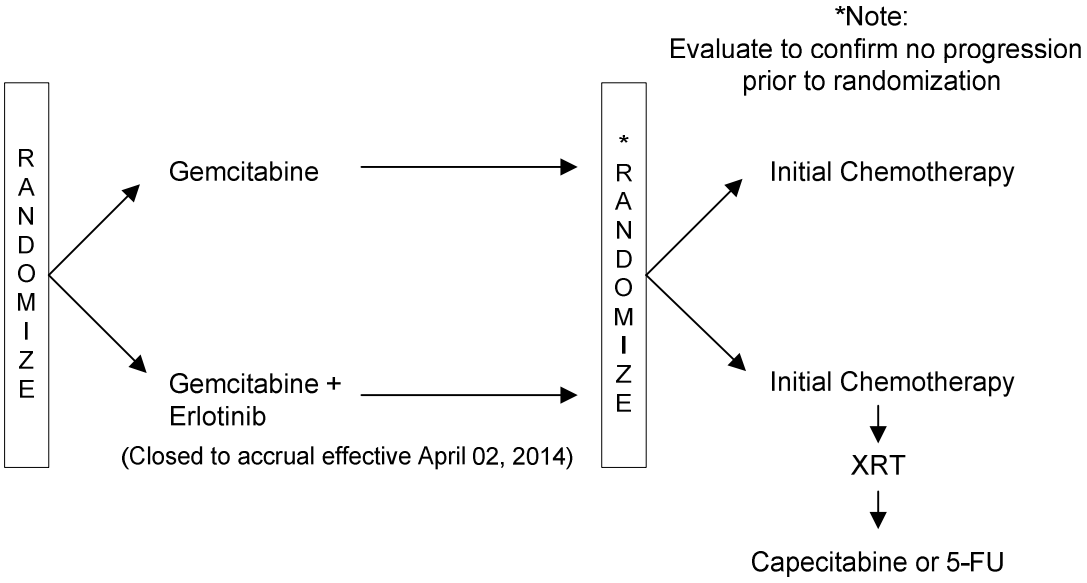
Participants:
NRG, SWOG, CTSU

Date Activated:
12/08/2009

Study Chairs:
R Abrams (NRG), P Philip (SWOG)

Statistician:
K Guthrie

SCHEMA



Objectives

To determine whether the addition of erlotinib to gemcitabine adjuvant chemotherapy improves survival as compared to gemcitabine alone following R0 or R1 resection of head of pancreas adenocarcinoma (including adenocarcinoma of the head, neck and uncinate process).

To determine whether the use of concurrent fluoropyrimidine and radiotherapy following adjuvant gemcitabine-based chemotherapy further enhances survival for such patients who are without evidence of progressive disease after five cycles of gemcitabine-based chemotherapy.

To evaluate disease-free survival of adjuvant chemotherapy followed by radiotherapy and concurrent fluoropyrimidine for patients with resected head of pancreas adenocarcinoma who are

disease-free after five cycles of adjuvant chemotherapy.

To evaluate disease-free survival of standard adjuvant gemcitabine chemotherapy with and without erlotinib for patients with resected head of pancreas adenocarcinoma.

To evaluate the disease-free and overall survival of standard adjuvant treatment with and without erlotinib for patients with resected head of pancreas adenocarcinoma by wild-type and mutant KRAS status.

To evaluate adverse events with and without erlotinib for patients with resected head of pancreas adenocarcinoma.

To evaluate adverse events of adjuvant chemotherapy with or without radiation therapy and concurrent fluoropyrimidine for patients with resected head of pancreas adenocarcinoma who are disease-free after adjuvant chemotherapy.

To evaluate preoperative cross-sectional imaging of the primary head of pancreas adenocarcinoma in order to determine the frequency with which objective criteria of resectability are present.

To determine the predictive roles of KRAS mutations and epithelial to mesenchymal transition (EMT) phenotype in response to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor in early-stage pancreas cancer.

To determine the frequency of EGFR-activated pathway and its influence on outcome in patients treated with gemcitabine and/or erlotinib, the association between developmental molecular markers and outcome of therapy, the phenotype and genotype of tumors in patients with recurrence after resection.

To determine if patients reporting low baseline fatigue, as measured by the FACIT-Fatigue, predicts survival and to explore correlations between baseline fatigue, as measured by PROMIS, and survival.

Patient Population

Patients must have histologic proof of primary head of pancreas invasive adenocarcinoma managed with a potentially curative resection. Patients with invasive adenocarcinoma that also contains a component of intraductal papillary mucinous neoplasm (IPMN) are eligible. Patients must have pathologic stage T1-3, N0-1 and M0 according to the 6th edition AJCC staging system. Patients with non-adenocarcinomas, adenosquamous carcinomas, islet cell tumors, cystadenomas, cystadenocarcinomas, carcinoid tumors, duodenal carcinomas, distal bile duct or ampullary carcinomas are not eligible.

Patients must have had removal of all gross tumor involving a classic pancreaticoduodenectomy, or a pylorus preserving pancreaticoduodenectomy. This surgery must have occurred within 21 and 56 days of registration. Patients managed with a total pancreatectomy, distal pancreatectomy, or central pancreatectomy are not eligible. Prior chemotherapy for pancreas cancer is not allowed. Patients with prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields are not eligible.

Patients must have adequate hematologic, hepatic and renal function and be at least 18 years of age. Patients must have a Zubrod performance status of 0 or 1. Patients with active HIV infection are eligible if their CD4 count is 499/mm^3 or greater and their viral load is 50 copies/ml or less (use of HAART is allowed).

Stratification/Descriptive Factors

At initial randomization patients will be stratified by (1) nodal status: involved vs uninvolved; (2) CA 19-9 results: 90 or less vs > 90-180; and (3) surgical margins: positive vs negative.

Accrual Goals

This study will accrue 950 patients. Three interim analyses will be performed.

Summary Statement

For the current status of this study, please refer to the Gastrointestinal chapter.

R1010 Phase III SWOG Supported CTSU Study

Coordinating Group: NRG

A Phase III Trial Evaluating the Addition of Trastuzumab to Trimodality Treatment of HER2-Overexpressing Esophageal Adenocarcinoma

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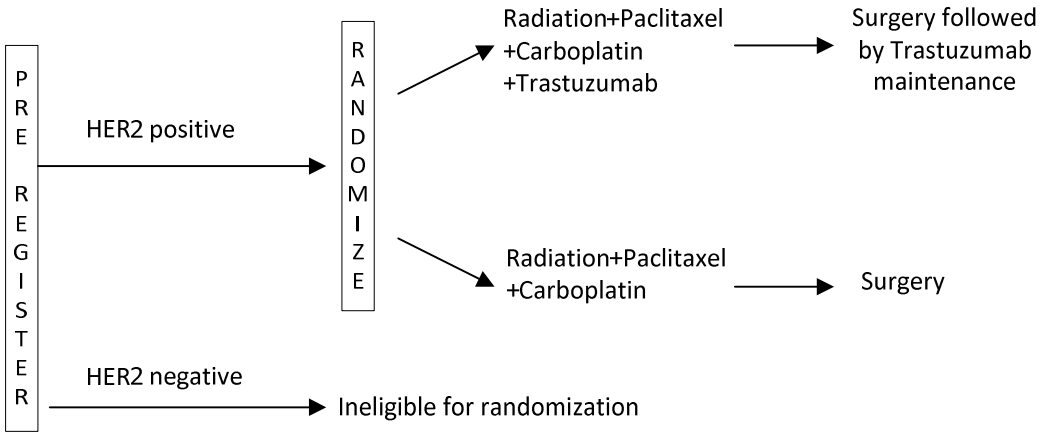
Participants:
NRG, SWOG, CTSU

Date Activated:
01/07/2011

Study Chairs:
H Safran (NRG), L Leichman (SWOG)

SCHEMA



Objectives

To determine if trastuzumab increases disease-free survival when combined with trimodality treatment (radiation plus chemotherapy followed by surgery) for patients with HER2-over expressing esophageal adenocarcinoma.

To evaluate if the addition of trastuzumab to tri-modality treatment increases the pathologic complete response rate and overall survival for patients with HER2-overexpressing esophageal adenocarcinoma.

To develop a tissue bank of tumor tissue from patients with non-metastatic esophageal adenocarcinoma.

To determine molecular correlates of complete pathologic response, disease-free survival, and overall survival for patients with HER2-overexpressing esophageal adenocarcinoma treated with neoadjuvant and maintenance trastuzumab.

To evaluate predictors of cardiotoxicity in patients with esophageal cancer treated with trastuzumab and chemoradiation.

To evaluate adverse events associated with the addition of trastuzumab to trimodality treatment for patients with non-metastatic esophageal adenocarcinoma.

To determine if the addition of trastuzumab to trimodality treatment improves the patient-reported Functional Assessment of Cancer Therapy for Esophageal Cancer (FACT-E) Esophageal Cancer Subscale (ECS) score.

To determine if an improvement in the FACT-E ECS score at 6-8 weeks post completion of neoadjuvant chemoradiation correlates with pathologic complete response.

To determine if pathologic complete response correlates with the FACT-E ECS score at one year and/or two years from the start of chemoradiation.

To determine if the addition of trastuzumab to trimodality treatment improves the Swallow Index and Eating Index Subscale scores of the FACT-E.

To determine if the addition of trastuzumab to paclitaxel, carboplatin, and radiation impacts quality-adjusted survival.

Patient Population

Patients must have pathologically confirmed primary adenocarcinoma of the esophagus that involves the mid (up to 25 cm), distal, or esophagogastric junction. The cancer may involve the stomach up to 5 cm. Patients must have had an endoscopy with biopsy. Patients must be stage T1N1-2, T2-3N0-2 according to the American Joint Committee on Cancer (AJCC) seventh edition staging, based upon the following minimum diagnostic work-up: chest/abdominal/pelvic CT or whole-body PET/CT; patients must have regional adenopathy including paraesophageal, gastric, gastrohepatic and celiac nodes; patients with tumors at the level of the carina or above must undergo bronchoscopy to exclude fistula. Patients with evidence of tracheoesophageal fistula or invasion into the trachea or major bronchi are not eligible. Patients with cervical esophageal carcinoma are not eligible.

Patients may not have received any of the following prior therapies: systemic chemotherapy for esophageal cancer, radiation for esophageal cancer, chest radiotherapy, anthracycline, taxane, any agent targeting the HER2 pathway or HER1 (EGFR) pathway, or trastuzumab.

Patients must be at least 18 years of age and have Zubrod performance status of 0-2. Patients must have adequate renal, hepatic, cardiac and bone marrow function, as defined in the protocol. Patients with medical contraindications to esophagectomy or prior allergic reaction to the study drugs involved in this protocol or to a monoclonal antibody are not eligible. Patients with acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration are not eligible.

Stratification/Descriptive Factors

Patient randomization will be stratified by presence of adenopathy: no vs yes - celiac absent vs yes - celiac present up to 2 cm.

Accrual Goals

The study is estimated to accrue 480 patients to randomize a total of 160 eligible HER2-positive patients.

Summary Statement

For the current status of this study, please refer to the Gastrointestinal chapter.