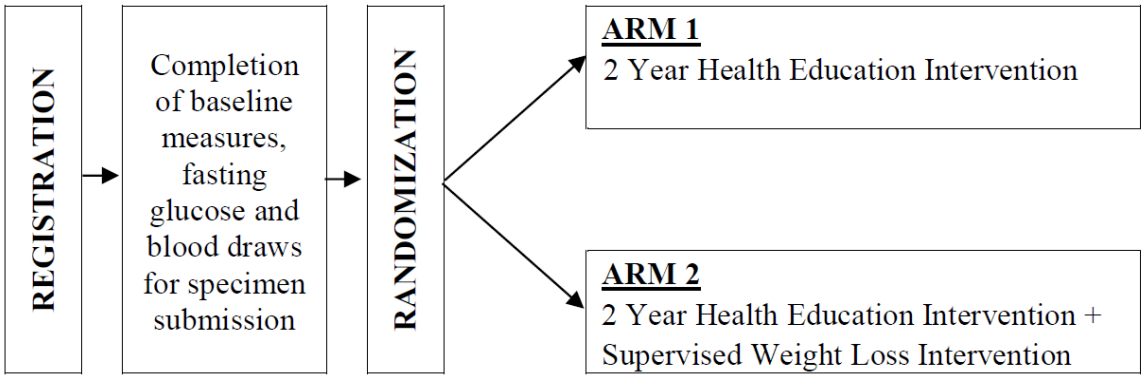
FAST FACTS

A011401 – Randomized Phase III Trial Evaluating the Role of Weight Loss in Adjuvant Treatment of Overweight and Obese Women with Early Breast Cancer

Schema



On-Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this treatment is appropriate.

Although they will not be considered formal eligibility (exclusion) criteria, physicians should recognize that the following may seriously increase the risk to the patient entering this protocol:
• Medical conditions such as uncontrolled infection (including HIV), or inflammatory bowel disease, which, in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.

In addition:
• Women should not be known to be pregnant or nursing, and should not plan to become pregnant within two years from registration.
• Patients should not be planning to undergo a major surgical procedure (e.g., hysterectomy) within 3 months after study registration. Breast reconstruction is allowed during study participation.

Documentation of Disease

- Subjects must have histologically confirmed invasive breast cancer and registration must occur within 16 months after the first histologic diagnosis of invasive breast cancer.
  - A core biopsy interpreted as invasive cancer meets this criterion; if no core biopsy is performed, the date of first histologic diagnosis will be the date of first surgical procedure that identifies invasive cancer (biopsy, lumpectomy or mastectomy).
  - Neoadjuvant subjects should have no evidence of clinical T4 disease prior to chemotherapy and surgery. See eligible cTNM classifications below. Eligibility for neoadjuvant patients can be

defined by either clinical stage prior to therapy or pathologic stage at surgery. If patient is eligible based on either, they are eligible for the study.

- Bilateral breast carcinoma is allowed provided either:
  1) Diagnoses are synchronous – that is, within 3 months of one another – and at least one of the two breast carcinomas meet the eligibility criteria and neither is Her-2 positive or inflammatory.
  OR
  2) The contralateral breast cancer was at least 5 years prior to the current diagnosis.
  • No evidence of distant metastatic or locally recurrent disease.

- Her-2 negative, defined as:
  - ISH ratio of < 2.0 (if performed)
  - IHC staining of 0-2+ (if performed)
  - Deemed to not be a candidate for Her-2 directed therapy.
- Eligible TNM Stages include:
  - ER and PR negative (defined as <1% staining for ER and PR by IHC):
    T2 or T3 N0, T0-3N1-3
    Note: Patients with T0N0, T1N0 and T1N1mi disease, and patients with T4 disease, are NOT eligible.
    ER and/or PR positive (defined as ≥ 1% staining for ER and/or PR on IHC):
    T0-3N1-3 or T3N0

Note:
Patients with T0N0, T1N0, T2N0, T1N1mi and T2N1mi disease
And patient with T4 disease are NOT eligible.

- The eligibility of neo-adjuvant subjects can be assessed on the basis of cTNM or ypTNM. The same eligible TNM combinations apply; patients may be eligible if they meet eligibility requirements at either time point, as long as they do not have T4 disease prior to therapy.
- No history of invasive breast cancer in 5 years prior to study registration other than the current diagnosis (prior DCIS at any time does not make a patient ineligible).
- Patients must have had a bilateral mammogram within 16 months prior to registration, unless the initial surgery was a total mastectomy, in which case only a mammogram of the remaining breast is required. (Subjects with bilateral total mastectomies do not require imaging).
- Investigations, including chest X-ray or CT chest, bone scan (with radiographs of suspicious areas) and abdominal ultrasound or liver scan or CT abdomen have been performed between the first histologic diagnosis and the time of registration as detailed below.
  - Chest X-Ray, 2 view (or Chest CT, or PET/CT) is required only if clinically indicated or recommended by NCCN guidelines.
  - Bone scans (with x-rays of abnormal areas) are required only if clinically indicated or recommended by NCCN guidelines.
  - Abdominal imaging is required only if clinically indicated or recommended by NCCN guidelines.

Prior Treatment

- All adjuvant or neoadjuvant chemotherapy, radiation, and surgery completed at least 21 days prior to registration.

- All triple negative patients must receive chemotherapy of the treating physician's choice.
- ER/PR+ patients must receive chemotherapy (of the treating physician's choice) unless Oncotype Dx or another genomic predictor score indicates that they are at low or intermediate risk of disease recurrence with endocrine therapy alone.
- Patients may have breast reconstruction during protocol participation, but definitive breast cancer surgery must be completed at least 21 days prior to registration.

Concomitant biologic therapy, hormonal therapy, and bisphosphonates are acceptable.

- Surgical margins must be clear of invasive carcinoma. If there is microscopic residual ductal in situ disease present at lumpectomy or total mastectomy margins, further excision is highly recommended. If further excision is not undertaken, the subject may still be entered on study, provided that in addition to breast or chest wall irradiation, a boost to the tumor bed is delivered. In situ lobular disease at the margin is acceptable.
- All subjects (both adjuvant and neoadjuvant) must have a sentinel lymph node biopsy and/or axillary lymph node dissection, as per pre-specified institutional guidelines.
- All women who undergo breast conserving therapy must receive concomitant radiotherapy. Radiation after mastectomy is to be administered according to pre-specified institutional guidelines. Radiation must be completed at least 21 days prior to registration.
- Patients with hormone receptor positive breast cancer as defined above must plan to receive at least 5 years of adjuvant hormonal therapy in the form of tamoxifen or an aromatase inhibitor, alone or in combination with ovarian suppression. (NOTE: for patients with ER and PR staining in less than 5% of cells, hormonal therapy for at least 5 years is strongly recommended but not required). Hormonal therapy can be initiated prior to or during protocol therapy.
- Participants must be women.
- Age ≥ 18 years
- ECOG Performance Status 0 or 1.

Comorbid Conditions

- No history of other malignancy within the past 4 years, except for malignancies with a >95% likelihood of cure (e.g. non-melanoma skin cancer, papillary thyroid cancer, in situ cervical cancer). Patients cannot have metastatic breast or other cancer.
- No diabetes mellitus currently treated with insulin or sulfonylureas.
- No history of serious digestive and/or absorptive problems, including inflammatory bowel disease and chronic diarrhea that preclude adherence to the study diet.
- No history of severe cardiovascular, respiratory or musculoskeletal disease or joint problems that preclude moderate physical activity. Examples would include unstable angina, recent myocardial infarction, oxygen-dependent pulmonary disease, and osteoarthritis requiring imminent joint replacement. Moderate arthritis that does not preclude physical activity is not a reason for ineligibility.
- No prior bariatric surgery or planning to undergo this procedure within the next 2 years after study registration.
- No use of weight loss medications (with the exception of metformin) at the time of study
- enrollment or plans to take these agents within the next 2 years after study enrollment.No comorbid conditions that would cause life expectancy of less than 5 years.

- No history of psychiatric disorders that would preclude participation in the study intervention (e.g. untreated major depression or psychosis, substance abuse, severe personality disorder) or prevent the patient from giving informed consent.
- No chronic (≥ 1 month) use of oral steroids at the time of study enrollment. Inhaled or topical steroids are acceptable. Patients previously taking oral steroids are required to undergo a 30-day washout prior to registration.

Other

- BMI ≥27 kg/m2 documented within 56 days prior to study registration. The most recent BMI obtained within that window must be used for eligibility. If most recent BMI is <27 then the patient is not eligible to enroll.
- Self-reported ability to walk at least 2 blocks (at any pace).
- Not participating in another weight loss, physical activity or dietary intervention clinical trial. Co-enrollment in some trials involving pharmacologic therapy is allowed. Participants in both arms are also allowed to pursue weight loss and physical activity programs on their own, as long as these programs are not provided as part of a clinical trial. For a list of acceptable trials for co-enrollment, please see the supplemental material titled "A011401 Acceptable Trials for Co-enrollment" document on the CTSU and Alliance websites.
- Able to read and comprehend spoken English or Spanish.
    a. *Eligibility is restricted to individuals who can comprehend and read English or Spanish given that participation in the study will require the ability to read lifestyle intervention materials and communicate with a coach through 42 phone calls over 2 years. The trial is unable to accommodate the needs of deaf participants as the study relies on spoken language to provide coaching.*