Colorado Cancer Wellness Conference 2019

Clinical Trials

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Clinical Trials

Colorado Cancer Wellness Conference
Saturday, September 14, 2019
UCHealth
Anschutz Medical Campus
Bruce Schroffel Conference Center

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Disclosures

None

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Learning Objectives

- Understand the different phases of a clinical trial
- Understand the benefits, risks and safety of a clinical trial
- Appreciate non-traditional clinical trials

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Clinical Trials

Taking part in any clinical trial is voluntary

Not all clinical trials study treatments

Some look at ways to prevent diseases

Many trials test new surgery or radiation therapy techniques

Trials will look at complimentary or alternative treatments

In cancer treatment patients always receive at least standard of care

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Phase I

Studies a new drug, typically first in human

The purpose is to find the highest tolerable dose of the new treatment

Must ensure the drug can be given safely without serious side effects

Safety is the main concern

The focus is to find out what the drug does to the body and what the body does to the drug

The number of people involved is small

Typically found in major cancer centers

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Phase II

If a new drug is found to be safe in Phase I, then it can move into Phase II to see if it works

The number of participants is typically 25 to 100

The patients have the same type of cancer

There is NO placebo

Mostly found at major cancer centers, but occasionally a community hospital or oncology offices will participate

If enough patients benefit with minimal side effects, the treatment will move on to Phase III

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Phase III

The main question being answered is whether the new treatment is better than the standard

Patients are randomized to either the standard treatment or the new treatment

These studies have large numbers of patients

They are often done in many locations even worldwide

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Phase 0 and Phase IV

Phase 0 trials are used to help speed up the drug approval process

The participants in Phase 0 clinical trials are less likely to benefit from the drug

Phase 0 studies are not used often, are very small, and only run for a short period of time

Phase IV studies look at drugs that are already FDA approved

Typically the safest trial because treatment is already been studied

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Benefits

The possibility of receiving the new treatment

More resources and access to more check-ups as part of your care

The opportunity to help others in the future receive better treatment

Access to additional resources that come with participating in a clinical trial

The ability to play an active role in your own health care

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Risks

Potential side effects from the new treatment

The new treatment may not be better than the standard of care

You may not get the new treatment

The trial could require additional time commitments for appointments or additional procedures

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Safety

There are laws now to protect study participants

Every clinical investigator is required to monitor and make sure that every participant is safe

Each clinical trial follows a detailed study plan that describes what the researchers will do

The principal investigator is responsible for making sure the protocol is followed

An Institutional Review Board (IRB), must approve every clinical trial

The IRB ensures that study participants are not exposed to unnecessary risks

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ALLIANCE A011401

Phase III Trial Evaluating the Role of Weight Loss in Adjuvant Treatment of Overweight

And Obese Women with Early Breast Cancer

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Study Status

Trial Activated August 29, 2016

Current Participating sites:

>1127 US sites /49 states

19 Canadian sites

Planned Enrollment 3136 Patients

Enrollment as of 8/15/2019

2249 Patients Randomized

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Background

Obesity is a growing health problem in the United States and increasingly, around the world.

Excess body weight has been linked to an increased risk of postmenopausal breast cancer and triple negative premenopausal breast cancer.

Growing evidence also suggests that obesity is associated with poor prognosis in women diagnosed with early stage breast cancer.

Despite the large body of observational data supporting a relationship between weight and breast cancer prognosis. **There is little information regarding the impact of weight loss upon the risk of recurrence and death in women with early stage breast cancer**.

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Objectives

Primary Objective

- To compare the effect of a supervised weight loss intervention plus health education materials versus health education alone upon invasive disease free survival in overweight (BMI 27-29.9kg/m^2) & obese (BMI ≥30kg/m^2) women diagnosed with HER-2 negative, stage II & III breast cancer.

Secondary Objective

- To determine the relationship between change in weight & iDFS, (invasive disease free survival) and to explore interaction between the level of clinical benefit from weight loss and the intervention.
- To evaluate the effect of a supervised weight loss intervention upon
  a. Overall survival
  b. Death from breast cancer
  c. Distant disease free survival
  d. Weight

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e. Body Composition

f. Insulin Resistance Syndrome associated conditions – diabetes, hospitalization for CV disease

g. Employment & work productivity

- Determine the impact of a supervised weight loss intervention on iDFS within subgroups of women
  1)HR + breast cancer
  2) HR- breast cancer.
- Determine the impact of a supervised weight loss intervention on iDFS within subgroups of 1) premenopausal women and 2) post-menopausal women.

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SCHEMA

REGISTRATIOn

Completion of baseline measures, fasting glucose and blood draws for specimen submission

RANDOMIZATION

ARM 1
2 Year Health Education Intervention

or

ARM 2
2 Year Health Education Intervention + Supervised Weight Loss Intervention

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Inclusion Criteria

Subjects must have histologically confirmed invasive breast cancer and registration must occur within 14 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.

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Inclusion criteria continued

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 & PR negative (defined as <1% staining for ER & PR by IHC): T2 or T3 N0, T0-3 N1-3
- ER &/or PR positive (defined as ≥ 1% staining for ER and/or PR on IHC): T0-3 N1-3 or T3N0

Neo-adjuvant patients are assessed on the basis of cTNM

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Inclusion criteria continued

No history of invasive breast cancer in 5 years prior to study registration other than current diagnosis(prior DCIS is acceptable)

TNBC pts. must have completed Chemo/Rad >21 days prior to registration

Age ≥ 18yrs

ECOG Status 0 or 1

BMI ≥27kg/m² documented within 56 days prior to registration

Self reported ability to walk at least 2 blocks

Be able to understand English or Spanish

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Exclusion Criteria

- No history of other malignancy within the past 4years, except for malignancies with a >95% likelihood of cure(e.g. non-melanoma skin cancer, papillary thyroid ca, in situ cervical 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 CV, Respiratory or Musculoskeletal disease or joint problems that preclude moderate physical activity.
- No prior bariatric surgery or planning to undergo this procedure within the next 2 years after registration
- No comorbid conditions that would cause life expectancy of less than 5 yrs
- No history of psychiatric disorders that would preclude participation in the study intervention.

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Prior/Concomitant Treatment

All adjuvant or neoadjuvant chemotherapy(at the discretion of the treating physician)& surgery completed at least 21days prior to registration.

Concomitant radiation, biologic therapy, hormonal therapy, & bisphosphonates are acceptable.

Surgical margins must be clear of invasive carcinoma.

All subjects must have sentinel lymph node biopsy & /or axillary lymph nodes dissection. SLN bx. alone criteria:

- SLN biopsy is negative/pN0
- SLN biopsy is positive for isolated tumor cells only/pN0

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Prior/Concomitant Treatment

Clinically node negative, T1-2 tumors with SLN positive in < 2 lymph nodes without matted nodes and undergoing breast conserving surgery and tangential whole breast irradiation, or undergoing mastectomy and chest wall irradiation.

All women who undergo breast conserving therapy must receive concomitant radiotherapy. Radiation can be administered either prior to or during protocol treatment.

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Prior/Concomitant Treatments

Patients with HR positive breast cancer, must 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. Hormonal therapy can be initiated prior to or during protocol therapy.

Concurrent enrollment in the other adjuvant trials involving pharmacologic therapies is allowed.

Participants can not participate in another weight loss, physical activity or dietary intervention **Clinical trial.**

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Study Calendars

Tests & Observations	Prior to Registra-tion	Randomi-zation	Month 6	Month 12 & 18	Month 24	Month 30 & 36	Annual Follow Up	iDFS events
History & Physical (within 56days prior to registration)	X		X	X	X	X	X	
Height (Section 8.3) (within 21days after registration, prior to randomizing)	X	X						
Weight (Section 8.3) (within 21days after registration ,prior to randomizing)	X	X	X	X	X	X	X	
Waist and Hip circumference (Section 8.3) (within 21 days after registration, prior to randomizing)	X		X	X	X	X	X	
Baseline patient Questionnaire(Appendix I (21days prior to registration)	X							
Follow Up patient Questionnaire			X	X	X	X	X	
AE assessment			X	X	X	X		
Outcome assessment			X	X	X	X	X	

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Staging	Prior to Registration	Randomization	Month 6	Month 12 & 18	Month 24	Month 30 & 36	Annual Follow up	iDFS events
Bilateral Mammogram(within 12months of registration)	X	Perform yearly while on study if applicable						
CXR or CT (Scans performed between 1st Histologic diagnosis and registration)	X	If clinically indicated						
Bone Scan	X	Required only if Alk Phos. is elevated or pt. is symptomatic If clinically indicated						
Abdominal x-ray or CT	X	Only required if Liver enzymes elevated or pt. is symptomatic						
Document initial breast cancer diagnosis, Histology(within 14months of registration)	X							
Laboratory (all Patients) (within 21 days of registration prior to randomizing)								
Fasting Status Validation Form		X	X		X			
Fasting Glucose(local)		X	X		X			
Fasting Blood draw (to Mayo BAP)		X	X		X			

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Specimen Collection

***12 hr. fasting**

	Baseline	Month 6	Month 24	Storage/ Shipping	Collection instructions	Submit to
For all patients registered to A011401, submit the following						
*Fasting Glucose (Gray top)	1 x 5ml	1x 5ml	1 x 5ml	Perform locally	Section 8.3	Do not ship
*Fasting plasma (Green top)	3 x 5ml	3 x 5ml	3 x 5ml	Frozen	Section 6.2.2	Mayo BAP
Fasting serum (Gold Top)	3 x 5ml	3 x 5ml	3 x 5ml	Frozen		Mayo BAP
For patients registered to A011401-Substudy1, submit the following						
Paraffin Block/cores of breast tissue from surgery	X Submit within 90 days of registration			Ambient/cold pack for summer months	Section 6.2.3	Mayo PCO
Whole Blood (lavender top)	2 x 5ml	2 x 5ml	2 x 5ml	Frozen	Section 6.2.4	Mayo BAP

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Specimen Processing

12hr Fasting Glucose will be performed locally
12hr Fasting Plasma collect 3 x 5ml in green top tube(lithium heparin).
Invert 9-10times & Centrifuge within 30minutes of draw.
Centrifuge for 15min @ 1300-2500 x g.
Remove plasma and transfer to 5ml tube. Repeat Centrifuge @ 2500 x g for 15min. Aliquot 1ml plasma in each 2ml cryovial.
Label specimen: Date & time of collection
Patient initials
Alliance Patient ID#
Alliance Study # A011401
Fasting plasma(PPP) or fasting serum (S)
Refer to pages 33-34 for collection of Substudy specimens;
Paraffin block & Blood sample.

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Specimen Submission cont.

All Specimens must be logged and shipped via Alliance Biospecimen Management System
URL:http://bioms.allianceforclinicaltrialsinoncology.org

After logging specimen, the system will create a shipping manifest.(Print 2 copies) 1 copy will go with shipment 2nd copy will be placed in chart.

Specimens should not be held at site for more than 60 days.

Shipping addresses for Specimens are located on page 31 of the Protocol.

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Treatment Plan/Intervention

Participants will be randomized 1:1 to a 2 year telephone-based weight loss intervention + health education or to a health education alone control arm.

The weight loss intervention will be delivered centrally through BWEL Call Center(located at Dana-Farber Cancer Institute) 42 telephone calls conducted over a 2 year time period. The intervention will include individual weight loss, caloric restriction, and physical activity goals administered by trained coaches.

The intervention will utilize a toolbox approach that will allow for tailoring for the individual participate.

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Intervention Goals

Weight Loss: 10% of baseline weight(1-2lbs/week) to a

BMI no less than 21kg/m².

Caloric intake: Recommended calorie levels will be based on body weight & on standardized tables.

Physical activity: Gradual increase in moderate intensity aerobic physical activity, target goal 150min/week during initial phase & 225-300min/week in maintenance phase.

To assist participants in achieving these goals, each participant will receive a workbook, commercially available cookbook, pedometer, measuring utensils, food scale & bathroom scale if they don't already have them.

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Collection of Study Measures & Evaluations

- Baseline & Follow up Questionnaires. (See Appendix 1 & 2, these appendix may be printed and administered to the patient)
- Anthropometric Measures: Standardized Weight, Height, Waist & Hip circumference(to be obtained by staff blinded to baseline measurements)
- Fasting Glucose (performed & resulted locally)
- Fasting Blood Specimens & Tissue collection, Mayo Biorepository
- Disease Outcome Assessment

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End of Treatment/Intervention

Duration of intervention will be 2 years. Criteria for discontinuation:

Disease recurrence

New invasive cancer diagnosis

Patient withdraws

Inter-current illness that prevents further administration of intervention.

Duration of Follow Up:

Completion of intervention, these patient will be followed up

Until invasive disease recurrence up to 10 years. If recurrence occurs patient will be followed for survival status up to 10 years.

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Additional Notes

Data for this study is entered through Medidata Rave

All Specimens must be logged and shipped via Alliance Biospecimen Management System(BioMS)

Specimens should not be held at the site for more than 60 days

If due to Institutional Policy a tissue block cannot be sent then 4 cores of tumor tissue and 4 cores of benign tissue (each measuring 1mm in diameter) is acceptable.

Slides are not an acceptable alternative.

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