# CALGB 40503:

# Endocrine Therapy With or Without Anti-VEGF Therapy: A Randomized, Phase III Trial of Endocrine Therapy Alone or Endocrine Therapy Plus Bevacizumab (NSC 704865) for Women With Hormone Receptor-Positive Advanced Breast Cancer

**ClinicalTrial.gov Identifier: NCT00601900**

## Study Background

### Trial Design

This randomized phase III trial studies tamoxifen citrate or letrozole together with bevacizumab to see how well it works compared with tamoxifen citrate or letrozole alone in treating women with stage III or stage IV breast cancer. Estrogen can cause the growth of breast cancer cells. Hormone therapy using tamoxifen citrate or letrozole may fight breast cancer by blocking the use of estrogen by the tumor cells. Monoclonal antibodies, such as bevacizumab, may help control breast cancer by stopping the growth of blood vessels to the tumor. It is not yet known whether giving hormone therapy is more effective with or without bevacizumab in treating advanced breast cancer.

*Arms:*

- Experimental: Arm I (endocrine therapy with monoclonal antibody)
- Active Comparator: Arm II (endocrine therapy)

### Objectives

*Primary:*

I. To compare the progression-free survival of letrozole therapy alone with the combination of letrozole therapy plus bevacizumab as first-line treatment in women with estrogen- and/or progesterone-receptor-positive advanced breast cancer.

*Secondary:*

I. Overall survival
II. Objective tumor response (measurable disease only)
III. Toxicity

### Stratification Factors

Disease measurability:

1) No

2) Yes

Disease free interval (months from initial diagnosis to first progression)

1) $\leq$ 24 months
2) $>$ 24 months

**Study History**

Nov 2008 Activation as double-blinded placebo-controlled study

May 2010 Update #2, changed study from double-blinded to open label with the intent of increasing accrual.

June 2011 Phase II tamoxifen trial permanently closed.

Nov 2011 Phase III letrozole trial permanently closed.

May 2015 Efficacy/safety results of phase III trial presented at ASCO Annual Meeting

May 2016 Published online, JCO.

# Publication Information

**Analysis Type:**

Primary Endpoint Analysis

**PubMed ID:**

27138575

**Citation:**

Dickler, M. N. et al. Phase III trial evaluating letrozole as first-line endocrine therapy with or without bevacizumab for the treatment of postmenopausal women with hormone receptor-positive advanced-stage breast cancer: CALGB 40503 (Alliance). J Clin Oncol. 34, 2602–2609, doi:10.1200/JCO.2015.66.1595 (2016).

**Associated Datasets:**
NCT00601900-D1 (efficacy)

NCT00601900-D2 (ae)

# Dataset Information

**Dataset Name: NCT00601900-D1 (efficacy)**

**Description:**

- Contains one record per patient enrolled in phase III letrozole trial (N=350)
- Efficacy analyses include only randomized and treated patients (N=343); use code treated=1 and arm in 1 or 2 to identify.
- Unless indicated in the Notes section of the table, missing data indicates the data was not collected.

Due to data cleaning efforts subsequent to publication, data may contain slight discrepancies from those reported in the manuscript.

Patients age 80 years and over were not included in the analysis for Figure 3.

| Variable description | Variable name | Codes | Notes |
|---|---|---|---|
| Identifier | patid | | deidentified patient # |
| Treated | treated | 0=no<br>1=yes | 1=yes included in efficacy and safety analyses |
| Arm | arm | 1=Bev<br>2=No Bev | |
| Amendment #2 | postamend2 | 0=pre amendment<br>1=post amendment | Amendment changed design from double-blinded to open label |
| Endocrine agent | strat1_endo | 1=letrozole | |
| Disease measurability | strat2_measdis | 1=non-measurable<br>2=measurable | |
| Vital status at reporting | sstat | 7=alive<br>8=deceased<br>65=w/d consent for survival f/up | w/d=withdrew |
| Age at registration (yrs) | ageatent | continuous | |
| Age Category at registration (yrs) | **agecat** | **1**= <=30<br>**2**= >30 and <=40<br>**3**= >40 and <=50<br>**4**= >50 and <=60<br>**5**= >60 and <=70<br>**6**= >70 and <=80<br>**7**= > 80 | |
| Patient race | race_id | 1=White<br>2=Black | |

| Variable description | Variable name | Codes | Notes |
|---|---|---|---|
| | | 4=Asian<br>9=All others | |
| ECOG performance score | PS | 0, 1, 2 | |
| Disease-free interval | dficat | 0= de novo<br>1= le 1 year<br>2= gt 1 yr and le 2 yrs<br>3= gt 2 yrs | years from initial DX to first recurrence |
| De novo disease | denovo | 1=yes<br>0=no | |
| Number metastatic sites at baseline | nmet_sites | | |
| Sites of mets | met_bone_only | 1=yes | Bone Only site(s)<br><br>Missing indicates patient was not identified as having only bone mets. |
| | met_visc_only | 1=yes | visceral only site(s)<br><br>Missing indicates patient was not identified as having only visceral mets. |
| | met_bone_visc | 1=yes | both bone and visceral.<br><br>Missing indicates patient was not identified as having both bone and visceral mets. |
| Tumor subtype | erstat | 1=negative<br>2=positive | tumoral ER |
| | pgrstat | 1=negative<br>2=positive | tumoral PgR |
| | her2stat | 1=negative<br>2=positive | tumoral HER2 |
| Prior treatment | priorht_tam | 1=yes<br>0=no | prior tamoxifen |
| | priorht_ai | 1=yes<br>0=no | prior aromatase inhibitor |
| | any_priorht | 1=yes<br>0=no | any prior hormone therapy |

| Variable description | Variable name | Codes | Notes |
|---|---|---|---|
| | any_priorcx | 1=yes<br>0=no | any prior chemo |
| Why rx ended | txendreas | -1=ended but unknown<br>2=disease progression<br>4=AE<br>11=w/d after starting rx<br>7=w/d before starting rx<br>8=other disease<br>5=death on study<br>10=alternative rx<br>12=other | w/d=withdrew<br><br>Missing indicates the patient did not have an end of active treatment form and was presumed to be still on treatment at time of data freeze.<br><br>Since this data was updated subsequent to the PFS analysis, the number of patients reporting a txendreas=2 (disease progression) is not indicative of the pfsstat below. |
| Overall survival | survmos | months from study registration to all-cause death; or censor at last f/up alive | |
| Survival status | survstat | 0=censor<br>1=dead any cause | |
| Follow-up | fumos | follow-up defined as survival months for surviving patients | per Gray method; only for surviving patients |
| Clinical follow-up (months) | clinfumos | follow-up for clinical evaluation defined as time from study entry until last clinical assessment for patients who are alive and without disease progression | per Gray method; only for patients who are alive and without disease progression |
| Progression-free survival | pfsmos | months from study registration to first disease progression or death without progression; censor last known alive and without disease progression | |
| PFS status | pfsstat | 0=censor<br>1=suffered disease progression or death without disease progression | |
| Best overall tumor response | bestresp | **1**=CR<br>**2**=PR<br>**3**=SD | For measurable disease only |

| Variable description | Variable name | Codes | Notes |
|---|---|---|---|
| | | **4**=PD<br>**5**=Could not be assessed | |
| duration stable disease | sd24 | 1=stable ge 24 wks<br>0=stable < 24 wks | only if bestresp above=3 |
| Number of treatment cycles taken | maxcycles | | |