# TARGIT U.S. Update

## Targeted Intraoperative Radiotherapy United States (TARGIT-US) Phase IV Registry Trial: An Update

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# Targeted Intraoperative Radiotherapy United States (TARGIT-US) Phase IV Registry Trial: An Update

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# TARGIT US

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# Primary Objective

- To study the efficacy and toxicity of breast radiotherapy given intra-operatively as a single fraction after breast conserving surgery, with or without whole breast radiation as indicated by pathologic risk factors, in women with early stage breast cancer.

# Objectives

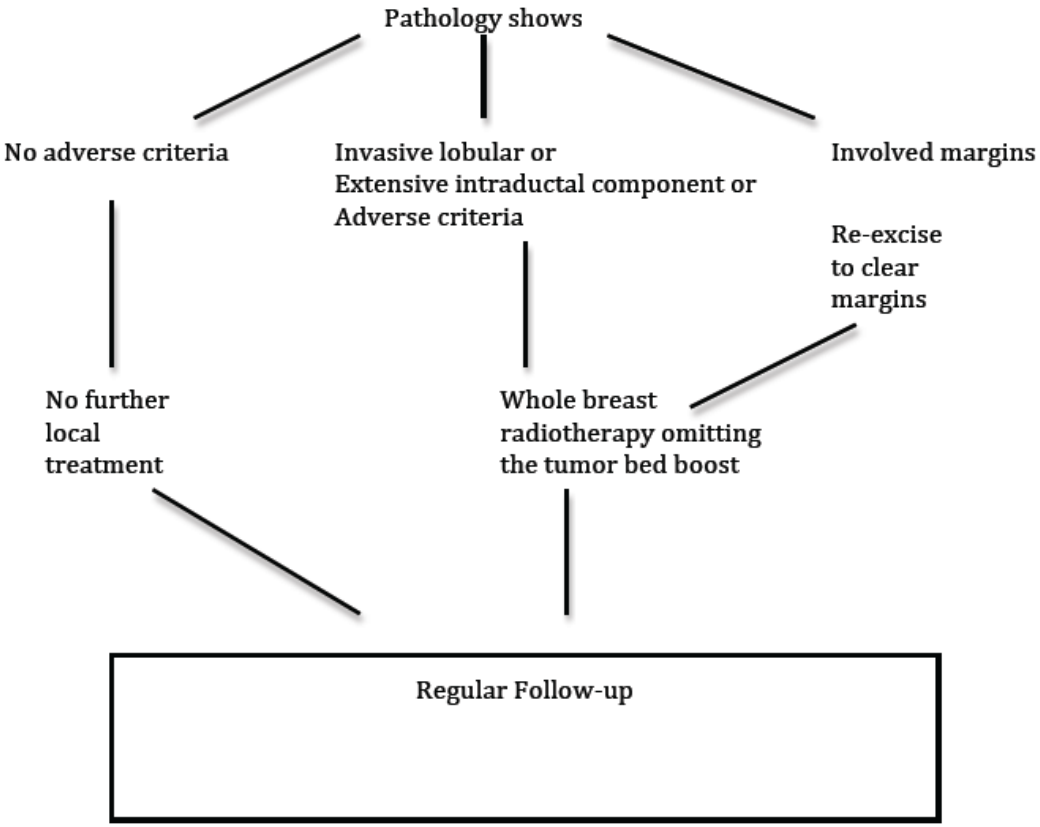
- 2.1.1 In-breast local failure and patterns of in-breast failure
- 2.1.2 Ipsilateral regional nodal failure
- 2.1.3 Toxicity and morbidity
- 2.1.4 Relapse-free survival
- 2.1.5 Overall survival

Breast cancer patient suitable for breast conserving therapy

NO RANDOMIZATION

Study Arm

Wide local excision of primary tumor
+ definitive sentinel node biopsy
+ IORT



# Eligibility

- Female
- Age 45 years old or older with operable invasive breast cancer
- T1 and T2 (<3.5 cm), N0, M0, confirmed by clinical, cytological or histological examination
- Suitable for breast conserving surgery and radiotherapy
- Ipsilateral diagnostic mammogram within 12 months of enrollment

# Exclusion Criteria

- Age < 45 years
- Known axillary lymph node positive breast cancer (FNA not required)
- Invasive lobular cancer
- Tumor size > 3.5 cm
- Multicentric cancer in the same breast as diagnosed by clinical examination, mammography, ultrasound. MRI or pathologic assessment, not amenable to excision with negative margins with a single lumpectomy.
- Synchronous bilateral breast cancer at the time of diagnosis.
- Ipsilateral breast had a previous cancer and/or prior in-field radiation.
- Patients known to have BRCA1/2 gene mutations (testing for gene mutations is *not* required).
- Patients undergoing primary systemic treatment (hormones or chemotherapy) as initial treatment with neoadjuvant intent of reducing tumor size.
- Previous history of malignant disease does not preclude entry if the expectation of relapse-free survival at 10 years is 75% or greater
- Any factor included as exclusion criteria in the participating center's Treatment Policy Statement.

# Statistics

| Background Rate | Current Rate | Delta | Alpha | Power | Sample size |
|---|---|---|---|---|---|
| 4.50% | 2.00% | 0.025 | 5% | 90% | 755 |

# Treatment

- Lumpectomy to be performed per institutional guideline.
- IORT is to be delivered with an appropriate size applicator keeping the applicator to skin distance of at least 1 cm.
- The prescribed dose of radiation is 20 Gy

# Additional Breast RT

- Axillary lymph node positive breast cancer
- Invasive lobular cancer
- Tumor size > 3.5 cm
- Extensive Intraductal Component (EIC= ≥ 25% of the lumpectomy specimen involved with ductal carcinoma in situ, DCIS) as assessed on surgical pathologic lumpectomy specimen.
- Multicentric cancer in the same breast as diagnosed by pathologic assessment, not amenable to excision with negative margins with a single lumpectomy.
- Inability to assess pathologic margin status
- Any factor included as exclusion criteria in the participating center's Treatment Policy Statement.

# Our Policy Statement

- Grade 3 disease
- Lymphovascular Space involvement

# Whole Breast Radiation

- Standard whole breast radiation is to be delivered and noted in the treatment policy document.
  - A dose of 45 to 50.4 Gy in 1.8 to 2 Gy per fraction, or 42.56 Gy in 2.66 Gy per fraction may be used.
  - Should start within 9 weeks or 6 weeks of last chemotherapy
  - Sequence of therapy not governed by the protocol.
- No lumpectomy bed boost is to be delivered

# Follow-up

- Patient’s are to be followed for 5 years.
- Treatment of recurrence is left to the discretion of the institution.

# Early Stopping

- Early stopping of this trial is within the power of the Steering Committee.  Reasons for early stopping include:
- Any grade V toxicity
- More than 5 grade IV toxicities within the first 50 patients reported at the 6 month follow-up
- More than 10 grade IV toxicities within the first 100 patients reported at the 6 month follow-up
- More than 5% local recurrences after the first safety report
- Skin breakdown and wound dehiscence (reported at 6 weeks of after procedure), which after detailed review of the Steering Committee as to time course and severity, were considered clinically significant
- There will be one formal interim analysis for efficacy of this single arm therapy once half the expected number of patients has been enrolled or once half of the expected events has occurred, whichever happens first. If at this time local recurrence is noted to be significantly different then the parent TARGIT trial (outside the initial 2.5% non-inferiority boundary; in which local recurrence is more than 5%) then early stopping will be undertaken.

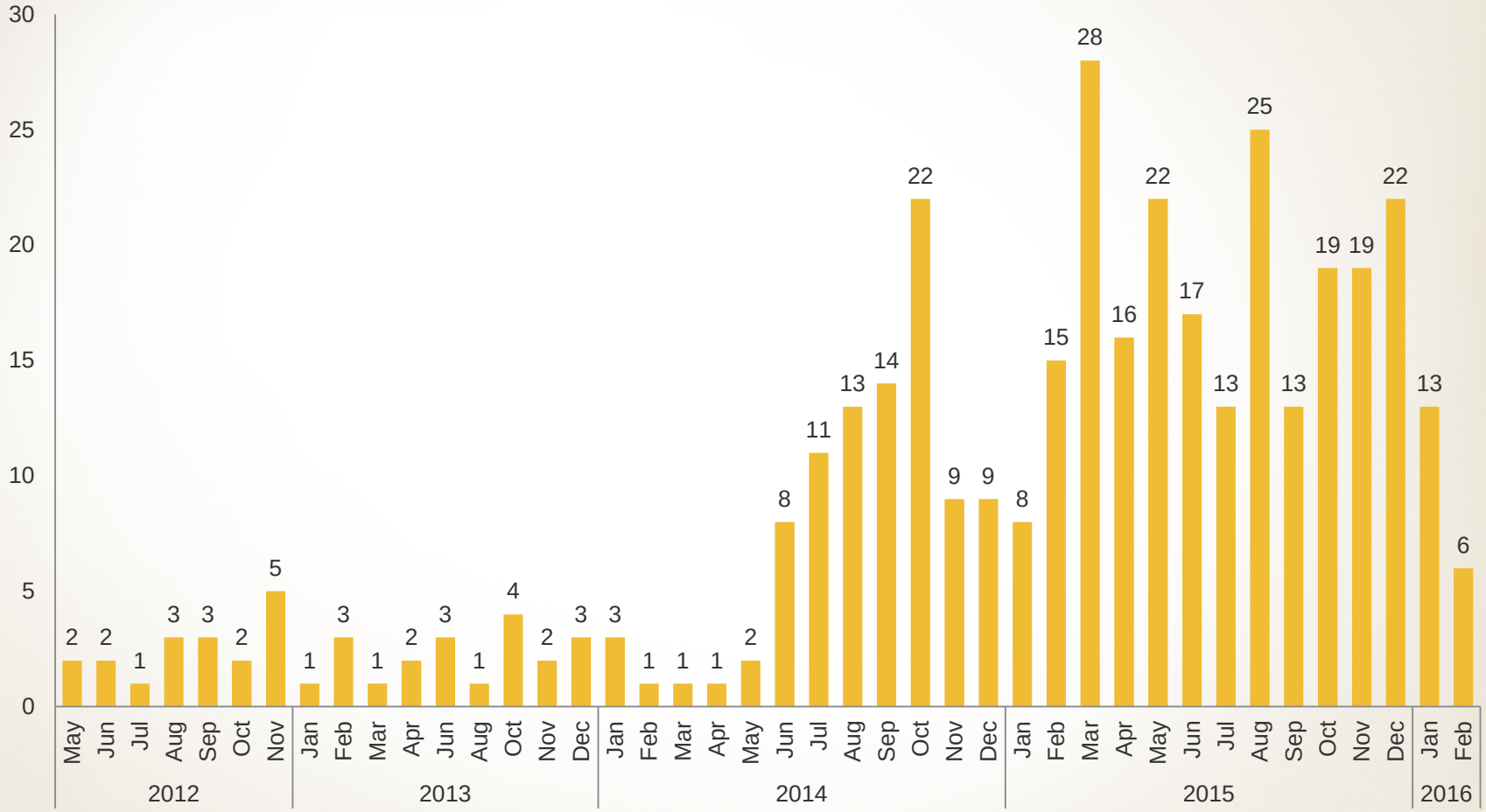
- Accrual goal is 793 (755 + 5% ineligible patients)
- Trial activated in 2012.
- Sub-contracts took longer than expected.
- Accrual picked up significantly in 2014,

# Current Status

| Site | Accrual |
|---|---|
| UCSF | 69 |
| John Muir | 8 |
| Dignity Health – Los Angeles | 8 |
| Cleveland Clinic | 6 |
| Georgetown | 9 |
| Washington Cancer Institute | 17 |
| Northwestern | 24 |
| Loyola | 3 |
| Vassar | 5 |
| Columbia | 27 |
| Dobbs Ferry Ashakari | 54 |
| Mercy Medical | 47 |
| Community Indiana | 26 |
| Lahey | 18 |
| Aurora | 23 |
| INOVA | 27 |
| Memorial Health | 8 |
| Greenwich Hospital | 2 |

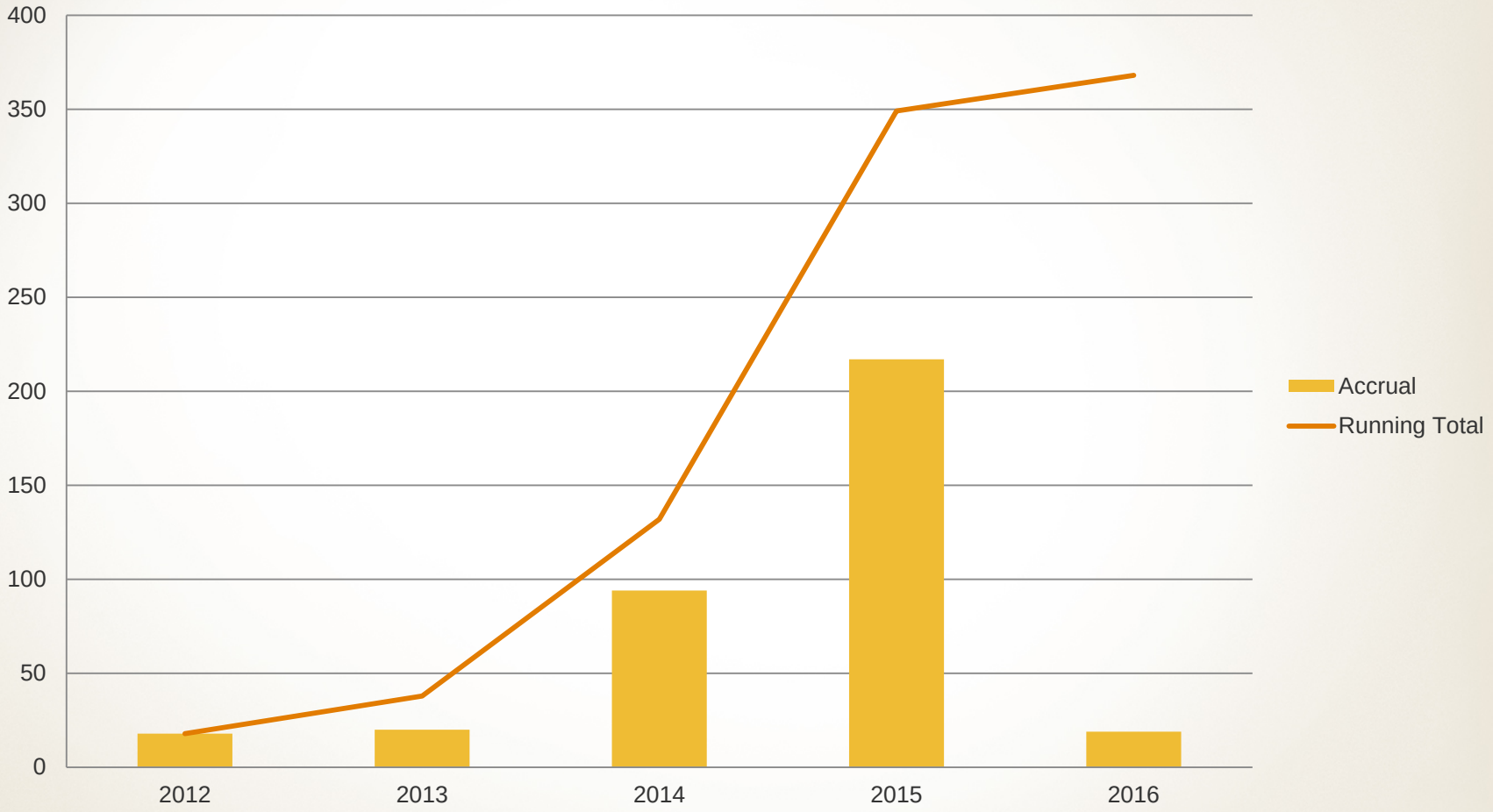
- 18 sites currently accruing patients
- 10 sites expected to begin accruing
- Total accrual of 381 patients

# Accrual by Month




*Includes known consent dates from 368 patients

# Accrual by Year




*Includes known consent dates from 368 patients

# Age, Race, and Ethnicity

| Age | Number |
|---|---|
| 45-49 | 3 |
| 50-59 | 84 |
| 60-69 | 159 |
| 70-79 | 89 |
| 80-89 | 15 |
| ≥90 | 1 |
| Unknown | 30 |

| Race | Number |
|---|---|
| White | 279 |
| Black or African American | 31 |
| Native Hawaiian or Other Pacific Islander | 2 |
| Asian | 21 |
| American Indian or Alaska Native | 3 |
| Unknown | 45 |

| Ethnicity | Number |
|---|---|
| Hispanic or Latino | 15 |
| Non-Hispanic | 330 |
| Unknown | 36 |

# Patient Characteristics

| Menopause status | Number |
|---|---|
| Pre-menopausal | 10 |
| Post-menopausal | 278 |
| Unknown | 1 |

| Previous contralateral breast cancer? | Number |
|---|---|
| Yes | 11 |
| No | 274 |
| Unknown | 4 |

| Tumor size (mm) | Number |
|---|---|
| 0-9 | 128 |
| 10-19 | 115 |
| 20-29 | 27 |
| 30-39 | 3 |
| ≥40 | 9 |
| Unknown | 7 |
| Median | 10 |
| Average | 13.3 |

*Data from 289 filled out forms

# Complications

| Hematoma | Number |
|---|---|
| Breast | 10 |
| Axilla | 0 |
| Both | 0 |
| No | 194 |

| Wound infection | Number |
|---|---|
| Breast | 11 |
| Axilla | 0 |
| Both | 1 |
| No | 192 |

| Seroma | Number |
|---|---|
| Breast | 17 |
| Axilla | 4 |
| Both | 3 |
| No | 180 |

| Skin Breakdown | Number |
|---|---|
| Breast | 2 |
| Axilla | 0 |
| Both | 0 |
| No | 202 |

*Data from 204 filled out forms

# Complications cont.

| Delayed wound healing | Number |
|---|---|
| Breast | 2 |
| Axilla | 1 |
| Both | 0 |
| No | 201 |

| Complication | Number |
|---|---|
| Rash: dermatitis associated with radiation | 0 |
| Telangiectasia | 0 |
| Pain in irradiated field | 1 (Grade 3) |
| Other toxicity | 0 |
| Other complications | 16 |

*Data from 204 filled out forms

# Questions

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