

**Nodal burden and nodal recurrence in patients with isolated tumor cells after neoadjuvant chemotherapy treated with axillary dissection or axillary radiation:
the OPBC-05/EUBREAST-14R/ICARO study**

Study design: Multicenter retrospective cohort study

Population: Consecutive patients with residual isolated tumor cells after neoadjuvant chemotherapy treated with either axillary lymph node dissection (ALND), axillary radiation (RT) or observation.

Eligibility:

- At least 1-year follow-up (inclusion should end in 12/2021)
- For cN0: any axillary staging technique including palpation is allowed
- For cN+: cytological or histological confirmation is required. Axillary staging should be performed with sentinel lymph node (SLNB) with dual mapping or targeted axillary dissection (TAD: imaging-guided localization of sampled node in combination with SLN procedure with or without dual mapping)

Primary outcomes:

- Patterns of treatment (TAD/SLNB +/- ALND +/- axillary RT) by geographic region and over time
- Incidence of additional micro- and macrometastases removed by ALND
- 3-year rate of axillary recurrence

Secondary outcomes:

- 3-year rates of any regional, locoregional and any invasive recurrence
- To compare 3-year rate of axillary recurrence in ypN0(i+) with ypN0 (historic OPBC-04/EUBREAST-06/OMA control)

List of variables to be collected:

- Center
- Age (at surgery)
- Race/Ethnicity (Asian, Black, Caucasian, Hispanic, other)
- cT at presentation
- cN0 or cN+ (biopsy-proven) at presentation
- if cN+ method of detection (palpable disease vs imaging-detected non-palpable)
- Date of surgery
- Type of breast surgery: BCT/mastectomy
- Type of axillary surgery
 - SLNB with dual mapping (in cN+ cases) or
 - TAD (in cN+ cases)
 - Type of localization (seed/wire/us/tattoo/others)
 - single or dual mapping?
 - SLNB with single tracer (in cN0 cases)
- Sampled node clipped y/n

- If yes: Clipped node removed y/n/unknown (documented by specimen radiography or operative/pathology reports)

- Number of SLNs removed
- Number of SLNs with ITCs
- Detection on frozen section? y/n
- Method of detection? H&E or IHC?
- ALND y/n
- Number of additional LNs removed
- Number of additional positive lymph nodes
- Size of the largest nodal metastasis found in the ALND specimen:
ITCs/micrometastasis/macrometastasis
- Histology (NST/lobular/other)
- Breast pCR: yes/no
- Residual tumor size in the breast: size (cm)
- Tumor grade
- Receptor status
 - ER+ and/or PR+ HER2-;
 - ER+ and/or PR+/Her2+;
 - ER-/PR- Her2+;
 - ER-/PR-/HER2-;
- Type of NAC regimen for HER2- (AC-T/AC-t + Carbo/AC-free regimen/other)
- Type of NAC regimen for HER2+ (AC-TH/AC-THP/TCHP/other)
- Adjuvant capecitabine: yes/no
- If HER2+: type of post-surgical anti-HER2 treatment (H/HP/TDM-1)
- If HR+: received adjuvant endocrine therapy: yes/no,
 - if yes: type of endocrine therapy

Radiotherapy: yes/no

- Target Volume:
Whole breast irradiation: y/no
Chest wall irradiation: y/no
Regional nodal irradiation y/no

Follow-up

Date of last follow up

- Recurrence: yes/no
- Type of recurrence: local/regional/locoregional/synchronous (regional and distant, local and distant, locoregional and distant)
- Type of regional recurrence: axillary only, axillary and supraclavicular or internalmammary, supraclavicular or internal mammary without axillary
- Date of recurrence
- Deceased: yes/no
- Date of death
- Cause of death