



Editorial on MSKCC prospective validation study of ACOSOG Z0011 Trial—what have we learned?

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De-escalation of axillary surgery in early breast cancer has been advocated to reduce early and late morbidity associated with extensive lymph node dissection. Several studies have shown that less surgery does not impact on patient survival in specific settings (1-3). The Memorial Sloan Kettering Cancer Center (MSKCC) latest study definitely shows the clinical applicability of American College of Surgeons Oncology Group (ACOSOG) Z0011 trial published by Giuliano *et al.* in 2011 and then updated in 2017 (1,4,5).

Despite criticisms, ACOSOG Z0011 trial has been a practice-changing trial.

The ACOSOG Z0011 trial demonstrated that a group of 891 breast cancer patients enrolled from 115 centres with residual tumour burden in the axilla (1–2 positive nodes) did not benefit from axillary lymph node dissection (ALND) when given systemic therapy at 6.3 years follow-up.

Five-year overall survival (OS) was 91.8% [95% confidence interval (CI), 89.1–94.5%] with ALND and 92.5% (95% CI, 90.0–95.1%) with sentinel lymph node dissection (SLND) alone; 5-year disease-free survival (DFS) 82.2% (95% CI, 78.3–86.3%) with ALND and 83.9% (95% CI, 80.2–87.9%) with SLND alone (1).

Longer follow up published in September 2017 confirmed this trend. At a median follow-up of 9.3 years, only one local recurrence was found in the SLND group alone. The 10-year OS was 86.3% *vs.* 83.6% in the SLND group and in the ALND group, respectively. HR, 0.85; 95% CI, 0–1.16; P=0.02. The 10-year DFS was 80.2% *vs.* 78.2%

in SLND group and in the ALND group, respectively. HR, 0.85; 95% CI, 0.62–1.17; P=0.32 (5).

The study from MSKCC has confirmed ACOSOG Z0011 findings and stimulate once again clinicians to be confident about the “real world” applicability of the conservative axillary approach introduced by Giuliano *et al.* (1,4) when axillary metastases are confined to 1–2 sentinel nodes. The study published by Morrow *et al.* (4) is unicentric and has enrolled 793 patients in 6-year time. Inclusion and exclusion criteria were prospectively defined as the same as Z0011. They did not found isolated axillary recurrence. Breast + nodal or nodal + distant recurrence rate was 0.7% for both (CI, 0–1%) and (CI, 0–2%), respectively.

Median follow up was 29 months and 5-year distant recurrence rate was 5% (CI, 3–7%).

Patient population was mainly postmenopausal (median age 58 years) with 84% of luminal cancers (ER positive; HER2 negative) and tumour median diameter of 1.7-cm. Despite this, 288 patients had at least one “high risk features” such as age <50 years, HER2 positive or triple negative breast cancer (TNBC).

Ninety-seven percent of the patients were given adjuvant systemic treatment. Whole breast radiation therapy (WBRT) was delivered to 94% of patients.

Noteworthy, Morrow *et al.* focused on radiation therapy (RT) aspects, which were widely discussed on the ACOSOG Z0011 trial as were not clearly specified. 484 patients were given WBRT with different RT fields. 21% of them had breast and nodes irradiated which means

axillary level III and supraclavicular fossa. Nodal recurrence (never alone, but concomitant either with in-breast or with distant recurrence) of about 1% was stratified according to three RT fields (prone, supine and nodal irradiation) and no difference was found among groups.

With regards to preoperative imaging, axillary ultrasound is considered by some to be an “overtreatment tool”, increasing the number of ALND by default. However, there are randomised ongoing trials which are testing the potential role of preoperative ultrasound-based staging of the axilla to avoid sentinel lymph node biopsy at all in small breast cancers (6,7).

According to Houssami *et al.* (8) preoperative ultrasound-based staging of the axilla has shown a median utility in about 20% of breast cancer patients who can be scheduled to receive axillary surgery based after a positive needle biopsy. However, ACOSOG Z0011 evidence as well as MSKCC confirmatory study may render preoperative axillary ultrasound needle biopsy less useful when SLND is already planned, but remains under investigations for those patients who will be potentially spared axillary surgery.

Recommendations for clinicians dealing with breast cancer

MSKCC validation study strengthens and amplifies ACOSOG Z0011 trial results, showing less than 1% of local recurrence among patients with 1–2 positive sentinel nodes treated with SLND alone and adjuvant therapies.

Indications for ALND in cT1-2N0 breast cancer remain gross nodal involvement, extracapsular extension, metastasis in more than 3 axillary nodes when breast conserving surgery is performed. Clinicians should consider radiotherapy in patients with a small tumour burden in their sentinel nodes.

When mastectomy is planned patients with 1–2 positive axillary sentinel node should still undergo complete axillary dissection. According to this and consistent with the latest guidelines from National Cancer Comprehensive Network (NCCN) (9), American Society of Clinical Oncology (ASCO) (10) and St. Gallen International Breast Cancer Conference (11) is now time to avoid useless and potentially harmful ALND for patients undergoing breast conserving surgery who meet Z0011 criteria.

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Footnote

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