

Neoadjuvant chemotherapy (NAC) is known to decrease the likelihood of axillary nodal positivity and thus can decrease need for axillary lymph node dissection (ALND) and nodal radiation. Axillary nodal staging information following NAC remains critical to guide adjuvant systemic therapy, with escalation of therapy (with use of T-DM1 for HER2+ disease, capecitabine for triple negative disease and CDK4/6 inhibitors for HR+/HER2- disease) in those patients found to have ypN+ disease after NAC. Since these therapies are associated with improvement in survival, accurate nodal staging remains important. Currently imaging techniques are not accurate enough to replace axillary surgery in this setting.

For patients presenting with clinically node negative disease (cN0) treated with NAC, surgical staging of the axilla is recommended to be performed after completion of NAC with use of sentinel lymph node (SLN) surgery. If the SLNs are found to be negative, then no further axillary surgery is indicated. In the setting of positive SLNs, then ALND remains the standard of care and nodal radiation is indicated.

Further evolution of axillary surgical management in patients presenting with cN0 disease is being evaluated with consideration of omission of axillary surgical staging for patients at lowest likelihood to have positive nodes. Retrospective studies have shown that in patients presenting with cT1-2N0 TNBC or HER2+ disease who are treated with NAC, the likelihood of nodal positivity after NAC is <2%. Studies, such as ASICS, EUBREAST-01 and are evaluating omission of axillary surgery in patients presenting with cT1-2N0 TNBC or HER2+ disease who are treated with NAC, with radiologic complete response. Additionally, the Neo-NAUTILUS and ASLAN trial is evaluating SLN surgery versus omission of axillary surgery in patients with cN0 Her2+ or triple negative disease treated with NAC with a good response on imaging (>30% decrease in breast tumor size or <2-4cm residual disease) after NAC.

For patients presenting with clinical N1 disease who are treated with NAC, ALND was historically the recommended axillary surgery after NAC. For patients who have a good imaging and clinical response in the breast and the nodes

to NAC, axillary surgical staging to assess for residual nodal disease is performed with SLN surgery (which is often performed along with marking the index biopsy proven node and pre-operative localization of that node to ensure resection at surgery – Targeted Axillary Dissection). If the SLNs are found to be negative, then ALND can be avoided.

Nodal radiation can also be omitted in the setting of cN1 disease converted to ypN0 disease, as shown in the NRG-NSABP B-51/RTOG 1304 trial, which showed that routine regional nodal irradiation (RNI) did not improve invasive recurrence-free survival, disease-free survival, or overall survival in this setting. These results support treating such patients as node-negative, avoiding unnecessary nodal radiation.

In the setting of positive SLN(s) after NAC, indicating chemotherapy resistant disease, ALND remains the standard of care and adjuvant nodal radiation is indicated. Consideration of axillary radiation in place of axillary dissection for patients with residual positive SLN(s) after NAC is currently being evaluated in prospective trials such as the Alliance A011202 and TAXIS trials.

Axillary management following NAC is becoming personalized based on tumor biology and treatment response and multidisciplinary team collaboration is crucial to enable de-escalation while optimizing oncologic outcomes.