Omission of Axillary Dissection in ypN1mi Breast Cancer Patients after Neoadjuvant Chemotherapy: Preliminary Results from the NEONOD2 Trial

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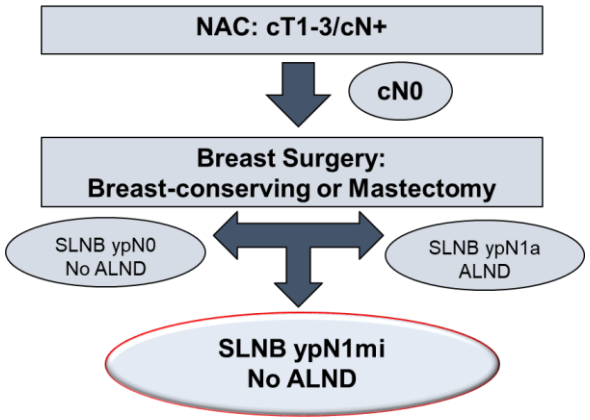
Introduction

The advent of sentinel lymph node biopsy (SLNB) and neoadjuvant chemotherapy (NAC) has progressively reduced the extent of axillary surgery in breast cancer (BC).

In early-stage BC, axillary lymph node dissection (ALND) is no longer recommended for patients with micrometastasis (ypN1mi) due to equivalent outcomes and reduced morbidity.

However, the role of ALND remains unclear in patients initially cN+ who convert to cN0 after NAC but present residual axillary micrometastasis.

NEONOD2: Design



Materials and Methods

NEONOD2 is a prospective, multicenter, non-inferiority trial designed to assess whether omission of ALND in cN+ patients downstaged to cN0 post-NAC and found to have sentinel lymph node (SLN) micrometastasis (ypN1mi) leads to recurrence or survival outcomes comparable to those with negative SLN (ypN0), for whom ALND omission is current standard. Eligible patients were cT1-3/cN+ BC candidates for NAC. After completion of NAC, only patients with clinical conversion to cN0 underwent SLNB. Those with micrometastatic SLN (ypN1mi) were enrolled in the experimental group; those with ypN0 were assigned to the standard group. Primary endpoint was recurrence-free survival; secondary endpoints included overall survival, loco-regional and distant recurrence-free survival.

Results

As of the current interim analysis, 449 patients have been enrolled across Italian Breast Units. The study population included 70 patients (15.6%) with SLN micrometastases (experimental group), 285 (63.5%) with negative SLN post-NAC (standard group), and 94 (20.9%) with macrometastatic SLN involvement. At a mean follow-up of 21.8 months (SD 13.0), nine recurrences (2.0%) were documented across the cohort. Three events occurred in the ypN1mi group, comprising one ipsilateral axillary-supraclavicular relapse, one ipsilateral breast recurrence following breast-conserving surgery, and one ipsilateral skin recurrence post-mastectomy. In the ypN0 group, four recurrences were observed, including two axillary (one supraclavicular), one ipsilateral breast, and one cutaneous recurrence. Two patients in the macrometastatic group experienced recurrence, including one breast and one distant brain metastasis. Notably, no isolated axillary relapse occurred in the micrometastatic group. Five deaths (1.1%) were recorded overall: three in the ypN0 group and two in the macrometastatic group. No deaths occurred among patients in the micrometastatic group.

Conclusions

Preliminary findings from the NEONOD2 trial suggest that omission of ALND in patients with SLN micrometastases following NAC does not result in a higher incidence of regional recurrence or mortality at early follow-up. The absence of isolated axillary failure and the lack of deaths in the experimental group are reassuring signals supporting the safety of de-escalated axillary management in this subset. Continued accrual and extended follow-up are ongoing to confirm the long-term oncologic safety of this approach.

Contact

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