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Applying SOUND Trial Results in the Real World:

New Study Identifies Appropriate Patients in a Multi-Disciplinary Clinical Practice

Abstract: Real World Implications of the SOUND Trial

Orlando, FL, April 11, 2024—Omitting sentinel lymph node biopsy (SLNB) in patients with early stage HR+HER2- breast cancer and a negative pre-surgical axillary ultrasound (AxUS) will not impact outcomes for a carefully chosen patient population in a real world setting, suggests a new study presented this week at The American Society of Breast Surgeons Annual Meeting in Orlando. The study identified patients meeting the SOUND (Sentinel Node vs Observation After Axillary Ultra-Sound) trial eligibility criteria in a large prospectively maintained surgical database and examined disease characteristics and outcomes.

Andreas Giannakou, MD, lead study author and breast surgical fellow at Brigham and Women's Hospital, Massachusetts General Hospital and Dana-Farber Cancer Institute, explains, "The SOUND trial, published in September 2023, randomized patients with early stage breast cancer (tumors < 2cm in size) who were node negative on both physical exam and axillary ultrasound to groups that underwent SLNB or did not. They found no difference in five-year year distant disease-free survival, the study's primary end point, based on the performance of surgical nodal staging. Additionally, no difference was found in the rate of axillary recurrences between the two study arms."

Today, SLNB is the standard-of-care in clinically node negative breast cancer to determine whether cancer has spread to the lymph nodes, and this information often helps determine next steps of care. By demonstrating that this patient population can be spared axillary surgery without impacting oncologic outcomes, the SOUND trial is an extremely important contribution to current efforts to de-escalate axillary surgery.

"Before applying clinical trial results to clinical practice, it is important to ensure that the trial population is representative of a real world patient population," says study senior author Tari A. King, MD, Professor of Surgery at Harvard Medical School and Chief of the Division of Breast Surgery at Brigham

and Women's Hospital. “In our study of patients meeting SOUND eligibility criteria who underwent SLNB as part of standard clinical care, the clinical and pathological tumor characteristics and nodal disease burden proved similar to the SLNB arm of the SOUND trial, suggesting that we can identify patients who can safely omit axillary surgical staging.”

The authors chose to restrict their analysis to patients with HR+HER2- tumors, the cancer sub-type comprising 90% of SOUND trial participants. Additionally, in this population, the need for adjuvant chemotherapy often is based on the results of genomic assays and not strictly guided by SLNB results.

The authors identified from the Dana-Farber Brigham Cancer Center surgical database 512 patients treated from 2016 to 2022 with HR+HER2- breast cancer who met SOUND trial eligibility criteria. SLNB was completed in 411 (80.5%) and omitted in 98 (19.2%). One procedure failed. “The patient population proved to be very similar to SOUND trial participants,” notes Dr. King. Of the patients who underwent lumpectomy, 88% had a negative SLNB and among those who had nodal disease on SLNB, 75% had only one positive node. Less than 1.0% had more than four positive lymph nodes. Cancer recurrence rates were very low and also similar to SOUND trial participants, although follow up was shorter.

At a median follow up of 26.3 months, three (0.7%) patients experienced a local recurrence, four (1.0%) patients developed a distant recurrence and three (0.7%) patients died. Kaplan-Meier estimates of three-year locoregional recurrences were 0%, distant recurrence 0.9%, invasive disease-free survival 98.4% and overall survival 100%.

“Given the similarity of our population to SOUND trial patients, our findings support thoughtful integration of these results into clinical practice,” states Dr. Giannakou. “Working closely with our multi-disciplinary colleagues in medical and radiation oncology, we have started to implement this data into practice for select postmenopausal patients with HR+HER2- breast cancer who would have met eligibility criteria for the SOUND trial.”

The authors note that multi-disciplinary conversations with radiation and medical oncology teams are important to ensure that omitting SLNB will not impact subsequent adjuvant therapy considerations.

“The SOUND trial results are very encouraging,” says Dr. King. “I am confident that multi-disciplinary groups around the country are looking at their own patient populations and determining how best to apply these data into their own practices.”

Real World Implications of the SOUND Trial

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Background/Objective

The SOUND trial randomized patients with cT1N0 breast cancer and negative axillary ultrasound (AxUS) to sentinel lymph node biopsy (SLNB) or no surgical staging and demonstrated that omission of SLNB is noninferior to SLNB for oncologic safety. While the SOUND trial included all breast cancer subtypes, to begin to examine the generalizability of these clinical trial results in real world practice, we chose to examine nodal disease burden and oncologic outcomes among cT1N0 HR+HER2- negative breast cancer patients who would have been eligible for the SOUND trial.

Methods

Patients with cT1N0M0, HR+HER2- breast cancer and negative preoperative AxUS or an isolated abnormal lymph node with negative preoperative biopsy (SOUND eligibility criteria), who underwent upfront surgery including SLNB from 2015-2022 were identified. Patient and tumor characteristics, disease burden, adjuvant treatment and oncologic outcomes were examined.

Results

Of 3938 patients with cT1N0M0 HR+HER2- breast cancer, 550 (13.9%) underwent AxUS, of which 510 (92.7%) met SOUND eligibility criteria. Compared to patients without preoperative AxUS, patients undergoing AxUS were younger (median age 59 vs 63 yrs, p=0.001), had higher grade tumors (p< 0.001) and were more likely to undergo mastectomy (20% vs 13.2%, p< 0.001). Oncologic outcomes at 3yrs including locoregional recurrence (LRR), distant recurrence (DR), invasive disease-free survival (iDFS) and overall survival (OS) were not different between patients with and without AxUS.

Of the 510 patients meeting SOUND criteria, SLNB was omitted in 98 (19.2%), failed in one and was completed in 411 (80.5%). Clinical and pathologic characteristics, overall nodal disease burden and recurrence rates for "SOUND eligible" patients and the published SOUND population (SLNB arm) were similar. (Table 1) However, it should be noted that our institutional cohort was limited to HR+HER2- patients, median follow up was shorter (26.3 vs 69.6 months) and there were fewer postmenopausal patients (57.4% vs 78.8%).

Among "SOUND eligible" patients, median age was 56 yrs (22 – 80yrs), median tumor size was 1.3 cm and the majority had grade 1 or 2 disease (n=336, 81.7%). Lumpectomy was performed in 312 (75.9%) patients, of whom 276 (88.5%) received whole breast radiation. At least one positive SLN was found in 59 (14.3%) patients. Of those with positive nodes, 15 (25.4%) patients underwent axillary dissection with

additional nodal disease found in 9 (15.2%). At a median follow-up of 26.3 months (0.3 – 84.4 months) there were 3 (0.7%) local recurrences, 3 (0.7%) regional recurrences, 4 (1.0%) distant recurrences and 3 (0.7%) deaths. 3-yr rates of LRR were 0.0%, DR 0.9%, iDFS 98.4% and OS 100%.

Conclusions

Examination of our real-world cT1N0 HR+HER2- "SOUND eligible" population suggests that nodal disease burden and oncologic outcomes are similar; providing support for careful implementation of these clinical trial results into multi-disciplinary clinical practice. Further investigation to determine the potential impact of omission of surgical axillary staging on adjuvant therapy recommendations in the era of evolving precision medicine is underway.

Table 1: Clinico-pathologic characteristics and outcomes among SOUND eligible patients

Characteristics	Patients, No (%) HR+HER- SOUND eligible with SLNB (n= 411)		SOUND population randomized to SLNB (n=708)	
Age at surgery (yrs)				
<40	33	8.0%	10	1.4%
40-49	102	24.8%	114	16.1%
50-65	188	45.7%	324	45.8%
≥65	88	21.4%	260	36.7%
Median (IQR) age	55.5	(46-53)	60	(52-68)
Menopausal status				
Premenopausal	167	40.6%	145	20.5%
Postmenopausal	236	57.4%	558	78.8%
Unknown	8	1.9%		
Histology				
Ductal	272	66.2%	551	77.8%
Lobular	56	13.6%	61	8.6%
Other	83	20.2%	96	13.6%
Pathologic tumor size				
pT1a	19	4.6%	71	10.0%
pT1b	97	23.6%	251	35.5%
pT1c	239	58.2%	355	50.1%
pT2	50	12.2%	31	4.4%
pT3	6	1.5%	0	0.0%
Median (IQR) tumor size (cm)	1.3	(0.8-1.5)	1.1	(0.8-1.5)
Grade				
G1	128	31.1%	194	27.4%
G2	208	50.6%	377	53.2%
G3	74	18.0%	130	18.4%
Unknown	1	0.2%	0	0.0%
Number of Pos SLNs				
0	352	85.6%	599	84.6%
1	44	10.7%	83	11.7%
≥2	15	3.6%	14	2.0%
No SLNB	0	0.0%	12	1.7%
Total number of Pos LN				
0	352	85.6%	599	84.6%
1-3	54	13.1%	93	13.1%
4-9	4	1.0%	2	0.3%
≥ 10	1	0.2%	2	0.3%
ALND				
ALND performed	15	25.4%*	97	13.7%
Final breast surgery				
Lumpectomy	312	75.9%	703	99.3%
Mastectomy	99	24.1%	5	0.7%
Oncologic outcomes				
Ipsilateral breast recurrence alone	3	0.7%	7	1.0%
Regional recurrence alone	1	0.2%	3	0.4%
Ipsilateral breast and axillary recurrence	2	0.5%	2	0.3%
Distant metastasis	4	1.0%	13	1.8%
Death from breast cancer	2	0.5%	0	0.0%
Death from unknown cause	1	0.2%	21	3.0%
Median (IQR) follow-up (months)	26.3	(11.4-39.6)	69.6	(64-82.8)

*among those with pos SLN