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Abstract #192

Omission of sentinel lymph node biopsy in early stage HR-positive HER2-negative breast cancer: impact on adjuvant CDK4/6 inhibitor candidacy and oncological outcomes

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Introduction

The SOUND and INSEMA trials established oncological non-inferiority of sentinel lymph node biopsy (SLNB) omission in many patients with small, clinically and imaging node-negative (cN0/iN0), hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer (BC)[1,2]. However, recruitment of these trials ended prior to the approval of adjuvant cyclin-dependent kinase 4/6 (CDK4/6) inhibitors. Therefore, the impact of SLNB omission on eligibility for adjuvant CDK4/6 inhibitor treatment and associated oncological outcomes is unknown.

How does nodal staging impact adjuvant CDK4/6 inhibitor candidacy and invasive disease-free survival (iDFS) in SOUND/INSEMA-eligible patients?

Methods

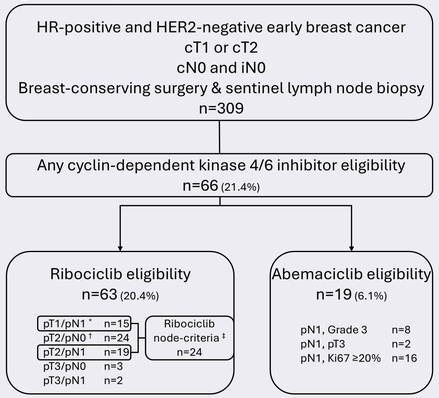
Retrospective cohort study of a prospectively maintained institutional database. Inclusion of patients with cT1 and cT2, cN0/iN0, HR+/HER2- early BC who underwent upfront breast-conserving surgery and SLNB between 01/2014-12/2024.

Eligibility criteria for adjuvant CDK4/6 inhibitors

Abemaciclib	monarchE	• ≥4 positive LNs • 1-3 positive LNs + grade 3 or tumor ≥5cm or Ki67 ≥20%
	FDA approved	• ≥4 positive LNs • 1-3 positive LNs + grade 3 or tumor ≥5cm
Ribociclib	node-criteria	• pT1 pN1 (macrometastasis) • pT2 pN1 provided no other eligibility criteria met for pT2 (grade 3; grade 2 and Ki67 ≥20%, grade 2 or Oncotype Dx RS ≥26)

Results

Figure 1. Study flow



* Excluding pN1mi.

† Additional criteria for eligibility: grade 3; grade 2 and high genomic risk (Ki67≥20% or Oncotype Dx ≥26 points).

‡ Ribociclib eligibility based on node-criteria was defined as either pT1pN1 or pT2pN1, provided that no additional criteria would render the pT2 status per se eligible for CDK4/6 inhibitor treatment (i.e., grade 3; or grade 2 plus Ki67 ≥20% or Oncotype Dx RS of ≥26), irrespective of nodal status.

Table 1. Estimates of invasive disease-free survival (iDFS) and the associated number needed to treat (NNT) with adjuvant abemaciclib and ribociclib

	iDFS experimental arm	iDFS comparator arm	iDFS benefit	NNT
Abemaciclib, 5-year follow-up[3]				
Stage II	89.1%	85.5%	3.6%	28
Ribociclib, 5-year follow-up[5]				
Stage II	91.7%	87.9%	3.7%	27

Table 2. Patient and tumor characteristics

Characteristic	Non-CDK4/6 inhibitor eligible n=243	CDK4/6 inhibitor eligible n=66
Menopausal status		
Pre, n(%)	51 (21.0)	14 (21.2)
Post, n(%)	190 (78.2)	52 (78.8)
Clinical tumor stage		
cT1, n(%)	193 (79.4)	30 (45.5)
cT2, n(%)	50 (20.6%)	36 (54.6)
Risk features		
Ki67 ≥20%, n(%)	52 (21.4)	40 (60.6)
Grade III, n(%)	20 (8.2)	17 (25.8)
LVSI, n(%)	26 (10.7)	29 (43.9)
Pathologic nodal stage		
pN0, n(%)	236 (97.1)	27 (40.9)
pN1, n(%)	7 (2.9)	39 (59.1)

Figure 2. Multivariable logistic regression analysis

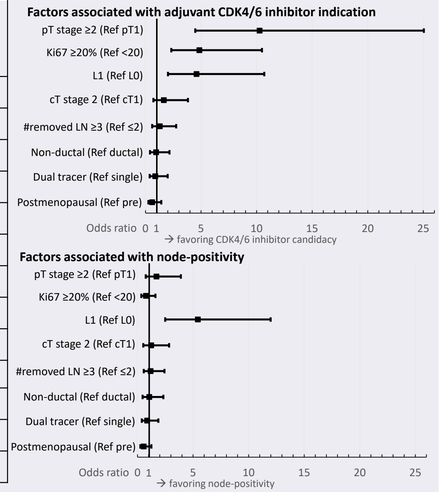


Table 3. Impact of SLNB in SOUND/INSEMA-eligible patients on CDK4/6 inhibitor indication and outcomes

Cohort	CDK4/6 inhibitor indication, n(%)	NNT with SLNB to identify one meeting CDK4/6 inhibitor indication	NNT with SLNB to prevent one iDFS event by use of a CDK4/6 inhibitor	Estimate of iDFS increase upon SLNB omission and missed treatment with CDK4/6 inhibitor
Abemaciclib, monarchE				
Total cohort, n=309	19 (6.1)	17 (95%CI 11-27)	456 (95%CI 287-723)	0.3% (95%CI 0.2-0.4%)
cT1, n=223	10 (4.5)	23 (95%CI 13-47)	625 (95%CI 324-1206)	0.2% (95%CI 0.1-0.3%)
Abemaciclib, FDA approved				
Total cohort, n=309	10 (3.2)	31 (95%CI 17-64)	866 (95%CI 447-1677)	0.2% (95%CI 0.1-0.3%)
cT1, n=223	5 (2.2)	45 (95%CI 20-137)	1249 (95%CI 471-3314)	0.1% (95%CI 0.1-0.2%)
Ribociclib, node-criteria				
Total cohort, n=309	24 (7.8)	13 (95%CI 9-20)	348 (95%CI 232-522)	0.3% (95%CI 0.2-0.5%)
cT1, n=223	18 (8.1)	13 (95%CI 9-21)	335 (95%CI 209-536)	0.3% (95%CI 0.2-0.5%)

Discussion

- Results on missed adjuvant CDK4/6 inhibitor indication and impact on iDFS are consistent between the total cohort and patients with cT1 BC.
- Lymphovascular invasion was found to be a common predictor for adjuvant CDK4/6 inhibitor indication and node-positivity.
- Patients in the present cohort followed eligibility criteria of the SOUND/INSEMA trials. However, they were more frequently cT2, ≥pT2, and grade III compared to patients included in the SOUND and INSEMA trials.

Conclusions

- SOUND/INSEMA-eligible patients may not receive adjuvant CDK4/6 inhibitor treatment in up to 8% of cases.
- Missing these treatment opportunities results in a minimal impact on iDFS.
- Therefore, SLNB should not routinely be performed in SOUND/INSEMA-eligible patients to inform adjuvant CDK4/6 inhibitor treatment recommendations.

References

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