



Erken Evre Meme Kanserinde Kimlere Aksiller Diseksiyon Gerekir?

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25 Mart 2017



Cevap Nerede Saklı?

- *ACOSOG Z0011 çalışması*
- *IBCSG 23-01 çalışması*
- AMAROS çalışması
- SINADOR ONE çalışması
- POSNOC çalışması
- OTOASOR çalışması

Surgical Complications Associated With Sentinel Lymph Node Dissection (SLND) Plus Axillary Lymph Node Dissection Compared With SLND Alone in the American College of Surgeons Oncology Group Trial Z0011

Anthony Lucci, Linda Mackie McCall, Peter D. Beitsch, Patrick W. Whitworth, Douglas S. Reintgen, Peter W. Blumencranz, A. Marilyn Leitch, Sukumal Saha, Kelly K. Hunt, and Armando E. Giuliano

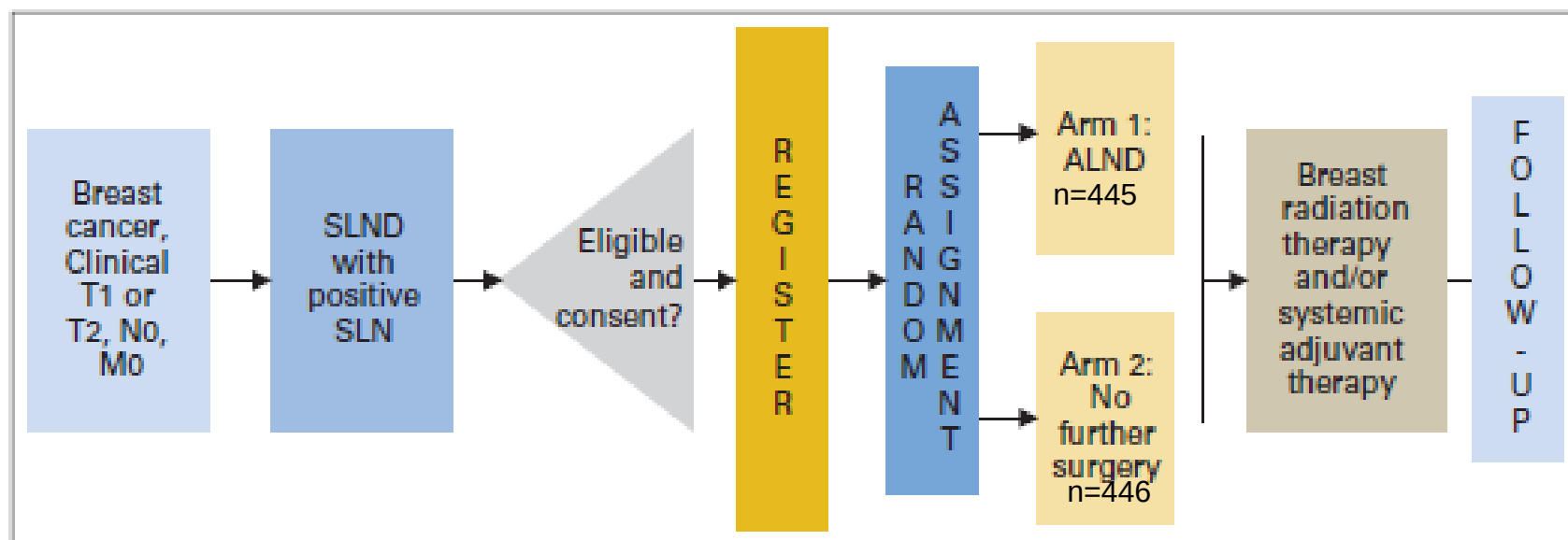


Fig 1. Study schema for American College of Surgeons Oncology Group trial Z0011. SLND, sentinel lymph node dissection; ALND, axillary lymph node dissection.

Adverse Surgical Effect	Study Group				<i>P</i>
	SLND + ALND		SLND Alone		
	No. of Patients*	%	No. of Patients*	%	
Wound Infections	31 of 373	8	11 of 371	3	.0016
Axillary seromas	53 of 373	14	21 of 371	6	.0001
Axillary paresthesias					
Present at 30 days	174 of 373	47	43 of 371	12	< .0001
Present at 6 months	146 of 335	44	35 of 288	12	< .0001
Present at 12 months	113 of 287	39	24 of 268	9	< .0001
Lymphedema (reported subjectively)					
Present at 6 months	27 of 327	8	19 of 339	6	.1772
Present at 12 months	37 of 288	13	16 of 268	2	< .0001
Present after 12 months	52 of 272	19	14 of 253	6	< .0001
Lymphedema (by arm measurements)					
Present at 30 days	23 of 255	8	17 of 272	6	.3609
Present at 6 months	29 of 270	11	21 of 271	8	.2296
Present at 12 months	26 of 242	11	14 of 226	6	.0786

Abbreviations: SLND, sentinel lymph node dissection; ALND, axillary lymph node dissection.
*Number of patients with adverse surgical effect of the total number of patients with available data.

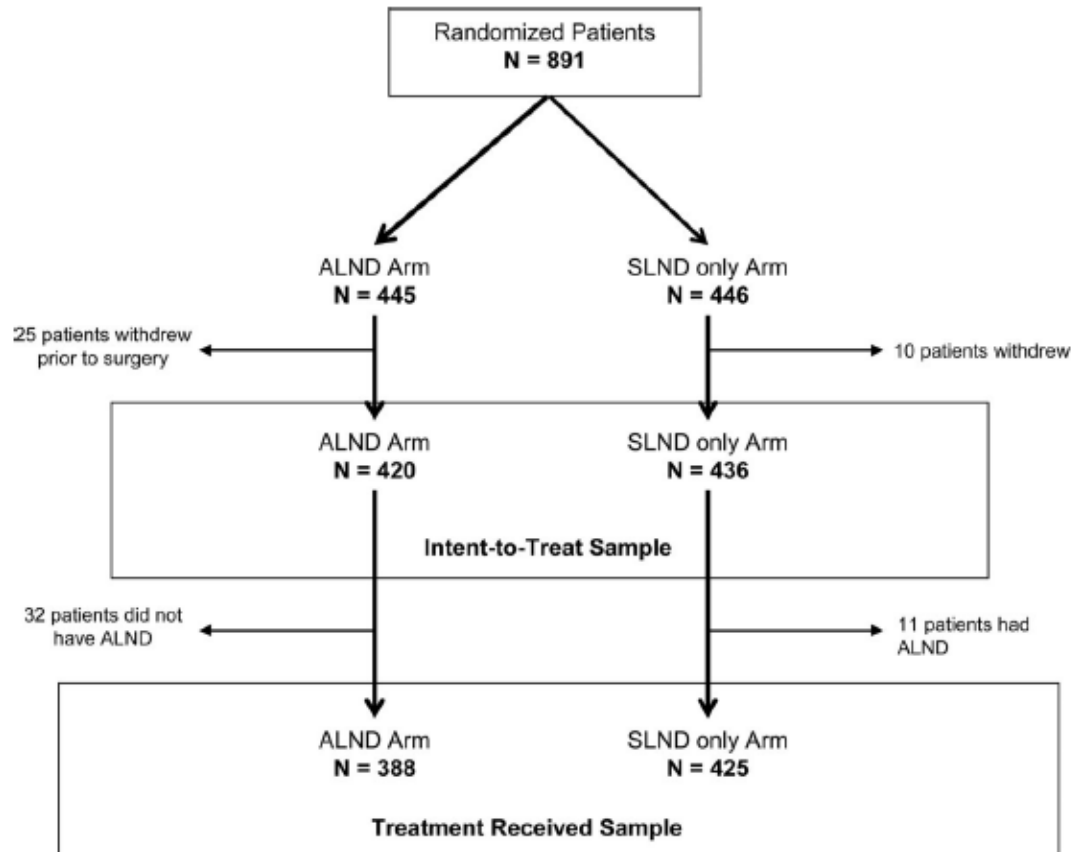
- * **ALND hastaların %75, SLND hastaların %25'inde morbidite görülmekte**
- * **ALMANAC çalışmasında ölçülerek saptanmış lenfödem oranı % 14**
- * **Çıkarılan lenf nodu sayısı ile lenfödem riski arasında ilişki yok**

Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases

The American College of Surgeons Oncology Group Z0011 Randomized Trial

Annals of Surgery • Volume 252, Number 3, September 2010

Median takip süresi 6.3 yıl

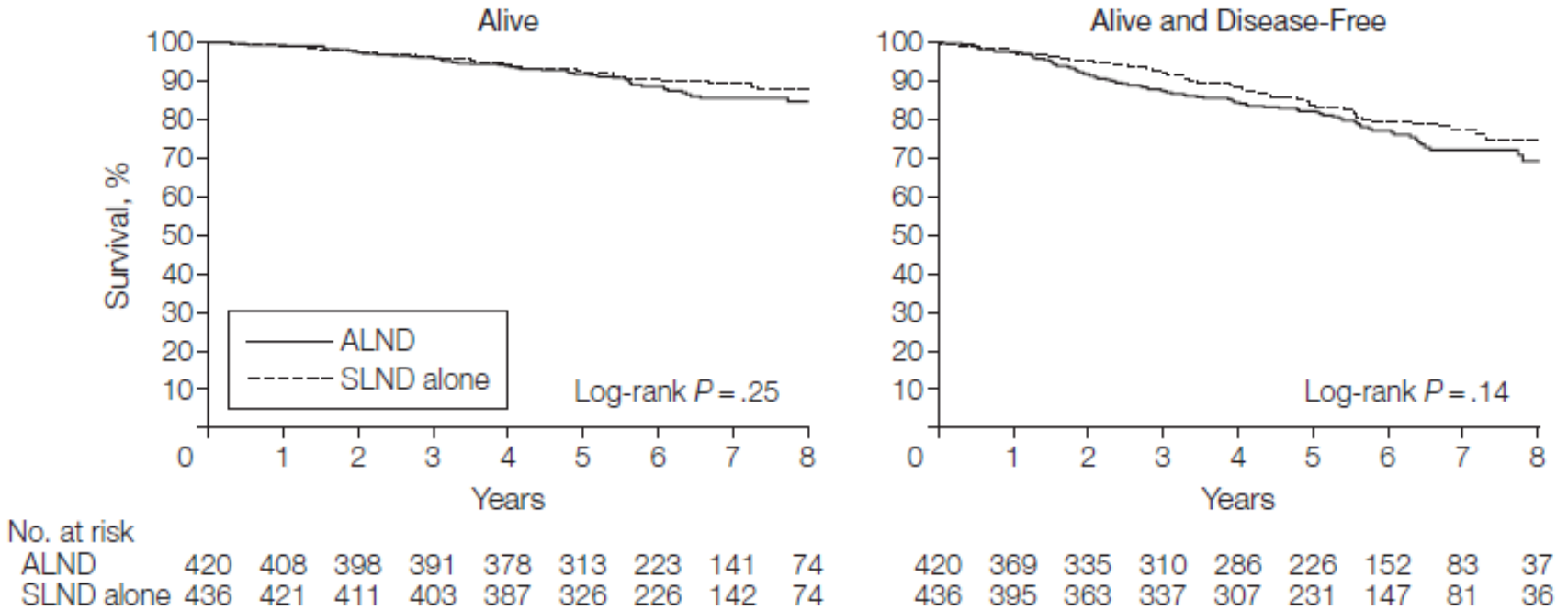


The American College of Surgeons Oncology Group Z0011 Randomized Trial

- ALND grubunda **388 hastanın 97'sinde (%27.3)** aksiller bölgede metastatik lenf nodu
- ALND grubunda; **137 hastada (%37.5)** → SLN mikrometastaz
- SLND grubunda; **164 hastada (%44.8)** → SLN mikrometastaz
- SLN mikrometastaz olanlarda aksillada ilave (+) LN ; **%10**
- Lokorejyonel nüks **29 hastada (%3.4)**
- Lokal rekürrens; SLND grubunda **8 hastada (%1.8)**
ALND grubunda **15 hastada (%3.6)**
- Rejyonel rekürrens SLND grubunda **4 hastada (%0.9)**
ALND grubunda **2 hastada (%0.5)**
- NSABP-04 çalışması (radikal mastektomi vs. total mastektomi+ nodal radyoterapi vs. total mastektomi + gecikmiş ALND); ALND lokorejyonel rekürrens riskini azaltır ancak 25 yıl sonuçları sağkalımda fark yok

The American College of Surgeons Oncology Group Z0011 Randomized Trial

Figure 2. Survival of the ALND Group Compared With SLND-Alone Group

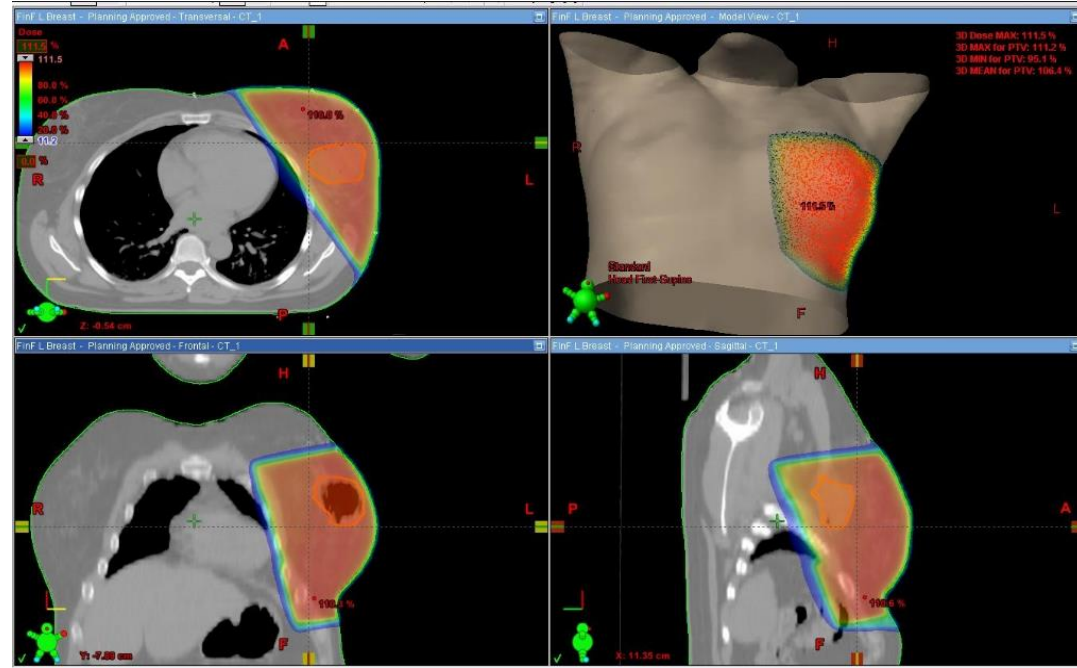


ALND indicates axillary lymph node dissection; SLND, sentinel lymph node dissection.

- 5 yıl sağkalım ALND grubunda %91.8, SLND grubunda %92.5
- 5 yıl hastalıksız sağkalım ALND grubunda %82.2, SLND grubunda %83.9

The American College of Surgeons Oncology Group Z0011 Randomized Trial

- %95 adjuvan sistemik tedavi (kemoterapi, hormonoterapi)
- Tüm meme radyoterapi (50Gy);
 - SLND bölgesinin tamamı
 - Level I ALN büyük kısmı
 - Level II ALN kısmı
- ER(-) oranı çalışmada az (her iki grupta %16) o yüzden lokal rekürrens az denilmekte, ancak ER(-) ve ER (+) hastalar arasında lokal rekürrens fark yok



ORIGINAL ARTICLE – BREAST ONCOLOGY

Presenting Features of Breast Cancer Differ by Molecular Subtype

Lisa Wiechmann, MD¹, Michelle Sampson, BS¹, Michelle Stempel, MPH¹, Lindsay M. Jacks, MS², Sujata M. Patil, PhD², Tari King, MD¹, and Monica Morrow, MD¹

¹Breast Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; ²Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY

TABLE 3 Multivariate logistic regression ($N = 4,971$)

Variable	Outcome					
	Multicentric/multifocal disease		Any nodal involvement (≥ 1 positive LN)		High-volume nodal involvement (≥ 4 positive LN)	
	Adjusted OR (95% CI)	<i>P</i> value	Adjusted OR (95% CI)	<i>P</i> value	Adjusted OR (95% CI)	<i>P</i> value
Subgroup						
Luminal A	1.0	0.0002	1.0	<0.0001	1.0	<0.0001
Luminal B	1.2 (0.9–1.5)		1.0 (0.8–1.2)		1.2 (0.9–1.7)	
<i>HER-2</i>	1.6 (1.2–2.1)		1.1 (0.8–1.5)		2.0 (1.4–2.8)	
Basal	0.9 (0.7–1.1)		0.6 (0.5–0.8)		0.7 (0.5–0.9)	
Tumor size	0.96 (0.9–1.0)	0.09	1.7 (1.6–1.8)	<0.0001	1.7 (1.6–1.8)	<0.0001
Nuclear grade						
Low/intermediate	1.0	0.74	1.0	0.009	1.0	0.0005
High	1.0 (0.8–1.1)		1.2 (1.1–1.4)		1.5 (1.2–1.8)	
LVI						
No	1.0	<0.0001	1.0	<0.0001	1.0	<0.0001
Yes	1.9 (1.7–2.2)		3.8 (3.3–4.4)		5.1 (4.2–6.3)	
Age	0.986 (0.98–0.99)	<0.0001	0.984 (0.98–0.99)	<0.0001	0.99 (0.98–1.00)	0.005

LN lymph node; OR odds ratio; 95% CI, 95% confidence interval; LVI lymphovascular invasion; ER estrogen receptor; PR progesterone receptor
Luminal A as referent group; ORs adjusted for age, tumor size, LVI, and nuclear grade. Data are provided for luminal A (ER+ or PR+ and *HER-2*–), luminal B (ER+ or PR+ and *HER-2*+), *HER-2* (ER– and PR– and *HER-2*+), and basal (ER– and PR– and *HER-2*–)

Annual Hazard Rates of Recurrence for Breast Cancer During 24 Years of Follow-Up: Results From the International Breast Cancer Study Group Trials I to V

Marco Colleoni, Zhuoxin Sun, Karen N. Price, Per Karlsson, John F. Forbes, Beat Thürlimann, Lorenzo Gianni, Monica Castiglione, Richard D. Gelber, Alan S. Coates, and Aron Goldhirsch

Table 3. Cumulative Incidence of Site-Specific First Breast Cancer Events by Year From Random Assignment

Event	Cumulative Incidence (%; SE)				
	Year 5	Year 10	Year 15	Year 20	Year 25
Local only					
ER positive	8.8 (0.7)	11.2 (0.7)	11.9 (0.8)	12.5 (0.8)	12.6 (0.8)
ER negative	6.9 (0.8)	8.0 (0.8)	8.1 (0.8)	8.3 (0.8)	8.3 (0.8)
Contralateral breast ± local					
ER positive	2.2 (0.3)	3.9 (0.5)	5.1 (0.5)	6.2 (0.6)	6.5 (0.6)
ER negative	1.3 (0.3)	2.7 (0.5)	3.8 (0.6)	5.3 (0.7)	6.2 (0.8)
Regional ± above					
ER positive	5.0 (0.5)	6.2 (0.6)	7.0 (0.6)	7.3 (0.6)	7.5 (0.6)
ER negative	9.0 (0.8)	10.0 (0.9)	10.0 (0.9)	10.0 (0.9)	10.1 (0.9)
Distant ± above					
ER positive	23.4 (1.0)	31.9 (1.1)	35.0 (1.1)	37.4 (1.2)	38.3 (1.2)
ER negative	27.1 (1.3)	31.8 (1.4)	33.4 (1.4)	34.1 (1.4)	35.3 (1.5)

NOTE. Data are shown as percentage (SE).

Abbreviation: ER, estrogen receptor.

Long-term Follow-up From the American College of Surgeons Oncology Group
(Alliance) ACOSOG Z0011 Randomized Trial

Annals of Surgery • Volume 264, Number 3, September 2016

- Medyan takip süresi; **9.25 yıl**

TABLE 3. Number and Cumulative Incidence of Locoregional Recurrences (%) at Specific Time Points

Time, y	ALND				SLND Only			
	No. at Risk	LRR Events	Local Events	Regional Events	No. at Risk	LRR Events	Local Events	Regional Events
1	375	1 (0.3%)	1 (0.3%)	0 (0.0%)	394	2 (0.5%)	1 (0.2%)	1 (0.2%)
2	342	9 (2.4%)	8 (2.1%)	1 (0.3%)	365	3 (0.7%)	1 (0.2%)	2 (0.5%)
5	286	15 (4.0%)	13 (3.5%)	2 (0.5%)	279	12 (3.3%)	8 (2.2%)	4 (1.1%)
10	130	21 (6.2%)	19 (5.6%)	2 (0.5%)	139	17 (5.3%)	12 (3.8%)	5 (1.5%)

ALND indicates axillary lymph node dissection; LRR, locoregional recurrence; SLND, sentinel lymph node dissection.

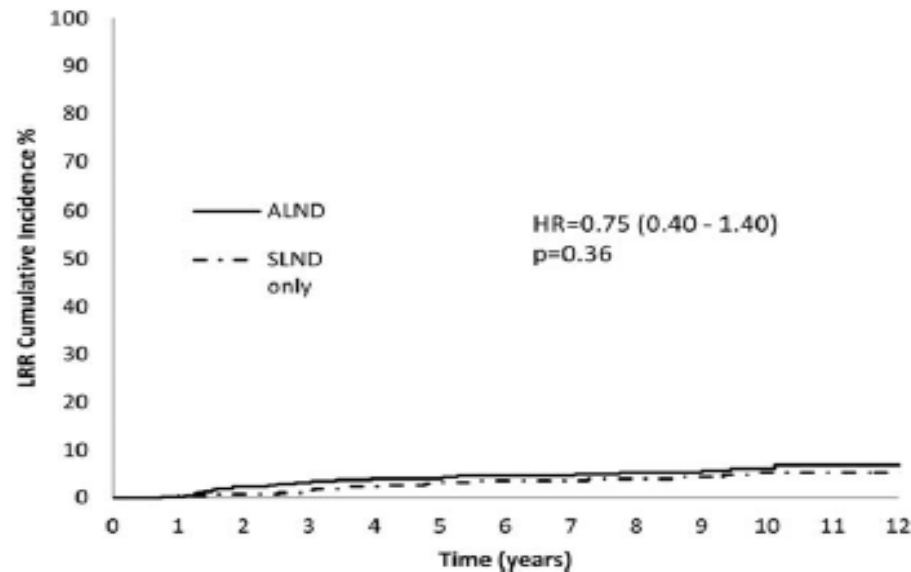


FIGURE 2. Cumulative incidence of locoregional recurrence by treatment arm.

*Long-term Follow-up From the American College of Surgeons Oncology Group
(Alliance) ACOSOG Z0011 Randomized Trial*

- Lokorejyonel nükste etkili prognostik faktörler; ***Yaş (?)***, ***Hormon rsp. durumu***, ***Tümör çapı***, ***Modifiye Bloom-Richardson skoru***
- ***ER (-) tümörler erken lokorejyonel nüks piki oluyor ve sonra hızla giderek azalıyor, ER (+) daha geç ortaya çıkıyor***
- Lenfovasküler invazyon, tümör histolojik tipi, mikro-makro metastaz; etkili bulunmamış

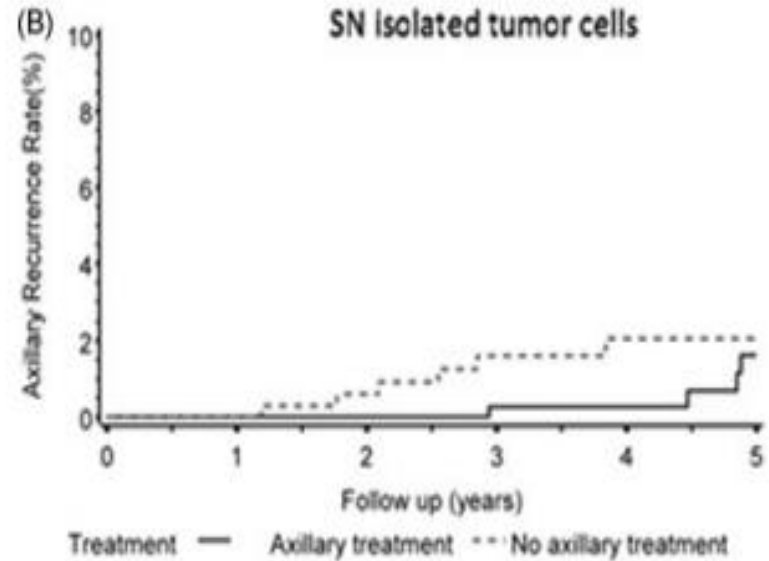
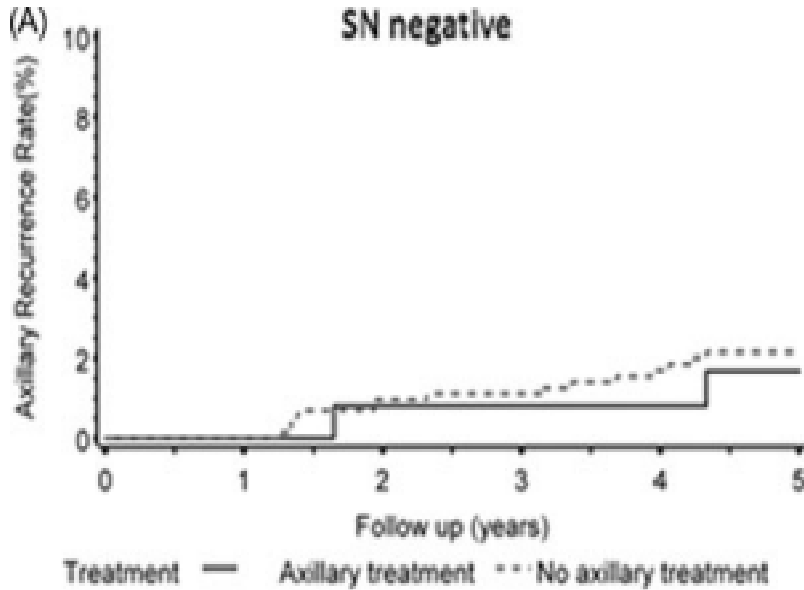
The American College of Surgeons Oncology Group Z0011 Randomized Trial

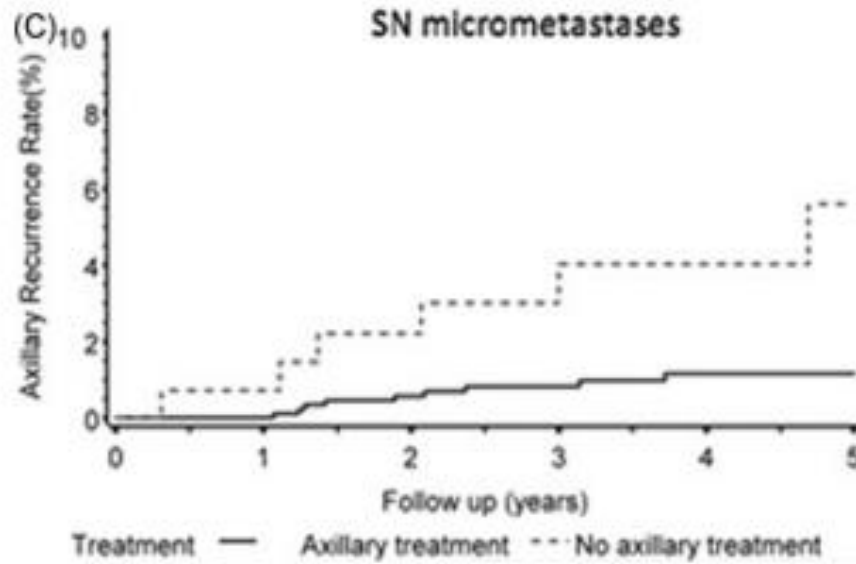
- ***Mastektomi***
- ***Radyoterapi ilavesiz lumpektomi***
- ***Parsiyel meme radyoterapisi***
- ***Neoadjuvan tedavi***
- ***Prone pozisyonda tüm meme radyoterapisi***



ITC-Mikrometastaz

- **Dutch Kohort study:** Mikrometastaz- ITC adjuvan tedavi verilmez ise 5 yıllık hastalıksız sağkalım %10↓
- **Hollanda Çalışması:** (Annals of Surgery Volume 255, Number 1, January 2012)





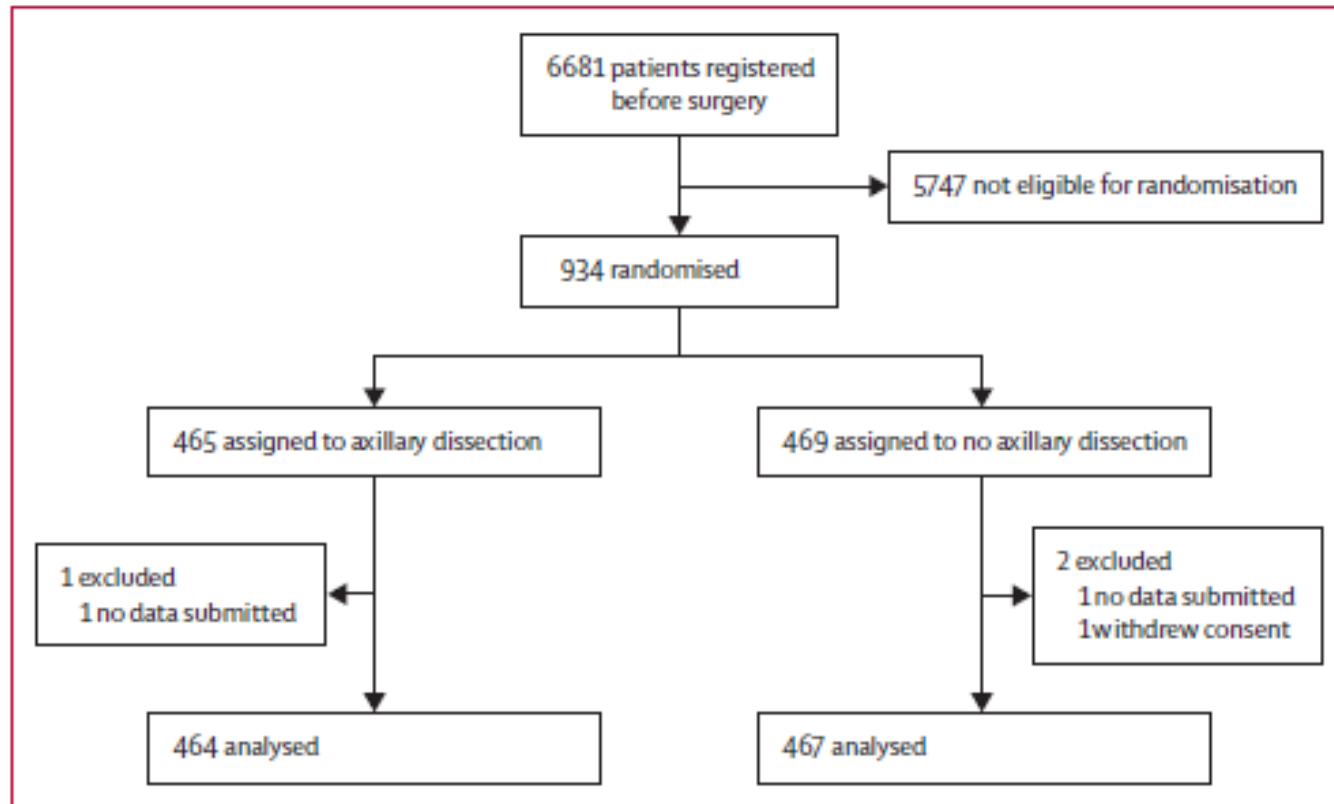
- Tümör çapı ↑
 - Histolojik grade 3
 - Hormon reseptörleri (-)
- Rejyonel rekürrens ↑**

Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial



Lancet Oncol 2013; 14: 297-305

- <5 cm tümör, SLNB sonucunda ≥ 1 mikrometastaz, ektrakapsüler tutulum yok



IBCSG 23-01

Local treatment*

Mastectomy	44 (9%)	42 (9%)
Breast-conserving surgery	420 (91%)	425 (91%)
Without radiotherapy	10/420 (2%)	12/425 (3%)
With radiotherapy	410/420 (98%)	413/425 (97%)
Intraoperative radiotherapy only	79/420 (19%)	80/425 (19%)
Postoperative radiotherapy only	293/420 (70%)	297/425 (70%)
Combination radiotherapy	36/420 (9%)	35/425 (8%)
Unspecified radiotherapy	2/420 (<1%)	1/425 (<1%)

Systemic therapy

Any systemic therapy	441 (95%)	451 (97%)
Hormonal therapy only	292 (63%)	315 (67%)
Chemotherapy only	42 (9%)	33 (7%)
Combination therapy	107 (23%)	103 (22%)

Data are number of patients (%) unless otherwise indicated. *Percentages for type of surgery are based on entire population, those for radiotherapy (no or yes) and for type of radiotherapy are based on only the breast-conserving surgery subpopulation.

Table 1: Patient characteristics and adjuvant therapies

	Axillary dissection (n=447)	No axillary dissection (n=453)	p value†
Sensory neuropathy	82 (18%)	55 (12%)	0.012
Grade 1	60 (13%)	40 (9%)	
Grade 2	15 (3%)	6 (1%)	
Grade 3	1 (<1%)	0	
Grade 4	0	0	
Unknown grade	6 (1%)	9 (2%)	
Lymphoedema	59 (13%)	15 (3%)	<0.0001
Grade 1	33 (7%)	10 (2%)	
Grade 2	20 (4%)	3 (<1%)	
Grade 3	2 (<1%)	0	
Grade 4	1 (<1%)	0	
Unknown grade	3 (<1%)	2 (<1%)	
Motor neuropathy	37 (8%)	13 (3%)	0.0004
Grade 1	25 (6%)	11 (2%)	
Grade 2	9 (2%)	1 (<1%)	
Grade 3	3 (<1%)	1 (<1%)	
Grade 4	0	0	
Unknown grade	0	0	

*Excludes 31 patients (17 in the axillary dissection group and 14 in the no-axillary-dissection group) who did not receive the randomly assigned treatment. †Based on Fisher's exact test comparison of the occurrence of any grade event across treatment groups.

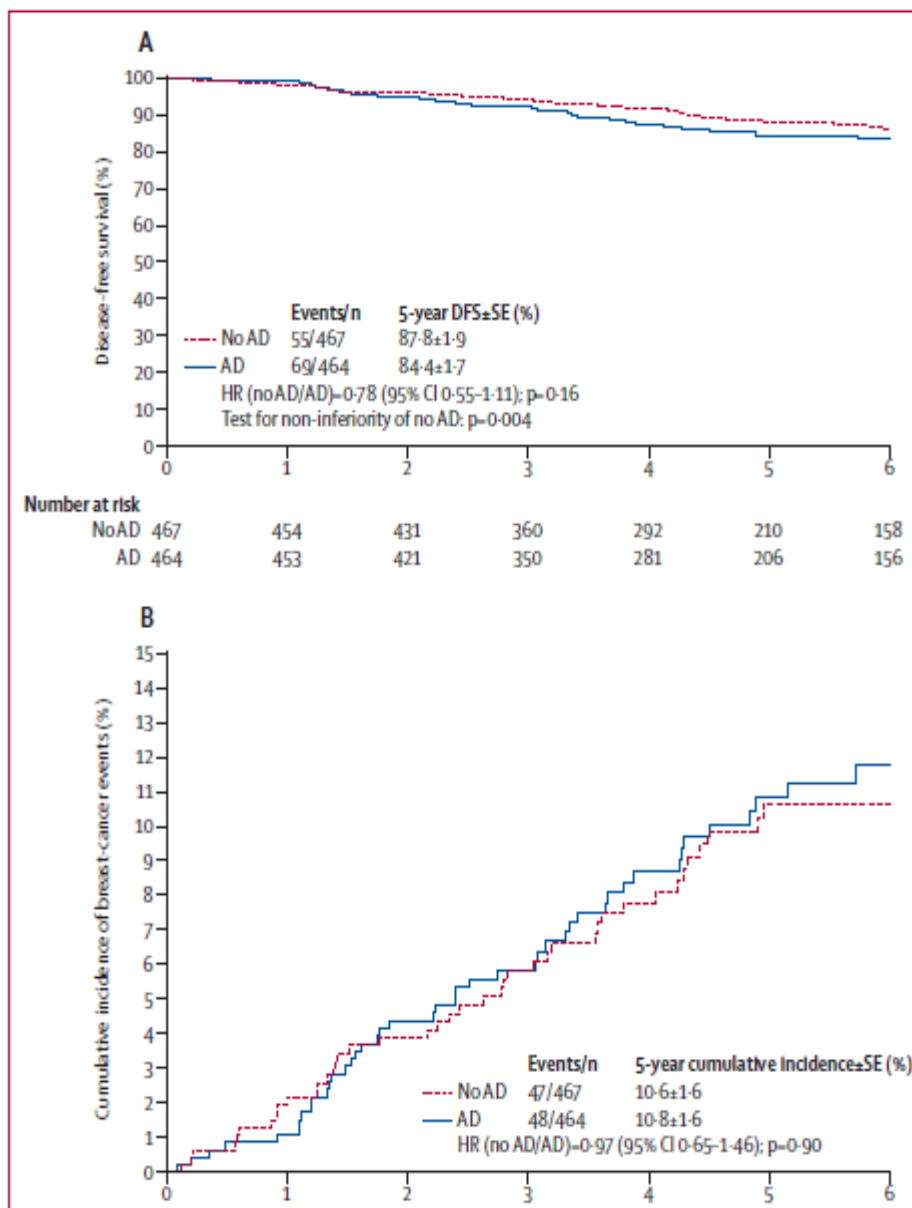
Table 2: Long-term surgical events*

IBCSG 23-01

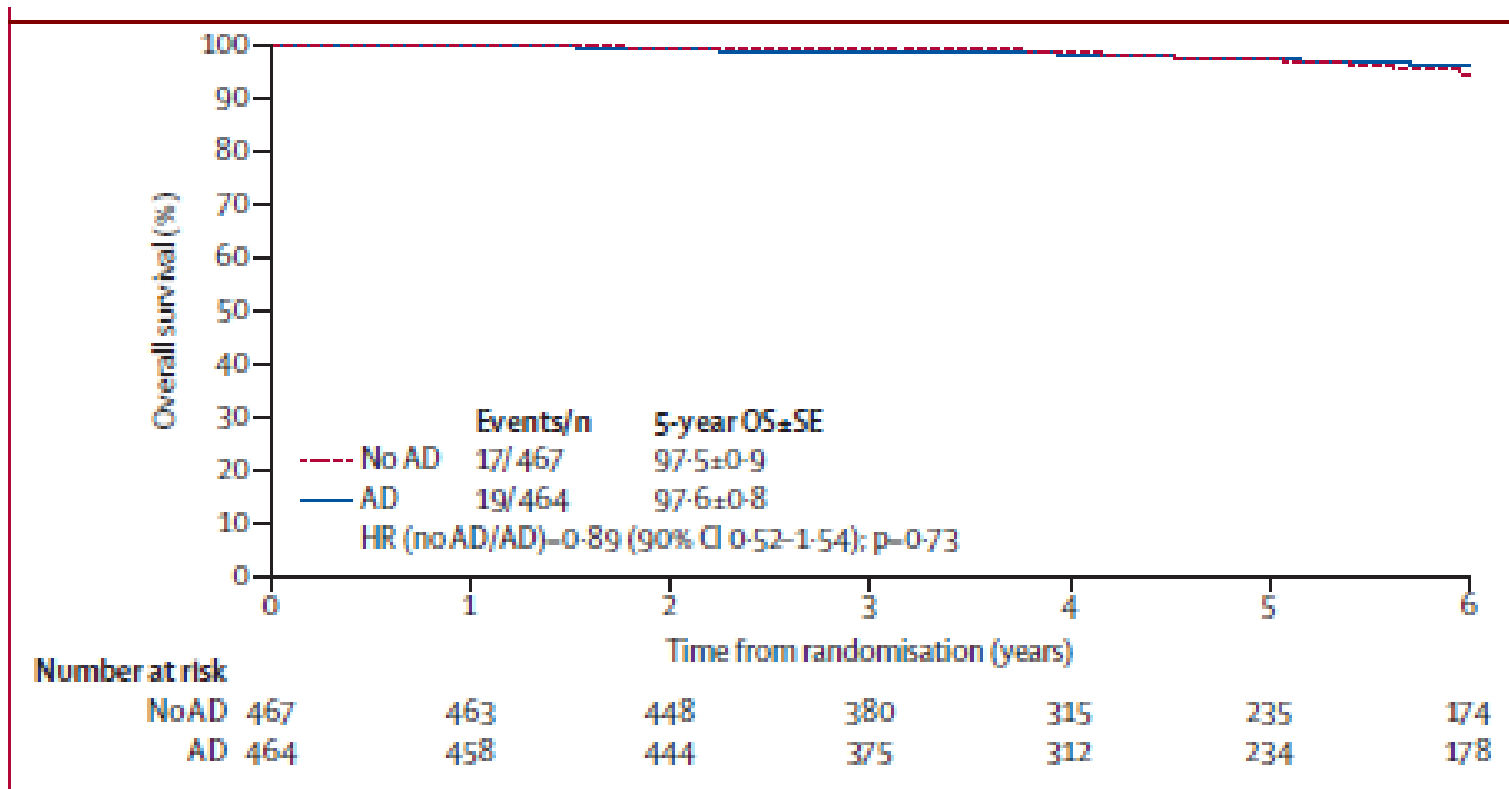
	Axillary dissection (n=464)	No axillary dissection (n=467)
Disease-free survival events*		
Total	69 (15%)	55 (12%)
Breast cancer events		
Local	10 (2%)	8 (2%)
Regional	1 (<1%)	5 (1%)
Distant	34 (7%)	25 (5%)
Contralateral breast	3 (<1%)	9 (2%)
Non-breast cancer events		
Second (non-breast) primary†	20 (4%)	6 (1%)
Death without cancer event	1 (<1%)	2 (<1%)
Deaths		
Total	19 (4%)	17 (4%)

*Includes all breast cancer events, all non-breast cancer events, and deaths with cause unknown. †Types (number) of second primaries in the group with axillary dissection were gastrointestinal (four), genitourinary (two), gynaecological (six), haematological (two), laryngeal (two), lung (one), and sarcoma (three). Types (number) in the group without axillary dissection were gastrointestinal (two), gynaecological (three), and melanoma (one).

Table 3: Disease-free survival events and deaths at 5.0 years median follow-up of intention-to-treat population



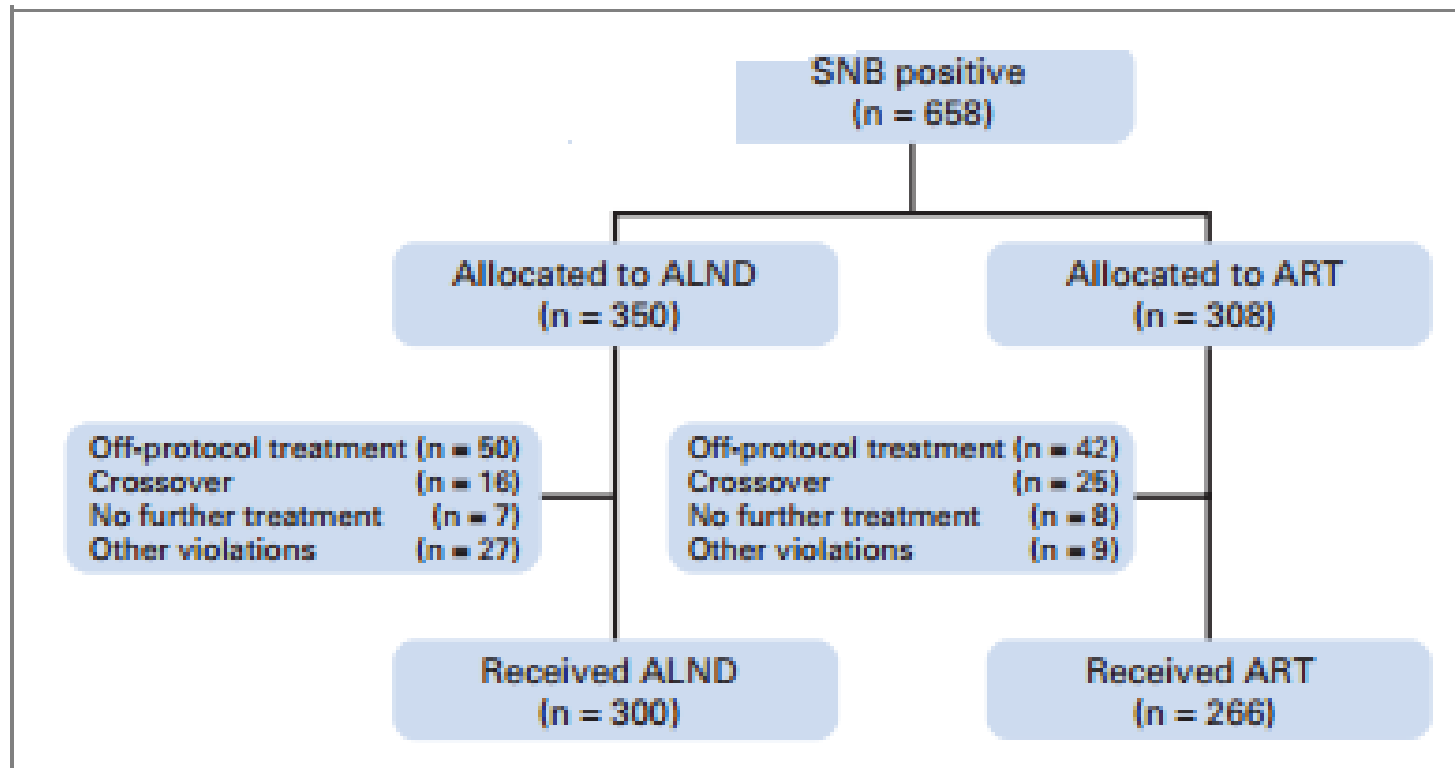
IBCSG 23-01



- %69 tümör çapı < 2cm
- ALND grubunda aksillada met. saptama %13
- Tümör çapı (>2cm) ve tümör grade (grade 3) aksiller diseksiyondan bağımsız hastalıksız sağkalım için en önemli parametre

Role of Axillary Clearance After a Tumor-Positive Sentinel
Node in the Administration of Adjuvant Therapy in Early
Breast Cancer

AMAROS trial



- Tümör çapı < 3 cm ve tek odak
- Cerrahiden sonraki 12 hafta içinde ART grubunda; supraklavikuler fossa ve Level I-II-III 25 fraksiyon, 50Gy

- MKC; ALND grubunda %88, ART grubunda %89

Table 2. Administration of Adjuvant Therapy

Therapy	ALND Arm (n = 300)		ART Arm (n = 266)	
	No. of Patients	%	No. of Patients	%
None	23	8	24	9
Endocrine therapy	95	32	80	30
Chemotherapy	35	12	39	15
Chemotherapy plus endocrine therapy	140	47	123	46
Missing	7	2	0	0
Radiotherapy (breast/chest wall)	257	86	237	89
Axillary radiotherapy	15	5	266	100

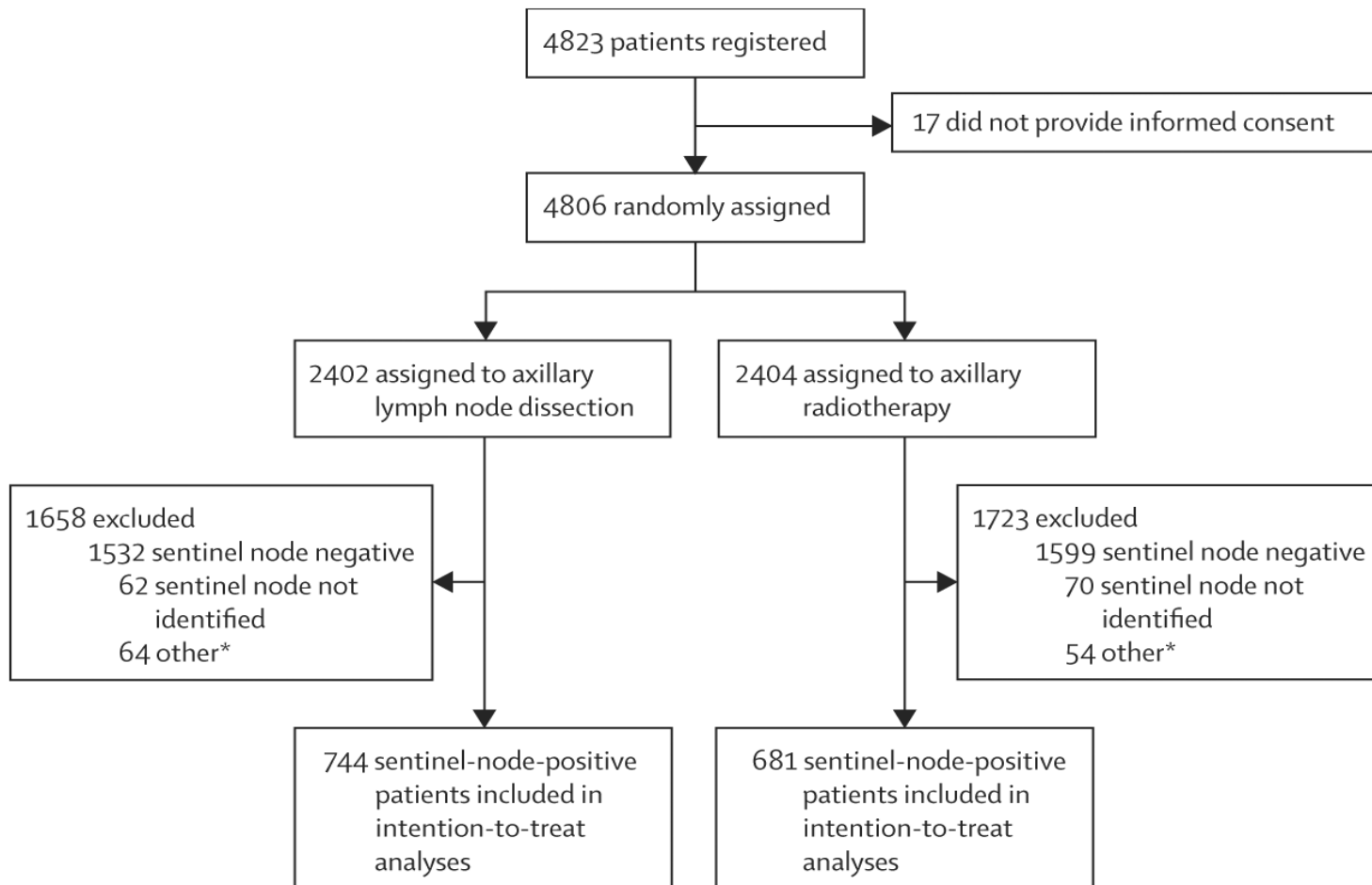
Abbreviations: ALND, axillary lymph node dissection; ART, axillary radiation therapy.

- Klasik bilgi: Aksillada (+) lenf nodlarının bilinmesi; adjuvan tedavi seçeneklendirmesinde de önem arzetmekte
- UICC TNM evrelemesi ???
- Adjuvan tedavi tiplendirmesi; hasta, tümör ve SLN karakteristiklerine bakılarak yapılabilir
- 70-gene profile (MammaPrint) ya da 21-gene profile (Oncotype DX) ???

Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial

Lancet Oncol. 2014 November ; 15(12): 1303–1310. doi:10.1016/S1470-2045(14)70460-7.

- Medyan takip 6.1 yıl
- 2008 sonrası <5 cm ve multifokal tümörlerde alınmış



Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial

- **5 yıl aksiller rekürrens;**
ALND; 4/744 hasta (%0.43)
ART; 7/681 (%1.19)
SLN (-) hastalarda rekürrens (%0.72)
- **5 yıl hastalıksız sağkalım;**
ALND; %86.9
ART; %82.7
SLN (-); %87.9
- **Meme kanserine bağlı ölüm;**
- ALND; 53 (%7)
- ART; 54 (%8)

Table 2**Lymphoedema**

	Axillary lymph node dissection	Axillary radiotherapy	p value
Clinical sign of lymphoedema in the ipsilateral arm			
Baseline	3/655 (<1%)	0/586 (0%)	0.25
1 year	114/410 (28%)	62/410 (15%)	<0.0001
3 years	84/373 (23%)	47/341 (14%)	0.003
5 years	76/328 (23%)	31/286 (11%)	<0.0001
Arm circumference increase >10% of the ipsilateral upper or lower arm, or both			
Baseline	33/655 (5%)	24/586 (4%)	0.497
1 year	32/410 (8%)	24/410 (6%)	0.332
3 years	38/373 (10%)	22/341 (6%)	0.080
5 years	43/328 (13%)	16/286 (5%)	0.0009

Data are n/N (%), unless otherwise specified.

- Kombine tedavi sonuçları lenfödem açısından çok kötü
- ROM (abduksiyon, adduksiyon, anteversiyon, retroversiyon) fark yok

Eight-year follow up result of the OTOASOR trial: The
Optimal Treatment Of the Axilla – Surgery Or
Radiotherapy after positive sentinel lymph node biopsy in
early-stage breast cancer:

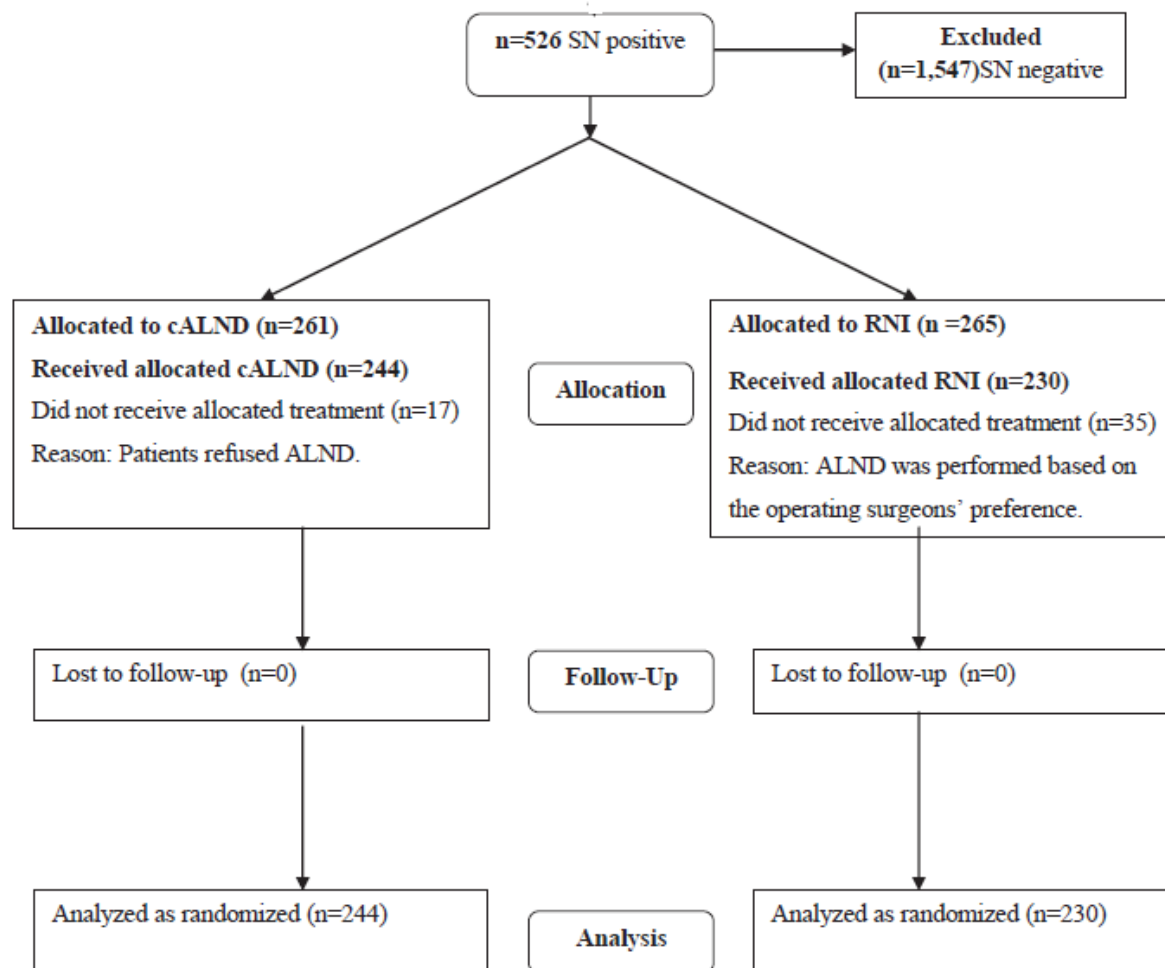
A randomized, single centre, phase III, non-inferiority trial

EJSO

the Journal of Cancer Surgery

www.ejso.com

EJSO xx (2017) 1–8



OTOASOR çalışması

- <3cm
- SLN ITC-mikro-makrometastaz
- MKC sonrası; tüm meme, level1-2-3 aksilla ve supraklavikulaer fossa 50 Gy
- Ortalama takip; 97 ay

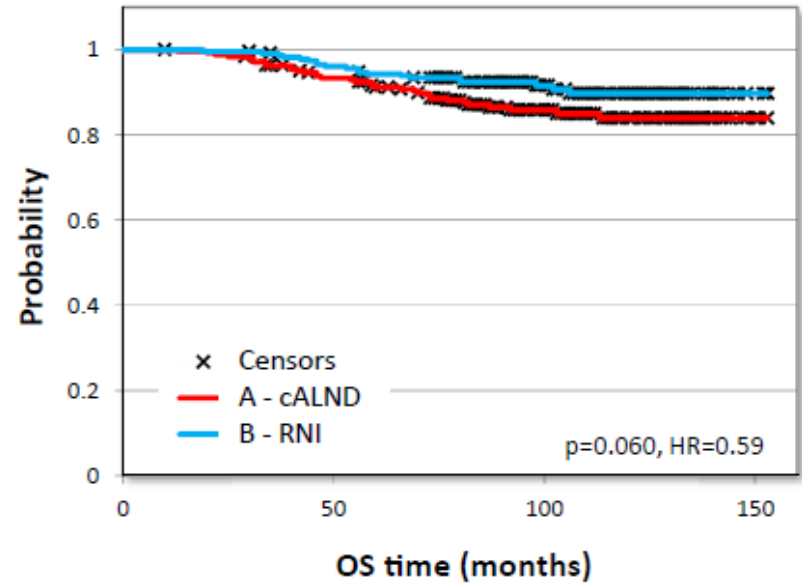
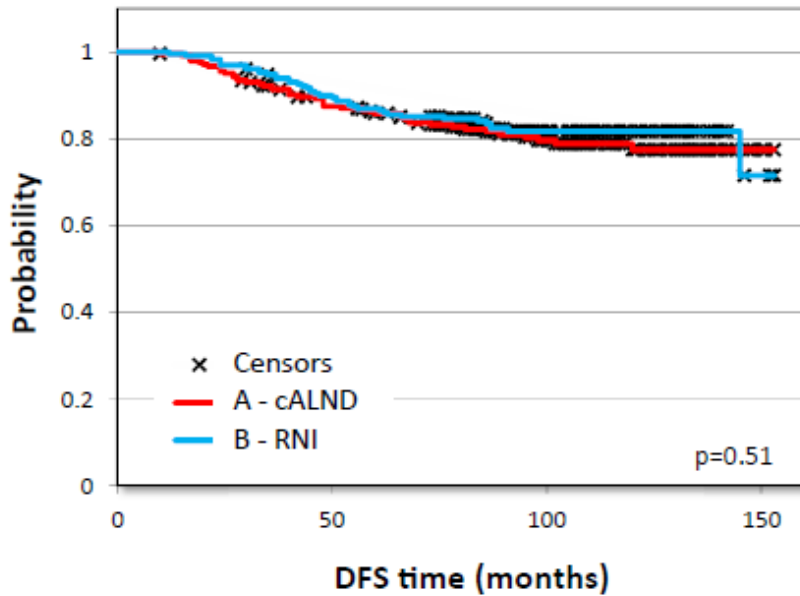
Table 1

Patient and treatment characteristics according to treatment arms.

Characteristic		Arm A (cALND) (n = 244) No. (%)	Arm B (RNI) (n = 230) No. (%)	p-value
Age (years)	Mean (range)	54.7 (26–74)	55.2 (27–74)	
Menopausal Status	Pre Post	83 (34) 161 (66)	62 (27) 168 (73)	0.095
Surgery	Breast-conserving ROLL (non-palpable)	200 (82) 71 (29)	200 (84) 76 (33)	0.164
cT category	Mastectomy cT1 cT2 (<3 cm)	44 (18) 152 (62) 92 (38)	30 (16) 157 (68) 73 (32)	0.173

OTOASOR çalışması

- Lenfödem, parestezi, şişlik, kol ağrısı, omuz ROM azalma ALND grubunda %15.3, ART grubunda %4.7



SINODAR ONE, an ongoing randomized clinical trial to assess the role of axillary surgery in breast cancer patients with one or two macrometastatic sentinel nodes



Corrado Tinterri ^a, Giuseppe Canavese ^a, Paolo Bruzzi ^b, Beatrice Dozin ^{b,*}

The Breast 30 (2016) 197–200

SINODAR ONE Trial

ACOSOG Z0011 eksiklikleri;

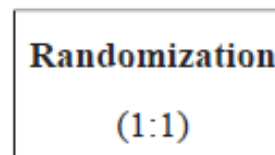
%70 T1 (<2cm)

%40 SLN mikrometastaz

%65 tek SLN (+)

%80 HR (+)

- Age ≥ 40 - ≤ 75 y
- T1-T2 unifocal invasive breast cancer
- Negative preoperative axillary ultrasound
- BCS / mastectomy
- 1 - 2 SLNs with macrometastases



- | | |
|--------------------------|--------------------|
| • No axillary treatment | • ALND |
| but | plus |
| • Adjuvant therapy alone | • Adjuvant therapy |

POSNOC: A Randomised Trial Looking at Axillary Treatment in Women with One or Two Sentinel Nodes with Macrometastases

A. Goyal ^{*}, D. Dodwell [†]

Clinical Oncology 27 (2015) 692–695

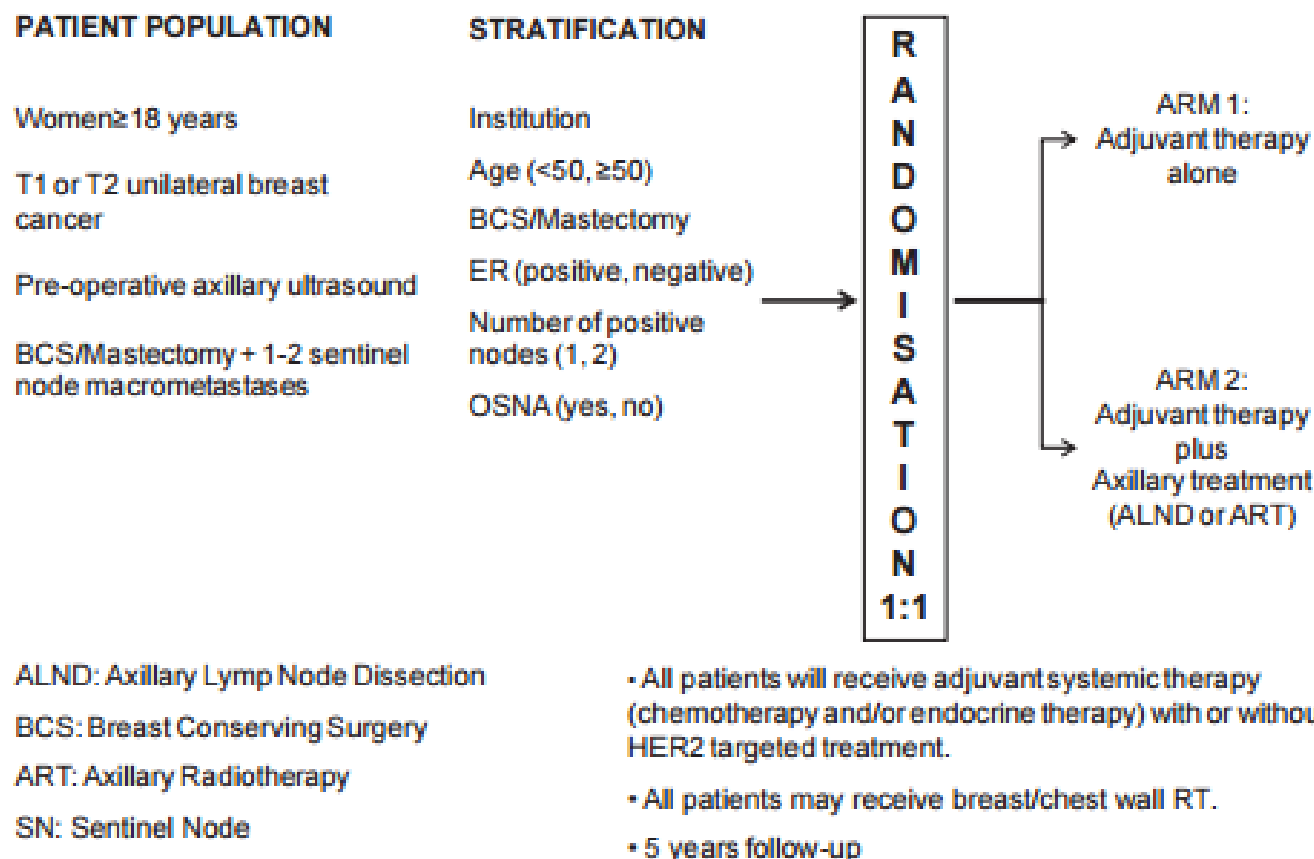


Fig 1. POSNOC trial design.

- *National Institute for Health and Care Excellence (NICE)*; 1-2 SLN makrometastaz ALND tavsiye etmekte (2014)
- *The European Society for Medical Oncology (ESMO)*; Z11 çalışmasının konfirme edilmesini ve farklı karakterde hastalarla tekrarlanmasını öneriyor (2013)
- *The Association of Breast Surgery in the UK*; Z11 çalışmasının kritik kısıtlılıklarının ortadan kaldırılarak tekrarlanmasını öneriyor (2015)
- *The American Society of Clinical Oncology* (2014);

Sentinel Lymph Node Biopsy for Patients With Early-Stage Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

- ***Clinicians should not recommend ALND for women with early-stage breast cancer who do not have nodal metastases. Type: evidence based; benefits outweigh harms. Evidence quality: strong. Strength of recommendation: high***
- ***The recommendations in response to this clinical question were split into two separate recommendations. The first recommendation was crafted to reflect the eligibility criteria of Z0011 (women with early-stage breast cancer and one to two SLN metastases, who underwent BCS with whole-breast radiotherapy).***
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Tailoring therapies—improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015

A. S. Coates¹, E. P. Winer², A. Goldhirsch^{3*}, R. D. Gelber⁴, M. Gnant⁵, M. Piccart-Gebhart⁶, B. Thürlimann⁷, H.-J. Senn⁸ & Panel Members[†]

Table 1. Recent research findings presented at the 14th International Conference on Primary Therapy of Early Breast Cancer and their implications for patient care

Field or treatment	Status of research/implications for patient care
Surgical management	Local regional recurrence is becoming less frequent over recent decades [28]. Meta-analysis of surgical series showed no further benefit from margins beyond ‘no ink on invasive tumor or DCIS’ [29]. This conclusion applies regardless of tumor characteristics such as lobular histology, extensive intraductal component, young age, and unfavorable biological subtype [7]. Avoiding axillary dissection for patients with one or two macrometastatic lymph nodes [30, 31] proved safe in a large institutional series, confirming the applicability of randomized trial approaches (ACOSOG Z011, AMAROS) for the majority of women with T1 and T2 clinically node-negative breast cancer [6].

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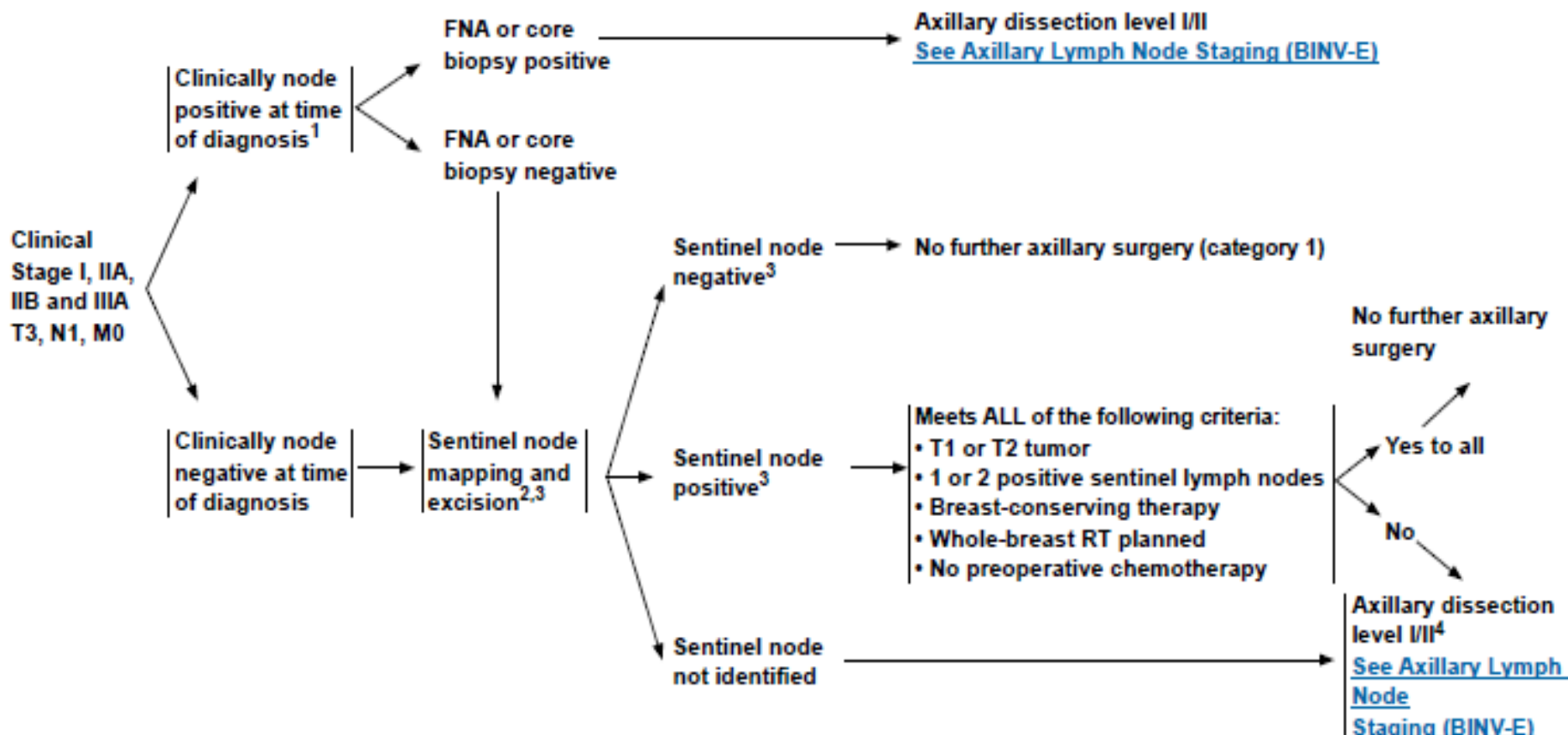
Surgery

A large US population-based study of more than 200 000 women noted that 7% underwent contralateral prophylactic mastectomy (CPM). Although a small survival benefit was observed [87], information was not available on BRCA status, which is known to be both a motivation for CPM and a marker for increased benefit from such surgery. Thus, selection bias could not be adequately addressed in this registry study [88]. There has been a substantial increase in the use of CPM over the past two decades in the United States, particularly in women <40 [89]. In Europe, the trend is less marked [90, 91]. Sentinel node biopsy is feasible and accurate after neoadjuvant chemotherapy and allows precise assessment of pCR [92–95]. In patients with nodal involvement at presentation, the false-negative rate of sentinel node biopsy is highly correlated with the number of sentinel nodes retrieved. Breast conservation after neoadjuvant chemotherapy is feasible even when the disease is multifocal or multicentric, provided that the margins are free of disease [96].

*Long-term Follow-up From the American College of Surgeons Oncology Group
(Alliance) ACOSOG Z0011 Randomized Trial*

Sentinel lymph node dissection (SLND) alone is widely accepted as axillary management for women with clinically node-negative breast cancer. However, SLND without axillary lymph node dissection (ALND) for selected SLN positive patients remains controversial even though 2 prospective randomized trials have demonstrated noninferiority of SLND alone to SLND and ALND for SLN positive patients.

SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB and IIIA T3, N1, M0





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The Breast

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Original article

Role of total tumour load of sentinel lymph node on survival in early breast cancer patients



- Tutulan lenf nodu ile prognoz arasındaki ilişki → SLN deki CK19 mRNA miktarı (SLN TTL, One Step Nucleic Asit Amplification-OSNA-) ile prognoz arasındaki ilişki
- T1-3 tümör, klinik ve USG negatif aksilla
- SLN makrometastaz = OSNA ++ $\geq 5 \times 10^3$ copies/ μ L of CK19 mRNA,
- SLN mikrometastaz = OSNA + 2.5×10^2 to 5×10^3 copies/ μ L,
- SLN non-metastaz = OSNA – $< 2.5 \times 10^2$ copies/ μ L.
- Tüm SLN lerdeki TTL toplamı
- 950 hasta medyan 5.1 yıl takip

Table 1
Demographic and tumour data.

Variable	Levels	N	%
Sex	Male	6	0.6
	Female	944	99.4
Menopause	Pre-menopause	300	31.6
	Post-menopause	573	60.3
	Missing	77	8.1
Tumour type	Ductal	797	83.9
	Lobular	83	8.7
	Other	70	7.4
Tumour grade	1	275	28.9
	2	465	49.0
	3	210	22.1
LVI	Yes	185	19.5
	No	765	80.5
HER2	Positive	108	11.4
	Negative	842	88.6
ER	Positive	837	88.1
	Negative	113	11.9
PR	Positive	767	80.7
	Negative	183	19.3
Molecular subtype	Luminal A	430	45.3
	Lum. B HER2 neg.	339	35.7
	Lum. B HER2 pos.	76	8.0
	HER2 enriched	32	3.4
	Triple negative	73	7.7

LVI: lymphovascular invasión; ER: Estrogen receptor; PR: Progesterone receptor.

Table 2
Demographic and tumour characteristics of the high risk group (TTL $\geq 25,000$) and the low risk group (TTL $< 25,000$).

Variable	Levels	Low TTL (N(%))	High TTL (N(%))
Sex	Male	4 (0.5)	2 (1.1)
	Female	766 (99.5)	178 (98.9)
Menopause	Pre-menopause	239 (31.0)	61 (33.9)
	Post-menopause	466 (60.5)	107 (59.4)
	Missing	65 (8.4)	12 (6.7)
Tumour type	Ductal	642 (83.4)	155 (86.1)
	Lobular	63 (8.2)	20 (11.1)
	Other	65 (8.4)	5 (2.8)
Tumour grade	1	231 (30.0)	44 (24.4)
	2	368 (47.8)	97 (53.9)
	3	171 (22.2)	39 (21.7)
LVI	Yes	112 (14.6)	73 (40.6)
	No	658 (85.5)	107 (59.4)
HER2	Positive	85 (11.0)	23 (12.8)
	Negative	685 (89.0)	157 (87.2)
ER	Positive	670 (87.0)	167 (92.8)
	Negative	100 (13.0)	13 (7.2)
PR	Positive	612 (79.5)	155 (86.1)
	Negative	158 (20.5)	25 (13.9)
Molecular subtype	Luminal A	347 (45.1)	83 (46.1)
	Lum. B HER2 neg.	270 (35.1)	69 (38.3)
	Lum. B HER2 pos.	60 (7.8)	16 (8.9)
	HER2 enriched	25 (3.2)	7 (3.9)
	Triple negative	68 (8.8)	5 (2.8)

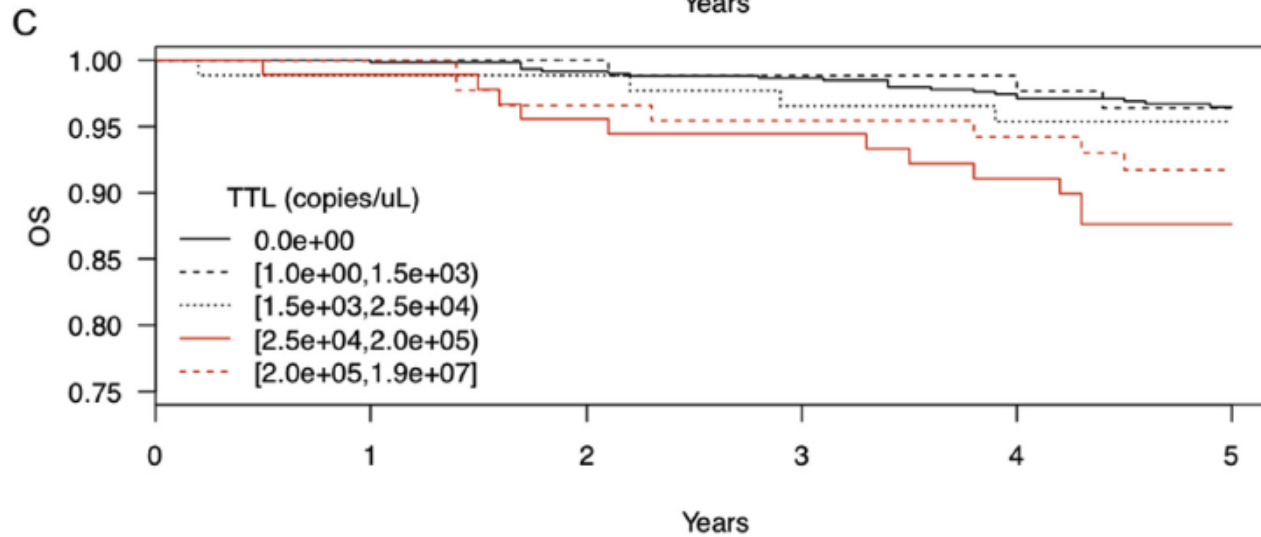
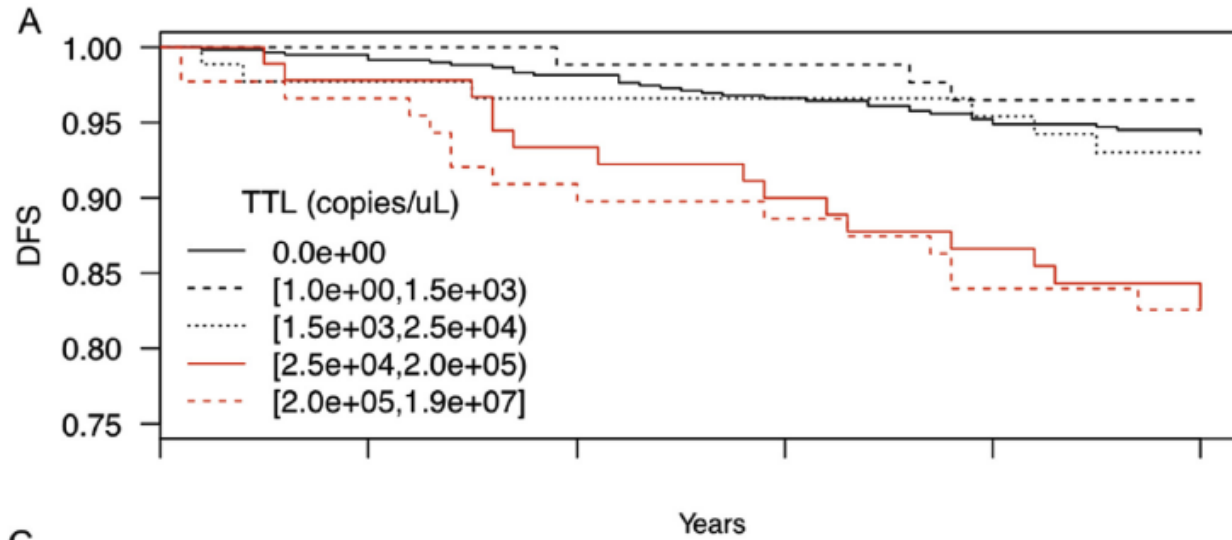
Low TTL: $< 25,000$ CK19 mRNA copies/ μ L; high TTL: $\geq 25,000$ CK19 mRNA copies/ μ L.

Table 3

Treatment characteristics of the high risk group (TTL $\geq 25,000$) and the low risk group (TTL $< 25,000$).

Variable	Levels	Low TTL (N(%))	High TTL (N(%))
Type of surgery	Lumpectomy	611 (79.3)	129 (71.7)
	Mastectomy	159 (20.6)	51 (28.3)
Lymphadenectomy	No	587 (76.2)	5 (2.8)
	Yes	183 (23.8)	175 (97.2)
Chemotherapy	No	312 (40.5)	27 (15.0)
	Yes	351 (45.6)	131 (72.8)
	Missing	107 (13.9)	22 (12.2)
Hormonal therapy	No	93 (12.1)	9 (5.0)
	Yes	572 (74.3)	148 (82.2)
	Missing	105 (13.6)	23 (12.8)
Radiotherapy	No	133 (17.3)	27 (15.0)
	Yes	464 (60.3)	124 (68.9)
	Missing	173 (22.5)	29 (16.1)
Axilar radiotherapy	No	478 (62.1)	105 (58.3)
	Yes	48 (6.2)	40 (22.2)
	Missing	244 (31.7)	35 (19.4)

Low TTL: $< 25,000$ CK19 mRNA copies/ μ L; high TTL: $\geq 25,000$ CK19 mRNA copies/ μ L.



TTL; yaş ve tümörün karakteristiklerinden bağımsız olarak DFS ve OS üzerinde tahmin edici etkinliğe sahip

