Gemeinschaftsklinikum Mittelrhein
Kemperhof

San Antonio 2023
Frühes Mammakarzinom

Lokale Therapie – Axillachirurgie
Beste Praxis –
Supportive Therapie -

A. Franzen
Frauenklinik, Brustzentrum

Themenübersicht

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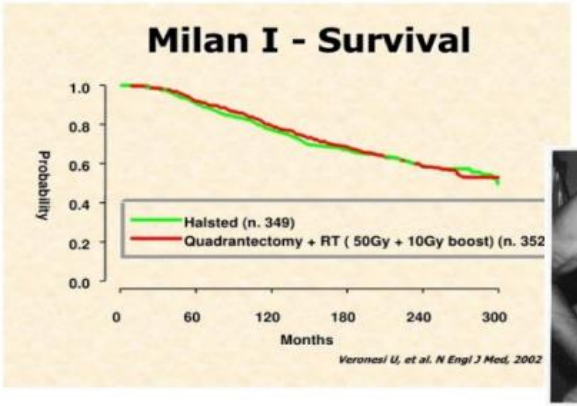
- De- Eskalation der axillären Chirurgie:
- Sentinel nach NA-Chemo ausreichend ?
- Langzeitergebnisse nach Konversion cN+ → ypN0
- Informationsverlust bei Verzicht auf ALND (>= 4LK´s +) ?
-
- Sentinel für alle Subgruppen sicher incl Mastectomien ? (Senomac)

- Axilläres Management im Langzeitverlauf : EBCCTG Metaanalyse

- Lebensqualität und Versorgung :
- Polyneuropathie nach NA-CHEMO
- Brustkrebsnachsorge ohne Facharzt/ - ärztin ?

Evolution der operativen Therapie – damals bis heute



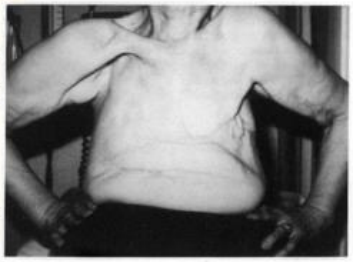
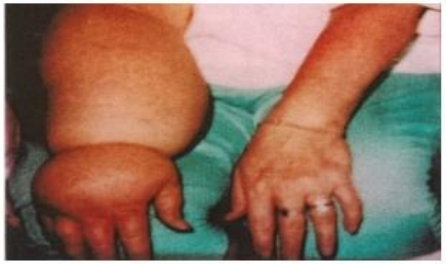
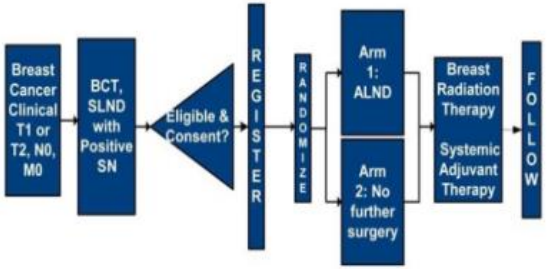
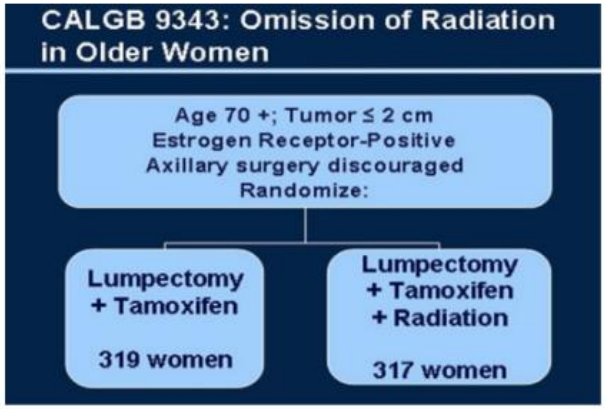
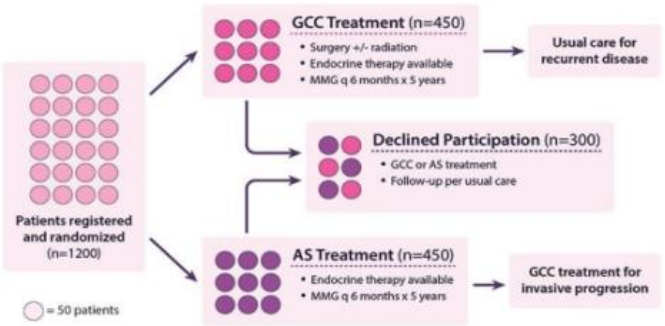


FIGURE 16–12. In the same patient, contraction of the intact pectoralis major muscle can be seen on the left. This photograph demonstrates the difference in the axilla and chest wall defects associated with the two operations.









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Axilläre Lymphknotendissektion (ALND) ohne neoadjuvante Chemotherapie

	Oxford LoE	Oxford GR	AGO
▪ **Endpunkt: Überleben (bei adäquater, multimodaler Therapie)**	3	D	-
▪ **Endpunkt: Staging**	3	A	-
▪ **Endpunkt: Lokoregionale Tumorkontrolle**	2a	A	+/-
▪ **pN+ (präoperativ histologisch gesichert)**	2a	B	+
▪ **cN0 pN0 (i+) (sn)**	1b	A	--
▪ **cN0 pN1mi (sn)**	2b	B	--
▪ **cN0 pN1 (sn) (T1/2, < 3 SN+*, BEO + RT + adäquate Systemtherapie)**	1b	A	-
▪ **cN0 pN1 (sn) und Mastektomie (keine Radiotherapie der Thoraxwand)**	1b	B	+**
▪ **cN0 pN1 (sn) und Mastektomie (T1/2, < 3 SN+, Radiotherapie der Thoraxwand)**	5	D	+/-**
▪ **ALND indiziert, aber nicht möglich**			
▪ **Radiatio analog AMAROS-Studie (evaluiert für cN0 pN1sn)**	1b	B	+

*ACOSOG Z0011 Studie ohne klare Definition eines extrakapsulären Wachstums; **Studienteilnahme empfohlen

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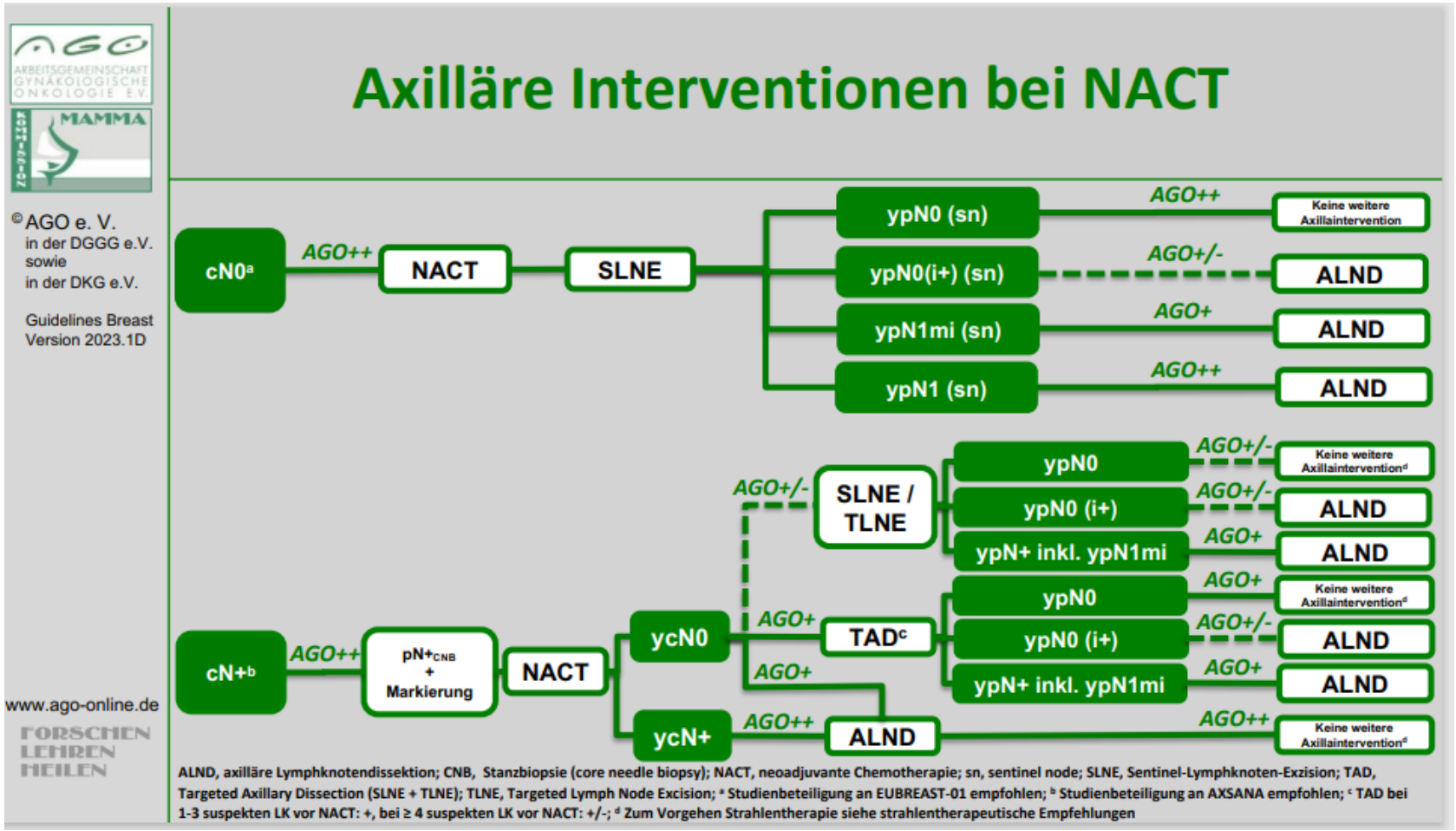

Hintergrund: Exkurs SABCS 2022

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Targeted Axillary Dissection

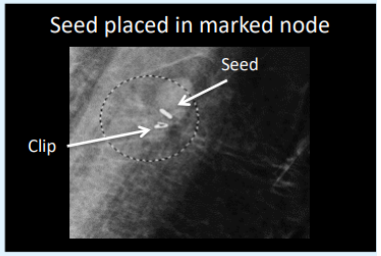
Metallic clip placed when FNA of lymph node shows metastases

At surgery, remove:

- LN with ***KNOWN*** disease (with clip)

and

- LNs most likely to harbor disease (SLN)



Caudle et al. *JAMA-Surg.* 2015;150(2):137-43

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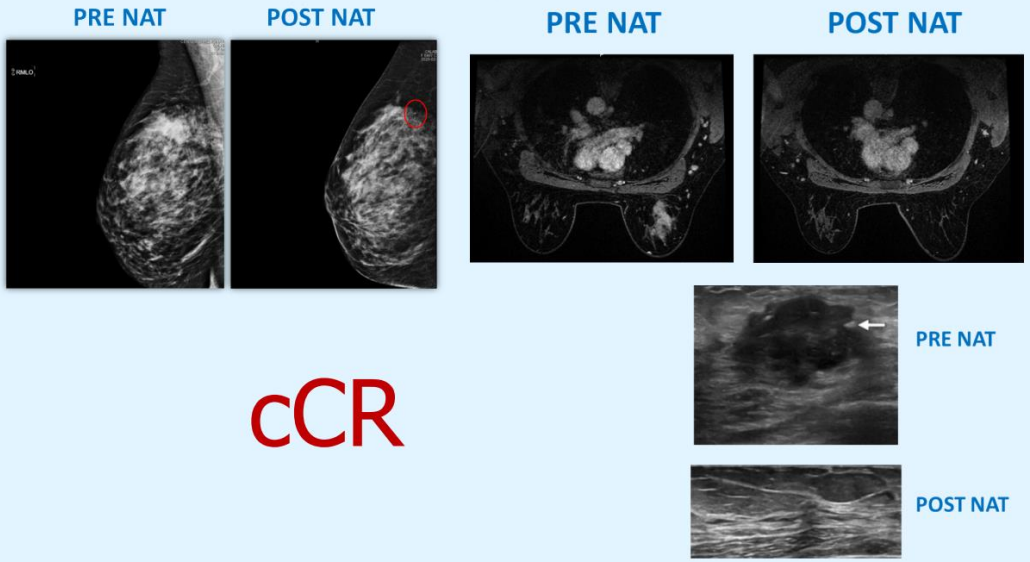

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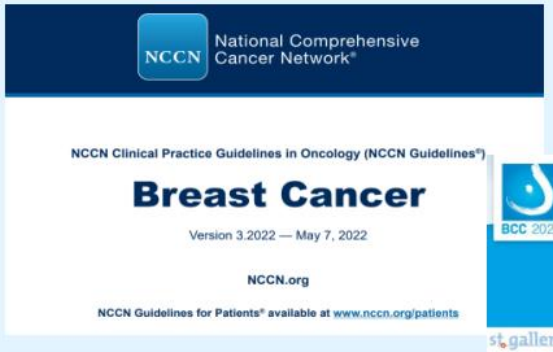

SNB is permitted instead of AD considered in a patient who presented with (cN1) and received NAT that downstage to clinically negative if…..

- **Marking of sampled axillary nodes with tattoo or clip**
- **Using dual tracer, and by removing more than 2 negative sentinel nodes.**

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Pro Clip

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Why Localize the Clipped Node?

Clipped node not retrieved as a SLN:

- MD Anderson[1]: 23%
- Turkey[2]: 19%
- SenTa[3]: 37%
- RISAS[4]: 29%

[1]Caudle et al. *JCO*, 2016
[2]Diego et al. *Ann Surg Onc*, 2016
[3]Kuemmel e
[4]Simons et a

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Evaluation of the Clipped Node Improves Accuracy

	SLND Alone	Marked Node Alone	SLN + Marked Node
MD Anderson	10.1%	4.2%	**2%**
SenTa	23.9%	7.2%	**4.3%**
RISAS	18.6%	6.8%	**2.5%**

Caudle et al. *JCO* 2016
Kuemmel et al. *Ann Surg*. 2022
Simons et al. *JAMA Surgery*. 2022

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Key Arguments

- Evaluating clipped node in addition to sentinel nodes is more accurate assessment of axillary response
- Residual small volume disease in the axilla has prognostic and therapeutic implications

Prognostic and Therapeutic Implications

Pro Clip

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Low Volume Disease Important

- Study of 702 CN+ patients who underwent NAC followed by SLND

SLND results	Additional Disease Found
Isolated Tumor Cells	17% (1/6)
Micrometastases	64% (28/44)
Macrometastases	62% (75/121)

Moo et al. *Ann Surg Oncol*. March 2018

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Adjuvant Decisions Impacted by Residual Disease

- HER2+ – T-DM1[1]
- TNBS – Capecitabine[2]
- HR+ - Abemiciclib[3]
- BRCA Patients – Olaparib[4]

1 Minckwitz et al. *NEJM*. 2019
2 Masuda et al. *NEJM*. 2017
3 Johnston et al. *JCO*. 2020
4 Tutt et al. *NEJM*. 2021

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Summary

- Evaluating the clipped node and the SLNs is the most accurate assessment or residual disease
- Small volume disease has prognostic and therapeutic implications

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Stand : Pro und Contra Clip

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Summing up

CLIP	NOT CLIP
FNR <10%	FNR <10% with >2 negative SNs
	FNR >10%with <2 SNs
More expensive	Less expensive
More time consuming	Easy to identify
More difficult to identify	Low axillary recurrence
Unknown how many nodes should be clipped	GOOD OUTCOMES
Unknown what to do in case of lost clip	
NO DATE ON OUTCOME	

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Oder ist trotzdem nur SNB ausreichend ?

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Axillary recurrence after SNB alone
cN+ ➡ ypN0 after NAT

Author	N. of pts	Axillary recurrence	Follow up
Kahler Ribeiro Fontana S	**123**	**1.6%**	**10 yrs**
Martelli G	81	0%	7 yrs
Wong SM	58	0%	5 yrs
Barrio A	234	1.6%	3 yrs
Piltin MA	139	0.7%	2 yrs

Kahler-Riberio Fontana , et al. EJSO 2020
Martelli G. et al Ann Surgery 2022
Piltin MA , et al. Ann Surg Oncol 2020

Wong SM, et al . Ann Surg Oncol 2021
Barrio A, et al. JAMA 2021

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journal homepage: www.ejso.com

ELSEVIER

Long-term standard sentinel node biopsy after neoadjuvant treatment in breast cancer: a single institution ten-year follow-up

Sabrina Kahler-Ribeiro-Fontana [a, g, *], Eleonora Pagan [b], Francesca Magnoni [a], Elisa Vicini [a], Consuelo Morigi [a], Giovanni Corso [a, h], Mattia Intra [a], Fiorella Canegallo [a], Silvia Ratini [a], Maria Cristina Leonardi [c], Eliana La Rocca [c, i], Vincenzo Bagnardi [b], Emilia Montagna [d], Marco Colleoni [d], Giuseppe Viale [e, h], Luca Bottiglieri [e], Chiara Maria Grana [f], Jorge Villanova Biasuz [g], Paolo Veronesi [a, h], Viviana Galimberti [a]

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Nach Sentinel

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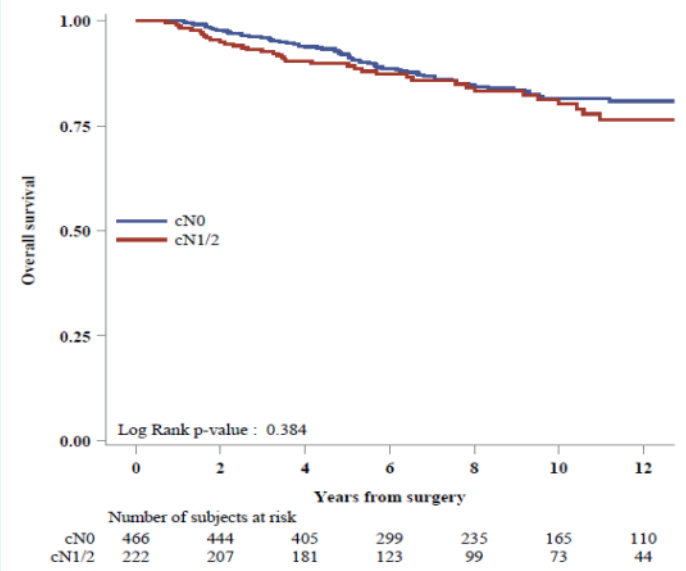
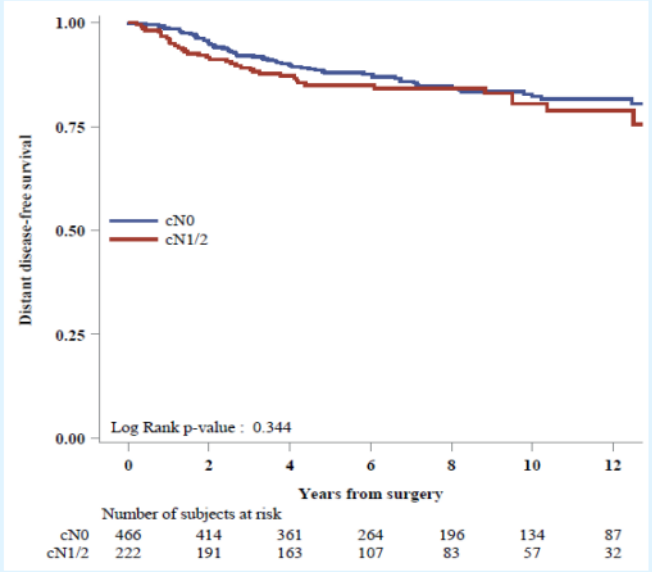
Overall survival and DDFS, according to cN status prior NAT





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Targeted Axillary Dissection (TAD)
= TLNE + SLNE

	Oxford LoE	Oxford GR	AGO
▪ Stanzbioptische Sicherung der LK-Metastase und Markierung	2b	B	++
▪ Markierung von mehreren Lymphknoten bei mehr als 1 suspekten LK	2b	B	+/-
▪ Evidenz für den Vergleich einzelner Marker (Clip / Coil, Kohle, magnetischer Seed, Radar-Reflexion, Radiofrequenzmarker etc.) nicht ausreichend*	2b	B	
▪ TAD bei 1-3 suspekten LK vor NACT	2b	B	+
▪ TAD bei ≥ 4 suspekten LK vor NACT	5	D	+/-
▪ Vollständige Aufarbeitung aller Lymphknoten am Paraffinschnitt mit Schnittstufen von ≤ 500 µm	5	D	++
▪ Immunhistochemie zum Nachweis von ITC	5	D	+/-
▪ ALND bei prä- oder intraoperativ nicht auffindbarem Marker	5	D	+
▪ Weitere Intervention zur Entfernung des nicht auffindbaren Markers (auch nach ALND)	5	D	-
▪ Alleinige TLNE ohne SLNE	2B	B	+/-

* Studienbeteiligung an AXSANA empfohlen

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Poster Spotlight Session 1

„Weniger ist mehr“

Minimierung der chirurgischen Behandlung bei Patientinnen mit Brustkrebs im Frühstadium

Poster Spotlight Session „Weniger ist mehr“
PS01-01:
Durchführbarkeit und onkologische Sicherheit einer TAD oder SNB bei Pat. mit cN+ nach NA-CHEMO : NEOSENTITURK-Studie

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San Antonio Breast Cancer Symposium - December 5-9, 2023

FEASIBILITY AND ONCOLOGICAL SAFETY OF TARGETED AXILLARY DISSECTION OR SENTINEL LYMPH NODE BIOPSY IN PATIENTS WITH CLINICALLY NODE-POSITIVE DISEASE AFTER NEOADJUVANT CHEMOTHERAPY IN THE PROSPECTIVE MF-1803 NEOSENTITURK-STUDY

N. Cabioglu, H. Karanlik, MA Gulcelik, H.B. Kocer, M. Muslumanoglu, A. Igci, M. Tukenmez, C. Uras, E. Ozkurt, G.G. Akgul, S. Emiroglu, S. Bademler, B. Mantoglu, A. Dağ, D.C. Trabulus, N. Yildirim, G.K. Cakmak, E.S. Oran, H. Kara, H.G. Kılıc, G. Basaran, A. Altinok, M.U. Ugurlu, K. Senol, B. Zengel, N. Karaman, E. Varol, E. Dilege, Y. Bolukbasi, A. Akcan, Y. E. Ersoy, A. Soyder, S. Ozbas, M. Velidedeoglu, B. Ozcinar, I. Jorani, N.Z. Utkan, B. Citgez, B. Celik, L. Zer, G. Sakman, L. Yeniay, L. Dogan, M. Dogan, F. Erozgen, B. Göktepe, O. Agcaoglu,T. Kivilcim, S. Yormaz, I.A. Özemir, A. Sevinç, K. Atahan, V. Veliyeva, FL Balci, B.M. Gulluoglu, A. Kamali Polat, A. Aydiner, A. Soran, K. Ibis, V. Ozmen, and the NEOSENTITURK STUDY GROUP, TURKIYE and AZERBAIJAN

Turkish Federation of Breast Diseases Societies

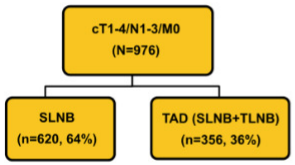
Breast Health Working Group International

BACKGROUND

- Prospective studies have shown decreased FNRs with removal of >2 SLNs, using dual tracer for SLNB, and using the TAD techniques in cN+ patients treated with NAC.
- Limited reports have studied the oncological safety of SLNB vs TAD in N+ patients after NAC.
- The objective of this prospective study is to compare the feasibility and the oncological safety of TAD with SLNB in cN+ patients, who became cN0 following NAC.

METHODS

- Between Feb 2019 to Jan 2023: 976 pts, prospective multicentre non-interventional NEOSENTITURK MF1803/BHWGI study (NCT04250129).
- Patients with distant metastases, pregnancy, inflammatory breast cancer, bilateral breast cancer, or previous malignancy were excluded from the study.
- Furthermore, patients with ALND were excluded for this subgroup analysis.
- All patients had regional and nodal irradiation.



RESULTS

Patient Characteristics	Total(n=976)	TAD(n=356)	SLNB(n=620)	p-value
Median age (min-max)	46(24-80)	46(24-76)	46(21-80)	0.835
Clinical T stage				<0.001
cT1/2	815(83.5)	327(91.9)	488(78.7)	
cT3/4	161(16.5)	29(8.1)	132(21.3)	
Clinical N stage				0.006
cN1	792(81.1)	305(85.7)	487(78.5)	
cN2-3	184(18.9)	51(14.3)	133(21.5)	
Method				<0.001
Single-agent (blue dye, 95%; radiocolloid, 5%)	681 (69.8%)	199(56%)	482 (78%)	
Dual tracer	295 (30.2%)	157(44%)	138 (22%)	
pCR (breast)				0.927
Complete	445(45.6)	163(45.8)	282(45.5)	
Partial	531(54.4)	193(54.2)	338(54.5)	
pCR (breast+axilla)				0.255
Complete	391(40.1)	151(42.4)	240(38.7)	
Partial	585(59.9)	205(57.6)	380(61.3)	
Tumor Subtype (IHC)				0.557
Luminal	672(68.9)	249(69.9)	423(68.2)	
Non-luminal	304(31.1)	107(30.1)	197(31.8)	

Median follow-up= 27 months (18-38)

Outcome	Overall (n=976)	TAD (n=356)	SLNB (n=620)	p-value	ypN0 (n=635)	ypN(+) (n=341)	p-value
Locoregional recurrence	8(0.8%)	2(0.6%)	6(1%)	0.718	5(0.8%)	3(0.9%)	0.999
Regional nodal recurrence	4(0.4%)	1(0.3%)	3(0.48%)	0.999	3(0.47%)	1(0.3%)	0.999
Ipsilateral axillary recurrence	2(0.2%)	1(0.3%)	1(0.2%)	0.999	2(0.3%)	0(0%)	0.545
Systemic recurrence	38(3.9%)	9(2.5%)	29(4.7%)	0.121	21(3.3%)	17(5%)	0.225
Mortality	7(0.7%)	2(0.6%)	5(0.8%)	0.999	4(0.6%)	3(0.9%)	0.700

Axillary/regional recurrences <0.5%

Lymph Node Characteristics (N, median IQR)	Overall	TAD (n=356)	SLNB (n=620)	p-value
Sentinel Lymph Nodes (SLNs)	3(2-4)	3(2-5)	3(2-4)	0.180
Total LNs	4(3-6)	4(3-6)	4(3-6)	0.085
Total LN: Mean (SD)	4.2(1.9)	4.4(1.9)	4.2(1.9)	
		ypN0		
	All	TAD (n=245)	SNB (n=390)	p-value
SLNs	3(2-4)	3(2-4)	3(2-4)	0.590
Total LN	4(3-5)	4(3-5)	4(2-5)	0.034
Total LN: Mean (SD)	4.0(1.9)	4.2(1.9)	3.9(1.9)	
		ypN+		
	All	TAD (n=111)	SNB (n=230)	p-value
SLNs	3(2-5)	4(3-5)	3(2-5)	0.062
Total LNs	5(3-6)	5(4-6)	5(3-6)	0.265
Total metastatic LNs	1(1-2)	1(1-2)	1(1-2)	0.212
LNR	0.33(0.2-0.5)	0.29(0.2-0.4)	0.33(0.2-0.5)	0.033
LNR: Mean (SD)	0.37(0.22)	0.33(0.19)	0.37(0.23)	
LN metastasis:				0.807
ITC/Micrometastasis	163 (47.8%)	52 (46.8)	111 (48.3)	
Macrometastasis	178 (52.2%)	59 (53.2)	119 (51.7)	
		ypN0	ypN(+)	
SLNs	3(2-4)	3(2-4)	3(2-5)	0.008
Total LNs	4(3-6)	4(3-5)	5(3-6)	<0.001

CONCLUSIONS

- Our results suggest that TAD may cause unnecessary LN removal in patients with an axillary pCR.
- However, TAD might be more feasible in patients with axillary residual disease.
- Patients with residual axillary disease were more likely to have LNs removed compared to those with an axillary pCR reflecting the surgeon's approach.
- Longer follow-up is needed to confirm the oncological safety of TAD or SLNB alone.

REFERENCES

Boughey J, JAMA 2013 ; Kühn T, Lancet Oncol 2013; Caudle AS, JCO 2016;Cabioglu N, 2018;

Classe J, Breast Cancer Res Treat 2019; Kuemmel S, Ann Surg 2022; Barrio A, JAMA Surg 2021;

Kahler-Ribeiro S, EJSO 2021; Cabioglu N, EJSO 2021, Kuemmel S, JAMA Surg 2023

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PS01-01: Hintergrund & Methoden

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Frühere propektive Studien berichteten über eine verringerte Falsch-Negativ-Rate bei Pat. mit T1-3/cN1-Erkrankung , bei der Entfernung von 2 oder mehr SLN´s ,unter Verwendung der kombinierten Technik für die SLN-Biopsie (SLNB) und durch gezielte axill. Dissektion (TAD) bei anfänglich klinisch nodal-positiven Patienten nach NA-CHEMO.

Ziel der Studie: die Durchführbarkeit und onkologische Sicherheit von TAD mit SLNB bei Patientinnen mit cN positivem / ycN0 – Brustkrebs nach NA-Chemo prospekiv multizentrisch zu vergleichen

METHODS

- Between Feb 2019 to Jan 2023: 976 pts, prospective multicentre non-interventional NEOSENTITURK MF1803/BHWGI study (NCT04250129).
- Patients with distant metastases, pregnancy, inflammatory breast cancer, bilateral breast cancer, or previous malignancy were excluded from the study.
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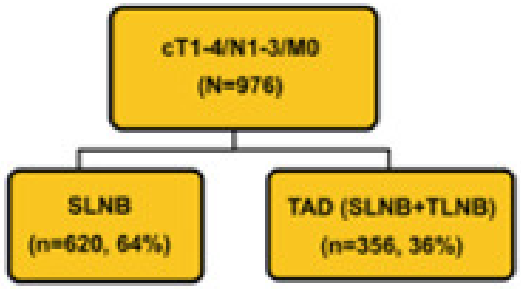

Ergebnisse

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Patient Characteristics	Total(n=976)	TAD(n=356)	SLNB(n=620)	p-value
Median age (min-max)	46(24-80)	46(24-76)	46(21-80)	0.835
Clinical T stage				<0.001
cT1/2	815(83.5)	327(91.9)	488(78.7)	
cT3/4	161(16.5)	29(8.1)	132(21.3)	
Clinical N stage				0.006
cN1	792(81.1)	305(85.7)	487(78.5)	
cN2-3	184(18.9)	51(14.3)	133(21.5)	
Method				<0.001
Single-agent (blue dye, 95%; radiocolloid, 5%)	681 (69.8%)	199(56%)	482 (78%)	
Dual tracer	295 (30.2%)	157(44%)	138 (22%)	
pCR (breast)				0.927
Complete	445(45.6)	163(45.8)	282(45.5)	
Partial	531(54.4)	193(54.2)	338(54.5)	
pCR (breast+axilla)				0.255
Complete	391(40.1)	151(42.4)	240(38.7)	
Partial	585(59.9)	205(57.6)	380(61.3)	
Tumor Subtype (IHC)				0.557
Luminal	672(68.9)	249(69.9)	423(68.2)	
Non-luminal	304(31.1)	107(30.1)	197(31.8)	

Lymph Node Characteristics (N, median IQR)	Overall	TAD (n=356)	SLNB (n=620)	p-value
Sentinel Lymph Nodes (SLNs)	3(2-4)	3(2-5)	3(2-4)	0.180
Total LNs	4(3-6)	4(3-6)	4(3-6)	0.085
Total LN: Mean (SD)	4.2(1.9)	4.4(1.9)	4.2(1.9)	
		ypN0		
	All	TAD (n=245)	SNB (n=390)	p-value
SLNs	3(2-4)	3(2-4)	3(2-4)	0.590
Total LN	4(3-5)	4(3-5)	4(2-5)	0.034
Total LN: Mean (SD)	4.0(1.9)	4.2(1.9)	3.9(1.9)	
		ypN+		
	All	TAD (n=111)	SNB (n=230)	p-value
SLNs	3(2-5)	4(3-5)	3(2-5)	0.062
Total LNs	5(3-6)	5(4-6)	5(3-6)	0.265
Total metastatic LNs	1(1-2)	1(1-2)	1(1-2)	0.212
LNR	0.33(0.2-0.5)	0.29(0.2-0.4)	0.33(0.2-0.5)	0.033
LNR: Mean (SD)	0.37(0.22)	0.33(0.19)	0.37(0.23)	
LN metastasis:				0.807
ITC/Micrometastasis	163 (47.8%)	52 (46.8)	111 (48.3)	
Macrometastasis	178 (52.2%)	59 (53.2)	119 (51.7)	
		ypN0	ypN(+)	
SLNs	3(2-4)	3(2-4)	3(2-5)	0.008
Total LNs	4(3-6)	4(3-5)	5(3-6)	<0.001

Median follow-up= 27 months (18-38)

Outcome	Overall (n=976)	TAD (n=356)	SLNB (n=620)	p-value	ypN0 (n=635)	ypN(+) (n=341)	p-value
Locoregional recurrence	8(0.8%)	2(0.6%)	6(1%)	0.718	5(0.8%)	3(0.9%)	0.999
Regional nodal recurrence	4(0.4%)	1(0.3%)	3(0.48%)	0.999	3(0.47%)	1(0.3%)	0.999
Ipsilateral axillary recurrence	2(0.2%)	1(0.3%)	1(0.2%)	0.999	2(0.3%)	0(0%)	0.545
Systemic recurrence	38(3.9%)	9(2.5%)	29(4.7%)	0.121	21(3.3%)	17(5%)	0.225
Mortality	7(0.7%)	2(0.6%)	5(0.8%)	0.999	4(0.6%)	3(0.9%)	0.700

Axillary/regional recurrences <0.5%

PS01-01:
Conclusio

Gemeinschaftsklinikum Mittelrhein

- **TAD kann unnötige LK Entfernung verursachen bei Pat. mit axillärer pCR (LK= ypN0) : NW Armbeweglichkeit / Lymphödem**
- **TAD mag mehr geeignet sein bei Pat mit axill. Resttumor (LK= ypN1):**
- **Pat mit axill. Resttumor hatten wahrscheinlicher eine LK Dissektion als Pat mit einer pCR**
- **Axill. und lokoregionäre Rezidive in ycN0 Pat., die mit SLN oder TAD ohne ALND behandelt wurde war sehr niedrig . Daher könnte das Weglassen von ALND bei < 2 befallenen LK´s sicher in Betracht gezogen werden, solange < 3 LK´s entfernt wurden und eine axilläre Radiatio erfolgt**
- **Längerer Follow Up ist notwendig zur Beurteilung der onkolog Sicherheit TAD vs. SLNB alleine**

Poster Spotligt Session „Weniger ist mehr“
PS01-02
Langzeitergebnisse der SNB nach NA-CHEMO bei initial nodal-positivem Brustkrebs : System. Übersicht und Metaanalyse

Gemeinschaftsklinikum Mittelrhein

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

Long-term outcomes of sentinel lymph node biopsy following neoadjuvant chemotherapy for initially node-positive breast cancer: A Systematic Review and Meta-Analysis.

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SAN ANTONIO BREAST CANCER SYMPOSIUM

Background

- Sentinel lymph node biopsy (SLNB) alone is frequently offered to women with initially node-positive breast cancer who convert to node-negative following neoadjuvant chemotherapy (NAC)
- Limited long-term data regarding the oncologic safety of this approach.

Objectives

- The aim of this meta-analysis was to evaluate the long-term oncologic outcomes associated with SLNB alone following NAC for initially node-positive breast cancer (BC).

Methods

- Systematic review and meta-analysis was conducted.
- Medline (Ovid), Embase, and Cochrane Central Registry were searched for studies comparing women undergoing SLNB vs ALND following NAC for initially clinically node-positive BC.
- Primary outcome: axillary recurrence (AR)
- Secondary outcomes: locoregional recurrence (LRR); disease-free survival (DFS); overall survival (OS).
- Random effects meta-analyses were used to calculate weighted pooled effect estimates (risk ratios, RR).
- Variability across studies due to heterogeneity was estimated using I^2 statistics.
- Subgroup analysis was performed by length of follow-up for each study.
- Risk of bias within studies was assessed using the Newcastle-Ottawa Scale (NOS).

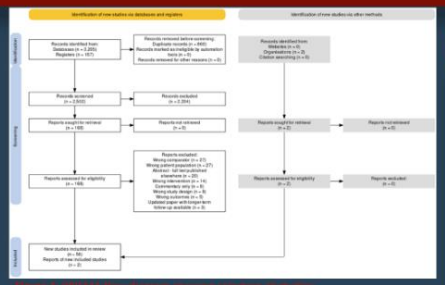

Figure 1: PRISMA flow diagram showing selection of studies

Study	Country	Accrual Period	Study Design	Participants (N)	Breast Cancer Population	Median / Mean Age (years)	Median / Mean Follow-up (months)	Primary Outcome	Other Outcome(s) Reported
Kim J.Y. et al. 2015	Korea	Jan 2007 - Aug 2013	Retrospective, multicenter	110	cN+, M0	47	19.5	AR	DR, DFS, OS
Peteiro et al. 2020	Croatia	May 2016 - 2018	Retrospective, cohort	22	cT1-3, cN1-3, M0	60	63.5	LRR, DR	AR, PFS
Pilitri et al. 2020	USA	Jan 2009 - Oct 2018	Retrospective, cohort	264	cT1-4, cN1-3, M0	51	34	LRR	AR, RFS
Kim H. et al. 2021	Korea	2006 - 2016	Retrospective, cohort	225	cT1-4, cN1-3, M0	47	77	OS	DFS, AR, LRR, DR, Postop. side effects
Kozak et al. 2021	USA	Jan 2005 - June 2015	Retrospective, cohort	96	cT1-3, cN1, M0	48	50	LRR	AR, DR, OS
Cabioglu et al. 2022	Turkey	Jan 2010 - Jan 2021	Retrospective, multicenter	1170	cT1-4, cN1-3, M0	47	39	AR	LRR
Lim et al. 2022	South Korea	Jan 2009 - Dec 2014	Retrospective, cohort	477	cT1-4, cN1, M0	NR	60	AR	DFS, OS
Martelli et al. 2022	Italy	2007 - 2015	Retrospective, cohort	121	cT2, cN0-1, M0	47	108	OS, DFS	AR
DFCI, unpublished	USA	2004 - March 2022	Retrospective, cohort	511	cT0-4c, cN1-3, M0	NR	51.2	AR	LRR, RFS, OS

Table 1: Characteristics of the studies included in the meta-analysis

Study	Median or Mean Number of SLNs	Intervention (SLNB)		Comparator (ALND)		Newcastle-Ottawa Scale (NOS) Quality Assessment		
(Author, Year)	(Intervention Group, SLNB)	Axillary recurrences	Number at risk	Axillary recurrences	Number at risk	Selection (out of 4)	Comparability (out of 2)	Outcomes (out of 3)
Kim J.Y. et al. 2015	3	1 (1.2%)	31	1 (1.3%)	79	4	1	2
Peteiro et al. 2020*	NR	0	9	0	13	4	0	3
Pilitri et al. 2020	3	1 (0.6%)	157	3 (2.6%)	107	4	0	2
Kim H. et al. 2021	2.7	1 (1.1%)	94	3 (2.3%)	129	4	1	3
Kozak et al. 2021	NR	4 (5.6%)	71	0	25	4	1	3
Cabioglu et al. 2022	NR	3 (0.3%)	1042	0	127	4	0	2
Lim et al. 2022	5	10 (3.2%)	314	3 (1.8%)	163	4	1	3
Martelli et al. 2022*	2	0	81	NR	40	4	2	3
DFCI, unpublished	3.5	1 (0.4%)	246	2 (0.8%)	264	4	0	3

*Excluded from analysis for primary outcome (axillary recurrence, AR)

Table 2: Data for the primary outcome, and quality assessment of included studies

Results

- Nine observational studies were eligible for meta-analysis.
- Rates of axillary recurrence (AR) were low (range 0.0% to 5.6%).
- For AR, data for 2,882 patients from 7 studies was synthesized (SLNB=1,964; ALND=917).
- No significant differences were observed in AR between patients undergoing SLNB alone versus ALND following NAC for initially node-positive BC: pooled RR 1.02 (95% CI: 0.46-2.29, I^2=0.0%).
- Similarly, no significant differences were observed in LRR (RR 0.70, 95% CI: 0.45-1.10, I^2=0.0%), DFS (RR 0.77, 95% CI:0.55-1.08, I^2=0.0%), nor overall mortality (RR 0.66, 95% CI: 0.33-1.33, I^2=0.0%) between the SLNB and ALND groups.

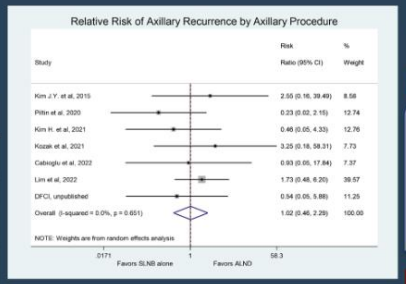

Figure 2: Primary Outcome, Axillary Recurrence

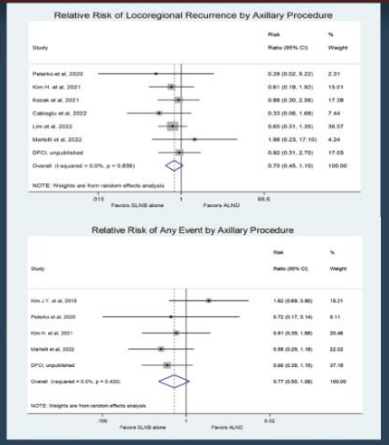

Figure 3: Secondary Outcomes: Locoregional Recurrence and Disease Free Survival

Conclusions

- Among patients who convert to node-negative following NAC, SLNB alone does not result in significantly different oncologic outcomes compared to ALND.
- De-escalation of axillary surgery to SLNB alone in this context may be safely considered in this patient population.

Acknowledgements

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PS01-02:
Hintergrund & Methoden

- Alleinige SLNB wird häufig angeboten bei Pat mit initial nodal positivem Brustkrebs, die nach NA-CHEMO nodal negativ werden = nodale pCR
- Daten zur onkologischen Sicherheit über einen längeren Zeitraum sind begrenzt.
- Ziel: Langzeitergebnisse nach alleinigem SLNB nach NA-CHEMO

- Systematischer Review: Medline, Embase, Cochrane
- Statist. Endunkte : Ax. Rezidiv, Lokoreg. Rez., DFS, OS
- Behandlungszeitraum : Jahr 2004 - 2022

- 9 Beobachtungsstudien waren auswertbar

- Mediane Nachbeobachtungen : 19,5 – 108 Monate

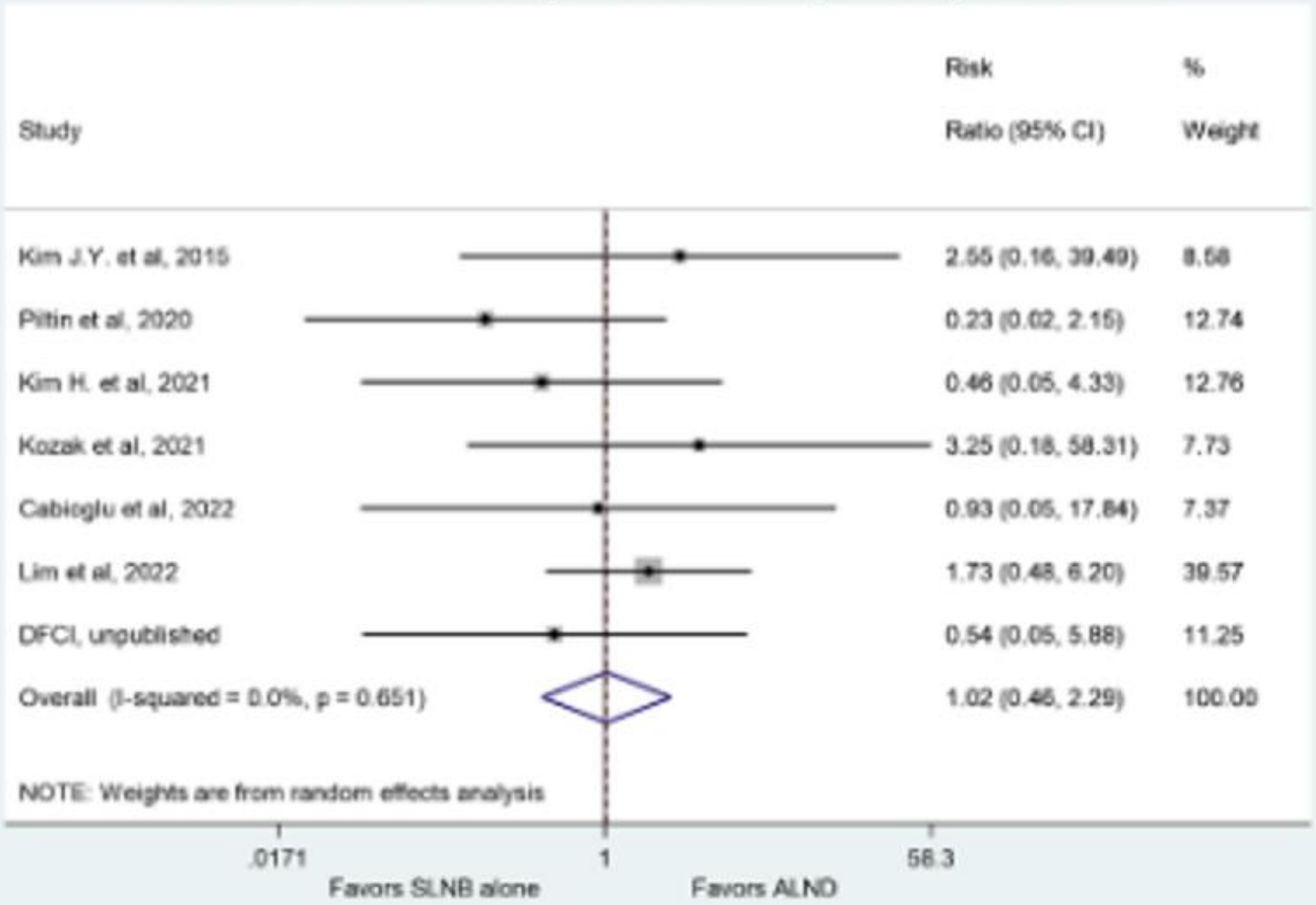
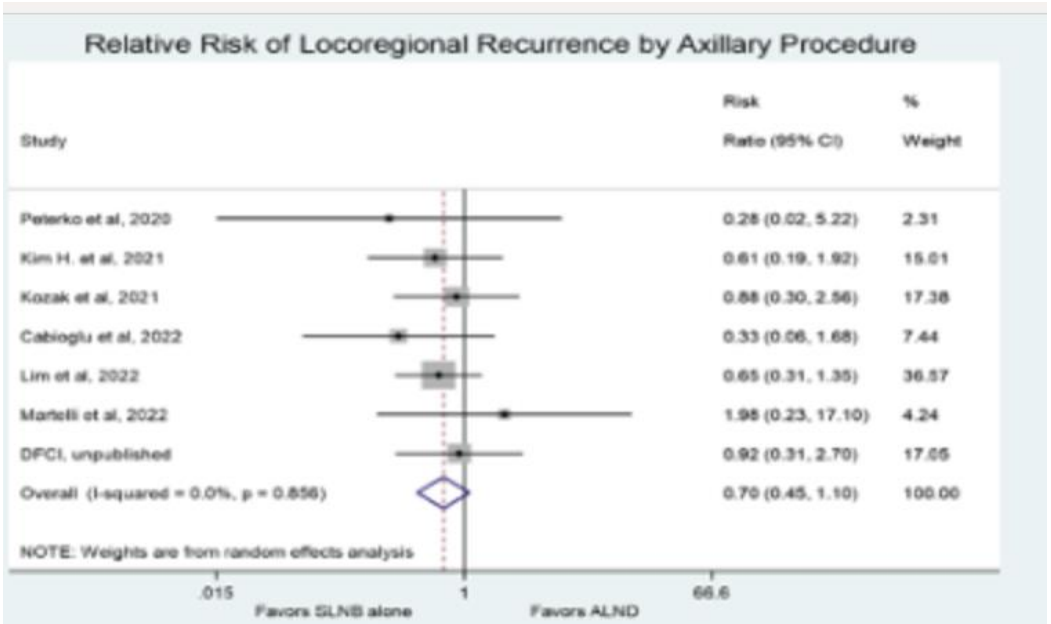
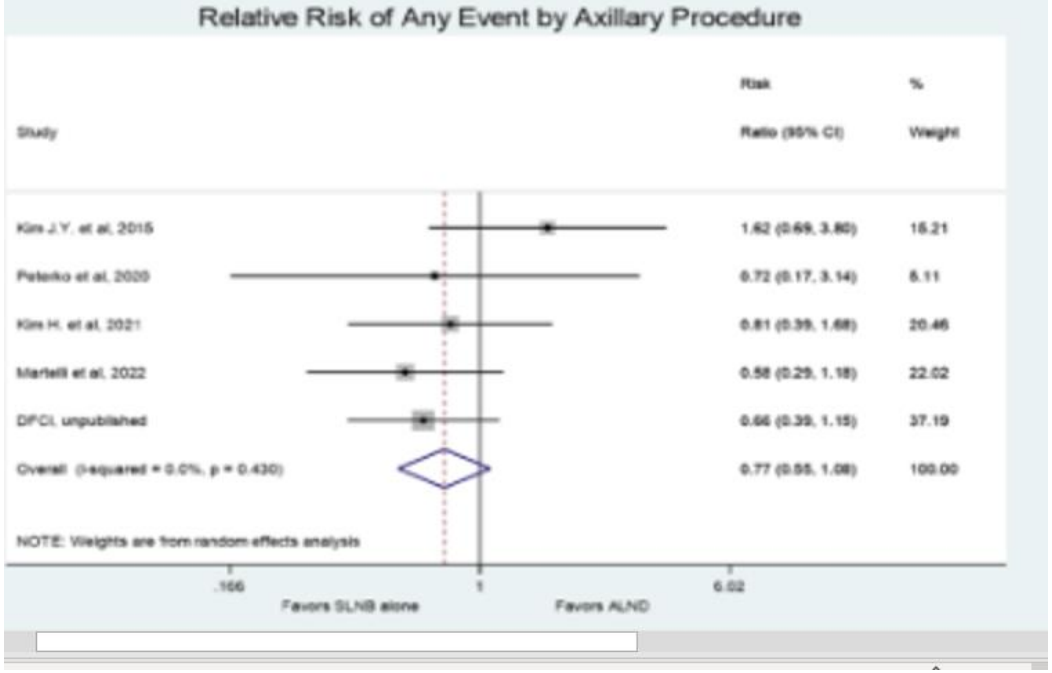


Figure 2: Primary Outcome, Axillary Recurrence





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PS01-02: „Weniger ist mehr“

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Ergebnisse & Conclusio

- Axilläre Rezidivrate (AR) war niedrig : 0 – 5,6 %
  (2882 Pat. aus 7 Studien : SLNB= 1964 ; ALND= 917)
- Kein signif. Unterschied beim Ax.Rez. zwischen SLNB und ALND nach NA-CHEMO, die davor cN+ waren (pooled RR 1.02)
- Kein signif. Unterschied bei Lokoreg. Rez. Rate (LRR , RR 0.70), DFS (RR 0.77) , und OS (RR 0.66) zwischen den SLNB und ALND Gruppen
- Bei Patientinnen, die nach NA-CHEMO zu nodal negativ konvertieren, führt SLNB alleine NICHT zu onkologisch unterschiedlichen Ergebnissen im Vergleich zur ALND
- Eine De-Eskalation der axillären Chirurgie auf SLNB alleine kann sicher in Betracht gezogen werden.

Poster Spotlight Session „Weniger ist mehr“
PS01-04: SINODAR – ONE Studie

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SABCS SAN ANTONIO BREAST CANCER SYMPOSIUM® DECEMBER 5–9, 2023 HENRY B. GONZALEZ CONVENTION CENTER SAN ANTONIO, TEXAS

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To dissect or not to dissect? The surgeon’s perspective on the prediction of ≥ 4 axillary lymph node metastasis in cN0 T1-2 breast cancer: A comparative analysis of the per-protocol population of the SINODAR-ONE clinical trial

Damiano Gentile, Wolfgang Gatzemeier, Andrea Sagona, Erika Barbieri, Alberto Bottini, Alberto Testori, Valentina Errico, Simone Di Maria Grimaldi, Giulia Caraceni, Shadya Darwish, Giuseppe Canavese, Corrado Tinterri

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Backgound: The role of axillary surgery in the management of breast cancer (BC) has evolved considerably over the past decades, with only a few routine indications for axillary lymph node dissection (ALND) remaining in clinical practice. However, de-escalation of axillary surgery, especially in BC patients with 1-3 positive sentinel lymph nodes (SLNs) challenges the recently established criteria for adjuvant treatment (i.e., combination therapy with abemaciclib, endocrine therapy, and chemotherapy in patients with ≥ 4 positive nodes). The question remains as to whether these patients should undergo further ALND to determine whether ≥ 4 nodes are positive. To further investigate the latest controversies in axillary management of BC patients and predict the presence of ≥ 4 axillary lymph node metastasis, we evaluated and compared patients ≥ 4 positive nodes in the per-protocol population of the SINODAR-ONE clinical trial.

Materials and methods: Patients in the standard arm (ALND) of the per-protocol population were evaluated, and a comparison of characteristics between patients with ≥ 4 metastatic lymph nodes versus patients with 1-3 metastatic lymph nodes was performed. Categorical variables were compared using the chi-square test or Fisher’s exact test, as appropriate. Multivariable analysis was performed using a logistic regression model to identify independent predictors of ≥4 axillary lymph node metastasis.

Results: Overall, 403 cN0 T1-2 BC patients in the per-protocol population were randomized to receive ALND. Of these, 65 and 338 patients presented with ≥ 4 or 1-3 axillary lymph node metastasis, respectively. Invasive lobular BC (26.2% versus 14.5% if other histology, odds ratio (OR)=4.185, 95% confidence interval (95%CI)= 1.284-1.443, p= 0.041), G3 (38.5% versus 21.3% if G1-2, OR=5.930, 95%CI= 2.134-2.289, p= 0.015), pT2 (46.2% versus 30.5% if pT1, OR=5.260, 95%CI= 15.330-16.346, p= 0.022), and 2 positive SLNs (32.3% versus 13.6% if 1 positive SLN, OR=13.188, 95%CI= 1.179-1.280, p< 0.0001) were found to significantly increase the probability to present ≥4 axillary lymph node metastasis at definitive histopathological evaluation.

Independent variables	Odds ratio (OR)	95% Confidence Interval (CI95%)	*p*-value
Lobular Carcinoma	4.185	1.284-1.443	0.041
G3	5.930	2.134-2.289	0.015
pT2	5.260	15.330-16.346	0.022
2 positive SLNs	13.188	1.179-1.280	<0.0001

Conclusions: The introduction of abemaciclib and other combination therapies has the potential to impact the surgical management of the axilla. Our results suggest that a minority of cN0 T1-2 BC patients may be understaged if ALND is not performed. However, the improvements and increasing effectiveness of combination therapies may sufficiently control and treat the axillary tumor-burden left behind, potentially reducing the need for extensive axillary surgery, as demonstrated by the promising 3-year oncological outcomes of the SINODAR-ONE trial. Although ALND may still be considered, after multidisciplinary team discussion, in individual patients presenting with specific risk factors for additional axillary disease (lobular, G3, pT2 BC with 2 positive SLNs), our suggestion is that routine ALND is not indicated for systemic therapy decision-making in the upfront surgical setting.

PS01-04: SINODAR – ONE Studie
Hintergrund & Fragestellung

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- **Nur noch wenige Routine-Indik. für ALND heutzutage**
- **„Problem“ dadurch: De-Eskalation bei 1-3 pos. SLN ´s stellt neu etablierte Kriterien für adjuvante Therapie in Frage (zB. Kombinationstherapie mit Abemaciclib, Endokrine Th., CHT ab >= 4 positive LK`s)**
- **Ist es sinnvoll, diese Pat. einer weiteren ALND zu unterziehen, um festzustellen , ob >= 4 LK´s befallen sind ?**
- **Statist. Auswertung / Multivariate Analyse:**
- **Standardarm ALND der Pro-Protokoll Population :**
  Merkmale zwischen Pat. Mit >= 4 + LK´s versus 1-3 + LK´s

PS01-04: SINODAR – ONE Studie Ergebnisse

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- 403 cN0 T1-2 Patientinnen random für ALND (65 : >= 4 pos LK`S = 16 % ; 338 : 1-3 pos LK´s)

- Wahrscheinlichkeit sign. erhöht für >= 4 axill. LK Metastasen bei definitiver histopath. Aufarbeitung :

Independent variables	Odds ratio (OR)	95% Confidence Interval (CI95%)	*p*-value
Lobular Carcinoma	4.185	1.284-1.443	0.041
G3	5.930	2.134-2.289	0.015
pT2	5.260	15.330-16.346	0.022
2 positive SLNs	13.188	1.179-1.280	<0.0001

PS01-04: SINODAR – ONE Studie Conclusio

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- Einführung von Abemaciclib und anderen Kombi.-Therapien hat Potential , die chirurg. Behandlung der Axilla zu beeinflussen
- Minderheit vom cN0 T1-2 Pat könnte unterversorgt sein bei Verzicht auf ALND
- Verbesserung von Komb.-Therapien können axilläre Tumorlast ausreichend kontrollieren = Notwendigkeit umfangreicher Operationen möglicherweise reduziert
- ALND kann bei einzelnen Risiko-Pat. immer noch in Betracht gezogen werden
- Autoren:
  Keine routinemässige ALND für die Entscheidungsfindung in der systemischen Therapie im Vorfeld der OP empfohlen

Gemeinschaftsklinikum Mittelrhein

Hauptsitzungen
Axilläres Management

Gemeinschaftsklinikum Mittelrhein

GS2-06 : SENOMAC Studie

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DECEMBER 5-9, 2023 | @SABCSSanAntonio

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Mays Cancer Center UT Health MD Anderson Cancer Center AACR

Recurrence-free survival following sentinel node-positive breast cancer without completion axillary lymph node dissection – first results from the international randomized SENOMAC trial

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Karolinska Institutet

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GS02-06 : Hintergrund

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- ACOSOG Z0011 (publ. 2010 & 2011)
- EORTC 10981-22023 AMAROS (publ. 2014)

- → Lehre daraus :

- Verzicht auf vollständige ALND bei positivem SLN bei cN0 Pat. Hat gleiche Überlebensdaten wie vollst. ALND bei BET mit adjuvanter Radiatio der gesamten Brust (Z0011 und IBCSG-23-01) und der axillären Radiatio unabhängig von der Brustoperation (AMAROS)

- Kritikpunkte waren : Statistische Power, Patientenselektion , Bestrahlungsfelder ,
- Unterrepräsentiert: ältere Pat, MASTEKTOMIEN ! , grosse Tumoren , Makro- vs. Mikromatastasen

Trial Design

Gemeinschaftsklinikum Mittelrhein

- Prospective 1:1 randomized clinical non-inferiority trial
  - **Standard of Care**: Completion axillary dissection
  - **Intervention**: No completion axillary dissection
- Primary endpoint: Overall Survival
- Non-inferiority margin 2.5% (hazard ratio 90% CI below 1.44)
- Target accrual 3000 patients
  - 190 events required for statistical power
- **Secondary endpoint: Recurrence-Free Survival**

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Patient Selection

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- T1-T3 primary invasive breast cancer
- Clinical node negativity (palpation)
  - Mandatory preoperative axillary ultrasound
- Male & female patients
- Breast-conserving surgery and mastectomy
- Up to 2 sentinel lymph node macrometastases
- No medical contraindications to adjuvant radiotherapy or relevant systemic treatment

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Results: Tumor

- Median tumor size 20 mm (0.2-155 mm)
  - T3 in 147 patients (5.8%)
- Lobular carcinoma in 504 patients (19.8%)
- Estrogen receptor positive & HER2 negative in 2200 patients (86.6%)

Results: Axilla

- 1 sentinel lymph node macrometastasis in 2151 patients (84.7%)
- Extranodal extension in 870 patients (34.3%)
- Removed lymph nodes median 15 (1-51) *versus* 2 (1-15)
- Additional sentinel lymph node micrometastases in 261 patients (10.2%)

Results: Axilla

- Non-sentinel lymph node (SLN) metastases on axillary dissection in 403 patients (34.5%)
  - If 1 SLN met: 31.3%
  - If 2 SLN met: 51.3%
- Pathological nodal stage (primary surgery)

	Standard of Care	Intervention
pN1	1016 (84.3%)	1311 (98.2%)
pN2	116 (9.6%)	7 (0.5%)
pN3	35 (2.9%)	0 (0%)

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Results: Treatment

- Mastectomy in 920 patients (36.2%)
- Adjuvant radiotherapy including nodal target volumes in
  - **Standard of Care** N=1060 (88.0%)
  - **Intervention** N=1193 (89.4%)
- Systemic treatment in all but 27 patients
  - Chemotherapy N=1649 (64.9%)
  - Endocrine treatment N=2335 (91.9%)
  - HER2-targeted therapy N=224 (8.8%)

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Gemeinschaftsklinikum Mittelrhein

Recurrence-Free Survival

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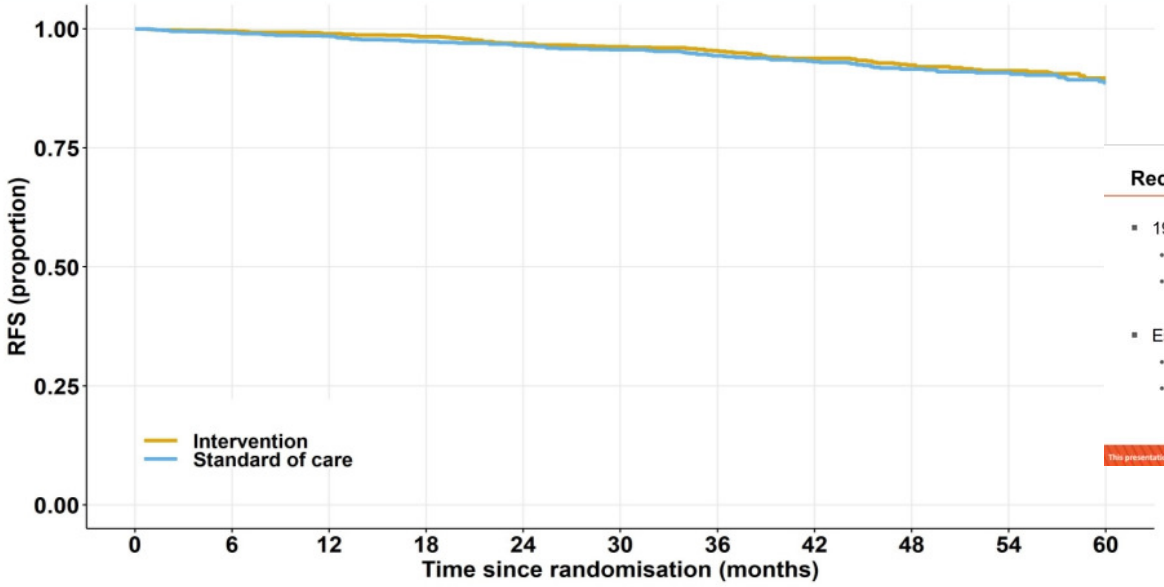

Number at risk

Intervention	1335	1276	1069	832	577	307
Standard of care	1205	1159	1009	772	544	274

Recurrence-Free Survival

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- 191 Recurrence-Free Survival (RFS) events
  - **Standard of Care** N=96 (8.0%)
  - **Intervention** N=95 (7.1%)
- Estimated 5-year RFS
  - **Standard of Care** 88.7% (86.3-91.1)
  - **Intervention** 89.7% (87.5-91.9)

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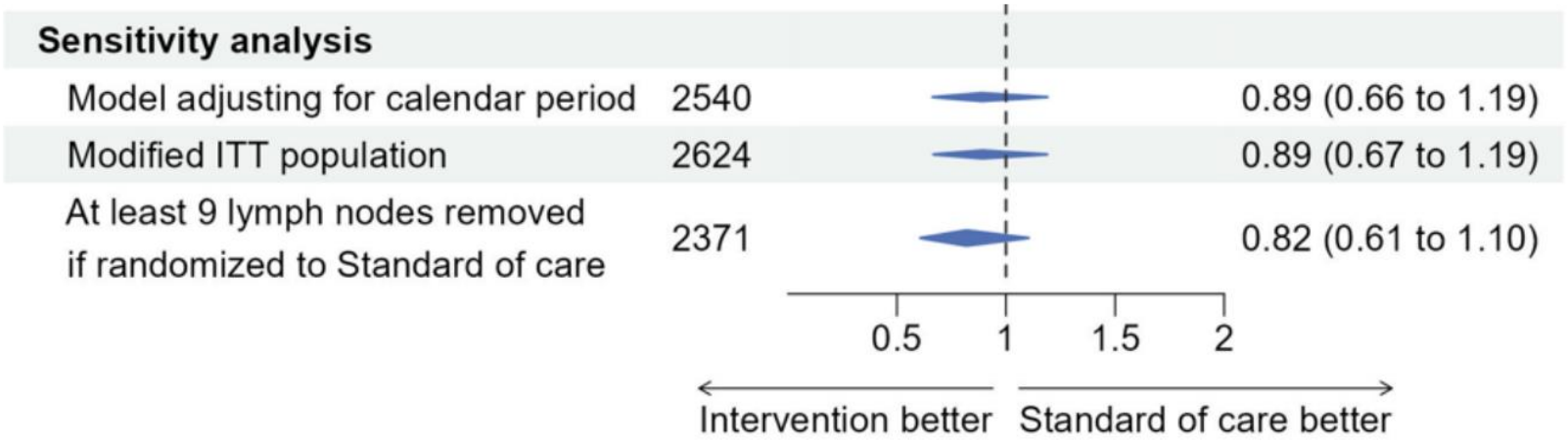
Results: Non-inferiority

- Hazard ratio 0.89 (0.66-1.19)
- Test of non-inferiority p<0.001



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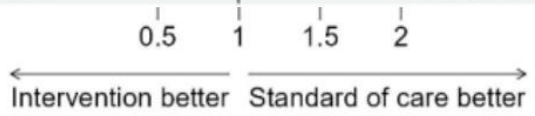
Subgroup analyses

Subgroup	N	HR (95% CI)
PP population	**2540**	**0.89 (0.66 to 1.19)**
Age		
<65 years	1515	0.77 (0.49 to 1.20)
≥65 years	1025	1.02 (0.69 to 1.51)
T stage		
T1-2	2393	0.94 (0.69 to 1.28)
T3	147	0.47 (0.16 to 1.39)
Number of macrometastases		
1	2151	0.92 (0.67 to 1.27)
2	389	0.79 (0.39 to 1.59)
Tumor type		
Lobular	504	0.91 (0.47 to 1.76)
Non-lobular	2036	0.88 (0.64 to 1.23)



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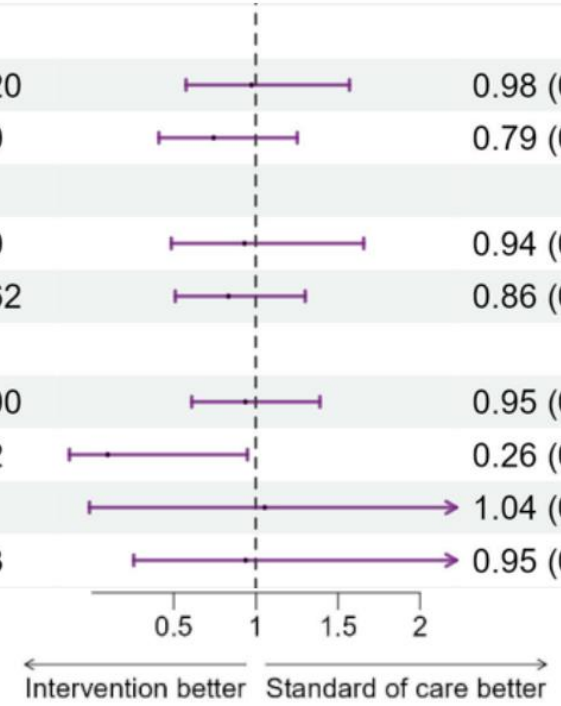
Subgroup analyses

Surgery		
Breast-conserving	1620	0.98 (0.65 to 1.47)
Mastectomy	920	0.79 (0.52 to 1.21)
Extracapsular extension		
Yes	870	0.94 (0.58 to 1.54)
No	1662	0.86 (0.60 to 1.25)
Subtype		
ER+HER2-	2200	0.95 (0.68 to 1.32)
ER+HER2+	172	0.26 (0.07 to 0.96)
ER-HER2+	57	1.04 (0.17 to 6.35)
ER-HER2-	103	0.95 (0.39 to 2.30)



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GS02-06: SENOMAC Studie
Conclusio

- **Trotz erweiterter Einschlußkriterien :**
- **KEIN Unterschied im rezidivfreien Überleben, ob komplette ALND weggelassen wurde oder nicht**
- **Mastectomien wurden in Subgruppenanalyse gezielt adressiert**
- **Langfristige Nachsorge ist bei hohem Anteil luminaler Erkrankungen von entscheidender Bedeutung**

Session: General Session 2

(GS02-05) Overview of Axillary Treatment in Early Breast Cancer: patient-level meta-analysis of long-term outcomes among 20,273 women in 29 randomised trials

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SAN ANTONIO BREAST CANCER SYMPOSIUM®

Mays Cancer Center UT Health MD Anderson Cancer Center

AACR

Overview of axillary management in early breast cancer

Presenter: Gurdeep S. Mannu D.Phil FRCS

University of Oxford

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)

Writing Committee: Gurdeep Mannu , Graham Beake, Richard Berry, David Dodwell, Robert Hills, Paul McGale, Stewart Anderson, Ian Campbell, Armando Giuliano, Reshma Jagsi, Thorsten Kuhn, Rebecca Llewelyn-Bennet, Terry Mamounas, Robert Mansel, Pascal Roy, Emiel Rutgers, Nisha Sharma, Sandra Swain*, Jonas Bergh*

(*joint senior co-authors)

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Session: General Session 2

(GS02-05) Overview of Axillary Treatment in Early Breast Cancer: patient-level meta-analysis of long-term outcomes among 20,273 women in 29 randomised trials

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Hintergrund & Methoden

- im Frühstadium ist die optimale Behandlung der Achselhöhle ungewiß
- Metaanalyse von random. Studien, in denen verschiedene Arten der axill. Behandlung verglichen wurden :
- Ziel: langfristiger Nutzen verschiedener Ansätze besser verstehen
- 29 Studien (20273 Frauen) zur axillären Chirurgie oder axillären Strahlentherapie
- Randomisierung : 1958 – 2009
- Mediane Nachbeobachtung : 10 Jahre

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History of trials of axillary treatment in breast cancer

Year	Randomised trials	
1950s - 1990s	**More *vs* Less axillary treatment**	Pre-SLNB era
1970s – 1990s	**Axillary dissection *vs* Axillary radiotherapy**	
1990s - 2010s	**More *vs* Less axillary treatment**	SLNB era
2000s - 2010s	**Axillary dissection *vs* Axillary radiotherapy**	
2012+	SLNB *vs* No SLNB	Post-SLNB era

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Comparisons of axillary treatment

	Comparison more vs. less	Trials	Women
Pre-SLNB era (1958-1995)			
AD vs no AD	Yes	4	1558
AD vs no AD*	Yes	1	773
Axillary/SCF RT vs no axillary/SCF RT	Yes	2	652
More vs less surgery to axilla	Yes	1	161
More vs less surgery to axilla*	Yes	3	4516
Axillary/SCF RT + AD vs Axillary/SCF RT *	Yes	1	233
AD vs axillary/SCF RT*	No	3	460
SLNB era (1998-2004)			
SLNB+AS/AD vs SLNB: (cN0/sN-)	Yes	10	8010
SLNB+AD vs SLNB: (sN+)	Yes	3	2023
AD vs Axillary RT: (sN+)	No	2	1899
Total		**30†**	**20285**

*confounded by extent of breast surgery

AD: axillary dissection, AS: axillary sampling, SCF: supraclavicular fossa, SLNB: sentinel lymph node biopsy, RT: radiotherapy

†3 trials contributes to two comparisons. Data for ~1000 women from 5 trials not available.

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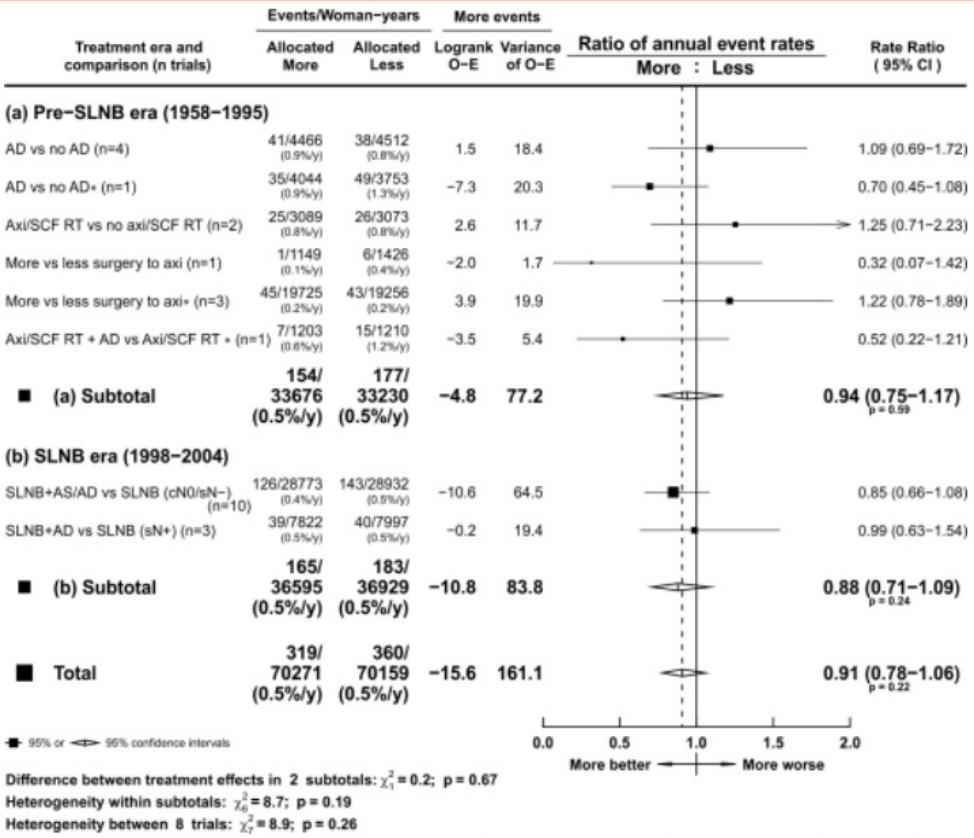
More vs Less axillary treatment
Locoregional recurrence



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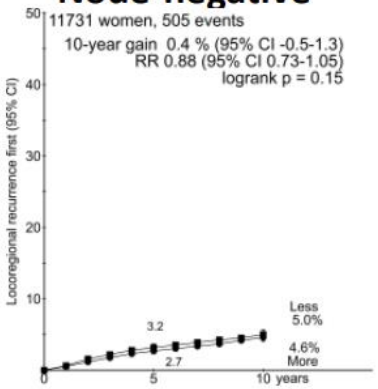
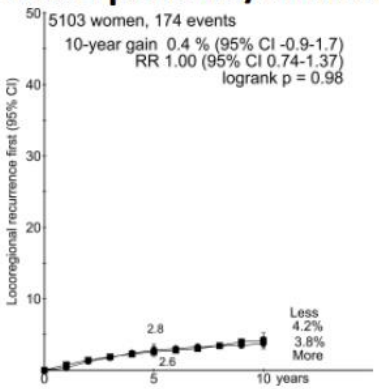
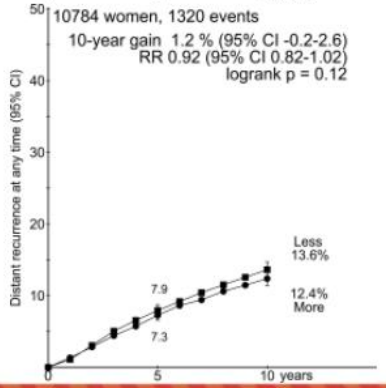
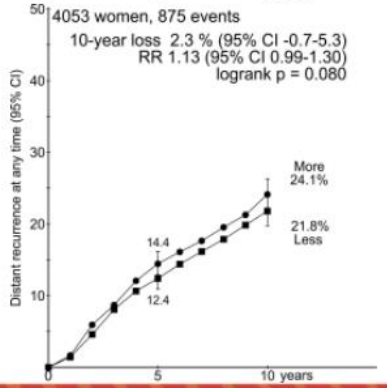
More vs Less axillary treatment by nodal status

	Node-negative	Node-positive/unknown
Locoregional recurrence		
Distant recurrence		

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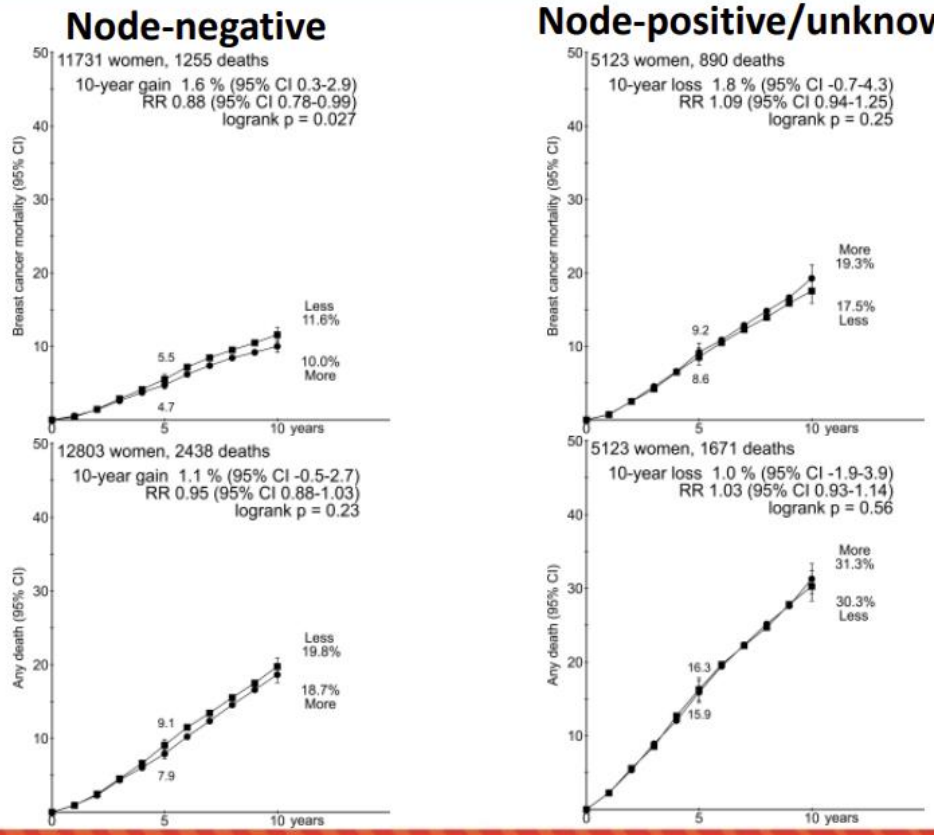
More vs Less axillary treatment by nodal status

Breast cancer mortality

Any death



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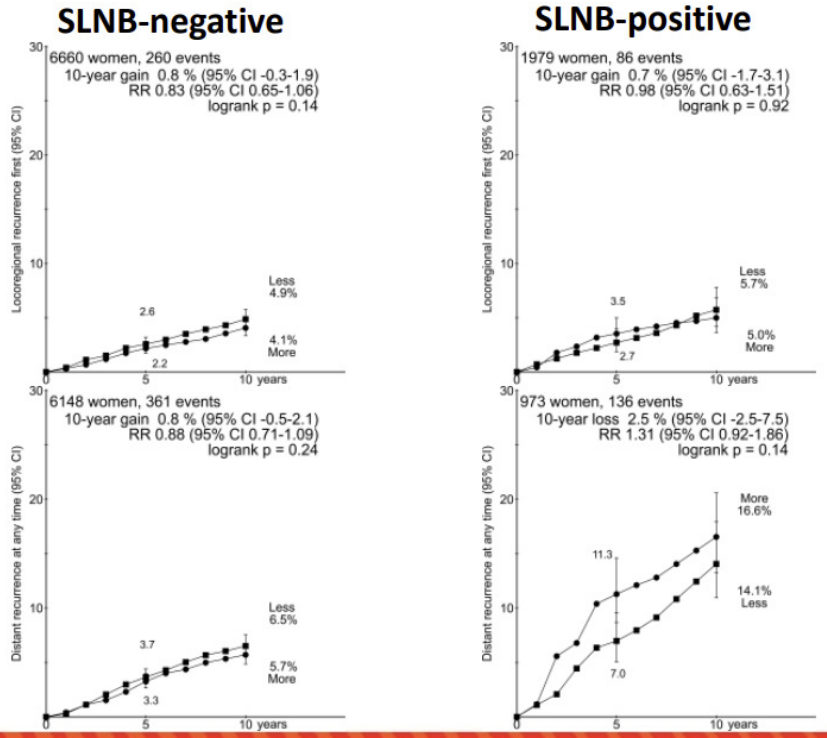
More vs Less axillary treatment by nodal status in SLNB trials



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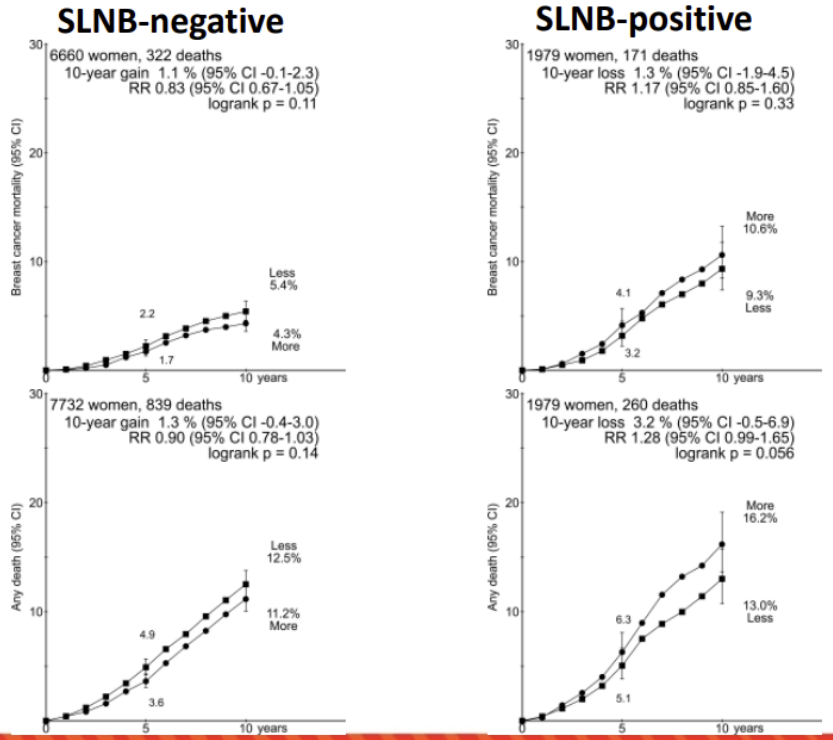
More vs Less axillary treatment by nodal status in SLNB trials

Breast cancer mortality

Any death



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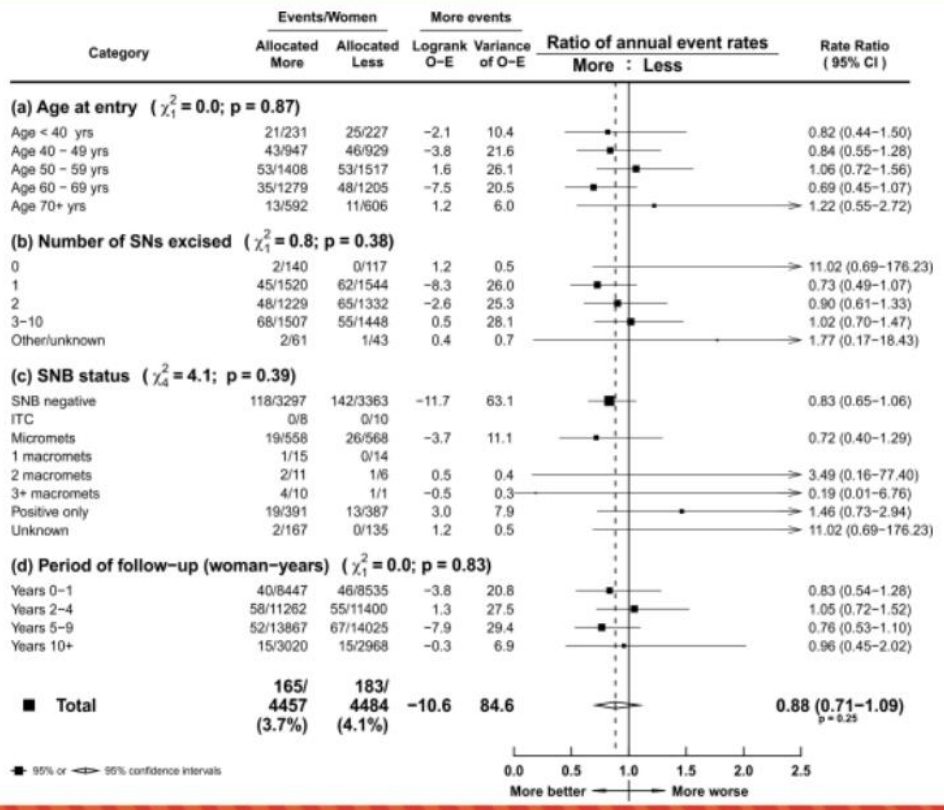
More vs Less axillary treatment Locoregional recurrence in SLNB trials



Category	Events/Women: Allocated More	Events/Women: Allocated Less	More events: Logrank O−E	More events: Variance of O−E	Rate Ratio (95% CI)
(a) Age at entry ($\chi^2_1 = 0.0$; p = 0.87)					
Age < 40 yrs	21/231	25/227	−2.1	10.4	0.82 (0.44−1.50)
Age 40 − 49 yrs	43/947	46/929	−3.8	21.6	0.84 (0.55−1.28)
Age 50 − 59 yrs	53/1408	53/1517	1.6	26.1	1.06 (0.72−1.56)
Age 60 − 69 yrs	35/1279	48/1205	−7.5	20.5	0.69 (0.45−1.07)
Age 70+ yrs	13/592	11/606	1.2	6.0	1.22 (0.55−2.72)
(b) Number of SNs excised ($\chi^2_1 = 0.8$; p = 0.38)					
0	2/140	0/117	1.2	0.5	11.02 (0.69−176.23)
1	45/1520	62/1544	−8.3	26.0	0.73 (0.49−1.07)
2	48/1229	65/1332	−2.6	25.3	0.90 (0.61−1.33)
3−10	68/1507	55/1448	0.5	28.1	1.02 (0.70−1.47)
Other/unknown	2/61	1/43	0.4	0.7	1.77 (0.17−18.43)
(c) SNB status ($\chi^2_4 = 4.1$; p = 0.39)					
SNB negative	118/3297	142/3363	−11.7	63.1	0.83 (0.65−1.06)
ITC	0/8	0/10			
Micromets	19/558	26/568	−3.7	11.1	0.72 (0.40−1.29)
1 macromets	1/15	0/14			
2 macromets	2/11	1/6	0.5	0.4	3.49 (0.16−77.40)
3+ macromets	4/10	1/1	−0.5	0.3	0.19 (0.01−6.76)
Positive only	19/391	13/387	3.0	7.9	1.46 (0.73−2.94)
Unknown	2/167	0/135	1.2	0.5	11.02 (0.69−176.23)
(d) Period of follow−up (woman−years) ($\chi^2_1 = 0.0$; p = 0.83)					
Years 0−1	40/8447	46/8535	−3.8	20.8	0.83 (0.54−1.28)
Years 2−4	58/11262	55/11400	1.3	27.5	1.05 (0.72−1.52)
Years 5−9	52/13867	67/14025	−7.9	29.4	0.76 (0.53−1.10)
Years 10+	15/3020	15/2968	−0.3	6.9	0.96 (0.45−2.02)
■ **Total**	**165/ 4457 (3.7%)**	**183/ 4484 (4.1%)**	**−10.6**	**84.6**	**0.88 (0.71−1.09)** p = 0.25

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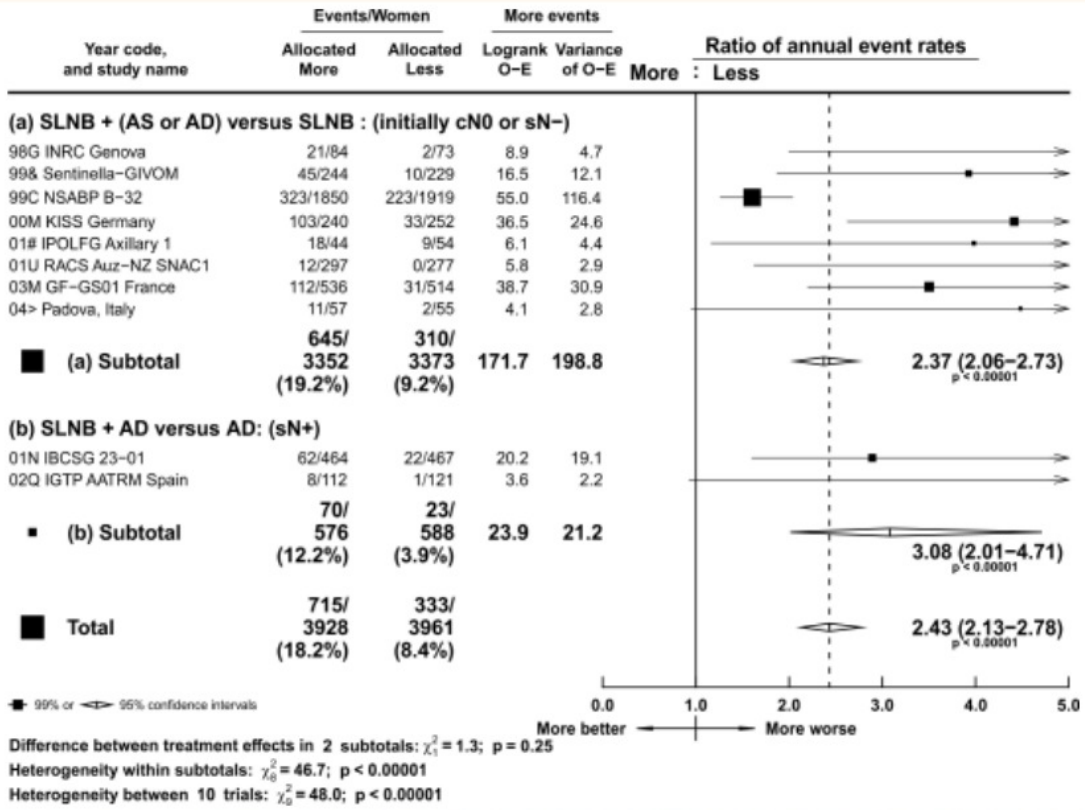
More vs Less axillary treatment Lymphoedema in SLNB trials



Difference between treatment effects in 2 subtotals: $\chi^2_1 = 1.3$; $p = 0.25$

Heterogeneity within subtotals: $\chi^2_8 = 46.7$; $p < 0.00001$

Heterogeneity between 10 trials: $\chi^2_9 = 48.0$; $p < 0.00001$

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History of trials of axillary treatment in breast cancer

Year	Randomised trials	
1950s - 1990s	**More *vs* Less axillary treatment**	Pre-SLNB era
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Axillary dissection *vs* Axillary radiotherapy

Trial	Recruitment	Women
Pre-SLNB era		
WSSA Glasgow	1972-1977	212
Edinburgh	1980-1983	167
Scottish	1987-1995	81
SLNB era		
AMAROS	2001-2010	1425
OTOASOR	2002-2009	474

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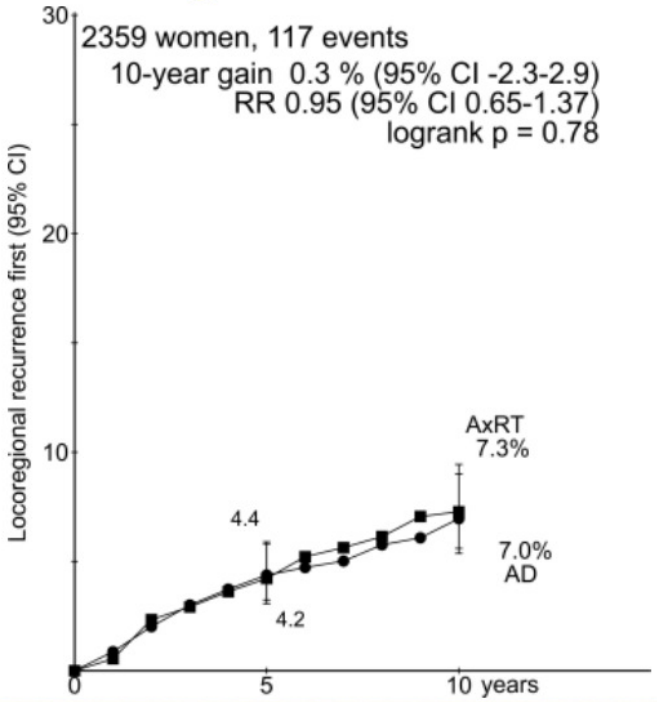
Axillary dissection *vs* Axillary radiotherapy

Locoregional recurrence



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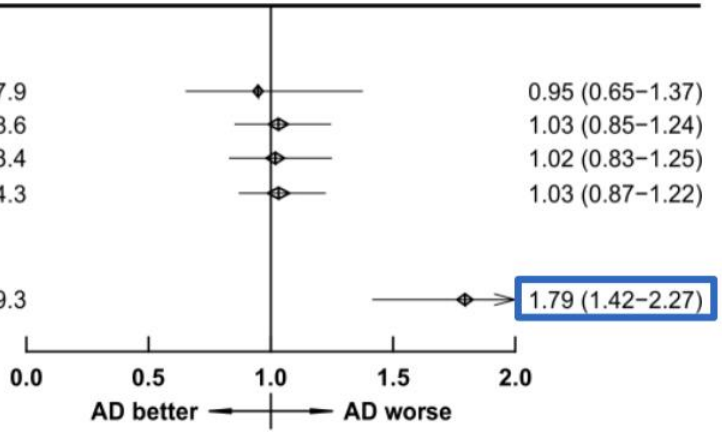
Axillary dissection *vs* Axillary radiotherapy

Summary of outcomes

Outcome	Events/Women: Allocated AD	Events/Women: Allocated AxRT	AD events: Logrank O−E	AD events: Variance of O−E	Rate Ratio* (95% CI)
Recurrence and mortality					
Locoregional recurrence	59/1235	58/1124	−1.5	27.9	0.95 (0.65−1.37)
Distant recurrence	252/1235	229/1124	3.3	108.6	1.03 (0.85−1.24)
Breast cancer mortality	227/1235	197/1124	1.7	93.4	1.02 (0.83−1.25)
Any death	323/1235	286/1124	4.2	134.3	1.03 (0.87−1.22)
Morbidity					
Any lymphoedema	263/612	174/592	40.5	69.3	1.79 (1.42−2.27)



95% or 95% confidence intervals

* odds ratio for lymphoedema

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Ergebnis

Conclusions for trials of more vs less axillary treatment

- Risk of locoregional recurrence low, <5% by year 10
  - RR 0.91 (95% CI 0.78 – 1.06)
- No evidence of an effect on breast cancer mortality
  - RR 0.96 (95% CI 0.87 – 1.05)
- In SLNB trials, increased lymphoedema from more treatment
  - OR 2.43 (95% CI 2.13 – 2.78)

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Ergebnis

Conclusions for trials of axillary dissection vs axillary radiotherapy

- Risk of locoregional recurrence ,~7% by year 10
  - RR 0.95 (95% CI 0.65 – 1.37)
- No evidence of an effect on breast cancer mortality
  - RR 1.02 (95% CI 0.83 - 1.25)
- In SLNB trials, increased lymphoedema from surgery
  - OR 1.79 (95% CI 1.42 - 2.27)

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Fazit:

- **Bisher umfassendster Überblick über die axilläre Therapie**
- **SNB oder axill. Radiatio führten zu deutlich weniger Lymphödemen im Vergleich zur axillären LNE**
- **Keine Hinweise auf einen Unterschied im lokoregionären Rezidiv (ein moderater Effekt kann nicht ausgeschlossen werden)**
- **Das Risiko für ein Fernrezidiv, Brustkrebs-/ Nicht-Brustkrebs- oder Gesamtmortalität unterschied sich nicht signifikant nach dem Ausmaß der axillären Behandlung oder beim Vergleich der axillären Clearance mit der Strahlentherapie**

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Supportive Therapie

Poster Spotlight Session 2

Verbesserung der Lebensqualität und Versorgung von Brustkrebspatientinnen

Poster Spotlight Session 2: Lebensqualität & Versorgung

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PS02-05: Verläufe und Prädiktoren der peripheren Neuropathie nach NA-CHEMO in einer prospektiven Kohorte von 11.014 Pat. mit Brustkrebs im Frühstadium

PS02-05

TRAJECTORIES AND PREDICTORS OF PERIPHERAL NEUROPATHY AFTER (NEO)ADJUVANT CHEMOTHERAPY IN A PROSPECTIVE COHORT OF 11,041 PATIENTS WITH EARLY BREAST CANCER

Youenn Drouet, PhD; Emilie Thomas, PhD; Florence Lerebours, MD, PhD; Barbara Pistilli, MD; Olivier Tredan, MD, PhD; Christelle Jouannaud, MD; Marion Fournier, MD; Philippe Rouanet, MD, PhD; Laurence Vanlemmens, MD; Charles Coutant, MD, PhD; Asma Dhaini Merimeche, MD; Baptiste Sauterey, MD; Christelle Levy, MD; Mario Campone, MD, PhD; Carole Tarpin, MD; Marie-Ange Mouret-Reynier, MD; Olivier Rigal, MD; Thierry Petit, MD; Sophie Guillermet, MD; Antoine Arnaud, MD; Mahmoud Ibrahim, MD; Sylvie Giacchetti, MD, PhD; Florence Dalenc, MD, PhD; Johanna Wassermann, MD, PhD; Olivier Arsène, MD; Ariane Darut-Jouve, MD; Sibille Everhard, PhD; Ines Vaz-Luis, MD, PhD; Anne-Laure Martin, PhD; Fabrice André, MD, PhD; Jean-François Deleuze, PhD; Alain Viari, PhD; Matthieu Carton, MD, PhD; **Paul Cottu, MD, PhD**

Centre Léon Bérard, Lyon; **Institut Curie, Paris** & Saint-Cloud; Gustave Roussy, Villejuif; Institut Godinot, Reims; Institut Bergonié, Bordeaux; Centre Oscar Lambret, Lille; Centre GF Leclerc, Dijon; Centre François Baclesse, Caen; Institut de Cancérologie de Lorraine, Nancy; Institut de Cancérologie de l'ouest, Angers & Saint-Herblain; Institut Paoli Calmette, Marseille; Institut Jean Perrin, Clermont-Ferrand; Centre Henri Becquerel, Rouen; Institut ce Cancérologie de Strasbourg, Strasbourg; Centre Eugène Marquis, Rennes; Institut Sainte-Catherine, Avignon; CHU La Source, Orléans; CHU Saint-Louis, Paris; IUCT, Toulouse; CHU Pitié-Salpêtrière, Paris; CH Blois, Blois; Clinique du Parc, Dijon; Labex GENMED, Evry; Lyrican, Lyon; Unicancer R&D, Paris - FRANCE

UCBG unicancer

canto CANcer TOxicities

Abstract

Background. Peripheral neuropathy (PN) is a debilitating adverse event in patients with early breast cancer (BC) receiving(neo)adjuvant chemotherapy (CT). We harnessed the CANTO cohort study to detail clinical trajectories and explore clinical and genetic predictors of PN.

Methods. CANTO (CANcer TOxicities - NCT01993498) prospectively enrolled invasive stage I-III BC patients (pts) of 26French comprehensive cancer centers. Pts were assessed at diagnosis, 3-6 (M6), 12 (M12), 36 (M36), and 60(M60) months after treatment, defined as completion of surgery, CT or radiotherapy, whichever comes last. At each time point, PN events including paresthesia, sensory and motor neuropathy were collected according to NCI-CTC v4.0 criteria. A genome-wide association study (GWAS) was conducted to identify genetic predictors of PN, using Illumina GSA BeadChips. Minimac4/1000G was used to impute additional single nucleotide polymorphisms (SNPs). After stringent quality control measures, 1,894,475 SNPs with a minor allele frequency (MAF) >0.05 were evaluated. Longitudinal trajectories of PN events were descriptively examined. Statistical associations between each SNP and PN events measured at different time points, and between SNPs and trajectories, were performed with logistic regression assuming a log-additive genetic model. All analyses were adjusted for key clinical parameters and the first ten axes of principal component analysis of the genetic data to control for population stratification.

Results. Of 12,012 included pts (data lock Aug. 2022), 11,014 (91.7%) were analyzed. Age was < 50 and > 65 in 3407 and 2759 pts (31% and 25%, respectively). Overweight/obesity and diabetes were recorded in 5328 (48%) and 458 pts (4%). A neurologic history was observed in 1360 pts (13%). Stage 0-I and II-III were observed in 5356 (49%) and 5512 pts (51%), and 4011 pts had an axillary dissection (37%). CT was administered in 5790 pts (53%), including a taxane (tax) in 5542 pts (96%).

Shortly, all grade and grade 2+ PN was observed in 29% and 12%; 27% and 10%; 20% and 10%; 13% and10% of pts at M6, M12, M36 and M60, respectively. We derived 5 trajectories of overall PN, deemed "never", "always", "appears", "transient" and "disappears", in respectively 54%, 10%, 9%, 7% and 19% of the pts. Similar trajectories were built for the 3 categories of PN events. We built 9 predictive nomograms including key clinical parameters and time of analysis. E.g., grade 2+ PN at M6 was independently predicted by a medical history of carpal tunnel syndrome, past neurologic history and exposure to tax. Grade 2+ PN at M36 was predicted by past neurologic history and exposure to tax, and largely by previous PN at M6 or M12.

The GWAS analysis included 7633 pts (84%). Four independent SNPs adding predictive value to the clinical nomograms were identified at a suggestive level of association ($p< 1e-6$), including one SNP in the NCAM1 gene (involved in neurogenesis) for M6 PN (OR=1.40, 95%CI 1.23-1.60, $p=4.8e-7$; see table) and one SNP in the CLDN11 gene (regulates oligodendrocytes) for M12 sensory PN (OR=1.47; 95%CI 1.17-1.49, $p=7.5e-6$). For rare (< 5%) toxicities, 10 independent suggestive SNPs were identified, including one SNP in the NELL1 gene (neural cell growth regulation and differentiation) for the "always" trajectory (OR=1.61, 95%CI 1.31-1.99, $p=7.6e-6$) and one SNP in the KCNIP1 gene (neuronal sensor) for M36 motor PN (OR=1.5, 95%CI 1.7-3.5, $p=3.1e-07$).

Conclusions. Risk of early peripheral neuropathy is associated with previous neurological history and taxane exposure. Patients with PN at M6 or M12 are highly exposed to long-term PN. Some key SNPs may add independent predictive value for specific PN endpoints. Exploratory results of interest were produced for rarer toxicities and typical clinical trajectories. Detailed results will be presented at the meeting.

Flow Chart

- 11400 • CANTO database, as of May 4, 2022 • Bilateral breast cancer n=264
- 11136 • Missing data /chemotherapy n=91
- 11045 • Trastuzumab only n=4
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- 7633 • => GWAS analyses

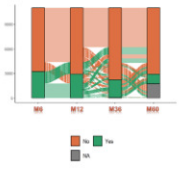
Population (key features)

	n	%
Age		
<50	3407	30.9
50-65	4875	44.1
>65	2759	24.9
Overweight/obesity (BMI>25)	5328	48.2
Diabetes	458	4.1
Past neurological condition	1360	12.3
Tumor stage		
I	5356	49.3
II-III	5512	50.7
Tumor subtype		
HR+/HER2-	8320	76.1
HER2+	1558	14.3
TNBC	1048	9.6
Axillary dissection	4011	36.9
Chemotherapy	5790	52.4
Taxane containing	5542	95.7

PN: global landscape

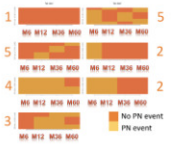
PN = paresthesia + sensory neuropathy + motor neuropathy

All patients	All grade PN	Grade 2-4 PN
M6 (n=11014)	29%	12%
M12 (n=11014)	27%	10%
M36 (n=10969)	20%	10%
M60 (n=9236)	13%	10%



PN : trajectories

7 classes were initially identified, then regrouped in 5 classes of trajectories
N=9236 patients M0-M60
All PN, all grades



Class	N	%
1 Never	4811	52.1%
2 Disappears	1883	20.4%
3 Appears	1223	13.2%
4 Always	823	8.9%
5 Passing	496	5.4%

No clinical predictor

PN : clinical nomograms (1)

N=9236 patients M6-M60
All PN, all grades

For each time point, we build multivariate models, considering
- Key clinical features
- PN diagnosis at previous time points for prediction at M12, M36, M60

Prediction of PN @M36

Clinical features only — AUC 0.590

Clinical features + previous PN — AUC 0.745

PN : clinical nomograms (2)

N=9236 patients M6-M60
All PN, all grades

Prediction of PN @M60

Clinical features only — AUC 0.579

Clinical features + previous PN — AUC 0.776

PN : clinical nomograms (3)

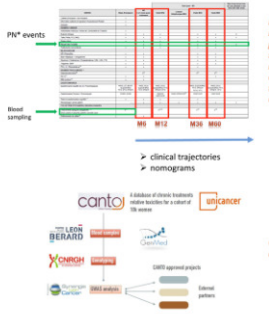
M6-M60
All PN, all grades
N=2934 patients with taxane exposure

Prediction of PN @M60

Clinical features only

Clinical features + previous PN — AUC 0.795

Methods



PN events including paresthesia, sensory and motor neuropathy were collected according to NCI-CTC v4.0 criteria

CANTO GWAS consortium

GWAS analysis (1)

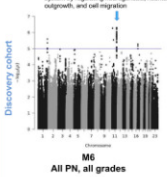
All PN, all grades
Timepoints

NCAM1 11q23.2
role in the development of the nervous system by regulating neurogenesis, neurite outgrowth, and cell migration

All PN, M6	Clinical model		Integrative model	
	OR	P	OR	p
Obesity	1.17	.013	1.1	.32
Carpal tunnel	1.44	<.001	1.49	<.001
Neurol. History	2.26	<.001	2.14	<.001
Taxane	3.08	<.001	3.0	<.001
NCAM1	-	-	1.40	4.8e-7

Following a power analysis, a validation cohort of N= 1811 (20% of the total cohort) is isolated for validation of the TOP SNPS. The p-value and OR of the TOP SNPS are calculated in the validation cohort.

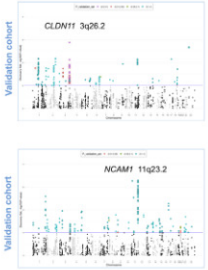
Otherwise, due to lack of statistical power, the whole cohort is used for discovery (i.e. there is no validation cohort)



GWAS analysis (2)

All PN, all grades
Timepoints

CLDN11 3q26.2
major component of central nervous system myelin and plays an important role in regulating proliferation and migration of oligodendrocytes



M12
Neurosensory PN, all grades

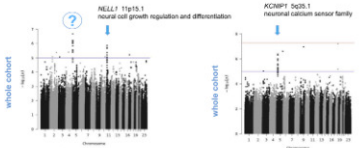
X: reversed Odds-ratio

GWAS analysis (3)

All PN, all grades
Trajectories and rare toxicities: exploratory analyses

NELL1 11p15.1
neural cell growth regulation and differentiation

KCNIP1 5q35.1
neuronal calcium sensor family



« always » trajectory
Sensory PN

M36
Motor PN

Conclusions

- ≈10,000 patients with 5 years follow-up, representative of current clinical care of early breast cancer
- PN is a frequent and durable adverse event (>10% grade 2-4 at 5 years)
- At baseline, clinical predictors associated with early and long term PN are
  - Past neurological condition
  - Taxane exposure
- After initial therapies (surgery, chemotherapy, radiation therapy), patients developing PN have a high risk of long-term PN
  - Almost 50% of those patients still suffer from PN at 5 years
  - Specific trajectories have been described, however with no clinical predictor
- Exploratory GWAS analyses suggested that specific SNPs in genes with neurological relevance may be associated with some PN endpoints, in addition to taxane exposure

Implication

Overall, these results suggest that the risk of PN should be assessed on an individual clinical and probably genetic basis, and must be re-assessed during clinical care

paul.cottu@curie.fr

**PN: peripheral neuropathy*

Gemeinschaftsklinikum Mittelrhein

PS02-05: Verläufe und Prädiktoren der peripheren Neuropathie nach NA-CHEMO in einer prospektiven Kohorte von 11.014 Pat. mit Brustkrebs im Frühstadium
Hintergrund & Methoden

- Periphere Neuropathie (PN) ist ein unerwünschtes Ereignis

- CANTO (CANcerTOxicities) Studie: 26 franz. Krebszentren

- Beschreibung klinischer Verläufe, Untersuchung klinischer u. genetischer Prädiktoren
- Erfassung klinischer Parameter 6 – 60 Monate nach Therapie (OP / Chemo / Radiatio)
- Genomweite Assoziationsstudie (GWAS) um genetische Prädiktoren für PN zu identifizieren
- Untersuchung von Einzelnukleotid-Polymorphismen (SNP´s)

- Statistik: Deskriptiv für Langzeitverläufe von PN ; mögliche Assoziation zwischen SNP´s

Gemeinschaftsklinikum Mittelrhein

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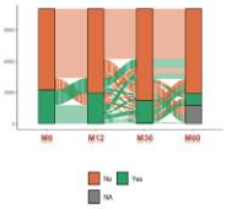

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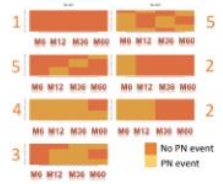

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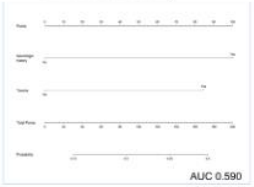
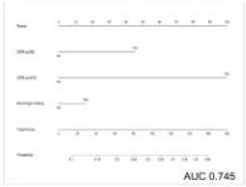
Prediction of PN @M36

Clinical features only



Clinical features + previous PN

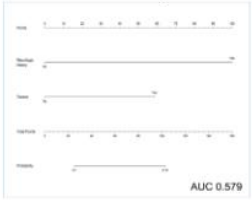


PN : clinical nomograms (2)

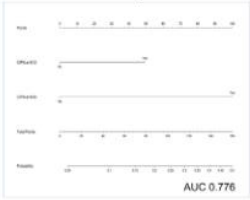
N=9236 patients M6-M60
All PN, all grades

Prediction of PN @M60

Clinical features only



Clinical features + previous PN

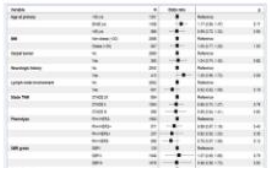


PN : clinical nomograms (3)

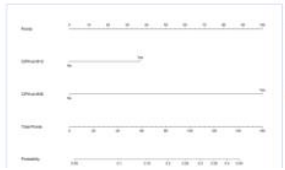
M6-M60
All PN, all grades
N=2994 patients with taxane exposure

Prediction of PN @M60

Clinical features only



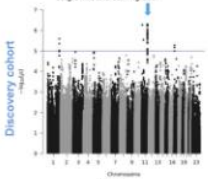
Clinical features + previous PN



GWAS analysis (1)

All PN, all grades
Timepoints

NCAM1 11q23.2
role in the development of the nervous system by regulating neurogenesis, neurite outgrowth, and cell migration



M6
All PN, all grades

All PN, M6	Clinical model		Integrative model	
	OR	P	OR	p
Obesity	1.17	.013	1.1	.32
Carpal tunnel	1.44	<.001	1.49	<.001
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Taxane	3.08	<.001	3.0	<.001
NCAM1	-	-	1.40	4.8e-7

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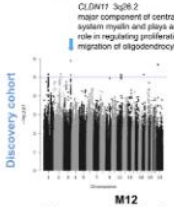
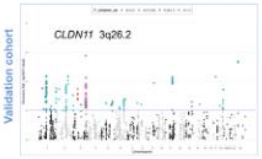
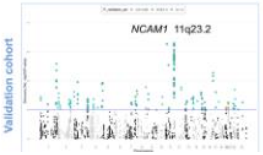
Timepoints

CLDN11 3q26.2
major component of central nervous system myelin and plays an important role in regulating proliferation and migration of oligodendrocytes



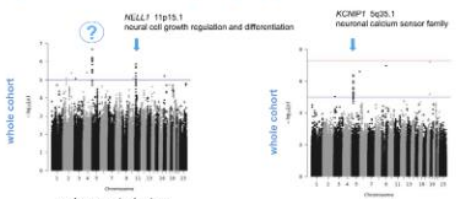
M12
Neurosensory PN, all grades





GWAS analysis (3)

All PN, all grades
Trajectories and rare toxicities: exploratory analyses



« always » trajectory
Sensory PN

M36
Motor PN

Conclusions

≈10,000 patients with 5 years follow-up, representative of current clinical care of early breast cancer
PN is a frequent and durable adverse event (>10% grade 2-4 at 5 years)

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Implication

Overall, these results suggest that the risk of PN should be assessed on an individual clinical and probably genetic basis, and must be re-

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Gemeinschaftsklinikum Mittelrhein

PS02-05: Verläufe und Prädiktoren der peripheren Neuropathie nach NA-CHEMO in einer prospektiven Kohorte von 11.014 Pat. mit Brustkrebs im Frühstadium

Conclusio

- Risiko einer frühen PNP ist mit der neurologischen Vorgeschichte und der Taxanexposition verbunden
- Relevant hoch : M6 : 29% ; M60 : 13 %
- Pat. mit PN bei M6 oder M12 sind einer Langzeit-PN stark ausgesetzt

- Einige SNP´s können einen unabhängigen prädiktiven Wert für bestimmte PN Endpunkte bieten :
- NCAM1.Gen: Neurogenese
- CLDN11-Gen: Oligodendrozyten
- NELL1-Gen: Neuronales Zellwachstum
- KCNIP1-Gen : Neuronaler Sensor

Poster Spotlight Session 2: Lebensqualität und Versorgung :

Gemeinschaftsklinikum Mittelrhein

PS02-09: Von Pflegenden geleitete individualisierte Nachsorge im Vergleich zu regelmäßigem ärztlichem Besuchen nach Brustkrebs im Frühstadium (MyHealth)

NURSE-LED INDIVIDUALIZED FOLLOW-UP VERSUS REGULAR PHYSICIAN-LED VISITS AFTER EARLY BREAST CANCER (MYHEALTH) - A RANDOMIZED CONTROLLED TRIAL

tbæk[1,2], Pernille E Bidstrup[3], Randi V Karlsen[3], Beverley L Høeg[3], Trine A Horsbøl[4], Federica Belmonte[5], Elisabeth AW Andersen[5], Vibeke Zoffmann[6], Anne S Friberg[1], Mads N Svendsen[2], Helle G Christensen[2], Vesna Glavicic[2], Dorte L Nielsen[7,8], Susanne O Dalton [1,2,8], Christoffer Johansen[1,3,8,9]

vivorship, Danish Cancer Institute, Copenhagen, Denmark; [2]Department of Oncology, Zealand University Hospital, Naestved, Denmark; [3]Cancer Survivorship, Research Team on Psychological Aspects of Cancer, Danish Cancer Institute, Copenhagen, Denmark; [4]National Institute of Public Health, University of Southern Denmark; [5]Statistics and Pharmaco-Epidemiology Unit, Danish Cancer penhagen, Denmark; [6]Research Unit of Women's and Children's Health, the Juliane Marie Center, Copenhagen University Hospital, Copenhagen, Denmark; [7]Department of Oncology, Herlev and Gentofte University Hospital, Denmark; [8]Department of Clinical Medicine, Faculty of Health, Copenhagen University; [9]CASTLE, Department of Oncology, Copenhagen University Hospital, Copenhagen,

CONCLUSION

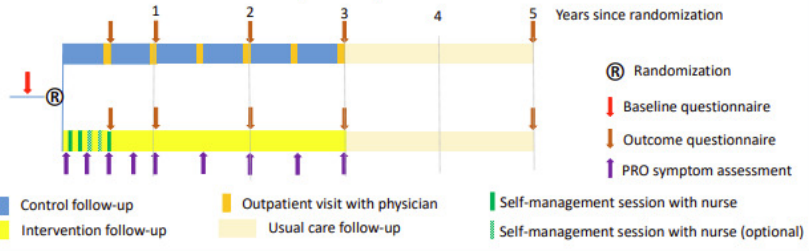
- **Nurse-led follow-up resulted in:**
  - **Significantly improved breast cancer-specific HRQoL, reduced fear of recurrence, anxiety and depression**
  - **Less outpatient visits with physician and more telephone consultations with nurse**
  - **No increase in the number of diagnostic imaging examinations**

OBJECTIVE

- Follow-up after breast cancer with regular visits has failed to prove superior to other strategies concerning detection of recurrence, cost-effectiveness, and in meeting the needs of breast cancer survivors
- Study aim:
  - To investigate if a nurse-led follow-up program with a self-management intervention, symptom assessment using PRO and nurse navigation can improve breast cancer-specific HRQoL compared with regular outpatient visits with physician
  - To investigate health care utilization in the two study groups

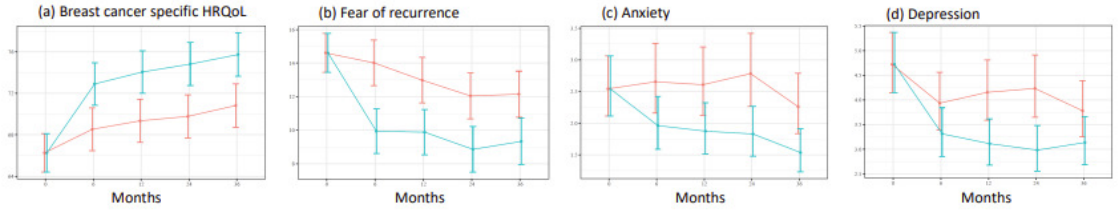
METHODS

- Patients with breast cancer stage I-II who recently completed surgery and chemotherapy/radiotherapy
- Randomization to intervention or control follow-up for three years



RESULTS

- 503 patients were randomized to intervention (n=251) or control (n=252) follow-up
- Intervention effects on breast cancer-specific HRQoL (a), fear of recurrence (b), anxiety (c), and depression (d) — Control follow-up — Intervention follow-up



- Number of contacts during three-year follow-up

	Intervention Mean (SD)	Control Mean (SD)	P-value
Physician visit	1.47 (1.81)	5.26 (2.32)	<0.001
Physician telephone	1.00 (1.34)	1.17 (1.12)	0.140
Nurse visit	0.40 (0.65)	0.05 (0.23)	<0.001
Nurse telephone	3.60 (2.71)	0.50 (1.14)	<0.001
Mammograms	1.99 (1.09)	2.07 (0.95)	0.384
Other diagnostic imaging	1.43 (1.68)	1.53 (2.13)	0.554

SABCS SAN ANTONIO BREAST CANCER SYMPOSIUM®
ECEMBER 5-9, 2023 | @SABCSSanAntonio

Contact: Lena Saltbæk, MD, PhD
E-mail: lsal@regionsjaelland.dk

Rigshospitalet

REGION SJÆLLAND SJÆLLANDS UNIVERSITETSHOSPITAL

Gemeinschaftsklinikum Mittelrhein

PS02-09: Von Pflegenden geleitete individualisuierte Nachsorge im Vergleich zu regelmäßigem ärztlichem Besuchen nach Brustkrebs im Frühstadium (MyHealth)

Hintergrund & Methoden

- Regelmässige Visiten bei Fachärzten in der Nachsorge hat sich gegenüber anderen Strategien nicht als überlegen erwiesen , aber ist Standard in vielen Gesundheitssystemen

- Nachsorge bei Hausarzt oder spezialisierter Krankenschwester ist kostengünstiger und sei nicht schlechter in Bezug auf Lebensqualität

- 503 Pat :
- Interventionsgruppe : Pflegekraft geleitet
- Kontrollgruppe : Onkologe alle 6 Monate ambulant

PS02-09:

Gemeinschaftsklinikum Mittelrhein

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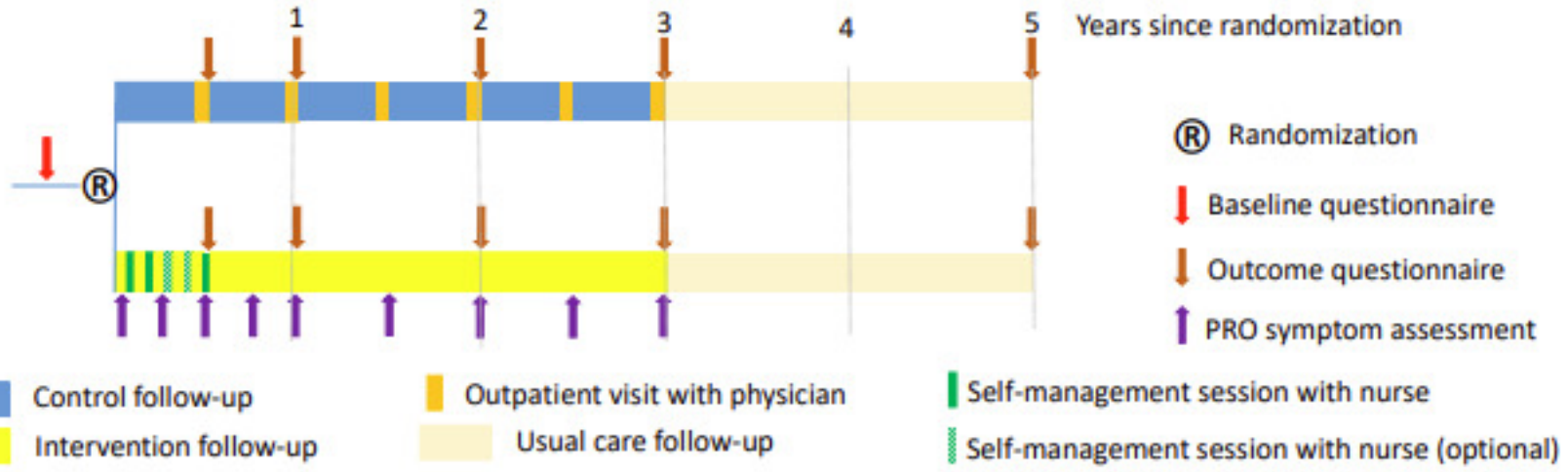
- Patients with breast cancer stage I-II who recently completed surgery and chemotherapy/radiotherapy
- Randomization to intervention or control follow-up for three years



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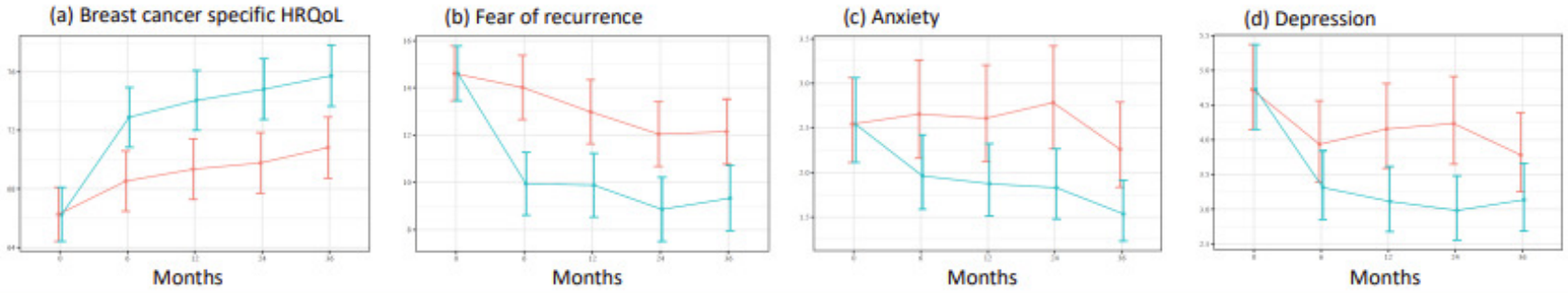
RESULTS

- 503 patients were randomized to intervention (n=251) or control (n=252) follow-up
- Intervention effects on breast cancer-specific HRQoL (a), fear of recurrence (b), anxiety (c), and depression (d)

Control follow-up — Intervention follow-up



- Number of contacts during three-year follow-up

	Intervention Mean (SD)	Control Mean (SD)	P-value
Physician visit	1.47 (1.81)	5.26 (2.32)	<0.001
Physician telephone	1.00 (1.34)	1.17 (1.12)	0.140
Nurse visit	0.40 (0.65)	0.05 (0.23)	<0.001
Nurse telephone	3.60 (2.71)	0.50 (1.14)	<0.001
Mammograms	1.99 (1.09)	2.07 (0.95)	0.384
Other diagnostic imaging	1.43 (1.68)	1.53 (2.13)	0.554

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Conclusio

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- **MyHealth- Studie :**
- **Autoren schlagen eine neue Strategie für die Nachsorge im Frühstadium vor:**
- **Verbesserung in QOL Parametern, Angst vor Rückfall, Depression**
- **Ohne zusätzliche Kosten für das Gesundheitswesen**
- **(Dänemark)**

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Zusammenfassung – Take Home

- **SNB statt TAD nach Neoadjuvanz ggf ausreichend (zumindest für ypN0), (PS01-01 Neosentiturk + 02 Harvard)**
- **Aber : möglicher Informationsverlust für weitere Therapien bei >= 4 + LK´s , (PS01-04, Sinodar One)**
- **Sentinel Konzept für alle Subgruppen als sicher bestätigt, incl Mastectomien (GS02-06, Senomac)**
- **De-Eskalation der Axillatherapie (SNB / Radiatio vs ALND) ist im Langzeitverlauf sicher (EBCTCG Metanalyse)**
- **Die taxaninduziere Polyneuropathie ist relevant , häufig und zeigt genetische Prädispositionen (PS02-05)**
- **Eine Nicht- Fachärztliche Nachsorge mit Interventionen ist in Bezug auf Lebensqualität überlegen und kostengünstiger (zumindest in Dänemark) PS02-09**

Danke für die Aufmerksamkeit

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Santo Antonio