

Brussels, January 30, 2021









What's new in Breast Cancer Surgery?

OFFICIAL -

SABCS



Marian Vanhoeij Medical Coördinator Breast Clinic UZ Brussel Coördinating Surgical Trainer VUB Guest Professor Surgery VUB



Financial Disclosure

Nothing to disclose



Surgery

- How?
- When?
- When not?



When not to?

- Urgent settings: experience, reasoning and gut feeling
- Planned situations: evidence-based

Do we have new evidence to help us decide?



SABCS 2020: de-escalation

- DCIS
- ALND in limited pN1
- Axilla in cN1 with ycN0 after NAC
- Breast after NAC



SSO-DCIS debate: Active monitoring vs Excision



Dr. Eun-Sil Shelley Hwang Duke University

Points of agreement:

High grade and/or extensive DCIS Young patients Symptomatic disease: palpable mass or mass on imaging

Frail High comorbidity



OFFICIAL

SABCS

best,

Dr. Sarah McLaughlin Mayo Clinic Florida



Occult invasive disease

Rates of Upstaging in DCIS

Variable	MSKCC:LORIS eligible (n=296) n (%)	S	Duke Cohor (n=307) n (%)	t	COMET eligible (n=81) n (%)	LORIS eligible (n=74) n (%)	LORD eligible (n=10) n (%)
Nuclear grade							
Low	53 (18)		15 (5)		12 (15)	12 (16)	10 (100)
Intermediate	244 (82)		95 (31)		69 (85)	62 (84)	0 (0)
High	0 (0)	+	197 (64)		0 (0)	0 (0)	0 (0)
Comedonecrosis		╈	157 (51)		0 (0)	0 (0)	0 (0)
Upgrade			13 (4)		8 (10)	7 (9)	3 (30)
Upstage	57 (18)		53 (17)		5 (6)	5 (7)	1 (10)
L							

6-18%

Grimm L et al, ASO 2017



6-18%

Occult invasive disease missed - so what?

ACOSOG Z0011

106 (27.4%) patients treated with ALND had additional positive nodes removed beyond SN.

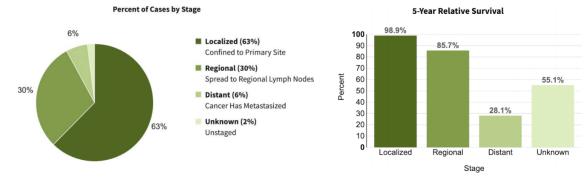
an an an an an an an an Anna an Anna an Anna an Anna an Anna. An an an anna an anna an an an an an an a	ALND	SLNB	р
Local regional recurrence	17%	15%	0.66
Disease free survival	78.2%	80.2%	0.51
Overall survival	83.6%	86.3%	0.72



6-18%

Occult invasive disease missed - so what?

Breast Cancer Outcomes in Patients With Localized Disease



63% of all breast cancers are localized at the time of diagnosis 5-year survival from localized breast cancer is **98.9%** compared to **99% for DCIS**

https://seer.cancer.gov/statfacts/html/breast.html



Occult invasive disease missed - so what?

Innocent DCIS does not always lead to "innocent" invasive disease.

Pilewskie et al. ASO 2016 reported a 20% upstage-rate

18% of them had adjuvant CT recommended

6% TN, HER2+, LVI, LN+

Alexander et al. Arch Path Lab Med 2019 reported a lower upstage rate of 8% but

10-14% of the low-intermediate grade group presented with

TN, HER2 or LN+ invasive cancers



SABCS 2020: no new evidence supplied

		COMET A Study for Low Risk DCIS Expanding Knowledge and Options		JCOG Japan Clinical Oncology Group
	LORIS	COMET	LORD	LORETTA
Country	UK	US	Netherlands	Japan
Age	<u>></u> 48	<u>></u> 40	<u>></u> 45	<u>></u> 40, <u><</u> 75
Design	RCT	RCT	Patient	Single arm
			preference	
Endocrine therapy	Possible	Possible	Not allowed	Tamoxifen
Primary outcome	10 years	2, 5, 7 years	10 years	5, 10 years
Opened	2014	2017	2017	2017
Patient accrual	166	600	40	60
Target	closed	1200 (900)	1240	340



SSO-DCIS debate: Active monitoring vs Excision

Until prospective studies are concluded and reported: multidisciplinary discussion & informed decision making



SABCS 2020: de-escalation

- DCIS
- ALND in limited pN1
- Axilla in cN1 with ycN0 after NAC
- Breast after NAC



ALND omission in limited pN1 disease

Sinodar One Trial: RESULTS

	SLNB N=446	SLNB + ALND N=442
Breast surgery		
Breast conserving surgery	79.9%	76.9%
Mastectomy	20.1%	23.1%
Median Number SLNs Removed	2	2
SLN micrometastsis	2	1
Outcomes	– median follow-up 30 month	S
Axillary recurrence	1	0
Distant relapse	3	3
Death	1	2
Non-Breast Cancers	1	3

5 year cumulative incidence of any recurrence 4.9% in SLNB arm vs 6.5% in ALND arm

Tinterri C, SABCS Spotlight Poster Discussion 2020



ALND omission in limited pN1 disease

DISCUSSION: Sinodar One VS ACOSOG Z0011

	Sinodar One		ACOSOG	6 Z0011
	SLNB N=446	ALND N=442	SLNB N=436	ALND N=420
Median Tumor Size	1.8cm	2.0cm	1.6cm	1.7cm
ER+	81%	83%	83%	83%
Median #LNs removed	2	16	2	17
SLN Macrometastases	99.6%	99.8%	55.2%	62.5%
Surgery Breast conserving surgery Mastectomy	79.9% 20.1%	76.9% 23.1%	100% 0	100% 0
	0	utcomes		
Follow-up	2.5 y	ears	6.3 y	ears
Axillary recurrences	1 (<0.01%)	0	4 (0.9%)	2 (0.5%)

ACOSOG Z0011

45% N1mic 100% BCS

Tinterri C, SABCS Spotlight Poster Discussion 2020



SABCS 2020: When not to?

- Excise DCIS
- ALND in limited pN1
- ALND in cN1 with ycN0 after NAC
- Breast resection after NAC



Axillary management after NAC

Subtype	Breast pCR rate	Axillary pCR rate
All patients	37%	49%
HR+/HER2-	10%	21%
HR+/HER2+	59%	70%
HR-/HER2+	70%	97%
HR-/HER2-	40%	47%



Elizabeth Mittendorf Dana-Farber Cancer Institute

Mamtani A, et al. Ann Surg Oncol, 23:3467-3474, 2016



SLNB in cN+ with ycN0 after NAC

	ACOSOG Z1071	SENTINA	SN-FNAC
Ν	649	592(cN+)*	153
Pre-tx biopsy?	Yes	Not required (25%)	Yes
Mapping	Apping Dual tracer recommended (79%)		Technetium required, IHC
Nodal pCR	41%	52%	35%
ID rate	92.7%	80.1%	87.6%
FNR (overall)	12.6%	14.2%	12.3% (H&E) 8.4% (IHC)
FNR by nodes retrieved 1 SLN 2 SLN ≥3 SLN	31.5% 21.1% 9.1%	24.3% 18.5% 7.3%	18.2% 4.9%

Boughey J et al. *JAMA*, 310:1455-61, 2013 Kuehn T et al. *Lancet Oncol*, 14:609-18, 2013 Boileua J et al. *J Clin Oncol*, 33:258-64, 2015



Reduce FNR of SLNB - tricks

Factor	ACOSOG Z1071	SENTINA	SN-FNAC
Dual tracer	10.8%	8.6%	5.2%
Clipped node	6.8%	-	-
≥ 3 SLN removed	9.1%	7.3%	-
IHC	8.7%	-	8.4%



Reduce FNR - RISAS trial Netherlands

Primary Radioactive Iodine Seed Localisation in the Axilla in Axillary Node Positive Breast Cancer Combined With Sentinel Node Procedure (RISAS) Following Neoadjuvant Chemotherapy

	Identification rate	FNR	NPV
SLNB ¹	89%	17%	57-86%
MARI ²	97%	7%	83.3%
TAD ^{3,4}	100%	2-4%	92-97%
RISAS	98%	3.5%	93.6%

Janine M. Simons, SABCS 2020



Oncological outcomes of ALND omission

Author (Year)	Yrs of Study	cN+→cN0 (n)	pN0, no ALND	Median f/u	Ax recurrences (rate)	Distant recurrence rate
Barrio (2020)	2014-2019	555	234	35mo	1 (0.4%)	4-yr distant recurrence rate = 6.1%
Galimberti (2016)	2000-2010	147	70	61mo	0	Absolute distant recurrence rate = 12.8%
Piltin (2020)	2009-2019	315	159	34 mo	1 (0.6%)	NR
Wong (2020)	2013-2018	132	60	36mo	0	5-yr distant recurrence rate = 13.7%



ALND after residual tumor in SN - does size matter?

Path nodal status	No. of patients	5-yr LRRFS (%)	5-yr DFS (%)
ypN0	524	95.7	88.4
ypN0i+	27	95.2	73.5
ypN1mi	61	96.6	74.7
ypN1	221	90.8	69.5
ypN2-3	134	84.3	57.4

Wong SM, et al. Ann Surg Oncol, 26:3502-3509, 2019



SABCS 2020: When not to?

- DCIS
- Axilla in older cN0 patients
- Axillary dissection in limited pN1
- Axilla in cN1 with ycN0 after NAC
- Breast after NAC



SSO: Eliminate surgery in excellent responders to NAC



Points of agreement:

Not enough science to indicate we can



Dr. Monica Morrow Memorial Sloan Kettering Cancer Center Dr. Jörg Heil Heidelberg University Hospital





Surgical excision after chemotherapy = important

Eliminate and measure residual disease

Measuring response : pCR - need for change in adjuvant strategy (Capecitabine for TNBC -T-DM1 for HER2 positive)

There is insuffcient data to support another method

The missing link?

Alternative to predict pCR



Alternative pCR-predictor

MR

- rCR is not accurate enough to serve as a surrogate marker for pCR on MRI after NAC. (Sener et al, JSO 2019)
- MRI is in fact not an accurate prediction of pCR (Yu et al, WJS 2019)

Image-guided biopsies

FNR varied from 5 to 49% in retrospective studies



	Seoul Nat'l University Hospital	German Multicenter study	Dutch MICRA Trial	NRG-BR005
Ν	40	398	167	98 (cCR)
Imaging characteristics	MRI Tumor < 5cm OR lesion/backgroung enhancement <1.6	Mam/US	MRI complete response OR > 30% size reductiion AND residual <2cm	rCR OR Mam: mass<1cm, no calcifications US: mass<2cm MRI: no mass with suspicious kinetics
Exclusion	Diffuse residual calcifications. Multifocal cancer >3 at presentatiion			
Biopsy	At least 5 cores. Alternating 14G CB and 10G VAB	US guided VAB (63% 7-8G)	8 US guided 14G cores of clip site	8-11G VAB, 4 cores
FNR	30.8% (95% Cl 14-70%)	17.8% (95% Cl 3.4-10.5%)	37% overall 45% in rCR group	FNR 22.5%
	In case of MRI ≤ 0.5, L-to-B SER ≤ 1.6, and cores ≥5 FNR 0 (n=27)	In case of normal mammo, US + VAB FNR 6.2% (95% Cl 3.4-10.5%)		
	Lee HB, BCRT 2020;182:97	Heil J, SABCS 2019	Vrancken Peeters M, SABCS 2019	Basik M, SABCS 2019



Invest in studies?

Combining negative VAB with promising radiological results

Larger-core VAB

Combining VAB and machine learning with deep learning algorithms

MRI guided biopsy (Sutton et al, JAMA Network Open 2021:4)

NPV 92.8%

accuracy 95%



General Conclusion SABCS

We are planting the seeds of change... Seeds of further surgical de-escalation





15 min

SABCS 2020: Take home message

- DCIS Seeds planted, waiting for fruit
- Omission ALND in limited pN1- Fruit tasted and approved
- Axilla (cN1-ypN0) after NAC Fruit ripe, plant our own Belgian seeds
- Breast after NAC Plant more seeds?

Questions? marian.vanhoeij@uzbrussel.be



Brussels, January 30, 2021





