

# Chirurgie axillaire en cas d'atteinte ganglionnaire

Prof. Walter P. Weber  
Breast Surgeon SSO

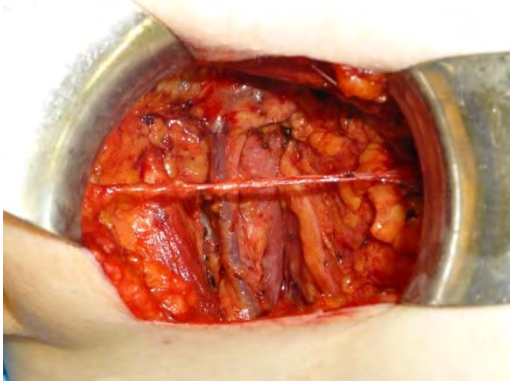
Chief, Breast Surgery Service, University Hospital Basel  
Chair, Oncologic Breast Surgery, University of Basel



# Evolution of axillary surgery

1895 → 1990

Always axillary  
dissection



20% Lymphedema

From 90's

Ax.  
dissection  
for positive  
sentinel  
and cN+



3% Lymphedema

2019

Ax. dissection  
or radiation  
for **high risk**  
pos. sentinel,  
dissection for cN+

Future

No more  
ax. dissection  
for **all**  
pos. sentinels?

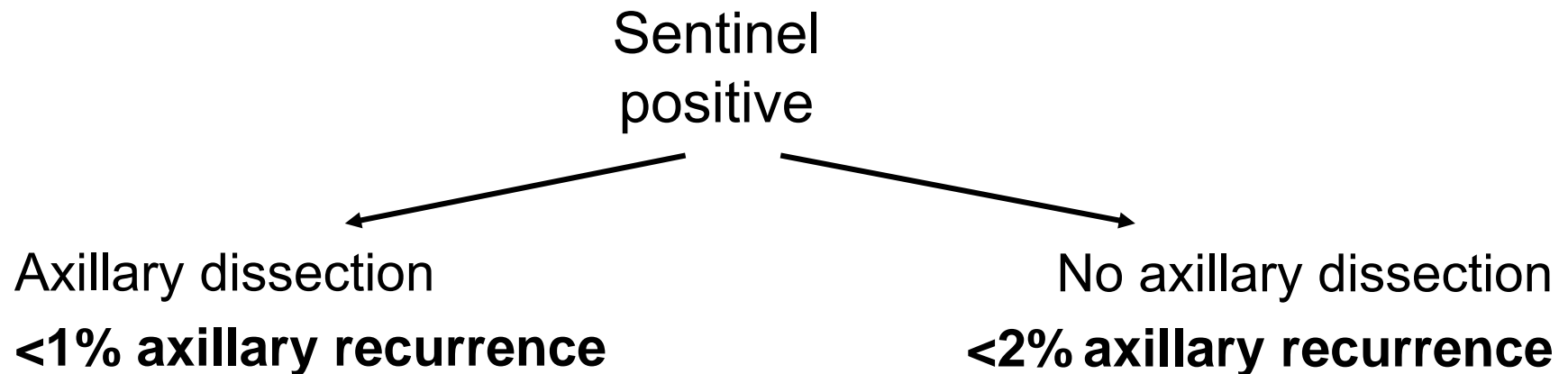
Ax. dissection  
for cN+?  
→ Tailored  
axillary  
surgery?

No sentinel  
for cN0?

# Omission of axillary dissection

## Clinically node-negative, sentinel positive

- <sup>1</sup>IBCSG 23-01 (n=934, follow-up 9.7y)
- <sup>2</sup>ACOSOG Z0011 (n=891, follow-up 9.3 y)



<sup>1</sup>Galimberti V, et al. Lancet Oncol. 2018 Oct;19(10):1385-1393.

<sup>2</sup>Giuliano AE et al, JAMA. 2017 Sep 12;318(10):918-926.

# ACOSOG Z0011

## Validation in clinical practice

- Single institution prospective study 2010-2016<sup>1</sup>
  - 793 patients, **Z0011-eligible** (cT1-2N0, 1-2 positive SLNs, BCT)
  - 16% ALND, no difference by age or subtype
  - Follow-up 29m: no isolated axillary recurrence
  - No difference in nodal recurrence by type of radiation
- Excellent regional control without axillary dissection or axillary-specific radiation

<sup>1</sup>Morrow M, et al. Ann Surg. 2017 Sep;266(3):457-462.

# ACOSOG Z0011

## Impact on clinical practice

- Multicentric retrospective study 2008-2015<sup>1</sup>
  - Germany
  - 13'741 Z0011-eligible patients
  - Use of axillary dissection: 95% → 47% ( $p < 0.001$ )

<sup>1</sup>Hennigs A, Heil J, et al. Breast Cancer Res Treat. 2019 Jan;173(2):429-438.

# Current indications for axillary dissection

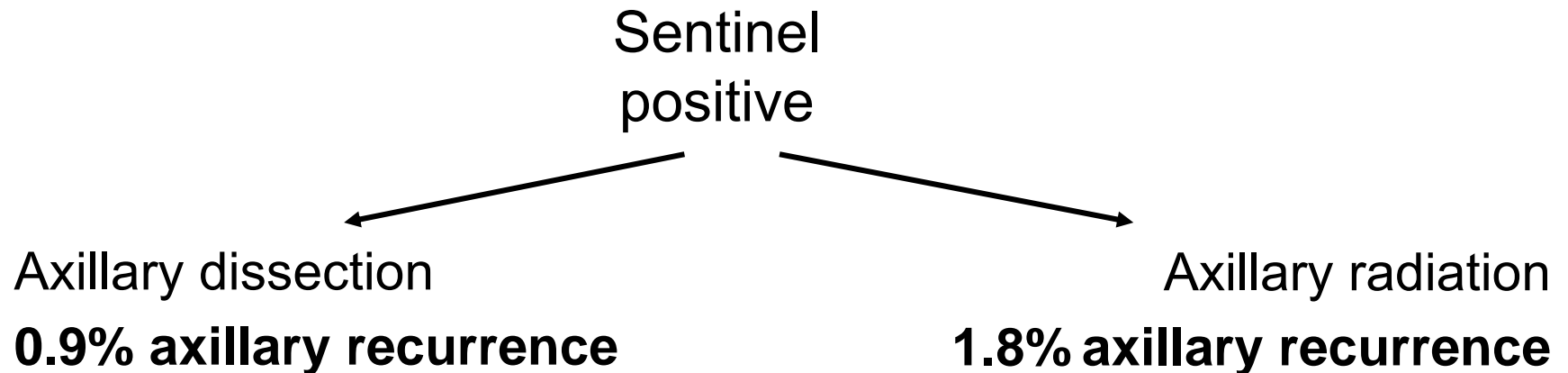
- Clinically node-positive (upfront surgery)
- Residual disease after NACT
- Locally advanced breast cancer (>2 pos. SLNs, gross extranodal disease, cT3-4, inflammatory)
- SLN macrometastasis and mastectomy
  - If post-mastectomy radiation is not indicated by the positive SLN or does not include the regional nodes

# Omission of axillary dissection

## Clinically node-negative, sentinel-positive

### ■ EORTC AMAROS

(n=1425, 248 mastectomies, 10y follow-up)



# Omission of axillary treatment?

## Ongoing trials: Clinically node-negative

- Imaging-positive? SLN pos. with mastectomy?
- >2 positive sentinels?

Ongoing trial	Inclusion	Design	PI	Accrual March 2019
SENOMAC	cT1-2 N0 cT1-2 iN1 1-2 pos SLN	ALND vs no ALND	Jana de Boniface	1300/3500
ERC/IPC 2012-001	cT1-2 N0 All pos SLN	ALND vs no ALND	Gilles Houvenaeghel	1961/2000



# Omission of axillary dissection?

## Ongoing trials: Clinically node-positive

- Residual disease after NACT?
- Clinically node-positive?

Ongoing trial	Inclusion	Design	PI	Accrual March 2019
Alliance A011202 USA	cT1-3 N1 NACT → Pos (S)LN	ALND vs ART, extended regional irradiation	Judy C. Boughey	1481/1576
TAXIS <sup>1,2</sup> Europe	cT1-4 N1-2 +/- NACT → Pos (S)LN	ALND vs ART, extended regional irradiation	Walter P. Weber	120/1500

<sup>1</sup>Weber WP. Ann Surg Oncol. 2018 Dec;25(Suppl 3):671-672.

<sup>2</sup>Henke G, Knauer M, Weber WP, et al. Trials. 2018 Dec 4;19(1):667.

# Omission of axillary dissection in clinically node positive BC today

- Meta-analysis on use of SLN after NACT<sup>1</sup>
  - 13 studies, 1921 patients, SLN → ALND
  - Identification rate 90% (95% CI: 87-93)
  - False negative rate 14% (95% CI 11-17)
    - Reduced to 11% with dual mapping
    - Reduced to 4% when  $\geq 3$  nodes are removed

<sup>1</sup>Tee SR, et al. Br J Surg. 2018 Nov;105(12):1541-1552.

# Localization and selective removal of initially positive nodes

- Meta-analysis of 20 studies (2217 patients)<sup>1</sup>

	n (studies)	n (patients)	Identification rate	False-negative rate
SLN only	17	2002	89%	Overall: 17%
				<3 SLNs: 22%
				≥3 SLNs: 8%
MARI	1	95	97%	7%
TAD	2	120	100%	2-4%

<sup>1</sup>Simons JM, et al. Ann Surg. 2019 Mar;269(3):432-442.

# Use of SLN after NACT in initially node-positive BC

- Single institution retrospective analysis of prospective database<sup>1</sup>
  - 430 cN1 patients undergoing NACT, 2009-2017
  - Use of SLN ( $\pm$  ALND): 28%  $\rightarrow$  86% ( $p < 0.001$ )
  - Use of ALND: 100%  $\rightarrow$  38% ( $p < 0.001$ )

<sup>1</sup>Nguyen TT, et al. Ann Surg Oncol. 2018 Sep;25(9):2596-2602.

# Oncologic safety of SLN after NACT in initially node-positive BC

- Single institution retrospective analysis of prospective database<sup>1</sup>
    - 70 patients, cN1/2 → NACT → cN0 → neg. SLN → no ALND
    - Single tracer (<sup>99</sup>Tc)
    - Isolated tumor cells considered SLN negative
    - Median follow-up 61 months
- No axillary recurrence**

<sup>1</sup>Galimberti V, et al. Eur J Surg Oncol. 2016 Mar;42(3):361-8.

# Omission of axillary dissection?

## Residual micrometastases after NACT

- Single institution retrospective analysis of prospective database<sup>1</sup>
  - 702 patients → pos. SLN after NACT → ALND
  - SLN **micromets**: 59% additional pos. nodes
  - SLN **macromets**: 63% additional pos. nodes
- Low volume disease in SLN does not indicate low risk of additional positive nodes
- Axillary dissection remains standard

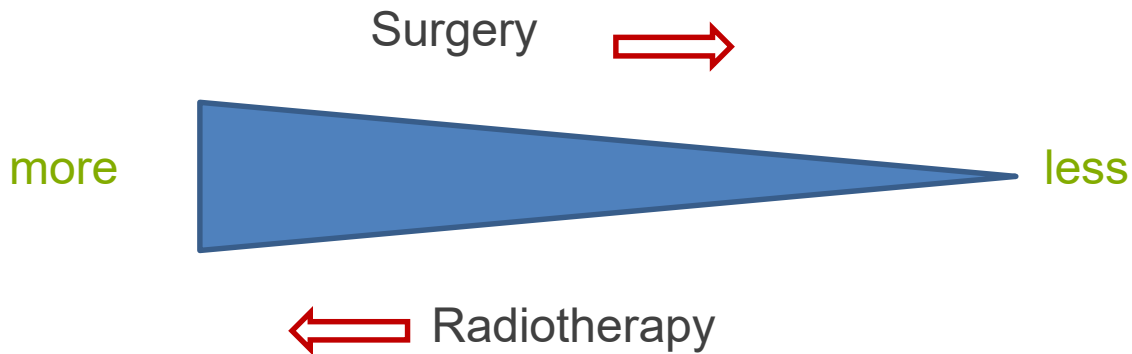
<sup>1</sup>Moo TA, et al. Ann Surg Oncol. 2018 Jun;25(6):1488-1494.

# Limitations of current strategies to minimize axillary surgery in cN+

- Only way to avoid ALND in cN+ is neoadjuvant chemotherapy, but most cancers are luminal
- In case of residual disease: ALND remains standard
- **We need to find ways to avoid axillary dissection**
  - **Without NACT**
  - **With NACT: For residual disease**

# Regional therapy for node-positive pts?

## Conflicting trends in the adjuvant setting



MA20, EORTC22922

significant improvement in  
disease-free survival with  
additional regional therapy  
after axillary dissection

IBCSG 23-01 / Z0011

regional recurrence ~1-5%  
without regional therapy

AMAROS

regional recurrence ~1%  
with regional radiotherapy  
instead of surgery



# New concept: Tailored axillary surgery (TAS)

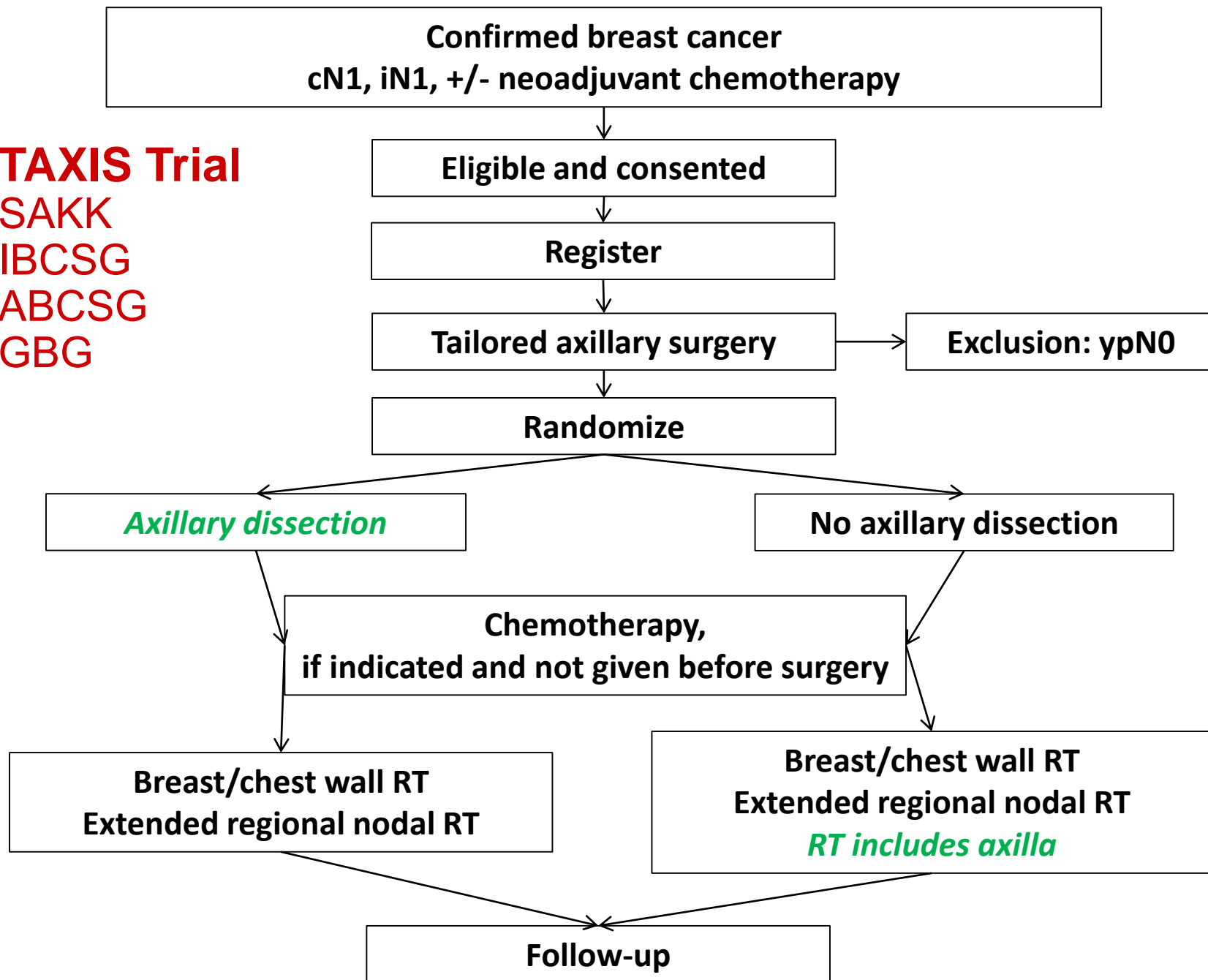
- Aim:

- **Selective** removal of positive nodes in axilla to reduce tumor load to the point where radiation can control it

- Steps:

1. Most suspicious node is clipped
2. Removal of palpably suspicious and sentinel nodes
  - Imaging-guided **localization** of clipped node **encouraged**
3. Specimen radiography documents clip removal

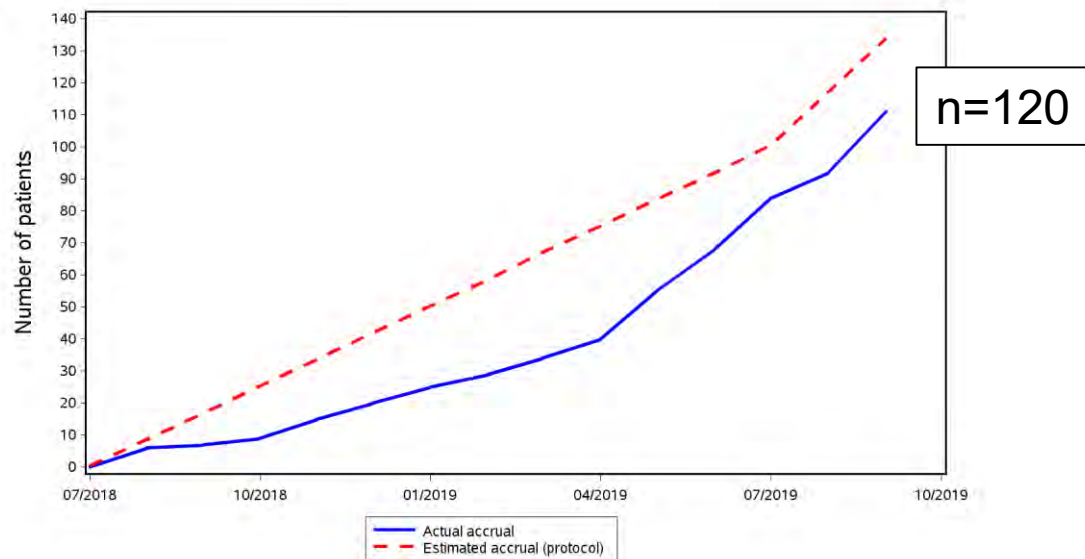
**TAXIS Trial**  
SAKK  
IBCSG  
ABCSG  
GBG



# SAKK / IBCSG / GBG / ABCSG TAXIS: Phase III non-inferiority RCT

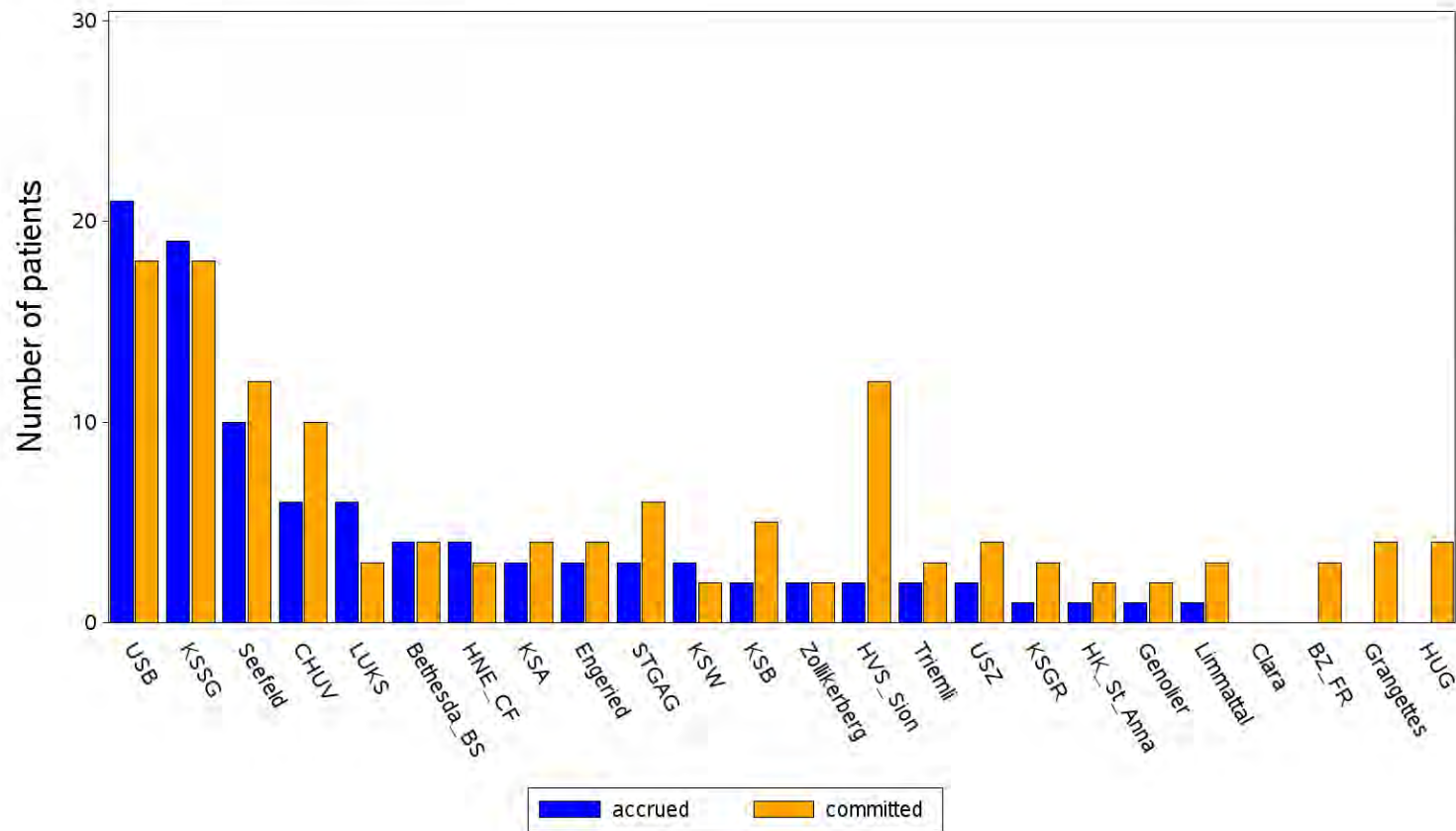
- Endpoints: 1°: DFS // 2° QOL
- 1500 pts in 6 years at 60 centers in 5 countries
- 8.5 Mio USD (1/3 covered)

SAKK 23/16 TAXIS - European Axilla Study  
Patient accrual curve  
30-SEP-2019



# SAKK / IBCSG / GBG / ABCSG TAXIS: Phase III non-inferiority RCT

SAKK 23/16 TAXIS - European Axilla Study  
Committed versus actual accrual by site (Switzerland)  
30-SEP-2019



# Tailored axillary surgery (TAS)

## Subproject

Site	Total	
Universitätsspital Basel	20	(19.0%)
Kantonsspital St. Gallen	17	(16.2%)
National Institute of Oncology, Budapest	11	(10.5%)
Brustzentrum (Seefeld)	10	(9.5%)
CHUV - Centre hospitalier universitaire vaudois	9	(8.6%)
Lindenhofgruppe - Engeriedspital	8	(7.6%)
Kantonsspital Winterthur	5	(4.8%)
Kantonsspital Baden	3	(2.9%)
Network - Spital Thurgau	3	(2.9%)
Basel Bethesda Spital	2	(1.9%)
Hôpital neuchâtelois - La Chaux-de-Fonds	2	(1.9%)
Kantonsspital Aarau	2	(1.9%)
Luzerner Kantonsspital Luzern	2	(1.9%)
Spital Limmattal	2	(1.9%)
Spital Zollikerberg	2	(1.9%)
Stadtspital Triemli	2	(1.9%)
UniversitätsSpital Zürich	2	(1.9%)
Centre du sein Fribourg/Brustzentrum Freiburg	1	(1.0%)
Clinique de Genolier	1	(1.0%)
Hirslandenlinik St. Anna	1	(1.0%)
<b>Total</b>	<b>105</b>	<b>(100%)</b>

# Clipping

## Tailored axillary surgery (TAS)

- Clipping of most suspicious lymph node: **n=105**

Imaging modality used to clip the node	
. Ultrasound	98%

Type of clip used to mark the positive node	
. Direct magseed	5%
. Direct radioactive seed	4%
. Nitinol ring marker (nickel titanium alloy)	30%
. Titanium or stainless steel marker with gel	42%
. Titanium or stainless steel marker without gel	19%

# Localization

## Tailored axillary surgery (TAS)

- Clipping of most suspicious lymph node: **n=105**

Imaging-guided localization of the clipped node		
Attempted	No	12%
	Yes	88%
Successful	Yes	83%
	Unsure	2%
	No	3%
Reason for failure	Clip not visible	2%
	Wire missed target	1%

# Localization

## Tailored axillary surgery (TAS)

- Localization of clipped node: **n=92**

Localization performed		
Before surgery		<b>64%</b>
	US	63%
	CT	1%
During surgery		<b>36%</b>
	US	36%



# Localization

## Tailored axillary surgery (TAS)

- Localization of clipped node: **n=92**

Type of localization used	
Magseed	7%
ROLL	8%
Radioactive seed	16%
Tattoo	5%
Wire	42%
US alone	17%
Other	2%

# **Radioguided seed localization**

## **University Hospital of Basel experience**

- Small titanium seed (4 x 0.8mm) labeled with I-125
  - Matched case-control study
  - 47 seeds (Nov 2017 - April 2018) vs 47 wires (May-Oct 2018)
  - Breast and axilla
- Duration of surgery was 15.8 min longer in the seed group (p-value 0.04, 95% CI 0.39 – 31.2)

# Tailored axillary surgery (TAS)

- Clipping of most suspicious lymph node: **n=105**

Removal of clipped node successful	
No	6%
Yes	93%
Missing	1%

Clipped node corresponds to (more than one applicable)	
Localized node	67%
Palpably suspicious node	49%
Sentinel node	68%

# Surgical removal of clipped node by type of clip

Type of clip	Direct magseed (N=3)	Direct seed (N=4)	Ring marker (N=31)	Marker with gel (N=44)	Marker without gel (N=20)
<b>Surgical removal successful</b>					
No	0	0	10%	5%	5%
Yes	100%	100%	90%	95%	95%

# Complete pathologic response after NACT

## Surgical removal of clipped node by type of clip

	Nitinol ring marker (N=8)	Titanium or stainless steel marker with gel (N=6)	Titanium or stainless steel marker without gel (N=2)
<b>Surgical removal successful</b>			
. No	0	1	0
. Yes	8	5	2

# TAS by type of node removed

	N=105	
	median	(min, max)
Total number of positive nodes	1.0	(0-21)
Total number of negative nodes	1.0	(0-23)

# TAS followed by axillary dissection

	Overall (N=38)	
	median	(min, max)
Number of lymph nodes removed during ALND	13.5	(2.0, 36.0)
Number of <b><u>positive</u></b> lymph nodes removed during ALND	1.0	(0.0, 24.0)

# Improved surgical removal of clipped node by imaging-guided localization?

Imaging-guided localization of the clipped node?	No (N=10)	Yes (N=92)
Surgical removal of clipped node		
. Yes	90%	95%
. No	10%	5%



# Implementing the concept of TAS in clinical practice

- Clipped node removed in  $> 90\%$
- US preferred method for clipping and to guide localization
- Localization performed in most cases
- Numbers too small to assess value of localization or compare performance of different devices
- Major heterogeneity in choice of equipment for clipping and localization in Switzerland

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Prof. Walter P. Weber

Breast Surgeon SSO

Chief, Breast Surgery Service, University Hospital Basel

Chair, Oncologic Breast Surgery, University of Basel

