

Chirurgie axillaire en cas d'atteinte ganglionnaire

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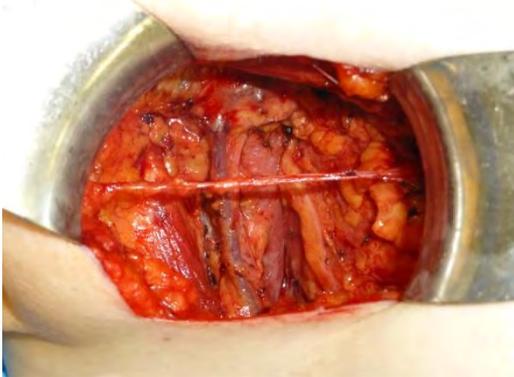
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Evolution of axillary surgery

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?

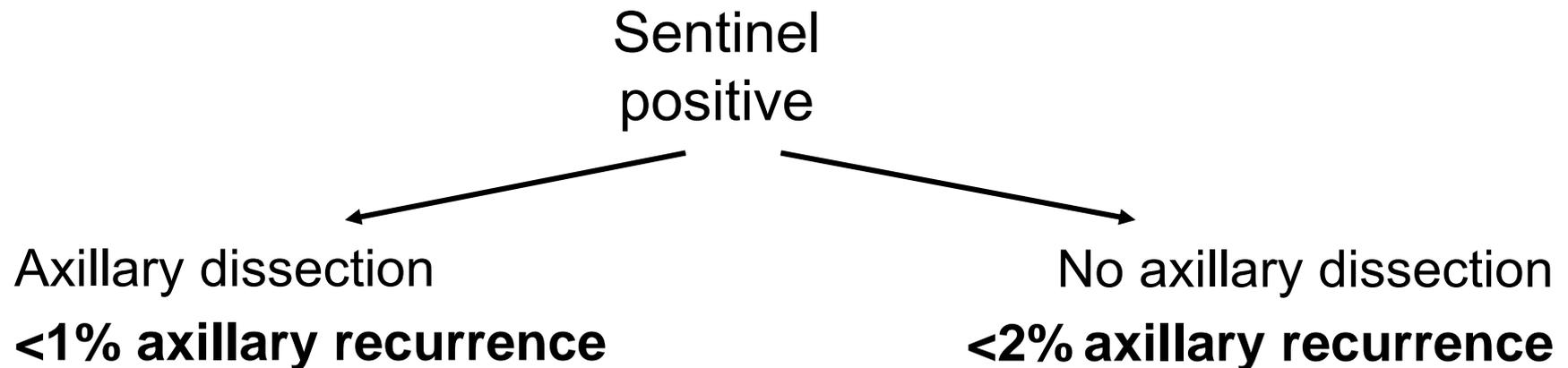
Ax. dissection
for cN+?
→ Tailored
axillary
surgery?

No sentinel
for cN0?

Omission of axillary dissection

Clinically node-negative, sentinel positive

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



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

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

ACOSOG Z0011

Validation in clinical practice

- Single institution prospective study 2010-2016¹
 - 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

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

ACOSOG Z0011

Impact on clinical practice

- Multicentric retrospective study 2008-2015¹
 - Germany
 - 13'741 Z0011-eligible patients
 - Use of axillary dissection: 95% → 47% (p < 0.001)

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

Current indications for axillary dissection

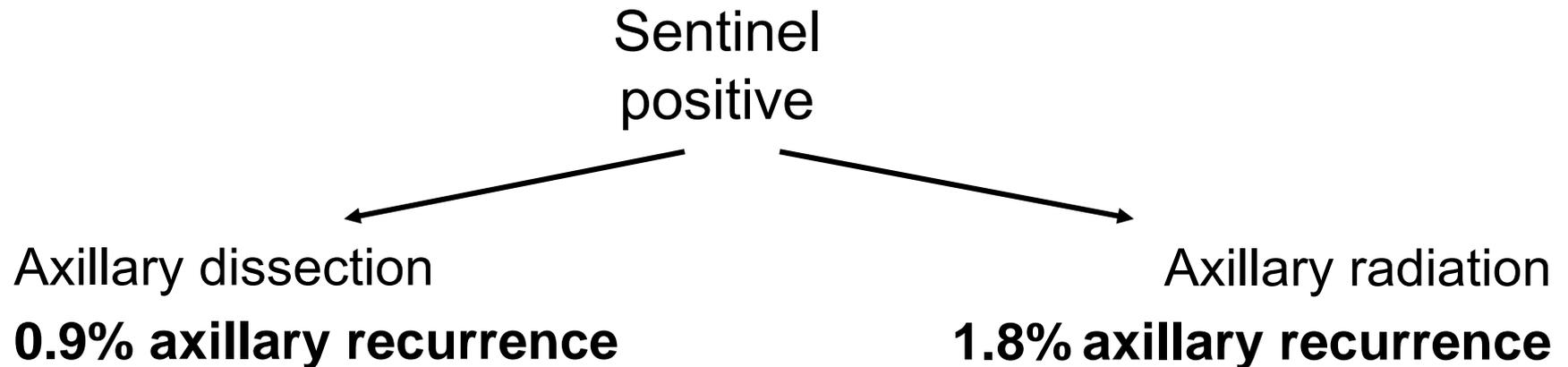
- Clinically node-positive (upfront surgery)
- Residual disease after NACT
- Locally advanced breast cancer (>2 pos. SLNs, gross extranodal disease, cT3-4, inflammatory)
- SLN macrometastasis and mastectomy
 - If post-mastectomy radiation is not indicated by the positive SLN or does not include the regional 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 ^{1,2} Europe	cT1-4 N1-2 +/- NACT → Pos (S)LN	ALND vs ART, extended regional irradiation	Walter P. Weber	120/1500

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

²Henke 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 NACT¹
 - 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 ≥ 3 nodes are removed

¹Tee 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)¹

	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%

¹Simons 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 database¹
 - 430 cN1 patients undergoing NACT, 2009-2017
 - Use of SLN (\pm ALND): 28% \rightarrow 86% ($p < 0.001$)
 - Use of ALND: 100% \rightarrow 38% ($p < 0.001$)

¹Nguyen 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 database¹
 - 70 patients, cN1/2 → NACT → cN0 → neg. SLN → no ALND
 - Single tracer (⁹⁹Tc)
 - Isolated tumor cells considered SLN negative
 - Median follow-up 61 months
- No axillary recurrence**

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

Omission of axillary dissection? Residual micrometastases after NACT

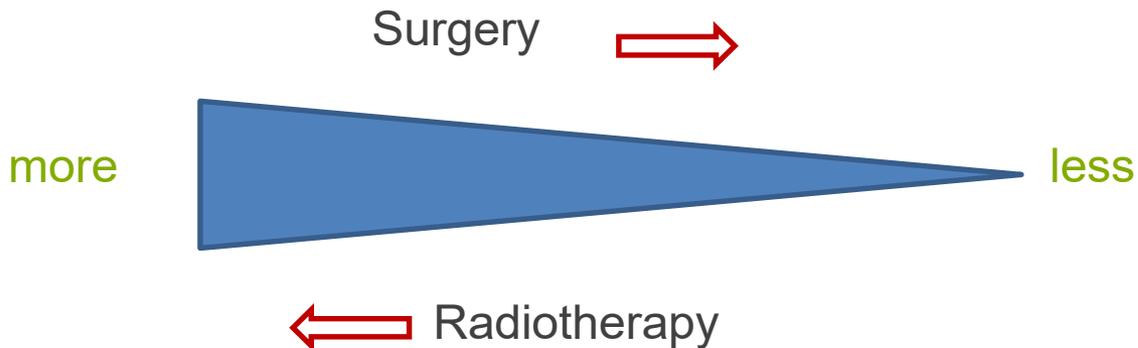
- Single institution retrospective analysis of prospective database¹
 - 702 patients → pos. SLN after NACT → ALND
 - SLN **micromets**: 59% additional pos. nodes
 - SLN **macromets**: 63% additional pos. nodes
- Low volume disease in SLN does not indicate low risk of additional positive nodes
- Axillary dissection remains standard

¹Moo 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

AMAROS
regional recurrence ~1%
with regional radiotherapy
instead of surgery

IBCSG 23-01 / Z0011
regional recurrence ~1-5%
without regional therapy

New concept: Tailored axillary surgery (TAS)

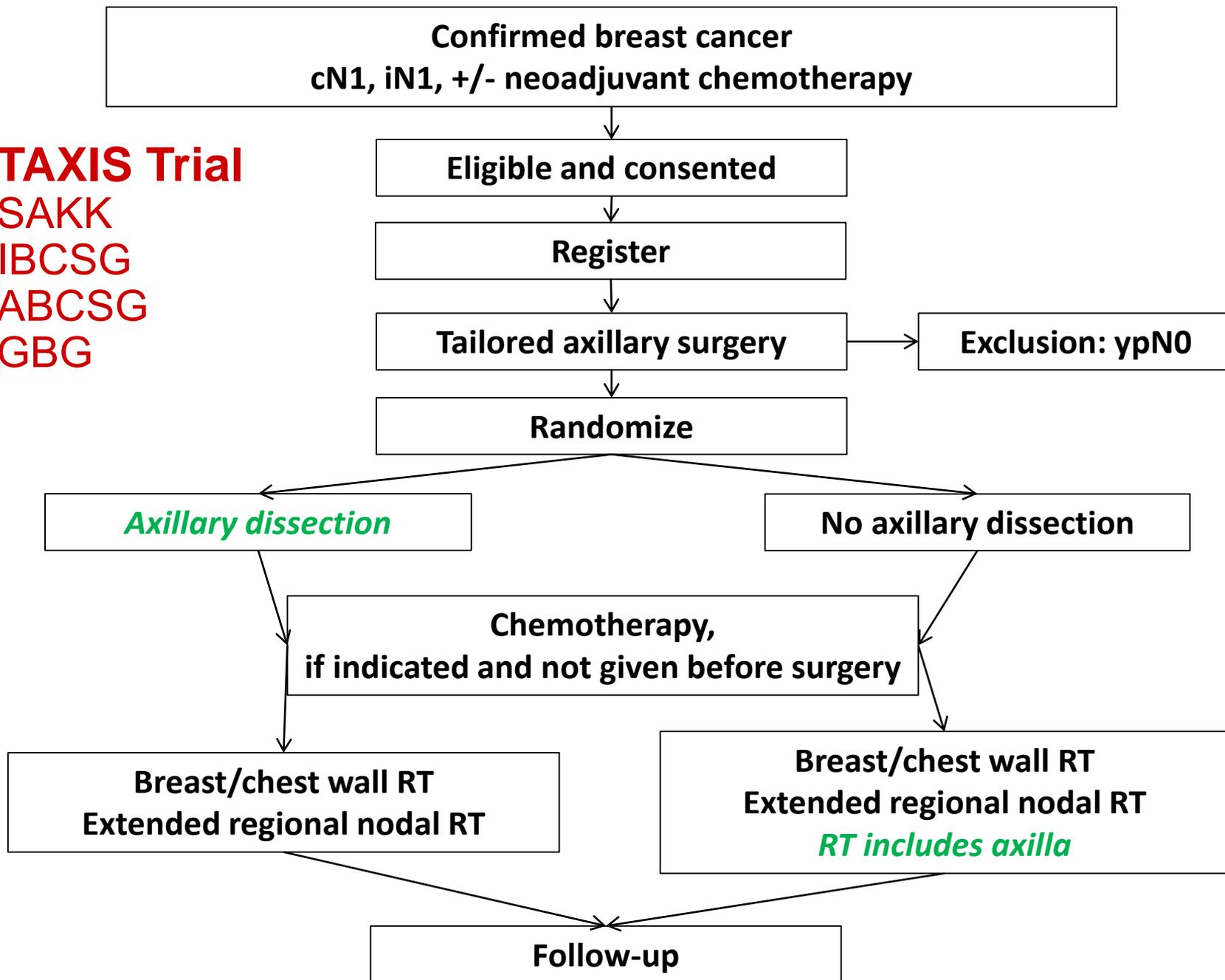
- Aim:

- **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

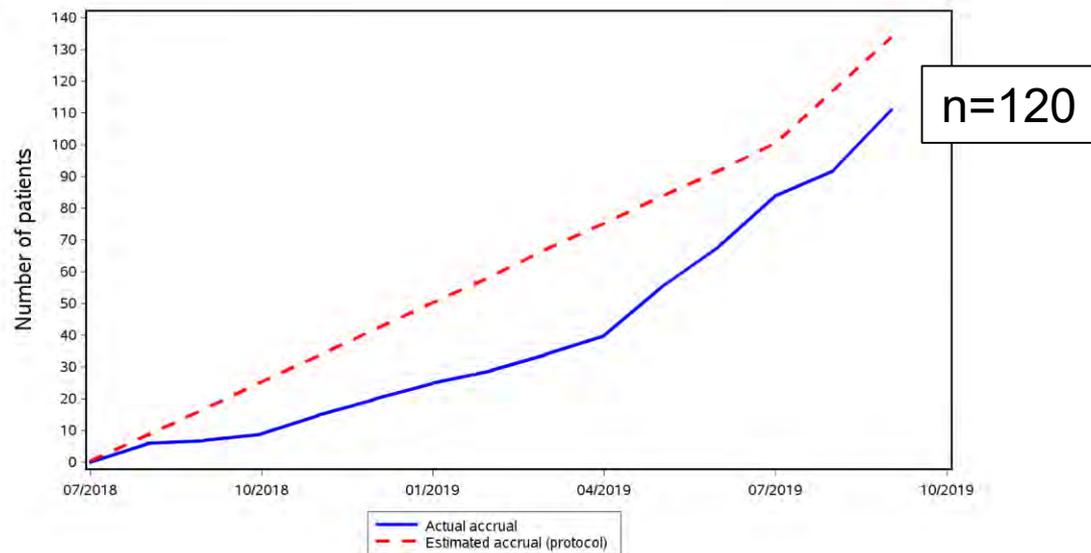
TAXIS Trial
SAKK
IBCSG
ABCSG
GBG



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

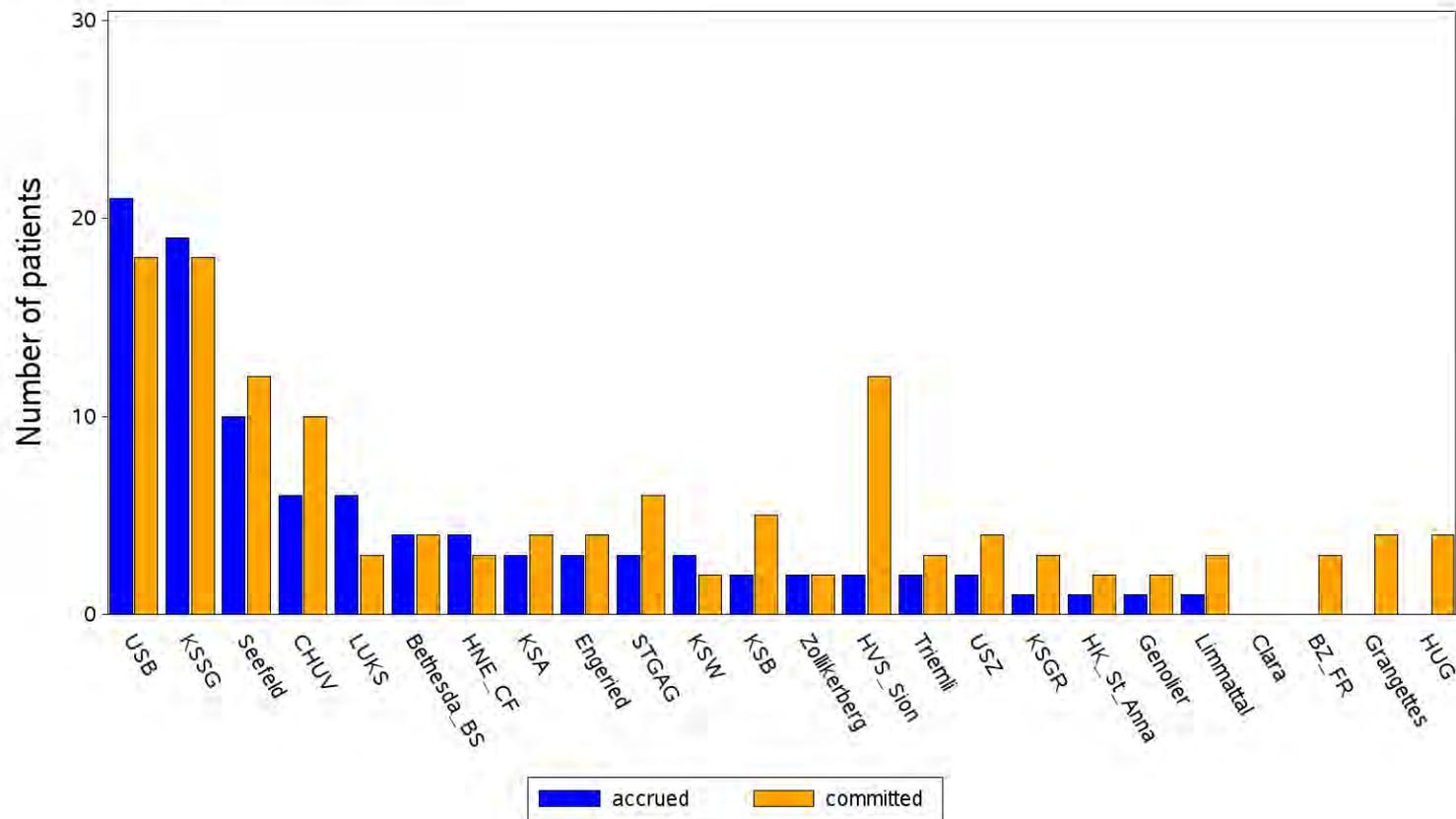
- Endpoints: 1°: DFS // 2° QOL
- 1500 pts in 6 years at 60 centers in 5 countries
- 8.5 Mio USD (1/3 covered)

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%)
Stadtpital Triemli	2	(1.9%)
UniversitätsSpital Zürich	2	(1.9%)
Centre du sein Fribourg/Brustzentrum Freiburg	1	(1.0%)
Clinique de Genolier	1	(1.0%)
Hirslandenklinik St. Anna	1	(1.0%)
Total	105	(100%)

Clipping

Tailored axillary surgery (TAS)

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

Imaging modality used to clip the node

. Ultrasound	98%
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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		64%
	US	63%
	CT	1%
During surgery		36%
	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)
Surgical removal successful					
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)
Surgical removal successful			
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 <u>positive</u> 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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