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Patient-reported outcomes (PROs) for the intergroup sentinel mamma study (INSEMA, GBG75, ABCSG43): Persistent impact of axillary surgery on arm and breast symptoms in early breast cancer

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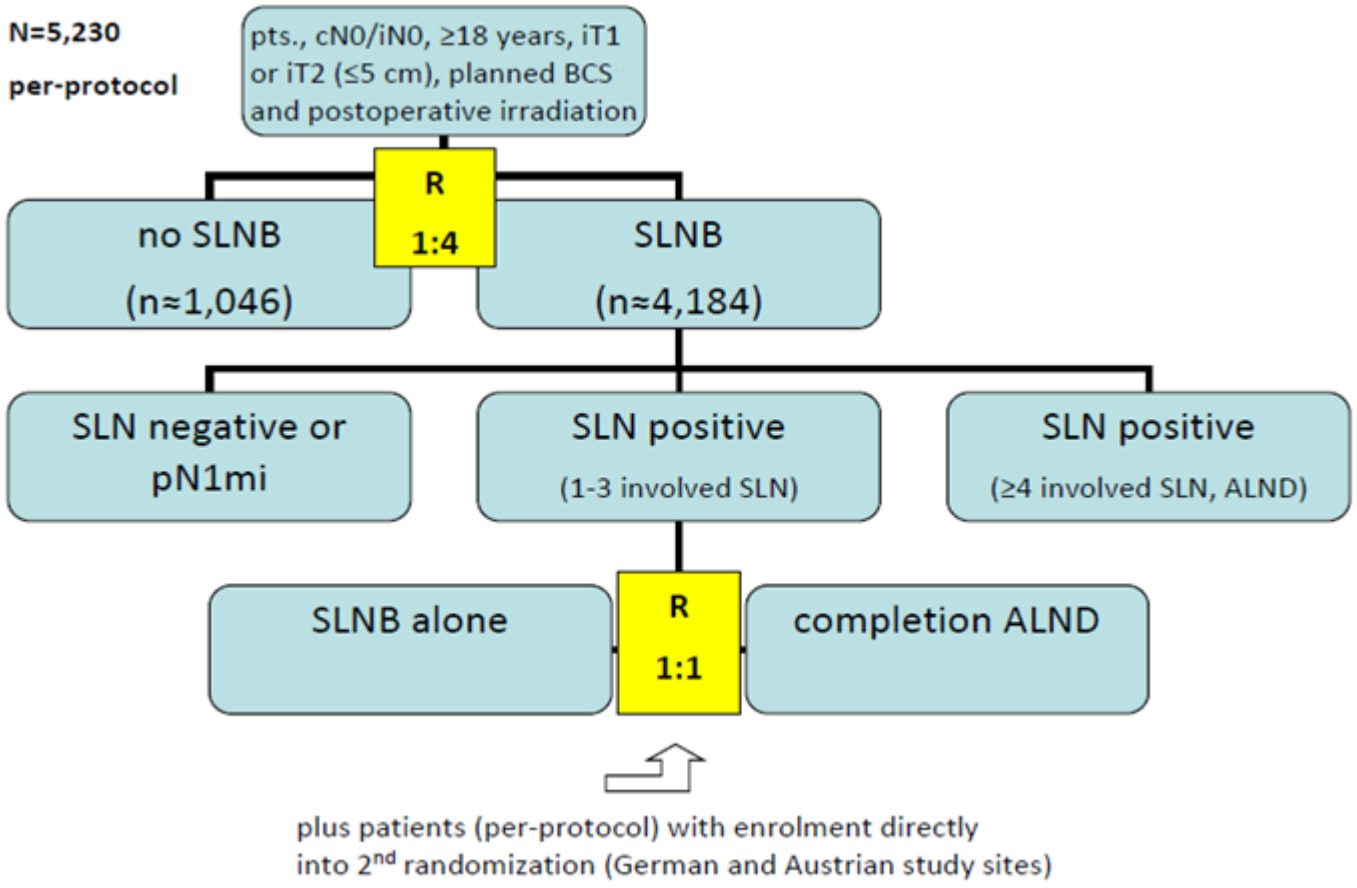
on behalf of the INSEMA investigators

Background

- Previous studies (NSABP B-04 / IBCSG 10-93) have shown a high loco-regional control rate even without axillary lymph node dissection (ALND).
- Despite increasing evidence supporting the sentinel lymph node biopsy (SLNB) alone, ALND remains part of breast cancer treatment guidelines.
- Current approaches including screening population, tumor biology, and more effective systemic treatment emphasize the need for ongoing re-evaluation of “standard” local therapy.
- Quality of life considerations are the primary motivation for abandoning SLNB.[1]

1 Jatoi & Kunkler Cancer 2021

Study Design (NCT02466737) and Main Inclusion Criteria



Primary objective:

- To compare iDFS after BCS (non-inferiority question) between no axillary surgery and SLNB patients (first randomization)

Key secondary objective:

- To compare iDFS after BCS (non-inferiority question) between SLNB alone and completion (c)ALND patients (second randomization)

Further secondary objective – topic of this talk:

- **Quality of life (QoL)**

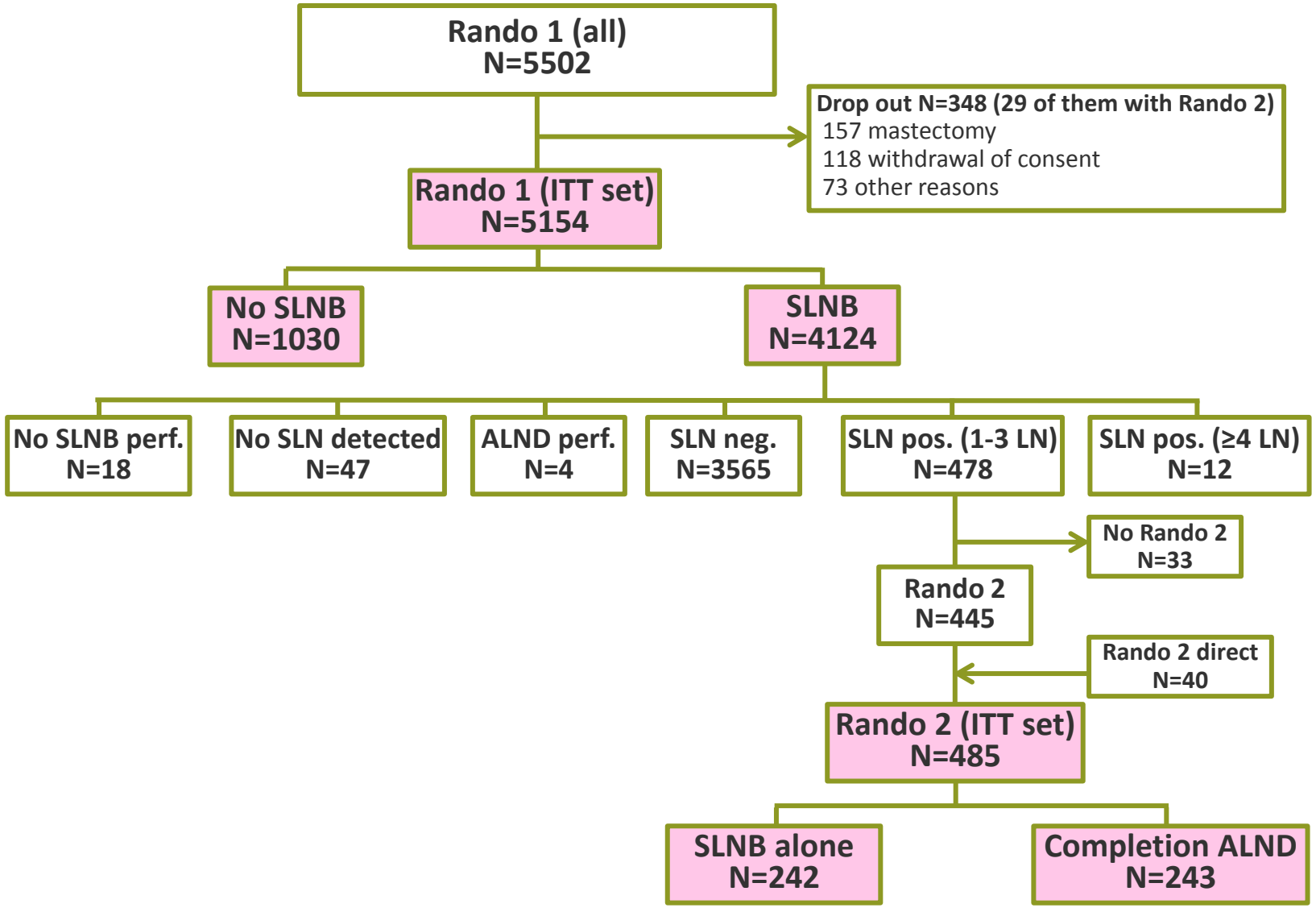
iDFS, invasive disease-free survival; BCS, breast-conserving surgery;
SLNB, sentinel lymph node biopsy; cALND, completion axillary lymph node dissection

Methods

- Patient-reported outcomes (PROs) were assessed at baseline (pre-surgery) and at 1, 3, 6, 12, and 18 months after final axillary surgery using the European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire (EORTC QLQ-C30) and its breast cancer (BR23) module.
- Higher scores of C30 and BR23 (range 0-100) indicate better functioning and global health status (GHS)/QoL or worse symptom severity, respectively; score difference of ≥5.0 points was considered as clinically meaningful difference.[1]
- The QoL scores were analyzed using repeated-measures of mixed-effects models leading to p-values for “treatment” and “time”, and for the interaction “treatment-by-time”.
- Postoperative whole-breast irradiation was mandatory for all patients. Ipsilateral axillary region was not included in the clinical target volume.[2]

1 Hamidou et al. Oncologist 2011
2 Hildebrandt et al. Int J Radiat Oncol Biol Phys 2020

Consort Flow Diagram



Baseline Characteristics, ITT set

First Randomization (SLNB vs No SLNB)

Paramenter	Category	SLNB N=4124 N(%)	No SLNB N=1030 N(%)
Age (strat.)	**<65 years**	**2514 (61.0)**	**623 (60.5)**
	≥65 years	**1610 (39.0)**	**407 (39.5)**
Tumor size (strat.)	**≤2 cm**	**3719 (90.2)**	**927 (90.0)**
	>2 cm	**403 (9.8)**	**103 (10.0)**
Grading (strat.)	**G1-2**	**3978 (96.5)**	**990 (96.1)**
	G3	**146 (3.5)**	**40 (3.9)**
cT	cT1	3719 (90.2)	927 (90.0)
	cT2	403 (9.8)	103 (10.0)
Tumor type	NST	2997 (72.7)	782 (75.9)
	Invasive/mixed lobular carcinoma	517 (12.5)	128 (12.4)
	other	2997 (72.7)	782 (75.9)
ER/PgR	both negative	63 (1.5)	16 (1.6)
	ER and/or PgR positive	4058 (98.5)	1013 (98.4)
HER2 status	negative	3972 (96.6)	982 (95.7)
	positive	141 (3.4)	44 (4.3)

Second Randomization (cALND vs SLNB alone)

Paramenter	Category	cALND N=243 N(%)	SLNB N=242 (N%)
Age (strat.)	**<65 years**	**160 (65.8)**	**158 (65.3)**
	≥65 years	**83 (34.2)**	**84 (34.7)**
Tumor size (strat.)	**≤2 cm**	**199 (81.9)**	**196 (81.0)**
	>2 cm	**44 (18.1)**	**46 (19.0)**
Grading (strat.)	**G1-2**	**232 (95.5)**	**230 (95.0)**
	G3	**11 (4.5)**	**12 (5.0)**
cT	cT1	199 (81.9)	196 (81.0)
	cT2	44 (18.1)	46 (19.0)
Tumor type	NST	182 (74.9)	171 (70.7)
	Invasive/mixed lobular carcinoma	36 (14.8)	28 (11.6)
	other	25 (10.3)	43 (17.8)
ER/PgR	both negative	2 (0.8)	6 (2.5)
	ER and/or PgR positive	241 (99.2)	236 (97.5)
HER2 status	negative	234 (96.3)	227 (94.2)
	positive	9 (3.7)	14 (5.8)

NST, invasive carcinoma of no special type; cT, tumor status by sonography/palpation

Questionnaire Completion Response, QoL Analysis Set

First Randomization (SLNB vs No SLNB)

QoL analysis set	SLNB	No SLNB	Overall
Pts, ITT set	4124	1030	5154
Pts treated not according to randomized arm	19	15	34
Pts included in the QoL analysis set	4120	1034	5154

Time point	Patients with available QoL data		
	SLNB N(%)	No SLNB N(%)	Overall N(%)
Baseline	3762 (91.3)	956 (92.5)	4718 (91.5)
1 month	3143 (76.3)	778 (75.2)	3921 (76.1)
3 months	3145 (76.3)	795 (76.9)	3940 (76.4)
6 months	3193 (77.5)	835 (80.8)	4028 (78.2)
12 months	3103 (75.3)	809 (78.2)	3912 (75.9)
18 months	2919 (70.8)	736 (71.2)	3655 (70.9)

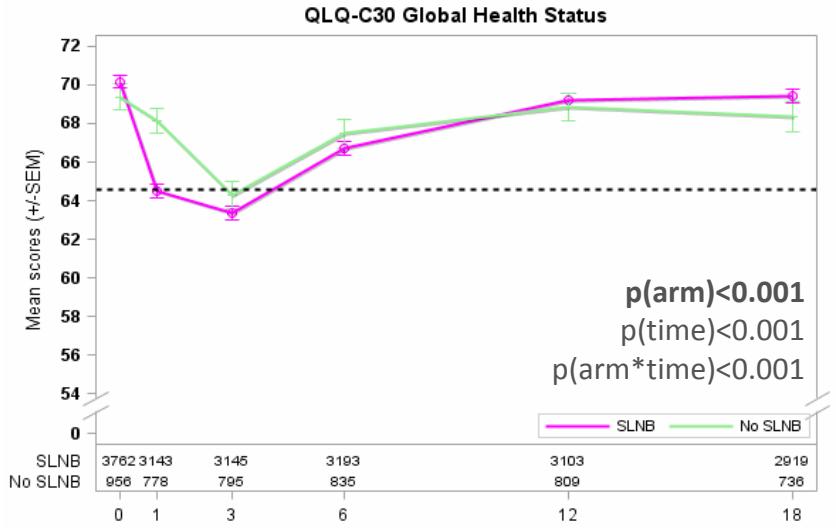
Second Randomization (cALND vs SLNB alone)

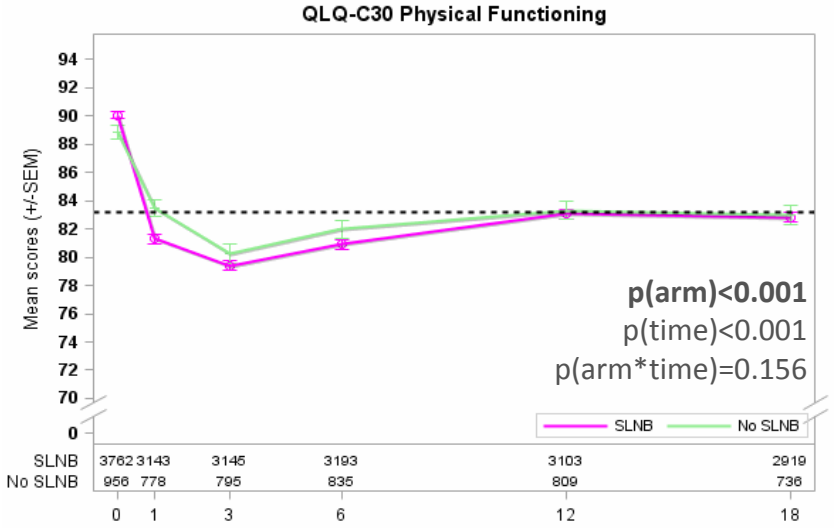
QoL analysis set	cALND	SLNB	Overall
Pts, ITT set	243	242	485
Pts treated not according to randomized arm	67	0	67
Pts included in the QoL analysis set	176	309	485

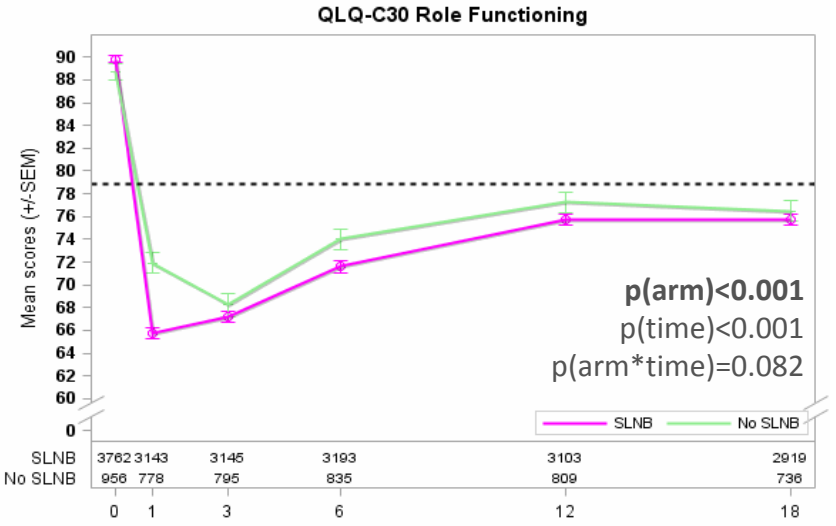
Time point	Patients with available QoL data		
	cALND N(%)	SLNB N(%)	Overall N(%)
Baseline	161 (91.5)	274 (88.7)	435 (89.7)
1 month	125 (71.0)	203 (65.7)	328 (67.6)
3 months	129 (73.3)	202 (65.4)	331 (68.2)
6 months	140 (79.5)	202 (65.4)	342 (70.5)
12 months	130 (73.9)	202 (65.4)	332 (68.5)
18 months	114 (64.8)	186 (60.2)	300 (61.9)

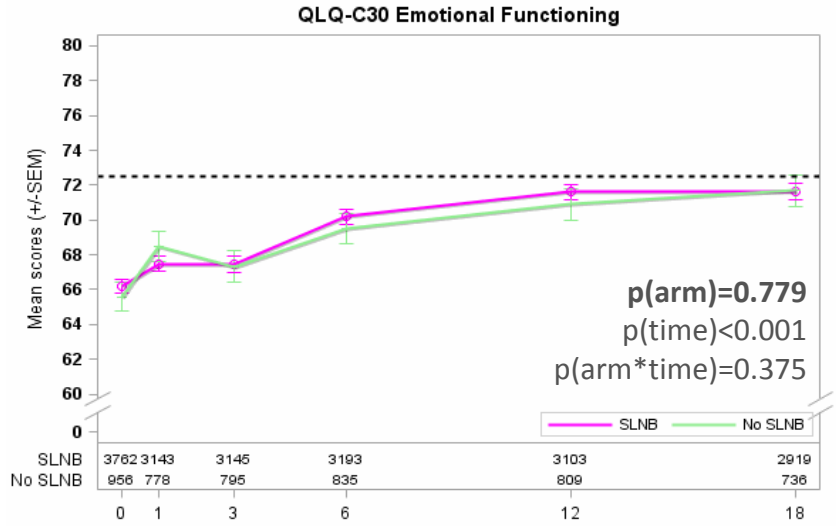
Questionnaire completion response remained high throughout the trial: over 60% at all time points

QoL – First Randomization (SLNB vs No SLNB)

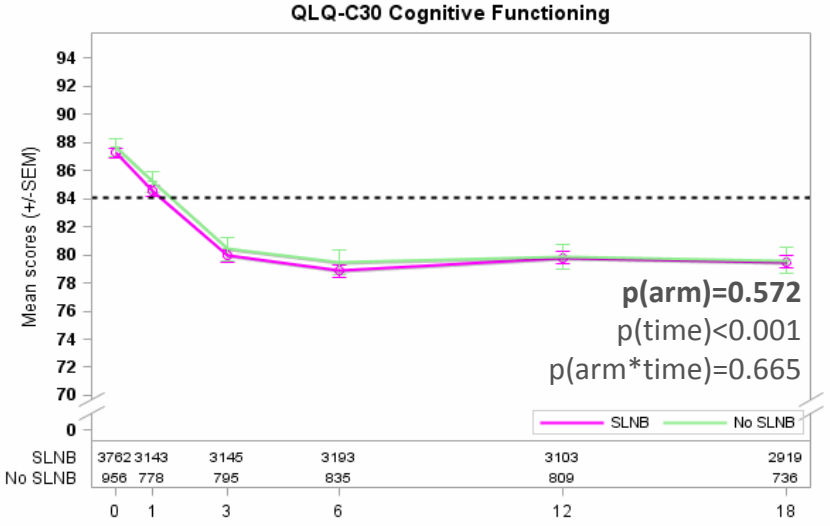


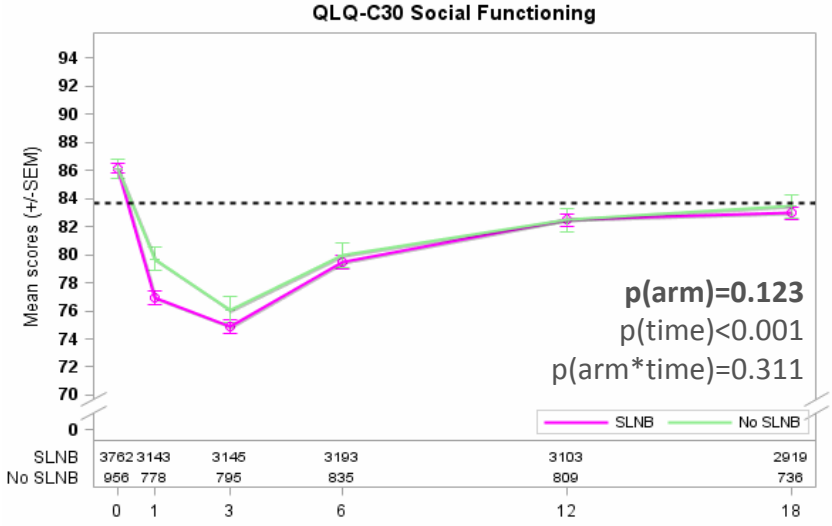






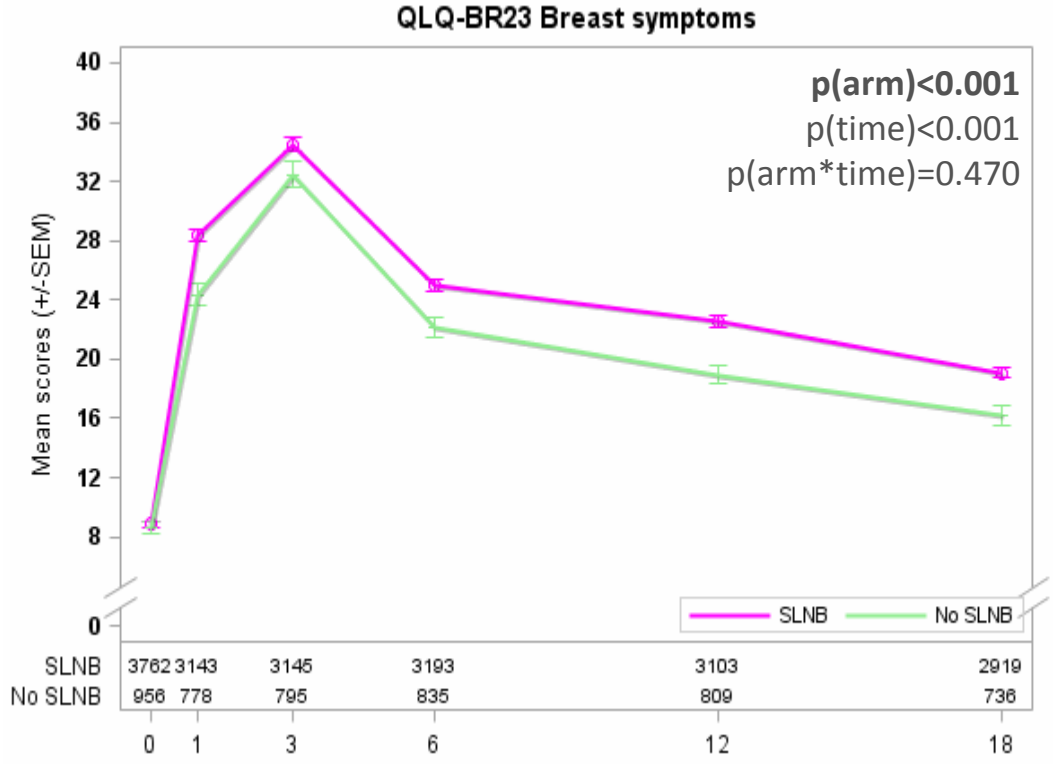
QoL – First Randomization (SLNB vs No SLNB)

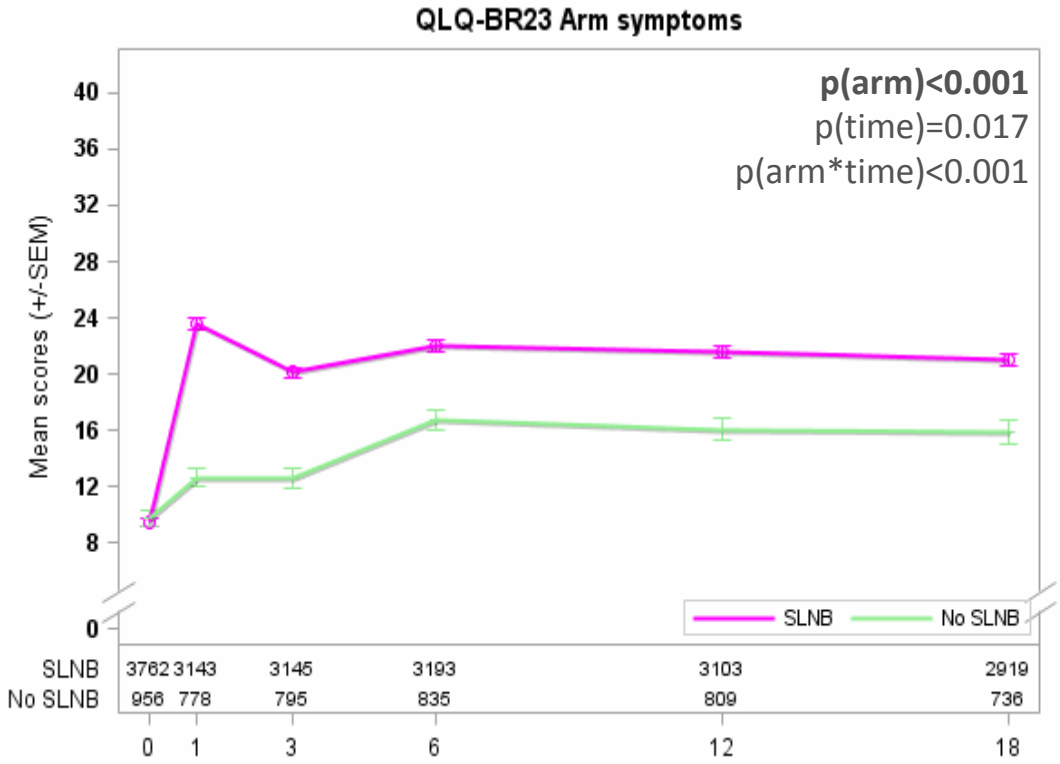




QoL – First Randomization (SLNB vs No SLNB)

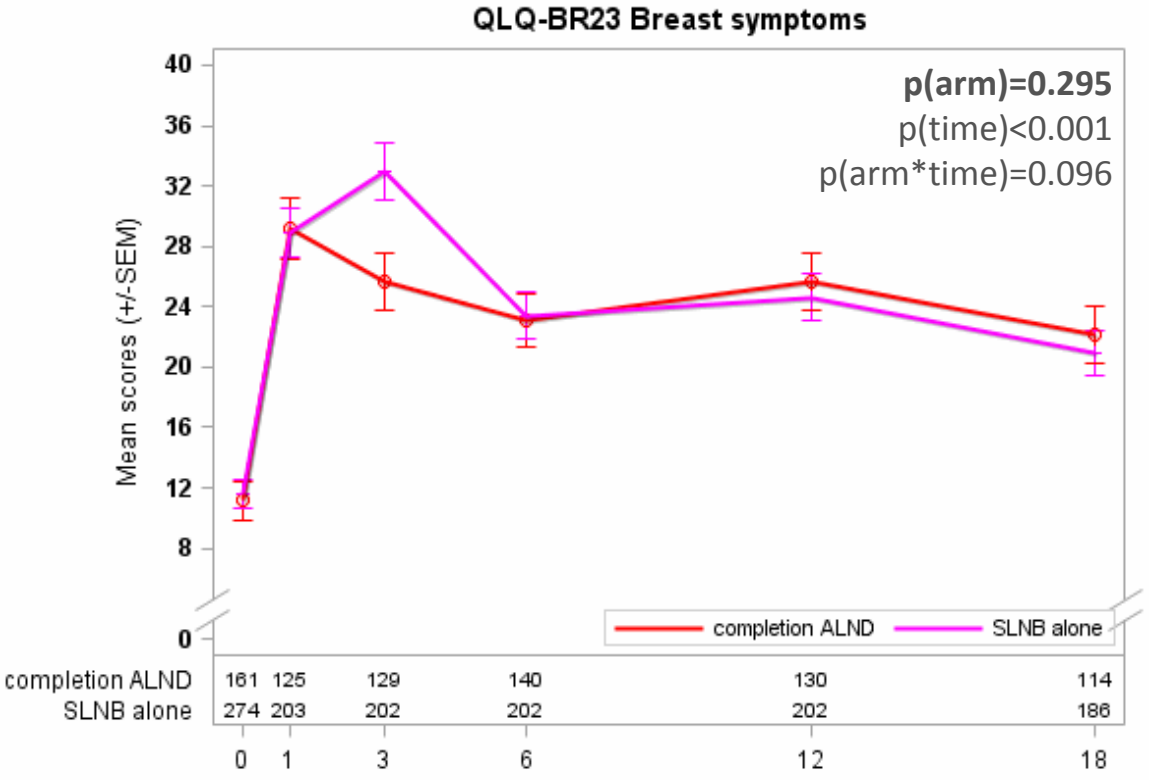
- There were significant differences for the BRBS (breast symptoms) and BRAS (arm symptoms) scores favoring the no SLNB group in post-baseline assessments. However, these differences were clinically meaningful only for the BRAS score.

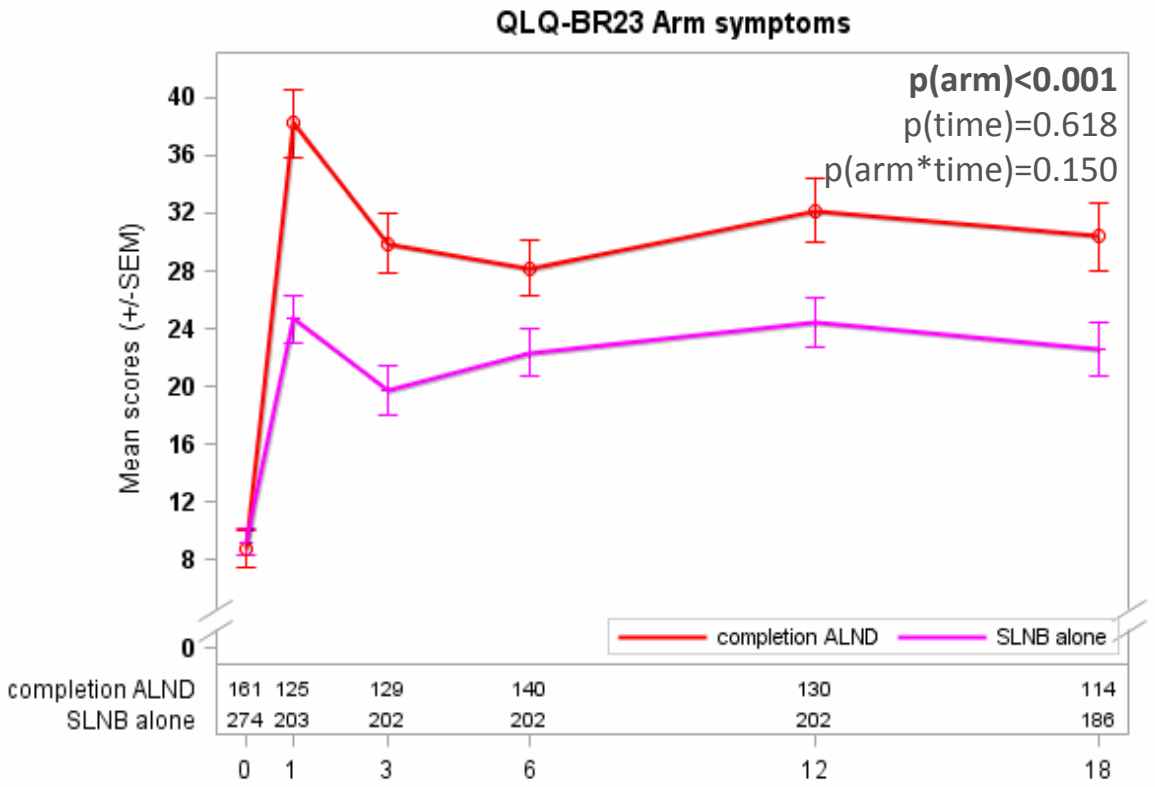




QoL – Second Randomization (cALND vs SLNB alone)

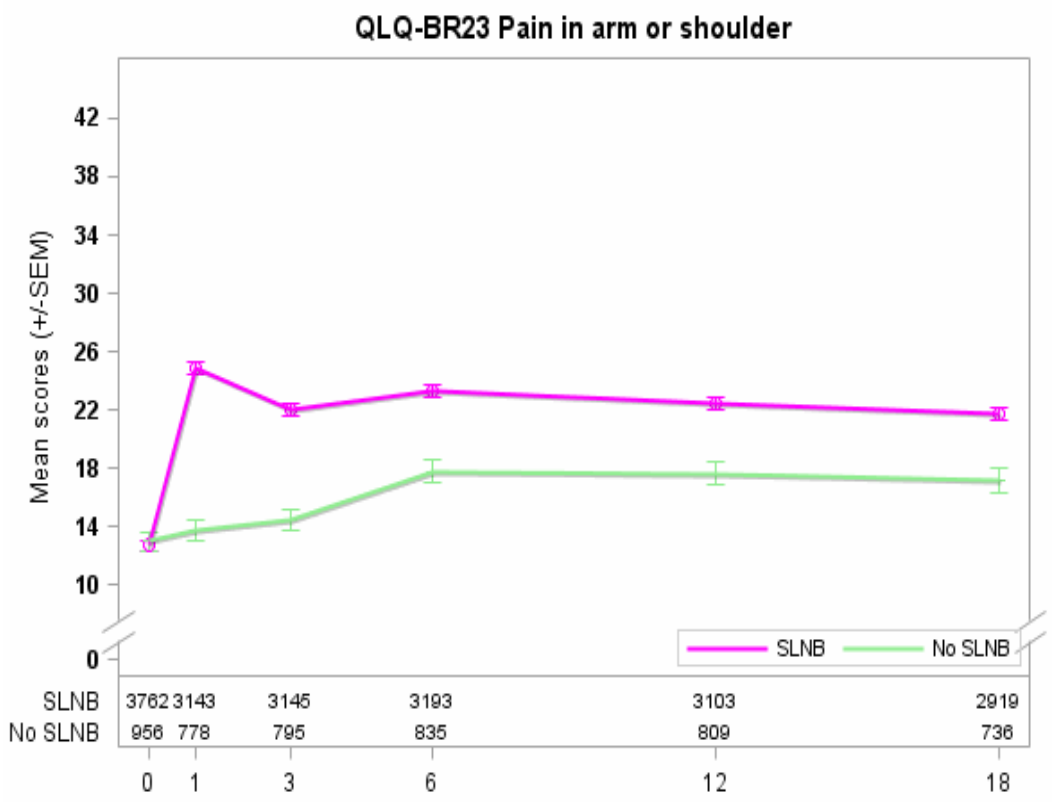
- There were also no relevant differences for GHS, functional scales and body image scales/items between cALND and SLNB groups.
- There were significant and clinically meaningful differences only for the BRAS (arm symptoms) scores favoring the SLNB group in post-baseline assessments.



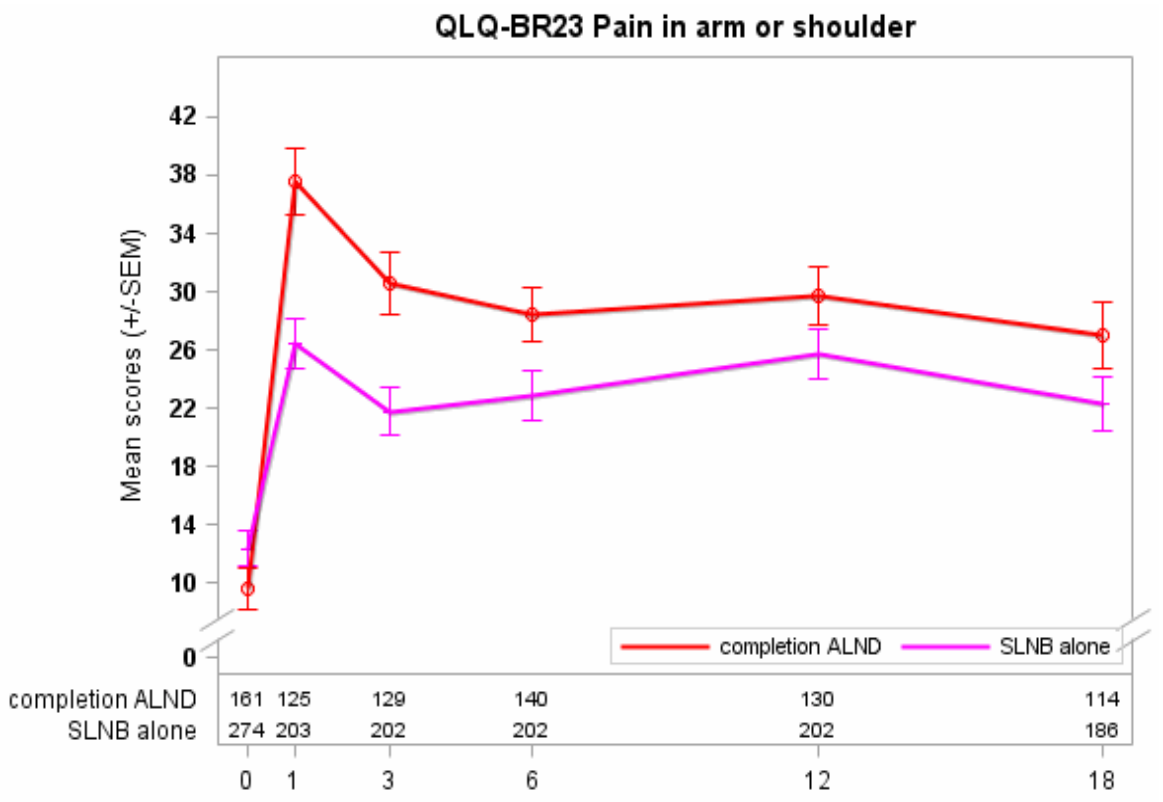


QoL – Arm Symptoms Separately

First Randomization (SLNB vs No SLNB)

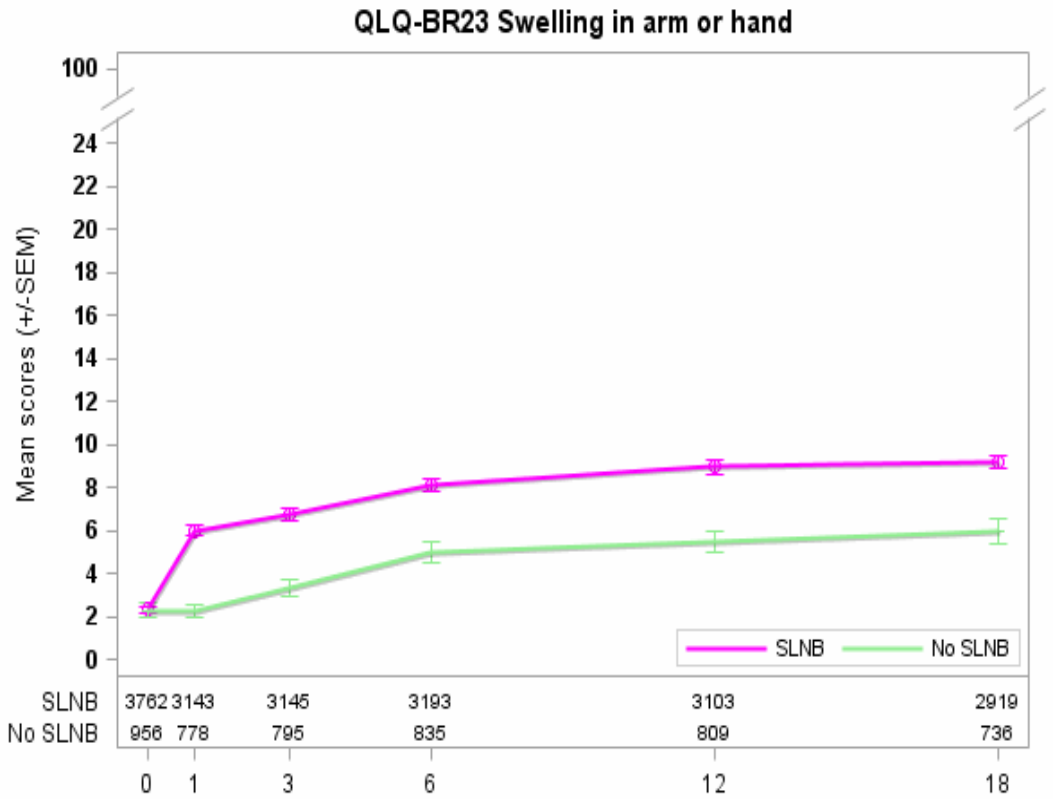


Second Randomization (cALND vs SLNB alone)

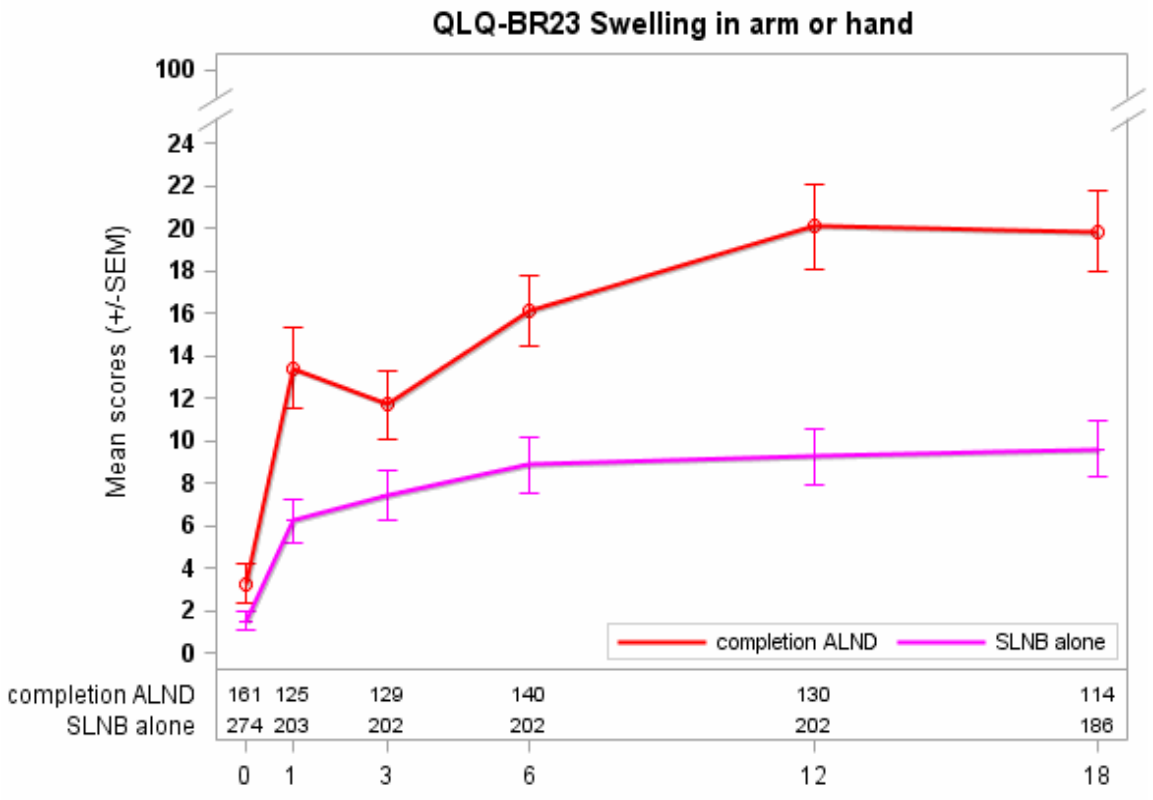


QoL – Arm Symptoms Separately

First Randomization (SLNB vs No SLNB)

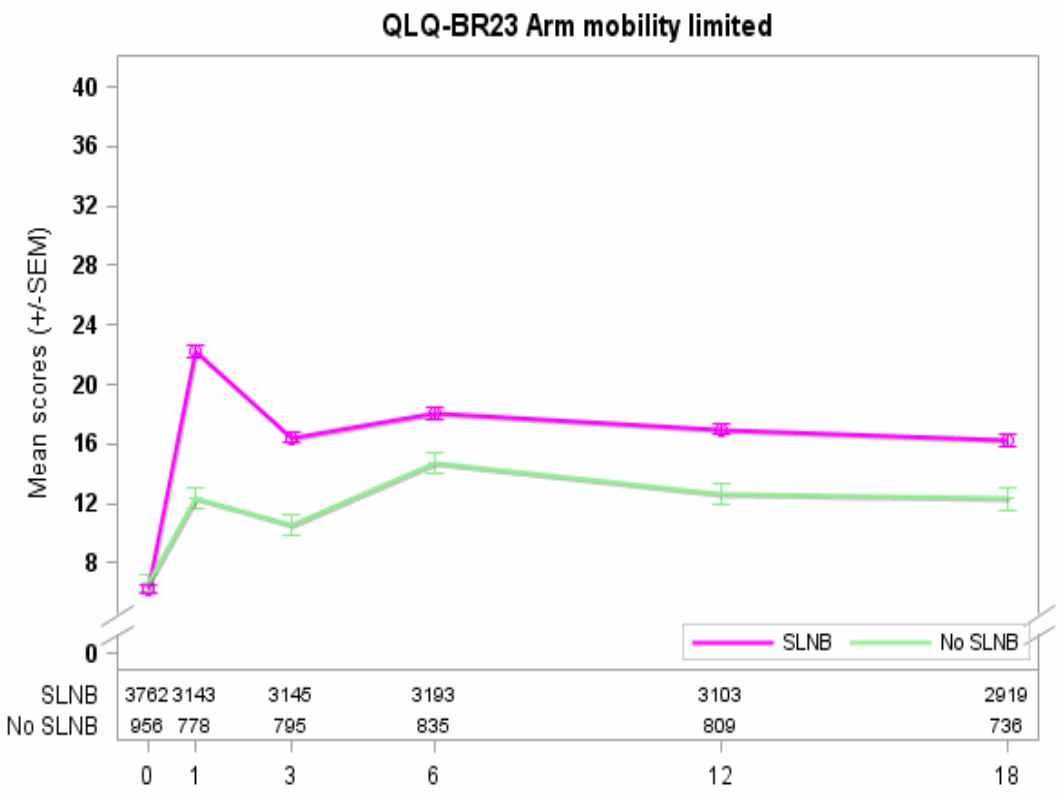


Second Randomization (cALND vs SLNB alone)

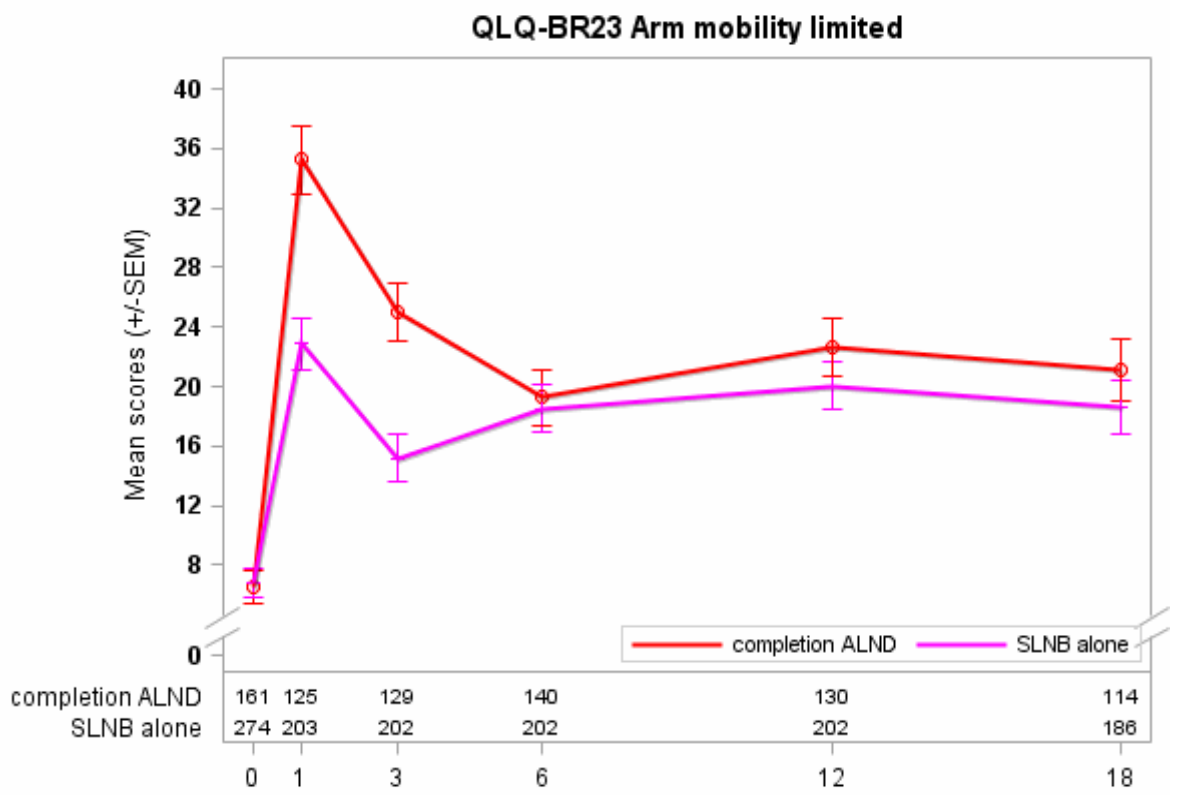


QoL – Arm Symptoms Separately

First Randomization (SLNB vs No SLNB)



Second Randomization (cALND vs SLNB alone)



Summary and Conclusion

- INSEMA (including over 5000 patients) is one of the first randomized trials investigating the omission of SLNB in clinically node-negative patients and the first to report QoL data.
- Patients with no SLNB had improved breast and arm symptoms compared to those with SLNB.
- Patients in the SLNB group had improved arm symptoms and functioning compared to those receiving completion ALND.
- No relevant differences in the other QoL scales were seen.
- iDFS data (primary outcome) are expected to be shown by the end of 2024.

Follow-up is ongoing, please continue to support the INSEMA trial

Acknowledgement

- All patients and their families, all participating sites, and IDMC

Cooperating partners

Collaborating study groups:

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Members of the Subboard GBG and AGO-B

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Medical Writing:
Valentina Vladimirova

HERZLICHEN DANK!

THANK YOU VERY MUCH!

Slides are available on the webpage of GBG www.gbg.de