Omitting Sentinel Lymph Node Dissection after neoadjuvant treatment in early breast cancer: Interim results from the VENUS randomized clinical trial

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Abstract

Introduction: Sentinel lymph node dissection (SLND) omission after neoadjuvant therapy (NAT) in early-stage breast cancer has not yet been studied, because most SLND omission trials do not allow recruitment of patients who undergo NAT. The VENUS trial (ClinicalTrials.gov NCT05315154, ReBEC RBR-8g6jbf, Ethics approved: CAAE:06805118.2.0000.5404) is an ongoing study that aims to evaluate the safety of omitting sentinel lymph node dissection in clinically and ultrasound node-negative early breast cancer (BC). The trial permits neoadjuvant treatment (NAT). **Objectives:** Evaluate the characteristics of patients enrolled in the VENUS trial until September 25th 2025, who underwent NAT and compare them to the other patients enrolled, in order to determine if it is safe to maintain the recruitment of women with early-stage breast cancer and neoadjuvant treatment indication. **Methods**: Descriptive interim exploratory analysis of the patients enrolled on the VENUS trial until September 25th 2025. The VENUS trial is a multicenter, prospective, non-inferiority, phase 3 clinical trial that includes women with T1/T2, N0 (clinical/ultrasound), M0 breast cancer, randomized to SLND or no axillary surgery (NAS). Initial treatment could be NAT or upfront surgery, and the axillary ultrasound must be negative before and after the neoadjuvant treatment (analysis groups: NAT-SLND, NAT-NAS, up-front-SLND, up-front-NAS). This interim analysis focuses on patient and tumor characteristics, SLND positivity, and axillary recurrence. **Results:** So far, 788 women were enrolled, with 287 randomized to SLND and 273 to NAS. Patients' epidemiological characteristics (body mass index, race and menopausal status) were similar in all randomization groups, but those who underwent NAT were younger (NAT-SLND and NAT-NAS mean ages were 53.4 and 53.7 years old *versus* up-front-SLND and up-front-NAS of 59.7 and 62.7 years old, p=0.01). Among all randomized patients, 45 (8%) underwent NAT, of which 25 had SLND performed and 20 no axillary surgery. They had more aggressive tumor profiles (37.7% HER2 positive tumors and 33.3% triple-negative tumors) and tumors' mean size of 28 mm. SLND positivity seems to be lower after NAT compared to upfront surgery (4.2% vs. 19.9%, p=0.1048), though this difference did not reach statistical significance. No axillary recurrences were observed during the 22-month follow-up. **Conclusions**: This interim analysis suggests that SLND positivity is lower after NAT and that omitting SLND in this context may be oncologically safe, with no axillary recurrences observed over 22 months of follow-up. However, the small NAT sample limits statistical power, and continued data collection is needed to confirm safety and feasibility. At this stage, continuing the inclusion of patients with indication for NAT in the VENUS trial appears justified. Recruitment will proceed through December 2025.

Introduction

SOUND and INSEMA trials demonstrated that it is possible to omit sentinel lymph node dissection in cT1 cN0 M0 breast cancer patients, who undergo upfront conservative surgery and radiotherapy [1,2]. These trials showed that axillary evaluation could be safely changed from surgery to clinical examination combined with axillary ultrasound. However, some features were not included in these trials, such as young women, T2 tumors, triple negative and HER-2+ tumors, mastectomy and neoadjuvant treatment (NAT). The sentinel lymph node dissection *VE*rsus no axillary surgery in clinically *N*ode negative early breast cancer with initial negative axillary *U*ltra*S*ound (**VENUS**) trial is a Brazilian ongoing multicenter, randomized clinical trial aimed at evaluating the oncological safety of omitting axillary surgery in specific subsets of non-metastatic breast cancer patients [3]. The **VENUS** trial differs from other studies (SOUND, INSEMA and NAUTILUS) [1, 2, 4] because it allows the recruitment of patients who have undergone NAT (neoadjuvant chemotherapy or hormone therapy). This distinction is important, as it addresses knowledge gaps left by such other studies, especially once many patients with early-stage (T1/T2 N0) breast cancer now receive NAT due to tumor molecular biology, such as triple-negative and Her2 positive breast cancer. Omitting SLND after NAT raises concerns due to the possibility of residual axillary disease and the potential lack of information for adjuvant treatment decisions.

Objectives

The purpose of this study is to present the interim and exploratory results of the **VENUS** trial for patients who underwent NAT, and to evaluate whether SLND omission after NAT can be safely maintained in this trial, as well as considered for other possible future trials.

Methods and Materials

Descriptive interim exploratory analysis of the patients enrolled on the **VENUS** trial until September 25th 2025. The **VENUS** trial is a Brazilian multicenter, prospective, non-inferiority, phase 3 clinical trial that includes women with T1/T2, N0 (clinical/ultrasound), M0 breast cancer, randomized to SLND or no axillary surgery (NAS) (Image 1). Initial treatment could be NAT or upfront surgery, and the axillary ultrasound must be negative before and after the neoadjuvant treatment (analysis groups: NAT-SLND, NAT-NAS, up-front-SLND, up-front-NAS). This interim analysis focuses on patient and tumor characteristics, SLND positivity, and axillary recurrence.

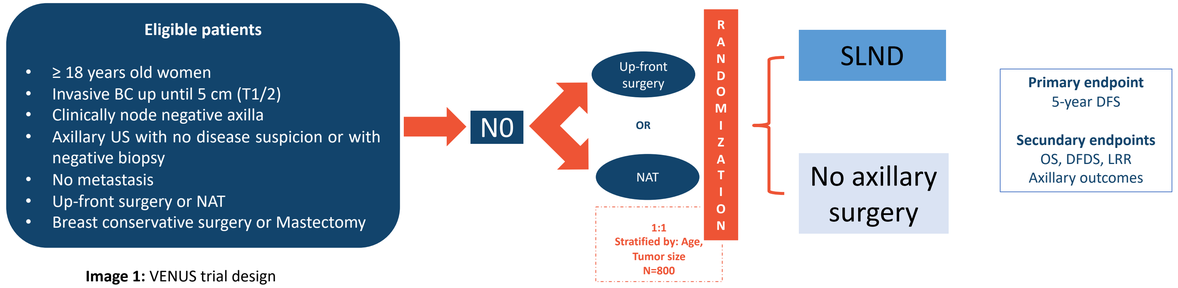


Image 1: VENUS trial design

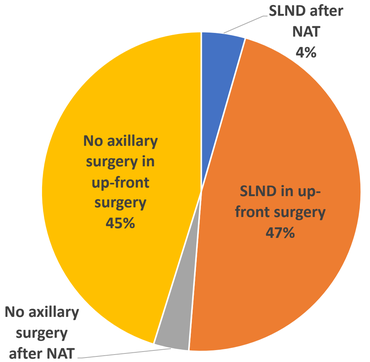
Results

Up until September 25th, 788 women had been enrolled, with 287 randomized to SLND and 273 to NAS. Patients', tumors', and treatments' characteristics are summarized in Table 1, and the mean follow-up time for all subjects is 22 months to date. Among all randomized patients, 45 underwent NAT, of which 25 had SLND performed and 20 no axillary surgery (Graphic 1). SLND positivity was 19.9% in the up-front group and 4.2% in the neoadjuvant treatment group (p=0.1048, Image 2). No axillary recurrences were observed during the 22-month follow-up.

Characteristic	SLND				No axillary surgery				P- Value
	NAT (n=25)		Up-front surgery (n=262)		NAT (n=20)		Up-front surgery (n=253)		
	n	%	n	%	n	%	n	%	
Mean age	53.4		59.1		53.7		62.7		0.01*
Mean Body Mass Index (Kg/m2)	28.9		28.8		28.9		28.4		0.8*
Race									
Caucasian	15	**60**	180	**68.7**	13	**65**	170	**67**	0.9**
Non-caucasian	10	**40**	82	**31.3**	7	**35**	83	**33**	
Postmenopausal women	17	**68**	187	**71.9**	12	**60**	180	**72.6**	0.65**
Histologial type									
Special	2	**8**	38	**15.5**	3	**15**	49	**19.7**	0.64**
Non-special	23	**92**	224	**84.5**	17	**85**	204	**80.3**	
Nuclear Grade									
I	1	**4**	56	**21.4**	1	**5**	63	**25**	<0.01**
II	13	**52**	176	**67.2**	14	**70**	161	**63**	
III	11	**44**	30	**11.5**	5	**25**	29	**12.1**	
Molecular subtype									
Luminal A *like*	2	**8**	184	**69.4**	5	**25**	186	**73.5**	<0.01**
Luminal B *like*	3	**12**	49	**18.5**	3	**15**	43	**17**	
Luminal Her	7	**28**	24	**9.1**	6	**30**	15	**5.9**	
Her2	1	**4**	4	**1.5**	3	**15**	1	**0.4**	
Triple negative	12	**48**	4	**1.5**	3	**15**	8	**3.2**	
Mean tumor size (mm)	25.4		15.6		25.5		16.1		<0.001*
Breast Surgery									
Breast conservative surgery	22	**88**	248	**93.6**	19	**95**	239	**94.1**	0.68**
Mastectomy	3	**12**	17	**6.4**	1	**5.1**	15	**5.9**	
Adjuvant treatment									
Chemo and Hormone theraphy	5	**20**	68	**27.7**	5	**26.3**	67	**28.6**	<0.001**
Hormone theraphy alone	5	**20**	159	**64.9**	6	**31.6**	145	**62**	
Chemotherapy alone	8	**32**	11	**4.5**	6	**31.6**	14	**6**	
No systemic adjuvant treatment	7	**28**	7	**2.9**	2	**10.5**	8	**3.4**	
Follow-up time (months)	21.7		24.3		26.8		13.52		0.54*

Kruskal-Wallis chi squared*; Pearsons chi-squared test**

Table 1. Patients', tumors', and treatments' characteristics



Graphic 1: Randomization distribution.

SLND positivity (NAT)	• **4.2%** • **There was residual breast disease** • **After axillary dissection, no additional lymph node disease was found**
SLND positivity (up-front surgery)	• **19.9%**

Image 2: Sentinel Lymph Node Dissection results

Conclusions

Sentinel lymph node positivity seems to be low after NAT (4.2%) in cT1/T2 c-usN0 M0 breast cancer patients. It is possible that omitting SLND in this context may be oncologically safe, once there was no axillary recurrences observed over 22 months of follow-up. However, the small NAT sample limits statistical power, and continued data collection is needed to confirm safety and feasibility. At this stage, continuing the inclusion of patients with indication of neoadjuvant treatment in the **VENUS** trial appears justified. Recruitment will proceed through December 2025.

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