



Radioactive Iodine Seed Localization in Axilla with Sentinel Node Biopsy: A Dutch Prospective Multicenter Trial on Axillary Staging After Neoadjuvant Chemotherapy in Node Positive Breast Cancer

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Background/Objective

As a result of neoadjuvant systemic therapy (NST), at least one out of every 3 patients with initial node positive (cN+) breast cancer achieves an axillary pathologic complete response (ax-pCR). In case of ax-pCR, axillary lymph node dissection (ALND), which is the current standard treatment, can be regarded as overtreatment. This urges the need for a less invasive axillary staging method after NST, such as sentinel lymph node biopsy (SLNB) or MARI (Marking Axillary lymph nodes with Radioactive Iodine seeds). However, both MARI and SLNB cannot yet, as independent procedures, safely replace the traditional ALND, since residual axillary disease can be missed. Recent studies suggest that, by combining these procedures, the accuracy of detecting residual axillary disease may be improved. We therefore developed the RISAS trial to validate the combination of MARI and SLNB (i.e. RISAS procedure) for axillary staging after NST in cN+ breast cancer with the potential to safely replace ALND.

Methods

In this currently recruiting prospective single arm multicenter validation study, a total of 225 cN+ patients will be needed to test non-inferiority of RISAS compared to ALND. Fourteen Dutch hospitals are participating in this trial. The RISAS procedure consists of performing MARI and SLNB and is directly followed by completion ALND (Figure 1). All RISAS lymph nodes are compared to ALND specimen lymph nodes.

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Figure 1. RISAS procedure followed by completion ALND. (RISAS consists of MARI(1) and SLNB(2))

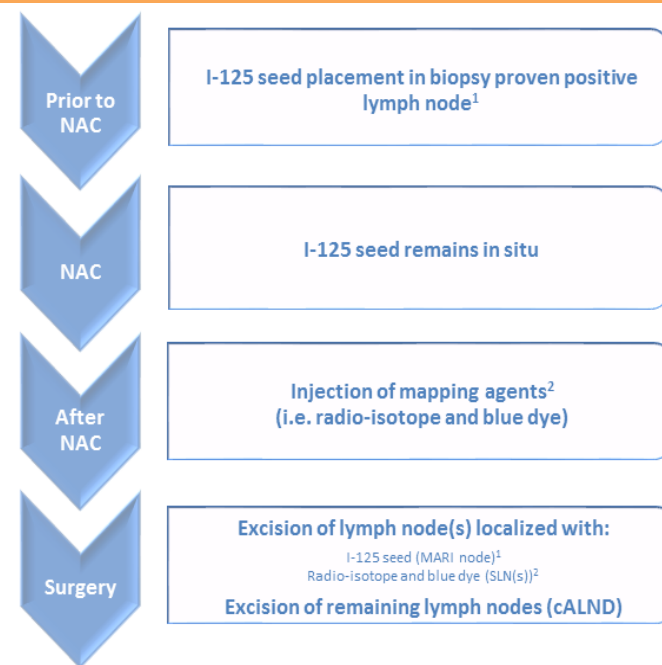
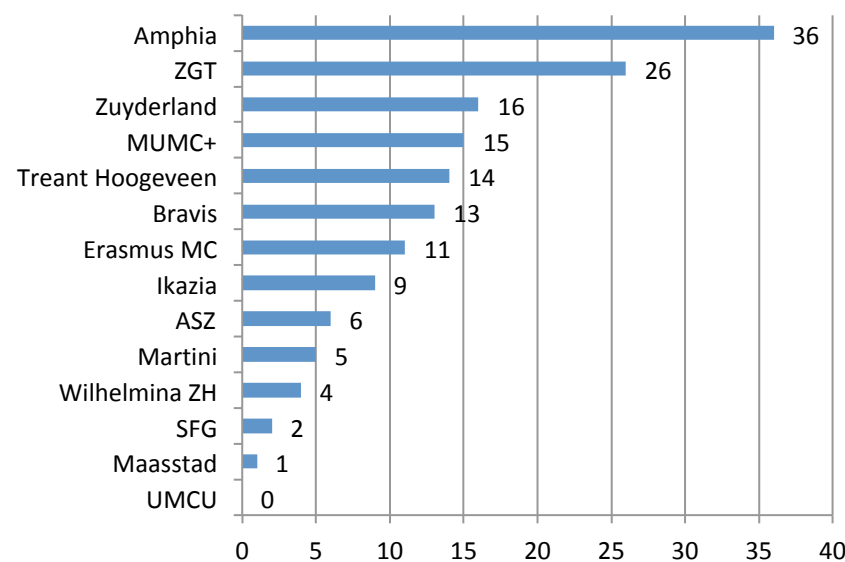


Figure 2. Accrual at each of the 14 participating institutions. (current total of included patients is 158/225)



Results

Female patients, aged 18 years or older, with invasive breast cancer and pathologically proven axillary nodal metastasis are eligible. All patients have to provide written informed consent. Patients with (oligo)metastatic breast cancer, previous axillary surgery or radiotherapy and patients with periclavicular metastasis (cN3a or cN3c) are not eligible.

Fourteen Dutch institutions are accruing patients with a current inclusion of 158 patients (see Figure 2). See table 1 for an overview of the diagnostic accuracy of different less invasive staging procedures compared to ALND.

Table 1. Overview of diagnostic accuracy of SLNB, MARI and TAD.

	SLNB ¹	MARI ²	TAD ³	RISAS
Sample size	2154	98	85	225
Prevalence axillary pCR	37.0	26.0	41.0	#
Identification rate (%)	89.0	97.0	100	#
FNR (%)	17.0	7.0	2.0	#
NPV (%)	57.0 to 86.0	83.0	97.2	#

¹Simons et al. Ann Surg. 2019 Mar. ²Donker et al. Ann Surg. 2015 Feb. ³Caudle et al. JCO. 2016 Apr.

Conclusion

RISAS will determine accuracy and safety of this combination procedure in order to optimize axillary staging and subsequent therapeutic management after NST in pretreatment cN+ patients.

If RISAS proves to be an accurate axillary staging procedure, ALND may safely be abandoned in case of pCR confirmed by the RISAS procedure.