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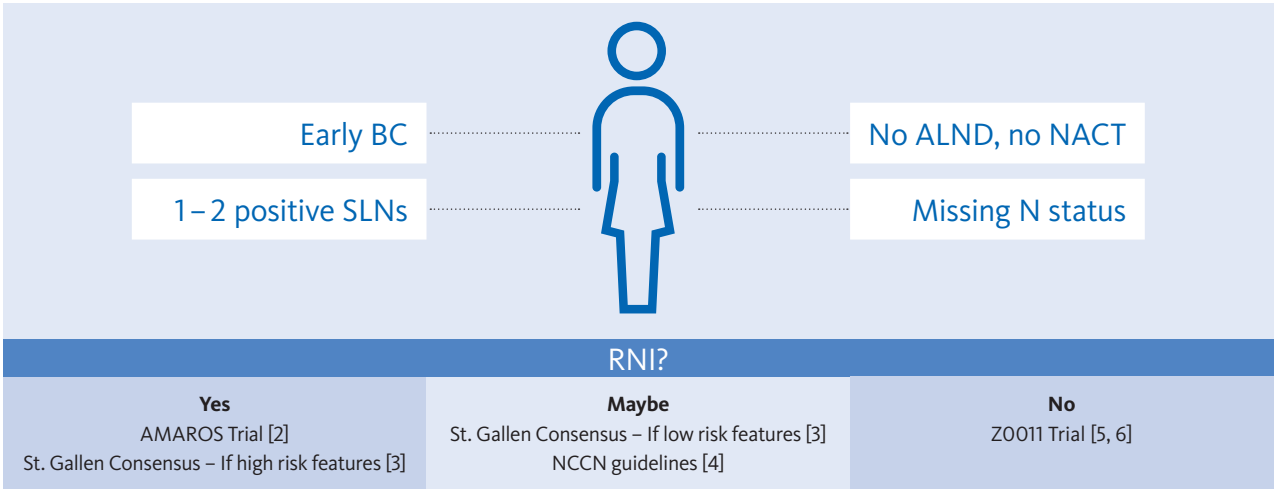
WHITE PAPER RXT

# OSNA® – fine-tune your radiation therapy with more differentiated information

## Challenges in selecting the appropriate radiation therapy for your patient

Although guidelines recommend considering regional node irradiation (RNI) in early stage breast cancer patients with 1–3 positive sentinel lymph nodes (SLN), consensus is mixed among clinicians. Should one apply RNI in these patients? Which patients benefit? And which can be spared the treatment? There is also no clear recommendation as to the extent of the radiation required. Getting the dose right is currently a subjective decision.

More questions have been raised by clinical trials that investigated less invasive treatment approaches as a replacement for axillary lymph node dissection (ALND). Methodological flaws in all trials have led to remaining uncertainty about the appropriate radiation therapy (RT) for individual patients [1]. Moreover, in case of omission of ALND, decision-making is even more challenging as staging information regarding the nodal status is missing and has to be based solely on the result of the SLN. This becomes even more relevant as SLN analysis by histopathology is not standardised, examines only part of the lymph node and so provides only limited diagnostic information.




Abbreviations: BC: breast cancer; SLN: sentinel lymph node; ALND: axillary lymph node dissection; NACT: neoadjuvant chemotherapy; N: nodal; RNI: regional node irradiation.

**Therefore, the question is: How do we address this information gap and is there a more standardised and comprehensive SLN assessment available that supports more reliable classification of patients?**

# OSNA® – more differentiated information to fine-tune treatment decisions

OSNA® – or One Step Nucleic Acid Amplification – is well established in routine and has proven its utility in many publications that show that the OSNA® result provides more differentiated diagnostic information than histopathology.

## Standardised and precise

- Quantitative determination of the metastatic burden of the sentinel lymph node by measurement of CK19 mRNA expression as marker
- Standardised and reliable results thanks to whole node analysis
- Included in European and several national guidelines

## Information beyond

- A better and independent predictor of the risk for non-sentinel node involvement than the number of positive SLN [7]
- The only independent predictor of ≥ 4 LN having metastases [8]
- Provides relevant staging information even in case no axillary dissection has been performed
- Provides also prognostic information [9]

**Individualised and targeted treatment for patients**

# Overtreatment? No thanks!

The clinical trend is moving towards de-escalation of treatment in suitable patients to increase treatment efficacy and reduce unwanted side-effects. However, uncertainty remains about the appropriate loco-regional treatment for early breast cancer patients with no or low tumour burden in the SLNs. Should they be spared RNI and the related morbidity?

In this context, the importance of a standardised SLN assessment as well as the predictive [8] and prognostic [9] information as provided by OSNA® have become even more relevant.

The ongoing trials Optimal I and IIa aim to answer this question by exploring the correct axillary treatment for those patients in the adjuvant and neoadjuvant setting (Table 1, Figure 1). Both studies use OSNA® for lymph node analysis and were presented at the ESTRO 35 conference [10] and at the 'Assisi Think Tank Meeting' in which the importance of adherence and active participation to these trials was underlined during the meeting as well as in the resulting review [1].

Preliminary results of Optimal I presented at the AIS congress in Florence indicate similar outcome in both study arms.

**Table 1**

| Trial | Type of study | Accrual time | Principal investigator, country | Cohort | Number of patients required | Main objective | Primary endpoint |
|---|---|---|---|---|---|---|---|
| Optimal I GIC-RAD-2014-0111 | International, multicentre, prospective | April 2015 to December 2021 | Manuel Ignacio Algara López, Spain | Early-stage BC, SLN assessed by OSNA® (250 – 15,000 copies/µL), no ALND | 1,400 | To demonstrate non-inferiority of incidental irradiation versus intentional irradiation to level I-III and supraclavicular nodes | 5-year DFS |
| Optimal IIa GIC-RAD-2016-01 | International, multicentre, prospective | January 2017 to January 2020 | Manuel Ignacio Algara López, Spain | Early-stage BC, cN+ before NACT and ypN0 after NACT (SLN assessed by OSNA®), no ALND | 1,212 | To demonstrate non-inferiority of irradiation to level I-II nodes versus irradiation to level I-III and supraclavicular nodes | 5-year DFS |

Abbreviations: ALND: Axillary lymph node dissection; DSF: Disease-free survival; NACT: neoadjuvant chemotherapy; SLN: Sentinel lymph node.

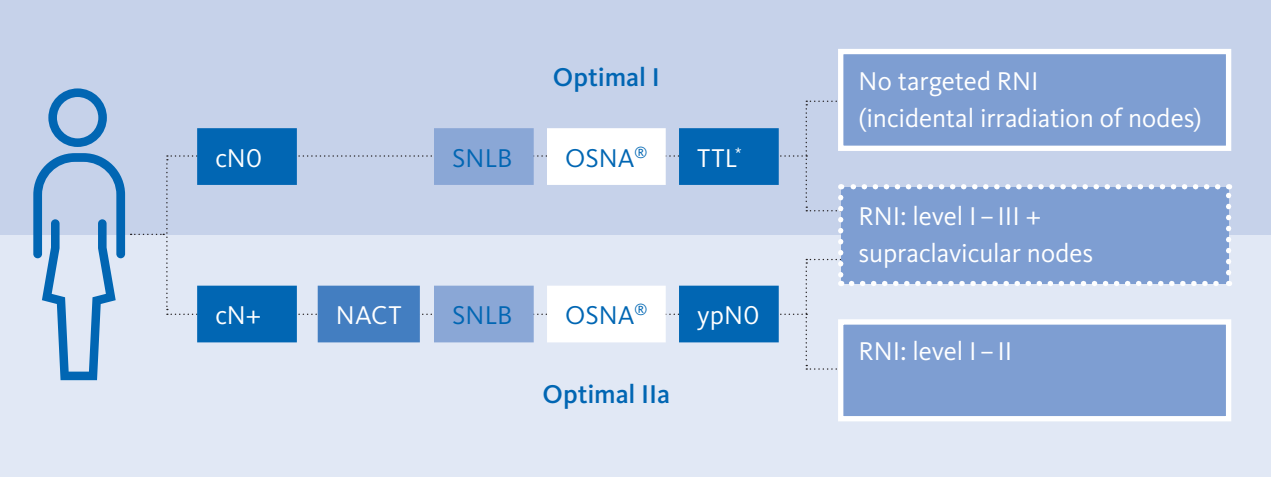



**Figure 1** Schema of both Optimal I and II trials. Abbreviations mean BC: breast cancer; cN0: clinically negative lymph nodes; cN+: clinically positive lymph nodes; NACT: neoadjuvant chemotherapy; SLNB: sentinel lymph node biopsy; OSNA®: One Step Nucleic Acid Amplification; TTL: Total Tumour Load; ypN0: pathologically negative lymph nodes after NACT; RNI: regional node irradiation. * TTL range: 250 – 15,000 CK19 mRNA copies/µL.

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