NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Review decision

Review of DG8: Intraoperative tests (RD-100i OSNA system and Metasin test) for detecting sentinel lymph node metastases in breast cancer

This guidance was issued in August 2013.

The review date for this guidance was August 2016. The review was deferred until the update of NICE clinical guideline on early and locally advanced breast cancer was complete. This guideline was published in July 2018.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Review decision

Transfer the guidance to the static guidance list and produce a technical supplement for the new RD-210i OSNA system.

The evidence gathered in this report will be passed to the Centre for Guidelines surveillance team and be considered during routine surveillance of NICE's guideline on early and locally advanced breast cancer.

At the Guidance Executive meeting of 28 January 2020, the proposal to transfer the guidance to the static list without consultation was agreed. A list of the options that were considered, and the consequences of each option is provided in Appendix 1 at the end of this paper.

2. Rationale

Although new evidence is available for both the OSNA system and the Metasin test, it is not expected that this new evidence would lead to changes in the results of the clinical and cost-effectiveness modelling from the original diagnostics assessment. In

addition, there appear to be limited changes to the cost of the technologies and associated costs.

There have been some changes to the care pathway in which the interoperative tests are indicated for use, however, it is expected these changes would have a limited impact on the results of the economic model. Further, although care pathway changes may reduce the size of the population requiring intraoperative testing of sentinel nodes, the potential value of these technologies remains the same.

Overall, changes to the technologies, evidence base and care pathway are unlikely to have a material effect on the recommendations in the published guidance, therefore the guidance will be transferred to the static list.

A technical supplement on the OSNA system will be produced because the RD-100i version of the technology assessed in the original guidance has now been superseded by the new RD-210i OSNA system.

3. Implications for other guidance producing programmes

No implications for other guidance producing programmes have been identified.

4. Original objective of guidance

To assess the clinical and cost effectiveness of intraoperative tests (RD-100i OSNA system and Metasin test) for detecting sentinel lymph node metastases in breast cancer.

5. Current guidance

Adoption recommendations

1.1 Whole lymph node analysis using the RD-100i OSNA system is recommended as an option for detecting sentinel lymph node metastases during breast surgery in people with early invasive breast cancer who have a sentinel lymph node biopsy and in whom axillary lymph node dissection will be considered. Details of the development of a national registry are included in section 7 of this guidance.

1.2 The Metasin test is not recommended for detecting sentinel lymph node metastases in people with early invasive breast cancer in routine clinical NHS practice. The Metasin test shows promise and the development of robust evidence is recommended to demonstrate its utility in clinical practice.

Research recommendations

7.1 NICE recommends that a national registry is developed to collect data on the use of the RD-100i OSNA system in detecting sentinel lymph node metastases during breast cancer surgery. It also recommends that data on all patients having whole lymph node analysis by the RD-100i OSNA system should be submitted to this registry. These data should be integrated with data from other registries for breast cancer where appropriate.

6. New evidence

The search strategy from the original diagnostics assessment report was re-run on Medline, Embase, Cochrane Library, Centre for Reviews and Dissemination (CRD) and Turning Research into Practice (TRIP) databases. References from 2012 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the diagnostic and care pathways. Companies were asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. Specialist committee members for this guidance topic were also consulted and asked to submit any information regarding changes to the technologies, the evidence base and clinical practice. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

6.1 Technologies

6.1.1 RD-100i OSNA system

At the beginning of 2018, the RD-100i system that performs the OSNA test was superseded by the RD-210i system. The RD-100i OSNA system is no longer available to purchase in the UK and support for the system will cease at the end of 2020. The consumable and capital costs of the RD-210i system appear to be similar to the RD-100i OSNA system (table 1).

Table 1: OSNA system costs

	Total cost (exc. VAT)	
	RD-100i system	**RD-210i system**
System	£70,000	£77,520.49
System supply parts		£2,468.23
Annual service contract,		

	Total cost (exc. VAT)	
	RD-100i system	**RD-210i system**
Annual service contract (year 2 onwards, 12-month warranty included)	£6,180	£7,554.65
Specific reagents and consumables		
Lynoamp CK19E	Approximately £150-£200 per patient	£2,399.11
Gene Ampl. Reagent Lynorhag EU		£219.87
Pipette Tips		£367.95
Detection Cells		£346.04
RD Sample Vial		£416.97
Lynoprep Blade Set (12)		£102.85
Lynoprep Tubes (24)		£87.12
Dualfiltertips 2-20µl 10x96		£208.25
Dualfiltertips 20-200 µl 10x96		£215.56
Dualfiltertips 50-1000 µl 10x96		£223.79
Dualfiltertips 100-5000 µl 5x24		£113.72
Microtubes 1,5ml (100)		£39.41

The RD-210i OSNA system uses an optimised LYNOAMP CK19E kit and has a larger throughput than the RD-100i system (14 samples per run). The amplification time is 5 minutes quicker (11 versus 16 minutes) and the requirement to prepare a dilute sample has also been removed. As a result of these changes, time to result is faster for the RD-210i system than for the RD-100i system (table 2).

Table 2: Time to results for the RD-100i and the RD-210i systems

No of samples	**RD-100i**	**RD-210i**
1 sample	23 minutes	16 minutes
2 samples	25 minutes	16 minutes
3 samples	27 minutes	18 minutes
4 samples	29 minutes	18 minutes
8 samples	52 minutes	22 minutes
14 samples	100 minutes	30 minutes

The original RD-100i OSNA system automatically calculated CK19 mRNA concentration in samples by comparison with a standard curve and a predetermined cut-off value of 250 copies/µL. Samples were judged as positive or negative according to the criteria as shown in table 3.

Table 3: Interpretation of results in the RD-100i OSNA system

Positive	(++)	CK19 mRNA concentration was ≥5,000 copies/μL (macro-metastatic tumour burden)
	(+)	CK19 mRNA concentration was ≥250 copies/μL and <5,000 copies/μL (micro-metastatic tumour burden)
	(+)I	Data indicates positive, but (++) and (+) were indistinguishable
Negative	(-)	CK19 mRNA concentration was less than 250 copies/μL

The RD-210i system also makes a qualitative determination of positive or negative and a semi-quantitative determination of (++), (+) and (-). The test thresholds from the RD-100i OSNA system are not included in the instructions for use (IFU) for the RD-210i. Sysmex have noted however, that the RD-210i and the RD-100i OSNA systems use the same thresholds for interpreting the results, but the (+)I category is no longer used for the RD-210i. The new system also calculates the CK19 mRNA concentration to give an indication for the total tumour load (TTL) burden, based on a standard curve. The TTL is based on whole node analysis rather than half or partial node analysis. However, there are no recommended thresholds in the IFU for the TTL burden result from the RD-210i OSNA test.

6.1.2 Metasin

Metasin remains a laboratory-developed test and uses CE marked lyophilised premix reagents produced by TIB MOLBIOL, in combination with Roche enzyme reagents. Centres that have not had formal training in the use of the TIB MOLBIOL reagents still use reagents prepared in-house.

The PCR platform that is used to run the Metasin test is being discontinued in December 2019. The PCRmax Eco 48 Real-Time qPCR system has been successfully evaluated as an alternative and will be phased in to all Metasin user sites. The unit cost for the Metasin test used in the original assessment was £74; the current costs relating to the Metasin test are presented in table 4.

Table 4: Metasin test costs

	Total cost (exc. VAT)
Test = controls (positive and negative) and up to 4 nodes per patient	
PCRmax Eco 48 Real-Time qPCR System	£10,045
CE marked reagents	£11.61 per test[†]
PCRmax Eco 48 Real-Time plate & seal	£1 per test
Homogeniser probes	£7.26 per test

	Total cost (exc. VAT)
Dependent on each site's account with the provider:	
Qiagen RNEASY (250)	£997.28 (£3.98 per node)
Roche Lightcycler 480 RNA Hydrolysis probes	£1028 (£2.06 per test)
Notes: † €13 - Euros converted @ XE.com rate on 18/06/2019	

6.2 Clinical practice

Since publication of DG8, NICE's clinical guideline on early and locally advanced breast cancer has been updated. The update has resulted in several changes to the diagnostic and care pathway in which the interoperative tests sit. The most relevant change for DG8 relates to the recommendations on who should be offered axillary treatment. The 2009 version of the guideline recommended that people with macrometastases or micrometastases in a sentinel lymph node should both be offered axillary treatment, with the preferred option being axillary lymph node dissection. The 2018 version of the guideline recommends that people who only have micrometastases in their sentinel lymph nodes should not be offered axillary treatment. For people with 1 or more sentinel lymph node macrometastases the guideline recommends axillary treatment is offered (axillary node clearance or radiotherapy), except for people with 1 or 2 sentinel lymph node macrometastases who have also been advised to have whole breast radiotherapy with systemic therapy. It also states that the benefits and risks of having no further axillary treatment after primary breast conserving surgery should be discussed with these people.

The Association of Breast Surgery consensus statement on the management of the malignant axilla in early breast cancer (2015) stated that:

- If the sentinel node(s) shows micrometastases, no further axillary treatment is required in addition to breast conserving surgery or mastectomy.
- If 1-2 sentinel nodes show macrometastases, further axillary treatment is not mandatory in patients having breast conservation with whole breast radiotherapy, that are post-menopausal and have T1, grade 1 or 2, oestrogen receptor positive and HER2 negative tumours.
- If 1-2 sentinel lymph nodes show macrometastases, further axillary treatment is recommended for patients undergoing mastectomy, or with tumours with 1 or more of the following features: T3, grade 3, oestrogen receptor negative or HER2 positive.
- If 3 or more sentinel nodes show macrometastases, further axillary treatment is recommended.

Clinical experts also agreed that care pathways relating to sentinel lymph node biopsies and further axillary treatment during breast cancer surgeries had changed since the publication of DG8. One expert stated that they no longer do routine axillary clearance for patients having radiotherapy, therefore use of intraoperative molecular tests is declining. Another expert noted that the total tumour load (TTL) burden in whole lymph node submission is now considered the important guidance figure, rather than the findings of any positivity in a sentinel node. TTL relates to the copy numbers of CK19 mRNA measured in the whole node and each laboratory may apply different cut-off levels to the test result.

Clinical experts advised that interoperative molecular tests may have value in patients who have had neoadjuvant chemotherapy, who were outside the scope for DG8. In these patients the tests could help guide further treatment decisions and provide information on prognosis.

6.3 New studies

A total of 8 studies in scope that have been published since the evidence review for DG8 were identified; 6 on RD-100i OSNA and 2 on the Metasin test. A single gate design was defined as a single sample of individuals with unknown metastatic status, with the sentinel lymph node assessed by both the intervention test and the reference standard (half-node analysis). A two-gate design was defined as 2 sets of patients, 1 with known metastatic status and 1 without, with the intervention test and reference standard performed on both (half-node analysis). Cohort studies were defined as using different patient populations for the intervention test and reference standard (whole node analysis).

6.3.1 RD-100i and RD-210i OSNA new studies

Three of the 6 new studies were of single-gate design, that is, people with unknown metastatic status were recruited and the sentinel lymph node was assessed by both the OSNA system and the reference standard (half-node analysis). There were also 2 cohort studies (whole node analysis) and 1 patient survey.

In summary, a common issue across the studies is that all single gate (half node analyses) are subject to tissue allocation bias, casting doubt on diagnostic accuracy results. Therefore, it is uncertain whether diagnostic accuracy data from the RD-100i OSNA system using half node analyses would be generalisable to the RD-210i, which requires whole node analysis to calculate total tumour load.

Shimazu et al. 2019 reported diagnostic accuracy data for the RD-200 OSNA system[1] compared with the RD-100i OSNA system and histopathology. Sixty-three patients from 3 hospitals in Japan with 150 sentinel lymph nodes or non-sentinel lymph nodes were prospectively included in half node analysis. Concordance rates, sensitivity and specificity results were found to be in good agreement between new and old OSNA systems.

Li et al. 2015 prospectively studied 115 patients with 370 clinically negative sentinel lymph nodes having half node analysis using the RD-100i OSNA system in a single centre in China. The concordance rate per node between OSNA and histopathology was 95.2% (95% confidence intervals [CI] 91.6–96.9%). However, 96% of macrometastatic nodes were diagnosed as positive by RD-100i OSNA, but only 54.5% micrometastatic nodes were diagnosed as positive.

Chaudhry et al. 2014 reported on 54 patients with 116 clinically negative sentinel lymph nodes having half node analysis using the RD-100i OSNA system in a single centre in the UK. In a second phase to the study, 168 patients with 324 sentinel lymph nodes had whole node analysis using the RD-100i OSNA system during routine use of the technology. The validation phase reported a sensitivity of 92.8%, specificity of 88.8%, PPV of 43.4% and NPV of 99.2%. In routine use, the median OSNA procedure time was 40.5 minutes and total operating time with intraoperative OSNA were prolonged by a median of 20 minutes.

Ruano et al. 2014 retrospectively analysed clinical outcomes from 148 patients who had whole node analysis using the RD-100i OSNA system compared with 153 historical controls who had histopathology in a single centre in Spain. More axillary lymphadenectomies were conducted after OSNA than after histopathology (34.5 % versus 24.2%, p=0.05). The authors concluded that whole lymph node analysis using the OSNA system can detect significantly more metastases than conventional histology.

Klingler et al. 2013 retrospectively analysed clinical outcomes from 100 patients who had whole node analysis using the RD-100i OSNA compared with 281 historical controls who had histopathology in a single centre in France. A statistically significant difference in second surgery rates was reported (9.0% from OSNA testing and 38.8% from histopathology, p=0.01). Operational outcomes for OSNA included transport time from theatre to laboratory of less than 10 minutes, and time from

[1] The RD-200 is the version of the RD-210i provided in Asia. The systems and reagents used are identical, but the RD-200 has the option to run a beta-actin control alongside the patient samples which reduces capacity to 7 samples from 14. The RD-200 is not available in Europe.

receipt of the samples in the laboratory to results reported back to the surgeon ranging from 30 to 94 minutes (mean 43 minutes) depending on the number of sentinel lymph nodes.

Athwal et al. 2016 reported results from a survey of 72 patients who had OSNA assessment at a single centre in the UK. Of 60 patients who responded, 25% reported pre-operative anxiety, but 96.7% of patients would choose the procedure (single operation) again over a staged approach.

6.3.2 Metasin studies

Both new Metasin studies are of single-gate design (half node analysis). No cohort or two-gate design studies were identified. In summary, although published studies are now available, it is difficult to draw conclusions on the diagnostic accuracy of Metasin because different cut-off thresholds have been used in each study.

Sai-Giridhar et al. 2016 is a two-part study reporting a retrospective analytical validation of the Metasin test based on samples from 448 patients, followed by a prospective clinical validation in 1388 patients in 3 hospitals across England and Wales. The clinical validation used half node analysis of alternate 2mm wide slices to compare Metasin with the local gold standard histology protocol. Per patient concordance between Metasin and histology was 94.1%, sensitivity 92% (95% CI 88–94%), specificity 97% (95% CI 95-97%), PPV 88% and NPV 98%.

Smith et al. 2016 prospectively evaluated the Metasin test at University Hospital, Southampton, UK. Different reagents and cut-off thresholds from the Sai-Giridhar et al. 2016 study were used. Per patient sensitivity was 91.4% (95% CI 80.3-96.8%), specificity 88.5% (95% CI 83-92.5%), PPV 70.7% and NPV 97.1%. The average turnaround time for the intraoperative test was 42 minutes, with an average of 5 minutes added for each additional node tested. Authors reported that 23% of patients proceeded to axillary clearance based on Metasin results and were considered spared a second operative procedure.

7. Summary of new evidence and implications for review

The recent changes to the care pathway described in NICE's clinical guideline on early and locally advanced breast cancer reduce the size of the patient population that are indicated for axillary node clearance, and offer a choice of axillary treatment (axillary node clearance or radiotherapy) to people who have 1 or more sentinel lymph node macrometastases. Therefore, if patients have a preference for radiotherapy over axillary node clearance, the size of the population requiring intraoperative testing of sentinel nodes would reduce because testing in those with a preference for radiotherapy would not need to be performed intraoperatively. The value of intraoperative testing remains in patients whose preference is axillary node

clearance because the OSNA system can identify sentinel lymph node macrometastases, axillary lymph nodes can be removed at the same time as the initial tumour, the need for a second operation can be avoided and subsequent treatments such as chemotherapy can begin earlier.

New evidence on the OSNA system is mainly on the older RD-100i version of the technology, which has now been superseded by the new RD-210i OSNA system. In addition, most new studies performed half node analysis and this evidence may not be generalisable to the new RD-210i OSNA system which requires whole node analysis to calculate total tumour load. Only 1 study is available that compared the old version of the OSNA system with the new version, therefore, if evidence on RD-100i is not generalisable to RD-210i, an assessment of the new OSNA system would be difficult. However, clinical opinion is that changes to the OSNA system are improvements and would not result in worse clinical outcomes from use of the RD-210i OSNA system compared with use of the RD-100i OSNA system. Further, there appear to be limited changes to the cost of the technology and associated costs. Therefore, it is likely that if the economic model was updated with new accuracy and cost inputs, the results of the cost-effectiveness analysis would be similar to those in the original assessment.

At the time of the original assessment there were no peer-reviewed studies available on the Metasin test, but 2 published studies are now available. Evidence on the Metasin test shows that diagnostic accuracy in the new studies is similar to that reported in the unpublished studies included in the original assessment. However, the 2 new studies each use different test thresholds, so uncertainty around the diagnostic accuracy remains. In addition, the Metasin test is still not fully CE marked, that is, it is a laboratory-developed test which uses CE marked lyophilised premix reagents produced by TIB MOLBIOL, in combination with Roche enzyme reagents. Further, centres that have not had formal training in the use of the TIB MOLBIOL reagents still use reagents prepared in-house. Therefore, the committee's concern about whether the Metasin test could be used effectively across many hospitals in the NHS remains an issue.

Overall, despite some new evidence becoming available on both tests and a change to the care pathway, new information and evidence is unlikely to have a material effect on the recommendations in the published guidance. Therefore, NICE is proposing to transfer the guidance to the static list and provide details of the new OSNA system in a technical supplement to the guidance.

8. Implementation

The OSNA system is in use in approximately 25 NHS hospitals and the Metasin test is in use in 4 hospitals.

9. Equality issues

People with a diagnosis of cancer are protected under the Equality Act 2010. The committee developed recommendations referring to people with early invasive breast cancer rather than women because breast cancer can also occur in men, although this is relatively rare and there is little published evidence. As the pathology of male breast cancer is similar to female breast cancer, treatment is usually based on knowledge of female breast cancer.

Paper sign off: Rebecca Albrow, Associate Director, 14 February 2020

Contributors to this paper:

Technical Lead:	Frances Nixon
Technical Adviser:	Rebecca Albrow
Project Manager:	Donna Barnes

Appendix 1 – explanation of options

If the published Diagnostics Guidance needs updating NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
Standard update of the guidance	A standard update of the Diagnostics Guidance will be planned into NICE's work programme.	No
Accelerated update of the guidance	An accelerated update of the Diagnostics Guidance will be planned into NICE's work programme. Accelerated updates are only undertaken in circumstances where the new evidence is likely to result in minimal changes to the decision problem, and the subsequent assessment will require less time to complete than a standard update or assessment.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Diagnostics Guidance does not need updating NICE must select one of the options in the table below:

Options	Consequences	Selected – 'Yes/No'
Transfer the guidance to the 'static guidance list'	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Diagnostics Guidance on the static list should be flagged for review.	Yes
Produce a technical supplement	A technical supplement describing newer versions of the technologies is planned into NICE's work programme.	Yes
Defer the decision to review the guidance to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Diagnostics Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant Institute work

Published

Early and locally advanced breast cancer: diagnosis and management (2018) NICE guideline NG101

Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013) NICE guideline CG164. Last updated: March 2017

Advanced breast cancer: diagnosis and treatment (2009) NICE guideline CG81. Last updated: August 2017

Improving outcomes in breast cancer (2002) NICE guideline CSG1

Abemaciclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2019) NICE technology appraisal guidance 579

Pertuzumab for adjuvant treatment of HER2-positive early stage breast cancer (2019) NICE technology appraisal guidance 569

Abemaciclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2019) NICE technology appraisal guidance 563

Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer (2018) NICE diagnostics guidance 34

Eribulin for treating locally advanced or metastatic breast cancer after 1 chemotherapy regimen (2018) NICE technology appraisal guidance 515

Pertuzumab with trastuzumab and docetaxel for treating HER2-positive breast cancer (2018) NICE technology appraisal guidance 509

Fulvestrant for untreated locally advanced or metastatic oestrogen-receptor positive breast cancer (2018) NICE technology appraisal guidance 503

Intrabeam radiotherapy system for adjuvant treatment of early breast cancer (2018) NICE technology appraisal guidance 501

Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017) NICE technology appraisal guidance 495

Ribociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017) NICE technology appraisal guidance 496

Trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane (2017) NICE technology appraisal guidance 458

Breast cancer (2011) NICE quality standard 12. Last updated: June 2016

Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016) NICE technology appraisal guidance 423

Everolimus with exemestane for treating advanced breast cancer after endocrine therapy (2016) NICE technology appraisal guidance 421

Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer (2016) NICE technology appraisal guidance 424

Early and metastatic HER2-positive breast cancer: subcutaneous trastuzumab (2013) NICE evidence summary 13

Fulvestrant for the treatment of locally advanced or metastatic breast cancer (2011) NICE technology appraisal guidance 239

Endoscopic axillary lymph node retrieval for breast cancer (2005) NICE interventional procedures guidance 147

Guidance on the use of trastuzumab for the treatment of advanced breast cancer (2002) NICE technology appraisal guidance 34

Ribociclib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer. (2019) NICE technology appraisal guidance 593.

In progress

Neratinib for treating early hormone receptor-positive HER2-positive breast cancer after adjuvant trastuzumab. NICE technology appraisal guidance. Publication expected November 2019

Atezolizumab for untreated, locally advanced or metastatic, triple negative, PD-L1 positive breast cancer. NICE technology appraisal guidance. Publication expected November 2019

Palbociclib in combination with fulvestrant for treating advanced, hormone-receptor positive, HER2-negative breast cancer after endocrine therapy. NICE technology appraisal guidance. Publication expected December 2019

Alpelisib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative, PIK3CA-positive breast cancer. NICE technology appraisal guidance. Publication expected December 2020

Entinostat for treating hormone receptor-positive breast cancer after hormonal therapy. NICE technology appraisal guidance. Publication date to be confirmed

Taselisib for previously treated ER-positive, HER2-negative, PIK3CA-positive breast cancer in postmenopausal women. NICE technology appraisal guidance. Publication date to be confirmed

Veliparib for treating HER2-negative, BRCA-positive breast cancer. NICE technology appraisal guidance. Publication date to be confirmed

Talazoparib for treating BRCA 1 or 2 mutated advanced breast cancer after prior chemotherapy. NICE technology appraisal guidance. Publication date to be confirmed

Pembrolizumab in combination with chemotherapy for neoadjuvant treatment of triple negative breast cancer. NICE technology appraisal guidance. Publication date to be confirmed

Trastuzumab emtansine for adjuvant treatment of HER2-positive breast cancer. NICE technology appraisal guidance. Publication date to be confirmed

Details of new technologies

No additional commercially available technologies or in-house NHS tests were identified.

Registered and unpublished trials

Trial name and registration number	Details
Medico-economic Study of Three Strategies of Sentinel Lymph Node Analysis in Operable Breast Cancer (SAGE) Clinicaltrials.gov identifier NCT02056886	An economic study of OSNA compared to histopathology in patients treated for invasive breast carcinoma (n=859) at a single institution in France. Cost comparisons will be made over a 9-month time horizon to incorporate the surgery, hospitalisation and follow-up. Due to complete January 2023.
Unlisted trial – details provided by Princess Alexandra Hospital NHS Trust (developer of the in-house Metasin test) [redacted]	[redacted]
Unlisted trial – details provided by Princess Alexandra Hospital NHS Trust (developer of the in-house Metasin test) [redacted]	[redacted]

Studies that aim to evaluate results from intraoperative tests as prognostic markers to aid treatment planning are not listed.

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Ruano MA, Lopez-Bonet E, Buxo M, et al. (2014) An improved axillary staging system using the OSNA assay does not modify the therapeutic management of breast cancer patients. *Scientific reports* 4:5743.

Sai-Giridhar P, Al-Ramadhani S, George D, et al. (2016) A multicentre validation of Metasin: A molecular assay for the intraoperative assessment of sentinel lymph nodes from breast cancer patients. *Histopathology* 68(6):875-87.

Shimazu K, Tanei T, Tamaki Y, et al. (2019) Performance of a new system using a one-step nucleic acid amplification assay for detecting lymph node metastases in breast cancer. *Medical Oncology* 36(6):54.

Smith GJ, Hodges E, Markham H, et al. (2017) Evaluation of the Metasin assay for intraoperative assessment of sentinel lymph node metastases in breast cancer. *Journal of Clinical Pathology* 70(2):134-9.