Minimizing inequality in access to precision medicine in breast cancer by real-time population-based molecular analysis in the SCAN-B initiative

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Background: Selection of systemic therapy for primary breast cancer is currently based on clinical biomarkers along with stage. Novel genomic tests are continuously being introduced as more precise tools for guidance of therapy, although they are often developed for specific patient subgroups. The Sweden Cancerome Analysis Network – Breast (SCAN-B) initiative aims to include all patients with breast cancer for tumour genomic analysis, and to deliver molecular subtype and mutational data back to the treating physician.

Methods: An infrastructure for collection of blood and fresh tumour tissue from all patients newly diagnosed with breast cancer was set up in 2010, initially including seven hospitals within the southern Sweden regional catchment area, which has 1.8 million inhabitants. Inclusion of patients was implemented into routine clinical care, with collection of tumour tissue at local pathology departments for transport to the central laboratory, where routines for rapid sample processing, RNA sequencing and biomarker reporting were developed.

Results: More than 10 000 patients from nine hospitals have currently consented to inclusion in SCAN-B with high (90 per cent) inclusion rates from both university and secondary hospitals. Tumour samples and successful RNA sequencing are being obtained from more than 70 per cent of patients, showing excellent representation compared with the national quality registry as a truly population-based cohort. Molecular biomarker reports can be delivered to multidisciplinary conferences within 1 week.

Conclusion: Population-based collection of fresh tumour tissue is feasible given a decisive joint effort between academia and collaborative healthcare groups, and with governmental support. An infrastructure for genomic analysis and prompt data output paves the way for novel systemic therapy for patients from all hospitals, irrespective of size and location.

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Introduction

Breast cancer heterogeneity is a well recognized concept, with implications for clinical decision-making related to systemic adjuvant and palliative therapy. Its description has evolved from a simplistic distinction of tumour steroid hormone receptor levels (hormone sensitive versus insensitive) into a refined molecular classification based on gene expression (GEX) patterns, as described by Perou and colleagues in 20001. The introduction of endocrine therapy to patients with hormone-sensitive tumours has improved the prognosis for those with endocrine responsive breast cancer2. Moreover, systemic polychemotherapy in the adjuvant setting has led to an increased cure rate and prolonged survival for the majority of patients with breast cancer who have node-positive and/or high-grade disease, despite the lack of a specific predictive biomarker3. Amplification of human epidermal growth factor receptor 2 (HER2) was recognized decades ago as an important factor...
associated with dismal outcome. With the subsequent introduction of adjuvant HER2-targeted therapy in the mid-2000s, the prognosis for patients with HER2-positive disease has become as favourable as that of patients without this genetic aberration, and the development of different HER2-directed therapies has much improved outcome even in metastatic HER2-positive disease.

In the clinical setting today, all newly diagnosed breast tumours are routinely characterized by immunohistochemistry for the treatment predictive biomarkers oestrogen receptor (ER), progesterone receptor (PR) and HER2, along with cell proliferation marker Ki-67 and Nottingham histological grade (NHG), and presented to a multidisciplinary conference that gives recommendations on postoperative locoregional and systemic therapy for individual patients. All these markers can be combined into the St Gallen molecular subtype system, a surrogate for the initial Perou–Sørlie classification of breast cancer, into luminal A-like, luminal B-like HER2-positive, luminal B-like HER2-negative, HER2-enriched and triple-negative subgroups. Today, the St Gallen algorithm is used in clinical decision-making, albeit imperfectly, to guide recommendations for adjuvant systemic therapy based on predictive biomarkers and risk of relapse. A question still of intense debate is the cut-off between luminal A- and luminal B-like HER2-negative disease. It is presumed that a substantial number of these women, either node-negative or -positive, treated with endocrine therapy for 5 years have a very low risk of distant recurrence and should be spared overtreatment with the addition of adjuvant chemotherapy. The choice is often made on the basis of fraction of nuclear staining of Ki-67. This distinction may be improved by multigene molecular assays, which are now being validated in large prospective studies. In many areas of the world, these specific multigene assays are already being applied in the decision-making process.

In Sweden, immunohistochemical in situ hybridization assessment of ER, PR, Ki-67 and HER2 is now mandatory for all patients with breast cancer, and reports on these biomarkers should be delivered within a short time frame according to national guidelines. Compliance with these recommendations is monitored by the National Swedish Quality Register on Breast Cancer (INCA). However, no laboratory-derived or commercially available genomic test has been approved by the Swedish National Board of Health.

In addition to tumour-related biomarkers, inherited germline mutations in breast cancer susceptibility genes, most notably BRCA1 and BRCA2, are gaining interest in the evaluation not only of families seeking an explanation for the occurrence of a familial aggregation of breast cancer, but also for optimal surgical and potentially medical management of incident breast cancer. Finally, circulating tumour markers such as circulating tumour cells and cell-free circulating tumour DNA are about to enter the clinical arena in breast cancer management.

This article describes the initiation and implementation of SCAN-B, a large and expanding population-based effort prospectively including all new patients with breast cancer from southern Sweden and beyond, with the aim of exploring and implementing new prognostic and predictive biomarkers in routine clinical care of breast cancer.

Methods

Early partnership between departments of surgery and experimental oncology

The Department of Oncology at Lund University began assessing hormone receptor status and flow cytometric S-phase fraction in fresh tumour tissue in the late 1970s. The assessment was implemented into clinical routine in the catchment area of the South Swedish Health Care Region, and paved the way for adjuvant clinical trials on the efficacy of adjuvant tamoxifen administered by the South Swedish Breast Cancer Group (SSBCG). In parallel with other national and international collaborative groups, the SSBCG was established in 1977 as a collaborative group between surgical departments at 15 hospitals as well as oncologists, pathologists and radiologists, with the goal of reducing inequality in delivery of care and promoting clinical trials of adjuvant therapy. In the early 2000s, routine analysis of hormone receptor status was shifted towards immunohistochemistry performed in the departments of pathology, and clinical trials were no longer undertaken by professional collaborative groups. The SSBCG continued its mission to promote best clinical care and diagnostics for patients, and supported continuous collection of fresh tumour material in its biobank for future diagnostics and as a research resource. Over time, new molecular techniques were set up in the Department of Oncology and introduced in a clinical setting. This was followed by early routine screening of inherited BRCA gene mutations in familial breast and breast–ovarian cancer. Such screening remains a national activity, but today these mutations are assessed by next-generation sequencing (NGS) methods. In parallel, new methods and bioinformatics tools for tumour characterization were introduced, including microarray and NGS for genomic and GEX profiling. However, facing the challenges of translating the new molecular tumour biomarkers into the clinic, the focus of the department remained on academic research rather than routine clinical analysis.
Formation of SCAN-B

Having undertaken a number of studies\textsuperscript{27–36} that generated experience and data from genomic and GEX-based classification of primary breast cancers, in 2009 the academic group in Lund and the SSBCG formed SCAN-B, an initiative to move these analyses closer to today’s patients and eventually into routine clinical practice\textsuperscript{17}. The mission was that all patients with newly diagnosed breast cancer would be offered these analyses within the clinical context, and that the analysis should be performed on the most modern platforms (NGS) using fresh (not formalin-fixed) tumour tissue samples in order to utilize the full potential of deep sequencing (Fig. 1). To be clinically meaningful, sampling and shipping of fresh tumour specimens was proposed to be continuous and in real time, and fully integrated into ordinary surgical and pathological practices, with delivery of the results from the analysis to the clinician at the time of the postoperative conference. The initial research programme for the SCAN-B initiative included consecutive retrieval of fresh tissue, and preoperative and postoperative blood samples.

The SSBCG acknowledged the initiative in 2009. The initiative had to be considered as a research project open to all patients with breast cancer. Ethical approval was given in 2009 and all (now centralized to 7) surgical departments in the South Swedish Health Care Region agreed to put necessary resources at hand for the project. Funding of technical equipment and reagents was granted by the Mrs Berta Kamprad Foundation, which provided a stable basis for the initial years of operation.

In the same interval, six regional cancer centres (RCCs) were established in Sweden to improve cancer care and clinical development\textsuperscript{38}. In 2010, the counties within RCC South, identical to the catchment area of the SSBCG, reached a decision and economic agreement that systematic biobanking of blood and unfixed tumour tissue from all consenting patients with cancer should be implemented as a support for clinical cancer research. To support this, an infrastructure for blood and tumour tissue collection and storage was established at all major hospitals in southern Sweden. This infrastructure was not limited to breast cancer research, and has also been implemented for other cancer diagnoses such as lung cancer\textsuperscript{59}. The decision and support of the regional governing body were instrumental in implementation of the same routines across a large geographical area, encompassing seven major hospitals and covering a population of 1.8 million (Fig. 1).

The start of this project was thus a fruitful partnership between enthusiastic researchers, an established collaborative group, seven hospitals, an important funding body and the regional governing body.

Early implementation of the SCAN-B initiative

After receiving approval from the Ethics Committee at Lund University, the SCAN-B steering group was formally constituted and a general start-up meeting was held for all clinical personnel related to breast cancer care, followed by separate start-up meetings at each of the participating hospitals. A project coordinator responsible for providing practical support to the enrolling centres was appointed.

As part of daily clinical routine, information about the project is provided to all patients with newly diagnosed breast cancer, with the help of specialist breast nurses, and the surgeon explaining the project and collecting the consent forms at the time of diagnosis. For patients receiving preoperative treatment, the corresponding procedure is carried out by oncology nurses and medical oncologists. After obtaining consent, specific SCAN-B referral forms are included with the patient’s documents. All written informed consent forms are sent to the project coordinator, who also deals with retraction of consent. A customized laboratory information management system (LIMS), BioArray Software Environment (BASE), has also been established to enable description of the representativeness of the population-based sample, as well as routines for the retraction of informed consent\textsuperscript{40–41}. The project is registered at clinical trials.gov (NCT02306096).

Implementation in the departments of pathology was instrumental for initiation of the project. Personal demonstration and coaching was carried out in all seven departments by the leading pathologist Dorthe Grabau and at regular meetings for breast pathologists. The breast specimen is delivered fresh on cooling wrap from the operating theatre to the department of pathology, with the SCAN-B referral form as a separate document. Common routines have been established at all departments of pathology as a consequence of the regional support of biobanking. Pieces of tumour are taken by the breast pathologist before fixation, if it is certain that this will not compromise the routine diagnostic work. One or several pieces (maximum $5 \times 5 \times 5$ mm) are placed in a microtube with RNAlater\textsuperscript{TM} (Invitrogen/Thermo Fisher Scientific, Carlsbad, California, USA), a solution optimized for preserving RNA and DNA, and stored in a refrigerator until shipment. If there is sufficient extra tumour material, fresh pieces are also taken and stored at $\sim 80$ °C. Preservation of tissue in RNAlater\textsuperscript{TM} allows regular transport from geographically distant sites in cool bags, between all pathology laboratories and the SCAN-B laboratory in the Department of Oncology in Lund. For patients eligible for neoadjuvant treatment, ultrasound-guided core needle biopsies are taken before the start of treatment and preserved in RNAlater\textsuperscript{TM}. If there is viable tumour left
in the final surgical specimen, new samples are collected. A subprotocol (referred to as preoperative SCAN-B) has been implemented at the largest study site (Malmö); patients receiving neoadjuvant chemotherapy are invited to participate in a project where serial blood samples are collected for analysis of circulating tumour markers before and during chemotherapy, as well as around the time of surgery and during follow-up. These patients are also asked to provide a second ultrasound-guided tumour biopsy after two treatment cycles to assess early signs of response in the tumour tissue.

To support the infrastructure for blood collection, routines for centrifugation, aliquoting and storage of samples at –80 °C have been established at all major hospitals.
in southern Sweden. After consenting to the SCAN-B study, the patients can go to the central unit in the hospital for blood tests and biobank samples can be drawn at the same time as blood samples for regular clinical analyses. The biobank samples are centrifuged, aliquoted and stored at \(-80^\circ\text{C}\) within 2 h after blood was drawn, providing a common standard for sample handling across the region.

The initial phase of SCAN-B study implementation was followed by regular reports and feedback at biannual regional meetings in which data were presented on the inclusion of patients and fraction of tumours assessed. Importantly, the project coordinator was also available on a hotline basis to address issues as needed.

Next-generation sequencing and library preparation

It was decided in 2009, during the early planning phase of the SCAN-B laboratory, to invest in the new and evolving NGS technology instead of microarray technology, the state-of-the-art technique for GEX analysis at that time. That choice resulted in an initial need to establish new instrumentation, computer capacity and sequencing library protocols that could be kept stable over an extended period for analysis of large cohorts of samples. Importantly, the LIMS and data processing and tracking system (BASE and Reggie\(^{40-42}\)) was instrumental in allowing the cost-effective and continuous processing of biopsies, as well as data storage, analysis and reporting. Tumour biopsies shipped in RNAlater\(^\text{TM}\) began to arrive in the laboratory in September 2010, and within a few months reached full volume from all seven participating sites.

Once registered, biopsies are divided; one part is used for extraction of RNA, DNA and flow-through (available for further processing and to permit isolation of soluble proteins), whereas an adjacent part is formalin-fixed and paraffin-embedded (FFPE), and placed in a small tissue microarray block to permit histopathological and cellularity examination; any remaining fresh tissue is stored frozen. An RNA aliquot from each sample is immediately processed using a directional dUTP library protocol, and further sequenced to a depth of approximately 30 million paired-end reads using a HiSeq\(^\text{TM}\) or NextSeq\(^\text{TM}\) instrument (Illumina, San Diego, California, USA). BASE enables well structured and curated data and biomaterial collections to be maintained, and provides continuous and automatic data management and analysis of raw sequence data, including demultiplexing, filtering, alignment and transcript quantification, as well as tools for biomarker result presentation.

Since the autumn of 2015, the SCAN-B initiative has continuously processed and subjected tumour biopsies to RNA sequencing (RNA-seq) in real time, with a turnaround time of less than 7 days from arrival of a sample to generation of a summary RNA sequencing GEX report. Routine clinicopathological data along with follow-up data are captured regularly from the INCA register. INCA is run and funded by the healthcare sector in collaboration with the RCC in each region, and includes all patients with breast cancer from 2009 onwards\(^{16}\), the majority of whom participate in SCAN-B. Research nurses have been recruited to collect comprehensive data on recurrences and recurrence-free status, as well as compliance with treatment.

Results

Prospective collection of tumour material, blood and clinical data

By April 2017, 6–7 years after the start, SCAN-B had included more than 10 000 patients, a resource that continues to expand at an accelerated rate as more hospitals in Sweden join the study (including Uppsala since 2013 and Jönköping since 2015). Very few invited patients decline participation; although some are lost, mainly owing to language barriers, the inclusion rate still reaches an average of 90 per cent or more of invited patients at most sites, showing the tremendous support and willingness of healthcare personnel and patients to contribute towards research. A preoperative blood sample is received from almost all participants; since 2012, patients have also been asked to provide a follow-up blood sample after 6, 12 and 36 months, and approximately 60 per cent comply. One or more samples of fresh tumour tissue are collected as described above from around 70 per cent of participants. The main reason for lack of sample is the tumour being too small to sample without jeopardizing routine pathology (less than 5 mm) or macroscopically poorly defined. It is clear that the cohort of accrued patients and available tumour tissue is a good representation of patients diagnosed in the catchment area (data from the cancer quality registry), with respect to most pathological data and clinical biomarkers, except for tumour size and grade (Fig. 2\(^\text{37}\)). Smaller tumours (and lower-grade lesions) are undersampled because pathologists prioritize available tissue to the routine clinical diagnosis. To date (September 2017), more than 7 500 tissue specimens have been processed and high-quality mRNA-seq data obtained from approximately 90 per cent of samples (Fig. 3). This material represents a unique consecutive and contemporary population-based cohort of patients with primary
Real-time population-based molecular analysis in breast cancer

| Year | Patients | With specimen |
|------|----------|---------------|
| 2011 | 1111     | 904 (81·4%)   |
| 2012 | 1077     | 866 (80·4%)   |
| 2013 | 1202     | 952 (79·2%)   |
| 2014 | 1357     | 986 (72·7%)   |
| 2015 | 1394     | 1028 (73·7%)  |
| 2016 | 1358     | 985 (72·5%)   |
| Total| 7499     | 5721 (76·3%)  |

a SCAN-B enrolment (1 January 2011 to 31 December 2016)

b SCAN-B accrual for catchment area

Oestrogen receptor status

Nottingham histological grade

Tumour size

Age at diagnosis

Lymph node status

Type of surgery

Fig. 2 SCAN-B enrolment statistics, and representativity of enrolled patients and sampled tumours. a Number of enrolled patients with operable invasive primary breast cancer by calendar year for 2011–2016 (partial years 2010 and 2017 not shown) and number of cases for which a preoperative untreated tumour specimen was received and processed for analysis. b Proportion of all operable invasive primary breast cancer diagnoses in the catchment area that were not accrued, accrued but without a tumour specimen or accrued with a specimen. The statistics are restricted to the original seven hospital sites where enrolment was fully operational by early 2010. c–h Bar graphs illustrating the distribution of clinicopathological characteristics for all operable invasive primary breast cancer diagnoses, all patients accrued in SCAN-B, and all patients accrued and with a processed tumour specimen: oestrogen receptor status (c), Nottingham histological grade (d), tumour size (e), age at diagnosis (f), lymph node status (g) and type of breast surgery (h)
Inclusion and sampling for SCAN-B is fully integrated into healthcare.

**Pathology**

Breast surgery

Inclusion and sampling

**Formalin**

Fresh tissue

Histological check of cellularity

**RNAIater™ SCAN-B**

Tissue homogenization

DNA/RNA extraction

**RNA pool**

**DNA pool**

RNA sequencing of all ~20,000 genes: activity, gene signatures, cell signalling, proliferation, etc.

Gene signatures for ER, PR, HER2, Ki-67, Nottingham histological grade, molecular subtype

**Fig. 3** Schematic illustration of the work flow from inclusion and surgical excision to output data via RNA/DNA extraction. ER, oestrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2
breast cancer for transcriptome biological and clinical studies, which will gain further in value with increasing size and follow-up time. It accomplishes one of the major goals of the SCAN-B initiative: a resource that will be shared publicly but needs continuous support to evolve optimally.

Use of SCAN-B output

The first clinical output from SCAN-B was used in a sub-project called BRCAs: BRCAsearch. This included patients from three study sites; 818 consecutive and newly diagnosed patients included in SCAN-B were offered screening for germline mutations in BRCA1 and BRCA2, after written genetic counselling with the possibility of telephone support. The clinical routine for BRCA testing in early breast cancer is currently being updated with BRCAs: BRCAsearch as the model.

Second, to verify the applicability and practicality of clinical implementation of GEX-derived molecular subtypes, a pilot test was started in late 2015. During a 4-month interval at a single participating central hospital, results of RNA-seq analysis presented in a specific document were reported to the multidisciplinary team meetings for 134 patients. The median interval between surgery or biopsy and reporting back the SCAN-B result was 7 days, and in no case was the multidisciplinary conference delayed because of missing RNA-seq data. In this pilot, the RNA-seq result was not used for clinical decision-making.

Third, in a validation project, a retrospective set of 405 specimens from patients with breast cancer underwent extensive conventional staining and evaluation for the five main biomarkers for early breast cancer (ER, PR, HER2, Ki-67 and NHG) in order to train GEX-based determinations of the clinical biomarkers. The GEX-based determinations were similar to those made by a pathologist, with the highest agreement for ER, PR and HER2, and somewhat lower agreement for NHG and Ki-67 (Fig. 3). Using the GEX-based determination on a large SCAN-B cohort with follow-up data, a group of patients could be identified in whom the conventional immunohistochemical determination and the GEX-based findings were inconsistent. The group with hormone receptor-positive disease determined by conventional immunohistochemistry, but for whom the GEX RNA-seq predictors indicated a non-endocrine responsive phenotype, had significantly poorer survival on adjuvant endocrine therapy alone than patients with a concordant endocrine responsive phenotype, indicating that these patients might benefit from the addition of adjuvant chemotherapy (L. H. Saal, unpublished observation).

Discussion

Developments in molecular biology over recent decades have shed light on the fundamental heterogeneity of breast cancer, and have had an immense effect on understanding the biology of the disease. Several of these aspects of breast cancer biology and new diagnostic techniques have already entered the clinical arena from prevention to palliative care, whereas others are still not ready for clinical use. The expanding team of clinicians and researchers involved in the SCAN-B initiative are working towards the goal of building a national consensus on how to introduce new NGS-based tests into routine healthcare, as well as guidelines on how these new biomarkers are used in breast cancer care. A key to minimizing inequality in healthcare is to establish routines that are suitable for smaller and geographically remote hospitals, but also to engage all participants in collaborative research and clinical studies.

The SCAN-B study was initiated with the main long-term goal of developing new tumour biomarkers for more precise diagnosis, prognostication and selection of adjuvant systemic treatment. Besides creating a large cohort of patients with tumour RNA-seq data for biomarker generation and validation, this project has included efforts to create infrastructure and build consensus, based on clinical validity and utility, among researchers and healthcare personnel for implementation of these biomarkers in routine clinical practice. SCAN-B is facing challenges from competing commercial GEX assays, some of which are gaining ground in other countries. These early tests build on rather simple gene signatures originally obtained from small patient cohorts, or conventional gene sets, but have been developed into robust assays suitable also for FFPE tissue; they have been validated retrospectively and prospectively in large cohorts. Such tests have obtained recommendations from international breast cancer organizations, but provide guidance for a defined purpose and specific types of breast cancer. It is plausible that the results from global RNA-seq resources such as SCAN-B will be able to provide biomarkers of equal or better performance than the current commercial alternatives, for all types of breast cancer and at a much lower cost. Implementation into routine clinical practice, however, requires data on clinical validity and utility for SCAN-B biomarkers compared with clinical biomarkers. This important step is addressed in specific subprotocols. Importantly, because RNA-seq provides sequence and information on driver and druggable gene mutations, data from the same sample run can also be used with a short turnaround time for prediction of targeted treatment. Combined with DNA-seq for genome
and epigenome characterization, as well as tissue quality control, SCAN-B can provide a comprehensive survey that reaches the demands of future precision medicine.

**BRCA** analysis is expanding from the context of familial breast cancer to include non-familial and eventually all newly diagnosed cases, **BRCA** status having an emerging role in the choice of surgery and postoperative treatment. This is being achieved by the development of new sensitive methods for high-speed and low-cost screening in larger sample volumes, including not only **BRCA1** and **BRCA2**, but also **PALB2** (partner and localizer of **BRCA2**) and other clinically validated breast cancer susceptibility genes. These methods should be suitable for screening of tumour tissue in order to identify somatically acquired mutations, **BRCA** status being important for choice of chemotherapy. In parallel, new biomarkers of homologous recombination deficiency (a hallmark of **BRCA**-mutated tumours) are being developed from genome sequencing data, potentially defining a larger subgroup of breast cancers with favourable response to certain types of chemotherapy. The SCAN-B resources and network offer unique possibilities to evaluate these new tests and introduce them into the clinic.

Currently, a large-scale prospective clinical evaluation of the GEX-based determination of endocrine responsiveness is planned in order to assess its clinical validity and utility based on the SCAN-B study. Other ongoing projects include: the development of prognostic profiles specific for the HER2-positive and triple-negative subtypes of breast cancer; the analysis of endocrine responsiveness in patients with ER-low breast cancer (1–10 per cent of nuclei stained positive for ER); comparisons of GEX-based subtyping between core needle biopsies and surgical specimens from patients not undergoing neoadjuvant chemotherapy; the effect of preoperative chemotherapy on GEX patterns after two and six cycles of chemotherapy; and somatic mutational profiles in early breast cancer.

In addition, a second large step in terms of infrastructure and interaction between the clinic and the translational researchers is currently being taken in the context of recurrent breast cancer; this involves building on the established infrastructure for consecutive inclusion and NGS-based diagnostics, including analysis of tumour tissue and circulating tumour markers. After providing informed consent, patients with advanced disease will be invited to participate in research on NGS-based GEX using FFPE tissues as well as those collected in RNAlater™. Finally, participation by any hospital in Sweden or the Nordic countries is still encouraged provided that they can maintain the enrolment, tissue sampling and handling standards.

The SCAN-B initiative is a large population-based academic project run in close collaboration between public healthcare providers, a professional collaborative group and academia. Over more than 6 years, more than 10 000 patients have successfully been included in the project, creating a platform for a broad range of translational research activities and facilitating the transition of actionable research results into clinical healthcare. The future close collaboration between healthcare providers and academics will facilitate dissemination of SCAN-B-derived results to all treating physicians in the catchment area. It is anticipated that SCAN-B results will be used clinically, with implications for the choice of surgical procedure based on **BRCA** status, recommendations on adjuvant therapy for luminal-like tumours and paving the way for the rapid introduction of novel targeted therapies. All patients included in the SCAN-B initiative can benefit from the shift in decision-making tools, minimizing inequality in access to precision therapy.

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