



New Zealand experience with implementation of the ESO-ESMO consensus guidelines for advanced breast cancer-report of achievements and lessons learned

M.J.J. Kuper-Hommel^{a,*}, Z. Little^b, A. Gautier^c

^a Department of Oncology, Waikato District Health Board, Private Bag 3200, Hamilton, 3240, New Zealand

^b School of Psychology, Victoria University of Wellington, New Zealand

^c Breast Cancer Foundation NZ, PO Box 99650, Newmarket, Auckland, 1149, New Zealand

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ABSTRACT

Background: People with advanced breast cancer (ABC) in New Zealand (NZ) have a poorer five-year survival than their peers in other developed countries. Comparisons of ABC care in NZ with other countries suggest that NZ is sometimes out of line with international standards and that inequities exist within the NZ healthcare system. Our aim was to develop nationwide consensus guidelines for diagnosis and treatment of ABC that are uniquely suited for the NZ context and can be applied across the nation. We describe the process of creating, voting on, and disseminating the guidelines, and provide insight into how we can better optimize these processes for the NZ context in the future.

Methods: The ABC5 ESO-ESMO consensus guidelines were used and adapted to the NZ clinical context. A panel of breast cancer clinicians voted on these guidelines using the same model of membership representation as ABC5. **Outcome:** Overall consensus was equally high between ABC5 and ABC-NZ. Four NZ specific guidelines were introduced. The European-style panel discussion needs some adaptations for the NZ situation and a wider and more thorough consultation process, before voting begins, is preferred. The NZ Breast Special Interest Group has endorsed and agreed to take ownership of these and future guidelines and to facilitate the next iteration of the ABC-NZ guidelines meeting.

Conclusions: The process was successful in creating the guidelines but can be improved in future meetings to streamline the process of creating and updating guidelines in the manner most suited to the NZ context and audience.

1. Background

Every year, around 350 people in New Zealand (NZ) will be diagnosed with advanced breast cancer (hereafter, ABC). People with ABC in NZ have a lower five-year survival than their peers in other developed nations, as median survival after an ABC diagnosis is 16 months. Five-year survival after metastatic diagnosis is only 5% in Māori populations, compared to 15% in non-Māori populations [1].

Some key areas of difference between ABC treatment in NZ and elsewhere have been identified. For one, healthcare professionals reported in 2018 that they lack publicly funded access to many of the latest medicines that are available in other nations [1] (since then, a HER2-targeted antibody-drug conjugate and a CDK4/6 inhibitor have

been funded). In NZ, there is no funding for re-trying previously failed HER2-targeted therapies, or continuing with HER2-targeted therapies after disease progression, two strategies that are commonly used overseas. International data also suggests that many patients can benefit from more than three lines of therapy. A 2018 report showed that only around 15% of NZ patients had received more than three systemic therapies [1].

These comparisons suggest that ABC care in NZ is out of line with international standards and is applied inconsistently across patients within NZ.

The problems experienced in NZ align with those identified as key actions for change by the ABC Global Alliance – including the need to improve quality of life, increase the availability of care from

* Corresponding author.

E-mail addresses: Marion.kuper@waikatodhb.health.nz (M.J.J. Kuper-Hommel), zoe.little@vuw.ac.nz (Z. Little), adeleg@nzbcf.org.nz (A. Gautier).

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multidisciplinary teams, and improve access to care regardless of patients' ability to pay [2]. These could potentially be addressed by adapting international ABC guidelines into a set of clear, nationwide guidelines on the diagnostic process and treatment of ABC that are uniquely suited for the NZ context and can be applied across the nation. Healthcare professionals have already suggested that there is a lack of awareness of or adherence to any treatment guidelines and that this may allow for suboptimal care and less ambitious treatment plans for ABC patients in NZ [1].

There are many possible benefits of having a clear set of national guidelines for the best treatment of ABC. Physician compliance with consensus recommendations is associated with improved survival of patients with breast cancer ([3,4]). Where guidelines exist, around 90% of physicians are likely to take them up [4]. Clear guidelines that are made accessible to patients may also help those with low health literacy to understand treatment options and make truly informed decisions [1]. Importantly, national guidelines that take into account socio-economic, cultural, geographical, and racial factors are crucial to making any consensus guidelines applicable and truly useful [5].

In November 2020, the first ABC-NZ consensus meeting was held in Wellington, NZ. In the previous year, representatives from NZ attended the international ABC conference (ABC5) in Lisbon for the first time. The format of the ABC-NZ meeting and guidelines was modelled on ABC5 [6]. The meeting was planned with the input and support of Dr Fatima Cardoso, the initiator and chair of the ESO-ESMO ABC guidelines group. Here we describe the process of creating, voting on, and disseminating the guidelines, and provide insight into how we can better optimize these processes for the NZ context in the future.

2. Method

2.1. Guideline creation

We selected 112 of the international ABC5 statements that were applicable to the NZ context. For our first set of guidelines, the criteria for inclusion were that the guideline is universally applicable to the NZ clinical practice and that recommended technologies and therapies are routinely available. We also created four new guidelines to meet needs relevant to ABC care in NZ. New guidelines are reported in Table 1.

2.2. Panel members

The panel had 20 members and was chaired by a medical oncologist (MK). The panel included nine medical oncologists, two breast surgeons, two radiation oncologists, two breast pathologists, one general practitioner/breast physician, one ABC Clinical Nurse Specialist, one Breast Cancer Research & Advocacy manager, two ABC patients and one palliative care physician (for the palliative care & integrative guidelines only). The makeup of this panel was designed to include representatives from different specialities involved in the diagnostic and therapeutic aspects of ABC care and used the same model of membership representation as ABC5. The panel included no breast radiologists due to time conflicts and did not include a geneticist or a psychologist.

The panel was designed to represent all cancer centres within NZ. The panel included representatives from all eight regional cancer centres within New Zealand and the number of representatives on the panel from each centre reflected the size of the centre.

2.3. ABC-NZ meeting

The ABC-NZ meeting took place at the Breast Cancer InSIGHTs conference held in Wellington, NZ, in November 2020.

Three weeks before the meeting, the 105 statements extracted from ABC5 along with 4 NZ-specific developed guidelines were circulated to the panel members. Panel members were asked to provide comments and feedback on the guidelines, as well as submitting their initial votes

Table 1

New guidelines created for ABC-NZ.

Section	Guideline statement	Consensus	Abstains
III. Assessment and general treatment guidelines	Preferred staging modality is CT imaging of chest, abdomen, and pelvis. A bone scan is only done for confirmation if CT imaging shows suspicious bone lesions.	89%	5%
VIII. Precision medicine	In patients with advanced/recurrent TNBC, TILs should be quantified (using light microscopy from a recent metastatic biopsy or from the primary).	63%	11%
VIII. Precision medicine	In patients with advanced/recurrent TNBC, PD-L1 status (assays SP142 Ventana assay >1% or more) should be assessed as well.	78%	22%
IX. Specific sites of metastases	For palliative radiation of an uncomplicated* symptomatic bone metastasis, a single 8 Gy fraction is recommended. ^a *Uncomplicated is no impending fracture or no spinal canal involvement and without significant neuropathic involvement.	74%	26%

CT, computed tomography; TILs, tumour-infiltrating lymphocytes; TNBC, triple-negative breast cancer. Percentages for "Disagree" votes have been left out of this table.

^a This is a national practice specified in an agreement between all radiation oncologists in New Zealand and is monitored as a KPI. It was introduced to create more consistency between private oncologists, who are paid per fraction, and public oncologists.

via email. Panel members also received a copy of the full ABC5 guidelines as supportive documentation for reference use. Panel members were asked to avoid abstaining from any vote if possible.

At the InSIGHTs meeting, panel members were able to attend presentations relevant to the guidelines they may have previously been unfamiliar with prior to the ABC-NZ voting session. At the ABC-NZ voting session, guidelines that had received 100% consensus from all 20 panel members were presented but not voted on. Statements that did not have 100% consensus prior to meeting, or had queries or comments raised by panel members, were discussed and voted on at the meeting.

Sixteen palliative care and supportive care guidelines were circulated to the panel members after the meeting and voted on by email. The chair (MK) wrote up the ABC-NZ guidelines for ratification by the Breast Special Interest Group; this took place in April 2021.

3. Results

The outcome of the meeting was the creation of 115 ABC-NZ guidelines for the treatment of ABC in New Zealand. Some of these guidelines, if implemented, would lead to significant practice changes in the treatment of ABC in NZ. For example, there was 100% consensus that "involvement of all specialities in a multidisciplinary team ... is crucial" (Section II). In NZ, multidisciplinary team meetings (MDM) are surgery-led; patients with *de novo* ABC may be presented at the MDM, but in some centres this is rare for patients with recurrent disease. There was 68% consensus for a guideline regarding biopsy of the metastatic lesion to identify biological discordance with the primary tumour (Section III), a practice which is at best inconsistent in NZ but has previously been recommended as a way to identify new lines of therapy for ABC patients [1]. There was also 100% consensus for considering "removal of the primary tumour in patients with *de novo* Stage Four breast cancer" "if this was required for local control" (Section III), another practice that is currently uncommon in NZ. The addition of this practice being used for

local control was made for ABC-NZ and was not in ABC5.

4. Discussion

4.1. Major comparisons to ABC5

The biggest difference between ABC-NZ and ABC5 is the introduction of four new guidelines (Table 1) that were required for the NZ context. The first states that “preferred staging modality is CT imaging of chest, abdomen, and pelvis. A bone scan is only done for confirmation if CT imaging shows suspicious bone lesions” (Section III). This guideline was introduced as CT imaging has become refined to the point of picking up bone lesions much better than a bone scan does. This practice has been adopted from the United Kingdom ([7,8]). The second states that “in patients with advanced/recurrent TNBC, TILs should be quantified ...” (Section VIII). This was added as PD-L1 testing in breast cancer is not easily available and is not funded in NZ, therefore quantification of TILs could be a good way to select candidates for unfunded immunotherapy with PD-(L)1 inhibitors [9–12]. We also added that “in patients with advanced/recurrent TNBC, PD-L1 status (assays SP142 Ventana assay >1% or more) should be assessed as well” [9] (Section VIII) to assess the willingness of physicians to use or request this test. Finally, we added a guideline recommending a single 8 Gy fraction for uncomplicated symptomatic bone metastasis (Section IX) to have our guidelines line up with recommendations made by radiation oncologists in NZ (as explained in Table 1) [13].

Other differences arise where ABC5 guidelines were reworded to more accurately describe the care available in NZ. For example, the ABC5 guideline “In ABC patients with long-standing stable disease or complete remission, breast imaging is an option” (Section II) became “the panel recommends that routine breast imaging is not undertaken in patients with ABC, even with long-standing, stable disease or complete remission”. The ABC5 guideline stating that the “Evaluation of response to therapy should generally occur every 2–4 months for [endocrine therapy] or after 2–4 cycles for [chemotherapy]” (Section III) was updated to specify evaluation after “3–4 cycles” of chemotherapy, to align with common practice in NZ. The ABC5 guideline recommending the “Use of an intrapleural catheter or intrapleural administration of talc or drugs” for malignant pleural effusions (Section IX) was amended to add that this should occur “after successful thoracentesis when the lung is fully expanded (not useful in case of a trapped lung or extensive pleural thickening)”.

We compared the degree of consensus reached for each guideline between ABC5 and ABC-NZ. Overall consensus was equally high between ABC5 (mean = 91%) and ABC-NZ (mean = 93%). The largest discrepancy in consensus between ABC5 and ABC-NZ was for the definition guideline stating that “Efficacy of [ovarian function suppression] must be initially confirmed analytically through serial evaluations of serum oestradiol, even in the presence of amenorrhea, especially if an [aromatase inhibitor] is administered” (Section I). This received 85% consensus by ABC5 but only 32% for ABC-NZ. In NZ, all endocrine interventions for premenopausal patients with endocrine-responsive ABC require indefinite OFS. Choosing one method over the other requires balancing the patient’s wish for potentially preserving fertility, compliance with frequent injections over a long period of time, and the risk of inadequate oestrogen level suppression and cost. As a result of the low consensus on this guideline we reworded an existing ABC5 guideline to simply state that “patients should be informed on the options of OFS/OFA and decisions should be made on a case by case basis,“. Another guideline that was endorsed much less by ABC-NZ (68%) than ABC5 (87%) is that regarding the biopsy of the metastatic lesion, which, as explained earlier, is not common practice throughout NZ.

Some guidelines were endorsed much more in ABC-NZ than ABC5. For example, the guideline defining primary and secondary (acquired) endocrine resistance (Section I) and the guideline specifying that “minimal staging workup for ABC includes a history and physical

examination, haematology and biochemistry tests, and imaging of chest, abdomen, pelvis and bones” (Section III) received 100% consensus by ABC-NZ and only 67% consensus by ABC5. Another definition statement, that defining oligo-metastatic disease as “low-volume metastatic disease with limited number and size of metastatic lesions (up to 5 and not necessarily in the same organ), potentially amendable for local treatment aimed at achieving complete remission status” was endorsed 100% by ABC-NZ and 78% by ABC5. Recently, identifying and treating oligo-metastatic disease with possible curative intent has become an area of increasing interest for some breast cancer clinicians in NZ, with stereotactic radiation techniques becoming more widely available across New Zealand. The guidelines stating that “removal of the primary tumour in patients with *de novo* stage IV breast cancer ... can be considered in selected patients with controlled systemic disease” and that “some studies suggest that surgery is only valuable if performed with the same attention to detail (e.g., complete removal of the disease) as in patients with early stage disease” (both Section III) received 100% consensus by ABC-NZ and only 70% consensus by ABC5. Otherwise, differences between the level of consensus to guidelines by ABC5 and ABC-NZ were small.

4.2. Dissemination of guidelines

The NZ Breast Special Interest Group membership includes senior medical and surgical breast cancer specialists and specialized breast nurses from all NZ cancer centres, along with representatives of advocacy non-governmental organisations; they are expected to relay the outputs of Special Interest Group meetings to their colleagues. The guidelines will be further disseminated in a direct communication (email or physical mail) to breast specialist medical officers and nurses. The guidelines will also be communicated to non-governmental organisations (including breast cancer support and advocacy organisations), Te Aho o Te Kahu (the NZ Cancer Control Agency), the Pharmaceutical Management Agency, and other stakeholders. They will also be submitted for publication to the websites of the NZ Ministry of Health and the Best Practice Advocacy Centre NZ (a primary care resource). Breast Cancer Foundation NZ will produce materials and modules for both individual patient use and for primary care. The guidelines will also be distributed at meetings and conferences within NZ, and various nurse meetings.

Around one third of breast cancer patients in New Zealand access treatment privately, either self-funded or through insurance, rather than through the national health system [1]. However, as 70% of breast cancer specialists working in public hospitals also work for private healthcare providers [14], guidelines that are encouraged within the public system should carry over to the private system. We will also make sure our guidelines are disseminated to private centres.

The role of the Breast Special Interest Group will be to endorse these and future guidelines, to officially take ownership of the guidelines, to nominate panel members for future meetings, and to facilitate the next iteration of the ABC-NZ guidelines meeting with the support of Breast Cancer Foundation NZ.

4.3. Future directions

As the guidelines are updated to continually reflect the availability of care and the standards of practice in NZ, the process of creating, voting on, and disseminating the guidelines can be informed by reflecting on which parts of the ABC-NZ process were successful and which could be improved.

One apparent issue is that too many guidelines were voted on within the single meeting at the InSIGhts conference and in too short a period pre-meeting. This can be improved at future meetings by voting on fewer guidelines disseminated with a longer lead-time before the meeting. Now that there exists an initial set of guidelines, in the future the only guidelines that will need to be voted on are: specific systemic therapies,

any updated or new international guidelines from the recent ABC6 meeting; guidelines related to symptom management that have not yet been reviewed; and, where appropriate, any changes that need to be made to existing ABC-NZ guidelines, including the addition of a guideline concerning the Treaty of Waitangi (Te Tiriti o Waitangi), the constitutional document that guides the relationship between the Crown and Māori (including the provision of health services). This reduction in votes required in future meetings should also improve the issue of some panel members being under-committed to the entire lengthy voting process, as some were not available to attend the entire meeting.

Indeed, the European-style panel discussion may not be suited to the NZ environment. The format was unfamiliar to many attendees, and with a high panel-to-audience ratio some people in the audience felt they should be part of the discussion. Future meetings may benefit from adopting a different meeting style that involves fewer topics of discussion with more room for debate around them. As an uncommon meeting format in NZ, this may also have been why some panel members were not prepared for the level of commitment the meeting would require. The processes and protocols for future meetings are to be documented in new Terms of Reference for approval by the Breast Special Interest Group.

In the future, a wider and more thorough consultation process will be initiated before voting begins. This process is currently in development but is likely to provide more opportunities for both clinicians and patient advocacy groups to provide feedback on the proposed guidelines before the meeting, for review by the Guidelines Panel. A wider consultation process will also address the concerns of some patients that their views were not represented in the current process. One of the disciplines not represented on the 2020 panel was breast radiology. In the future, a breast radiology advisory group will be invited to provide feedback on the proposed guidelines and be represented in the panel discussion.

The aim of the first iteration of ABC-NZ guidelines was to adapt the existing set of guidelines so that they would be applicable in NZ. For future iterations, the scope of the guidelines will be broadened to include statements ensuring that cancer treatment is delivered with respect to the principles of Te Tiriti o Waitangi and is equitable for Māori patients. This will be done with consultation from Hei Āhuru Mōwai – the Māori Cancer Leadership Group.

As the guidelines now reflect both what is common and what is possible in NZ, they should be more easily implemented by NZ clinicians. However, there are some foreseeable challenges involved in encouraging clinicians to implement these guidelines. While NZ is smaller in geography than other countries that have implemented ABC guidelines [15] and is a single health system [16], there will still be challenges involved in encouraging uptake of the guidelines across the country. With only six tertiary cancer treatment centres across the country, patients in rural areas currently have fewer options presented to them. These guidelines ought to encourage all ABC patients to be offered the same treatments, but there will be little point of this if a patient in a rural area cannot travel to receive the recommended treatments [1]. Strategies to ensure that all physicians, rural and non-rural, will feel able to take up these guidelines will need to be identified. Currently, different geographic areas in NZ are served by separate district health boards which make their own recommendations for care. For example, different health boards vary in the stage at which they offer palliative care; in one region, this is only when life expectancy reaches six weeks, which falls well short of what is recommended by the guidelines. As NZ transitions to a new, centralised healthcare system and disestablishes district health boards [17], physicians across regions will hopefully feel equally able to implement these guidelines. Under the new health system, specialist services will be managed in wider regional networks and expertise shared nationally through digital and virtual care, allowing for greater standardisation across the country [18].

Another consideration is how the efficacy of these guidelines will be assessed. Currently, data on breast cancer diagnoses, treatments, and mortalities is collected and in Te Rēhita Mate Ūtaetae, the Breast Cancer

Foundation National Register [19]. This is one of the world's most comprehensive collections of data on ABC diagnosis (*de novo* and recurrent) and treatment, with 99% of breast cancer cases now being recorded in the Register. Data from the Register is used to create regular reports on the state of ABC care in NZ [1]. Trends in this data will help us to identify the impacts of the ABC guidelines. Focused investigations and audits of practices comparing them to the guidelines will also demonstrate where the guidelines are being used and what effect this has. We also plan to provide oncologists and clinicians involved in advanced breast cancer care with contextualised feedback as they begin to adopt the guidelines, using data from the National Register to show them how they compare to other practices.

The international guidelines will be updated following the ABC6 meeting in Lisbon in November 2021. The next iteration of ABC-NZ guidelines will therefore be updated and voted on in 2022. We hope to provide access to recordings of ABC6 sessions on the latest developments relevant to the guidelines to the panel members to bring them up-to-date before voting. We are welcoming feedback and suggestions for the next meeting.

5. Conclusion

ABC-NZ was the first ABC meeting held in NZ and its output is the first set of guidelines attempting to define and reach consensus on best practice in the treatment of ABC across NZ. We endorse the ABC-NZ guidelines as an important step towards optimising ABC care and improving equity in NZ, with the ultimate goal of improving the quality and longevity of life of people with ABC in NZ. The above process was successful in creating the guidelines but can be improved in future meetings to streamline the process of creating and updating guidelines in the manner most suited to the NZ context and audience. We expect challenges in implementing these guidelines based on the unique geography of cancer care in NZ that we will aim to address in future meetings.

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