ABC-NZ

3rd New Zealand Consensus Guidelines for Advanced Breast Cancer (ABC-NZ3)

September 2025

Contents

Abbreviations guide:
TNBC = triple negative breast cancer
QoL = quality of life
CT = chemotherapy
ET = endocrine therapy
RT = radiation therapy

Introduction

Personal note from the chair of the Breast SIG

It is my true honour and pleasure to present this new set of clinical guidelines for the treatment of advanced breast cancer (ABC). These guidelines have been developed by the Breast Special Interest Group (Breast SIG), a group of passionate practitioners - doctors and nurses - specialising in the diagnosis and treatment of breast cancer, with the assistance of Breast Cancer Foundation NZ (BCFNZ). Our expert panel, including several patient advocates, produced these guidelines to be a framework for everyone involved in the management of ABC. They provide an evidence-based summary of what New Zealand clinicians consider is best practice to manage ABC, a complex disease requiring specialist care, if we are to help our patients live as long as possible with the best possible quality of life.

We want our patients to be informed about the expected standard of care when they are diagnosed with and treated for ABC, and want them to receive the best care, regardless of their ethnicity and their location of residence within New Zealand. We want all healthcare providers to be familiar with the expected standard of care that should be delivered to our patients. We want government health organisations to be up to date with what should be available and funded for New Zealand patients with ABC. As the standard of care evolves, these guidelines are a living document which will be updated every two years.

Dr Marion Kuper-Hommel
Chair of the Breast SIG and Specialist Medical Oncologist

Background

Consensus guidelines offer opinions or recommendations on management of a specific condition and are meant to encourage safe, high-quality, evidence-based patient care. While they constitute the general opinion of a group of experts, they are not necessarily a unanimous view of those experts (a percentage of agreement is published for each statement). The guidelines are not rules for clinicians to follow; rather, they are a snapshot of what their peers consider to be best practice.

The ABC-NZ guidelines are adapted for Aotearoa New Zealand from the international ABC guidelines in consultation with ABC Global Alliance chair Dr Fatima Cardoso. The voting panel was made up of New Zealand breast cancer experts including medical oncologists, radiation oncologists, breast surgeons, ABC clinical nurse specialists, GP/breast physician, patient advocates.

Our vision

To provide the best care to all patients in NZ with ABC, with equity of access, regardless of their ethnicity and their location of residence within NZ.

Our mission

For these guidelines to be endorsed and implemented by all stakeholders involved in management of ABC.

Important information about medicines

- If a **medicine is funded by Pharmac**, it is available for use in the public system. If a **medicine is not Pharmac-funded**, patients will need to pay for the medicine and usually for its administration in a private oncology clinic.
- For **medicines that are not Pharmac-funded but are approved by Medsafe**, patients with health insurance may be able to claim some of these costs against their policies. Medsafe approves medicines for specific uses, but they can also be used off-label for different conditions. **Medicines that are neither Pharmac-funded nor Medsafe-approved** may still be prescribed to patients by clinicians under section 29 of the Medicines Act.
- These guidelines include **medicines that may not be Medsafe-approved or Pharmac-funded** but can still be accessed privately. Including them is important as it also acknowledges international standards of care, and where we expect New Zealand to head in the future.
- The terms "Medsafe-approved" and "Pharmac-funded" in these guidelines refer to indications in advanced breast cancer.
  For example, a drug that is Medsafe-approved in renal cancer, but not for ABC, will be described as "not Medsafe-approved". For Pharmac-funded drugs, clinicians should check the specific eligibility critieria.
- The **ESMO Magnitude of Clinical Benefit Scale (MCBS)** is reported for newer medicines in these guidelines. This score indicates the overall efficacy of the medicine as reported in clinical trials, and can be a useful tool for clinicians and patients in treatment decision-making. However, it is important to note that these scores may be too general to apply to individual patients, for example where a subgroup may have reported better or worse trial outcomes than the overall MCBS score suggests, or where a low MCBS score results from lack of phase 3 trial evidence.

Section I. ABC Definitions

Guideline statement	LoE / GoR	NZ Consensus
Visceral crisis is defined as severe organ dysfunction as assessed by signs and symptoms, laboratory studies and rapid progression of disease. Visceral crisis is NOT the mere presence of visceral metastases, but implies important ORGAN COMPROMISE, leading to a clinical indication of the most efficacious therapy. Examples: • *Liver visceral crisis:* rapidly increasing bilirubin >1.5x ULN, in the absence of Gilbert's syndrome or biliary obstruction. • *Lung visceral crisis:* rapidly increasing dyspnea at rest, not alleviated by drainage of pleural effusion.	Expert opinion/ n/a	100%
ET NAIVE: Unknown if there is sensitivity of resistance to endocrine therapy (ET) since has never received ET **PRIMARY ENDOCRINE RESISTANCE is defined as:** Relapse while on the first 2 years of adjuvant ET, or progressive disease (PD) within first 6 months of 1st line ET for ABC, while on ET. **SECONDARY (ACQUIRED) ENDOCRINE RESISTANCE is defined as:** All other clinical situations of endocrine resistance. Examples include: 1) Relapse while receiving adjuvant ET but after at least 2 years; 2) PD after at least 6 months of 1st line ET-based therapy for ABC; 3) PD after any duration of 2nd+ line ET-based therapy for ABC; 4) Known ESR1 mutation. (note: definition unaffected by therapy with CDK4/6i, mTOR/PI3Ki, or other adjunctive drugs) **ENDOCRINE INSENSITIVITY** is defined as PD within 2 months of later-line ET-based therapy for ABC and no additional ET-based approaches likely to result in clinically meaningful benefit.	Expert opinion/ n/a	100%

Patients with multiple chronic conditions (MCCs) are defined as patients with additional comorbidities (cardiovascular, impaired renal or liver function, autoimmune disease), which may decrease tolerance to treatment and impact outcomes and the incidence of toxicities. This limits the ability to extrapolate existing data and make evidence-based recommendations for care.	Expert opinion/ n/a	100%
Adequate ovarian function suppression (OFS) for premenopausal patients with ABC can be obtained through bilateral oophorectomy, continuous use of LHRH agonists or ovarian function ablation (OFA) through pelvic radiotherapy (the latter is not always effective and therefore is the least *preferred option).*	I/A	100%
If a LHRH agonist is used in this age group, it should usually be given on a q4w basis to optimise OFS.	II/B	89%
Efficacy of OFS must be initially confirmed analytically through serial evaluations of serum estradiol, even in the presence of amenorrhea, especially if an AI is administered.	Expert opinion/B	Yes 32% No 47%
As all endocrine interventions for premenopausal patients with endocrine-responsive ABC require indefinite OFS, choosing one method over the other requires balance of patient's wish for potentially preserving fertility, compliance with frequent injections over a long period of time, risk of inadequate estrogen level suppression, and cost.		Abstain 21%
Maintenance therapy, in the context of ABC Guidelines, refers to the continuation of anti-HER2 therapy and/or endocrine therapy after discontinuation *of chemotherapy.*	Expert opinion/ n/a	100%
Complementary and integrative medicine (CIM) represents the use of complementary treatments side by side with conventional approaches in a proper *therapeutic environment*	Expert opinion/ n/a	100%
HER2 LOW To be eligible for treatment with trastuzumab-deruxtecan, the presence of low HER2 status on one sample is sufficient, regardless of the stage of the disease at which it was assessed (primary tumour or metastatic lesion). It is therefore advisable to systematically reassess HER2 status during the course of the disease if the initial HER2 status is zero.	I/A	95%

HER2 LOW The pathology report must detail the HER2 score according to ASCO/CAP 2023 recommendations [0,1+,2+ (amplified or not amplified) or 3+]. It is desirable to report the percentage of labelled cells. It is recommended to detail in the conclusion: HER2 ultra-low (IHC:0), HER2 low (1+ or 2+ non-amplified), HER2+ (HER2 3+ or ISH amplified).	Expert opinion/ A	95%

Section II. General guidelines

Guideline statement	LoE / GoR	NZ Consensus
The management of ABC is complex and, therefore, involvement of all appropriate specialties in a multidisciplinary team (including but not restricted to medical, radiation, surgical oncologists, imaging experts, pathologists, gynaecologists, psycho-oncologists, social workers, nurses and palliative care specialists), is crucial.	Expert opinion/A	100%
From the time of diagnosis of ABC, patients should be offered appropriate psychosocial care, supportive care, and symptom-related interventions as a routine part of their care. The approach must be personalised to meet the needs of the individual patient.	Expert opinion/A	100%
Following a thorough assessment and confirmation of ABC, the potential treatment goals of care should be discussed. Patients should be told that ABC is incurable but treatable, and that some patients can live with ABC for extended periods of time (many years in some circumstances). This conversation should be conducted in accessible language, respecting patient privacy and cultural differences, and whenever possible, written information should be provided.	Expert opinion/A	100%
Doctors should ensure that patients are involved, as far as possible, in understanding the nature of their problems, the range of possible solutions, and the likely benefits, risks and costs, to assist them in making informed choices.	Expert opinion/NA	100%
All ABC patients should be offered comprehensive, culturally sensitive, up-to-date and easy to understand information about their disease and its management. Doctors should provide adequate information to their patients about their assessment and treatment options, which are considered standard of care, even if these options are not readily available in NZ.	Expert opinion/NA	100%

Patients (and their families, caregivers or support network, if the patient agrees) should be invited to participate in the decision-making process at all times. When possible, patients should be encouraged to be accompanied by persons who can support them and share treatment decisions (e.g. family members, caregivers, support network).	Expert opinion/A	100%
Every ABC patient must have access to optimal cancer treatment and supportive care according to the highest standards of patient centred care, as defined by: • Open communication between patients and their cancer care teams as a primary goal. • Educating patients about treatment options and supportive care, through development and dissemination of evidence-based information in a clear, culturally appropriate form. • Encouraging patients to be proactive in their care and to share decision-making with their healthcare providers. • Empowering patients to develop the capability of improving their own quality of life within their cancer experience. • Always taking into account patient preferences, values and needs as essential to optimal cancer care. • Patients should have easy access to well-designed clinical studies, since these are crucial for further improvement in the management of ABC.	Expert opinion/A	100%
Every ABC patient should:		
• Have access to the most up-to-date, effective and best tolerated treatments at specialised Cancer Centres.	Expert opinion/A	95%
• Be treated by a practitioner experienced in the management of ABC and the potential side effects of treatment and who has regular access to a multidisciplinary breast cancer specialist team.	I/A	100%
• Survivorship issues and palliative care should be addressed and offered at an early stage. Referral to palliative care does not preclude continuation of active treatment.	Expert opinion/A	100%
• Quality Assurance Programmes undertaken in specialised Cancer Centres should specifically include treatment and support of ABC patients. A Quality Assurance Programme covering the entire breast cancer pathway from screening and diagnosis to treatment, rehabilitation, follow up and palliative care including services and support for ABC patients and their caregivers, should be implemented by specialised Cancer Centres.	Expert opinion/B	100%

ABC strategies, care and treatment protocols should recognise and acknowledge the principles and obligations underpinned by Te Tiriti o Waitangi (The Treaty of Waitangi). This includes assisting Māori to access relevant services and support, and where possible incorporating a "by Māori, for Māori" approach to help address ethnic inequities, consulting with iwi and Māori to meet their needs. Health providers should look to restore mauri, enhance mana and recognise and respect the role of whānau.	Expert opinion	100%

General Statements: PROs, e-PROs and quality of life assessments

Guideline statement	LoE / GoR	NZ Consensus
Strong consideration, as part of routine clinical care, should be given to the integration of patients' reports of symptoms of disease and side effects of treatment. Several remote measurement systems exist but these must be evidence-based and shown to be simple enough for use in clinical practice, in particular employ user-friendly collection platforms e.g. tablets or smartphones appropriate for different patient groups. Such regular systematic monitoring may facilitate communication between patients and their treatment teams about the toxicities of anticancer therapies. Reporting does not have to be tied to regular follow-up visits so that it may permit earlier introduction of ameliorative interventions and supportive care services.	I/B	100%
Trials evaluating QoL in ABC should employ standardised PROMs and not focus exclusively on reporting CTCAE symptom grades. If generic measures are used, then appropriate symptom and treatment specific modules or subscales that exist within the EORTC and FACiT systems should be incorporated. Additionally, attention must be paid to collection methods, timing of assessments and handling of missing data. More sophisticated statistics should also be employed to ensure that clinicians have better, reliable data to help patients choose between treatment options.	Expert opinion/A	100%

General Statements: Clinical Trials

Guideline statement	LoE / GoR	NZ Consensus
After appropriate informed consent, inclusion of patients in well-designed, prospective, independent trials must be a priority, whenever such trials are available, and the patient is willing to participate.	Expert opinion/A	100%
The ABC community strongly calls for clinical trials addressing important unanswered clinical questions in this setting, and not just for regulatory purposes. Clinical trials should continue to be performed, even after approval of a new treatment, to provide real world data on its performance, efficacy and toxicity.	Expert opinion/A	100%
Maximum tolerated dose vs. minimal effective dose When using chemotherapy in the palliative setting, the optimal dose level and the best schedule for treatment should be individualised for every patient. This should be based on what is the most effective and best tolerated dose, which, in most cases, is the minimal effective dose and not the maximum.	Expert opinion/NA	100%

General Statements: Affordability/Cost Effectiveness

Guideline statement	LoE / GoR	NZ Consensus
The medical community is aware of the problems raised by the cost of ABC treatment. Balanced decisions should be made in all instances; patients' wellbeing, length of life and preferences should always guide decisions.	Expert opinion/A	100%
Biosimilars The ABC community strongly supports the use of appropriately developed and validated biosimilars both for treatment of breast cancer (e.g. trastuzumab) and for supportive care. To be used, the biosimilar must be approved after passing the stringent development and validation processes required by Medsafe, EMA or FDA or other similarly strict authority. *For use in NZ public practice the biosimilar needs to be Medsafe-approved and Pharmac-funded.* *One trastuzumab biosimilar is Medsafe-approved (but not Pharmac-funded) as of September 2022.*	I/A	100%

General Statements: Survivorship issues

Guideline statement	LoE / GoR	NZ Consensus
As survival is improving in many patients with ABC, consideration of **survivorship issues** should be part of the routine care of these patients. Health professionals should therefore be ready to change and adapt treatment strategies to disease status, treatment adverse effects and QoL, patients' priorities and life plans. Attention to chronic needs for home and family care, job and social requirements, should be incorporated in the treatment planning and periodically updated.	Expert opinion/A	100%
ABC patients who desire to work or need to **work** for financial reasons should have the opportunity to do so, with due consideration to safety, and with needed and reasonable flexibility in their working schedules to accommodate continuous treatment and hospital visits.	Expert opinion/A	100%
The impact of the anticancer therapies on fertility should be discussed with all women with ABC of childbearing age and their partners, before the start of treatment. The discussion must also include appropriate information about the prognosis of the disease and the potential consequences of pregnancy (e.g. stopping ongoing treatment).	Expert opinion/B	100%
The panel recommends that routine breast imaging is not undertaken in patients with ABC, even with long-standing, stable disease or complete remission.		84%
Breast imaging could be considered when there is a suspicion of loco-regional progression.	I/A	100%

The wellbeing of all informal and formal caregivers of patients with ABC is frequently ignored and their pivotal role in supporting patients underestimated and undervalued. They, too, often need appropriate psychological and practical support. Working carers require protection from discrimination in the workplace (current and future). With the patient's agreement, culturally sensitive, up-to-date, and easy to understand information about their loved one's disease and its management throughout the whole trajectory from diagnosis to end-of-life should be provided by the healthcare team and needs to be congruent with that given to patients. Identification of formal and informal carers' needs and referral to appropriate resources should be available for all patients with ABC. For working carers, entitlement to continued employment and requests for reasonable adjustments, such as flexible working, to accommodate their caring responsibilities should be addressed.	Expert opinion/A	100%

General Statements: Caring for patients with ABC and pre-existing serious mental health illness

Guideline statement	LoE / GoR	NZ Consensus
Individuals diagnosed with serious mental illness (SMI) (including but not limited to major depression, bipolar disorder and schizophrenia) are more likely to be diagnosed with advanced stage cancer and to have poorer outcomes than individuals without SMI. Attention needs to be given to the special needs of patients with ABC and SMI and there should be no discrimination against them. The oncology team should endeavour to work together with the patient's psychiatrist and mental illness care team and endeavour to engage carers in order to ensure optimization, compliance and continuity of oncology care. Special attention needs to be given to drug-drug interactions between psychiatric medication and oncological therapies. Under certain circumstances steroid and medicinal cannabis use should be minimized to avoid triggering episodes of mania and psychosis.	IV/B	100%

General Statements: Access of patients to ICU

Guideline statement	LoE / GoR	NZ Consensus
Patients with ABC should receive patient-centred communications regarding their prognosis and treatment options and have the right to forgo treatment as well as to pursue treatments to the degree they desire where available and appropriate for the disease setting. They should not be denied access to ICU (intensive care units) based solely on their ABC diagnosis, in particular in cases of potentially reversible serious adverse events or complications of comorbidities other than ABC.	Expert opinion/B	100%

General Statements: Treatment holidays

Guideline statement	LoE / GoR	NZ Consensus
Planned treatment holidays, with careful supervision, can be an acceptable option in the case of long-term responders with controlled disease.	IV/B	95%
Stopping treatment in patients with long-term complete remissions has not been adequately studied but should be considered on a case-by-case basis, after extensive discussion with the patient. It is crucial that resuming the treatment if progression of disease occurs is allowed in New Zealand.	Expert opinion/B	100%

General Statements: Other

Guideline statement	LoE / GoR	NZ Consensus
Specialised oncology nurses (if possible specialised breast nurses) should be part of the multidisciplinary team managing ABC patients. This role may be played by a physician assistant, Medical Officer of Specialist Scale (MOSS) or another trained and specialised health care practitioner.	Expert opinion/A	100%
The use of **telemedicine in oncology** to help management of patients with ABC living in remote places is an important option to consider when geographic distances are a problem and provided that issues of connectivity and the need for physical examination are solved.	Expert opinion/B	100%

Section III. Oligometastatic disease

Oligometastatic disease – Definition

Oligometastatic disease is defined as low volume metastatic disease with limited number and size of metastatic lesions (up to 5 and not necessarily in the same organ), potentially amenable for treatment, aimed at achieving a complete remission status.

Oligometastatic disease – Modifications done in view of the NRG-BR002 trial.

A randomized phase 2 trial (NRG-BR002) in patients (n=125) with oligometastatic breast cancer (<4 extra-cranial sites) evaluated use of SBRT and/or Surgical Resection to all oligometastatic sites, in context of <12 months of first-line systemic therapy without progression. Most enrolled patients had oligometastatic recurrence (78%) and ER+/HER2- negative breast cancer (80%). The results showed no difference in median PFS and 3-yr OS, no difference in the rate of metastases outside index area, and the trial did not proceed to phase 3.

A small, randomized phase 2 trial (SABR-COMET) in patients with different types of advanced cancers including breast (18 patients only), evaluated the use of SABR or SBRT to all sites of oligometastatic disease, in the context of a controlled primary tumour, and showed a significant OS benefit.

Guideline statement	LoE / GoR	NZ Consensus
Oligometastatic disease – Management Systemic therapy should be the 1st treatment initiated and decision about possible local-regional treatments should be taken based on disease response. However, locoregional treatments may be considered prior to systemic therapy in patients where rapid symptom control is required. Results of additional ongoing trials are awaited. Further data specific to patients with de novo oligometastatic breast cancer is needed, as well as a better characterization of the subset of patients likely to benefit from a local-regional approach.	II/B	89%

Oligometastatic disease – Management Based on available data, routine ablation of extra-cranial asymptomatic oligometastatic sites to improve survival is not recommended, outside a clinical trial, until further data is available. It may be discussed on a case-by-case basis in a multidisciplinary tumour board, and the patient should be informed about the uncertainty about benefit and impact on OS seen so far.	II/D	90%
Oligometastatic disease in contralateral axilla Contralateral axillary nodal metastasis (in the absence of contralateral primary) as initial diagnosis of recurrent disease is considered stage 4 metastatic breast cancer. However, after prior local therapy to ipsilateral axilla for early breast cancer, subsequent metachronous contralateral axillary nodal metastasis, either alone or concurrent with an in-breast ipsilateral recurrence, could be considered and treated as a regional metastasis (due to altered lymphatic drainage), and has the potential for long survival or cure with a multidisciplinary approach.	Expert opinion/NA	95%

Section IV. Assessment and treatment general guidelines

Guideline statement	LoE / GoR	NZ Consensus
Minimal **staging workup for ABC** includes a history and physical examination, haematology and biochemistry tests, and imaging of chest, abdomen, pelvis and bones.	II/A	100%
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.	Expert opinion	89%
For staging of non-special type (NST) invasive breast cancers, PET-CT, if available, is preferred instead of and not in addition to CT-scans and bone scan. Note: PET-CT should be used for specific indications, to characterise/clarify equivocal findings (and this is usually based on CT findings). Small bone and liver lesions might be missed on PET-CT. Low grade and lobular cancers and small <1 cm metastases have relatively high false negative rates on FDG-PET.	II/B	53%
CT-scans and bone scans are preferred for invasive lobular breast cancers.		83%
Brain imaging should *not* be routinely performed in asymptomatic patients. This approach is applicable to all patients with ABC including those with HER2+ and/or triple negative ABC.	II/D	95%
The clinical value of **tumour markers** is not well established for diagnosis or follow-up after adjuvant therapy, but their use (if elevated) as an aid to evaluate response to treatment, particularly in patients with non-measurable metastatic disease, is reasonable. A change in tumour markers alone should not be used to initiate a change in treatment.	II/C	100%

Evaluation of response to therapy should generally occur every 2 to 4 months for ET or after 3 to 4 cycles for CT, depending on the dynamics of the disease, the location and extent of metastatic involvement, and type of treatment. In certain patients, such as those with indolent disease, less frequent monitoring is acceptable. Additional testing should be performed in a timely manner, irrespective of the planned intervals, if PD is suspected or new symptoms appear. Thorough history and physical examination must always be performed.	Expert opinion/B	95%

Biopsy of Metastatic Lesion(s)

Guideline statement	LoE / GoR	NZ Consensus
A biopsy (preferably providing histology or cytology) of a metastatic lesion should be performed, if possible, to confirm diagnosis particularly when metastasis is diagnosed for the first time.	I/B	95%
Biological markers (especially ER, PR and HER2) should be reassessed at least once in the metastatic setting, if clinically feasible. Depending on the metastatic site (e.g. bone tissue), technical considerations need to be discussed with the pathologist.	I/B	100%
The value of PR in the metastatic setting is limited and reserved only for confirmation of triple negative status. In the very rare cases of ER-/HER2-/PR+ ABC, approved therapies for triple negative ABC can be used. Depending on the metastatic site (e.g. bone tissue), technical considerations need to be discussed with the pathologist and the interventional radiologist. The quality of IHC assessments is crucial to ensure adequate treatment decisions.	Expert opinion/B	80%

If the results of ER and HER2 in the metastatic lesion differ from the primary tumour, it is currently unknown which result should be used for treatment-decision making. Since a clinical trial addressing this issue is difficult to undertake, we recommend considering the use of endocrine therapy or anti-HER2 therapy, respectively, when ER or HER2 are positive in at least one biopsy, regardless of timing. When reporting HER2 status of a metastatic lesion, the IHC or FISH score should be reported (not just a positive or negative status).	Expert opinion/B	85%
For tumours with confirmed triple negative histology in the primary tumour, if the results of any receptor status in the metastatic lesion differ, it is currently unknown which result should be used for treatment decision making. Since a clinical trial addressing this issue is difficult to undertake, the use of therapies specifically approved for triple negative, ER+/HER2 negative or HER2+ ABC should be discussed on a case-by-case basis. When reporting HER2 status of a metastatic lesion, the IHC or FISH score should be reported (not just a positive or negative status).	Expert opinion/B	100%

Locoregional Treatment General Guidelines

Guideline statement	LoE / GoR	NZ Consensus
Surgery of the primary tumour To date, the removal of the primary tumour in patients with de novo stage IV breast cancer has not been associated with prolongation of survival. However, it can be considered in selected patients, particularly to improve quality of life, always taking into account the patient's preferences, after a multidisciplinary discussion. Examples of situations where surgery of the primary may be considered include: • Symptomatic disease control of the primary site (for palliation) • Progression of the primary tumour when distant disease is controlled • No evidence of disease except in the primary tumour.	I/C	100%
Of note, 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.	II/B	89%

Systemic Treatment General Guidelines

Guideline statement	LoE / GoR	NZ Consensus
Systemic treatment choice should take at least these factors into account: • HR & HER2 status & germline BRCA status • Patient's preference • Need for rapid disease/symptom control • Previous therapies and their toxicities, disease-free interval • Tumour burden (defined as number and site of metastases) • Biological age, performance status, co-morbidities (including organ dysfunctions), • Menopausal status (for ET) • Socio-economic and psychological factors • Available therapies • PIK3CA in HR+ and PD-L1 in TNBC, if targeted therapies are accessible.	Expert opinion/A	100%
The **age** of the patient should not be the sole reason to withhold effective therapy (in elderly patients) nor to over-treat (in young patients). Age alone should not determine the intensity of treatment.	I/E	100%

Chemotherapy General Guidelines

Guideline statement	LoE / GoR	NZ Consensus
Both combination and sequential single agent CT are reasonable options. Based on the available data, we recommend **sequential monotherapy** as the preferred choice for ABC. Combination CT should be reserved for patients with rapid clinical progression, life-threatening visceral metastases or the need for rapid symptom and/or disease control.	I/A	95%
If given in the adjuvant setting, a taxane can be re-used as 1st line therapy, particularly if there has been at least one year of disease-free survival.	I/B	95%
Metronomic chemotherapy is a treatment option for patients not requiring rapid tumour response. Available options are low dose oral cyclophosphamide and methotrexate, capecitabine and vinorelbine. Randomised trials are needed and underway to accurately compare metronomic CT with standard dosing regimens.	I/B	95%
Duration of each regimen and number of regimens should be tailored to each individual patient.	Expert opinion/A	100%
Usually each regimen (except anthracyclines) should be given until progression of disease or unacceptable toxicity. What is considered unacceptable should be defined together with the patient.	I/B	89%

HER2- ABC

Guideline statement	LoE / GoR	NZ Consensus
For patients with HER2-negative ABC for whom chemotherapy is appropriate, and in the absence of medical contraindications or patient concerns, single agent chemotherapy from the available options would usually be preferred as 1st line CT. The decision should be individualised and take into account different toxicity profiles, previous exposure, patient preferences and breast cancer subtype. Available options include anthracyclines, taxanes, capecitabine, vinorelbine or gemcitabine.	I/A	67%
In patients with taxane-naive and anthracycline-resistant ABC or with anthracycline maximum cumulative dose or toxicity (i.e. cardiac) who are being considered for further CT, single agent chemotherapy would usually be considered the treatment of choice. A taxane would be an option; other options include capecitabine, vinorelbine or gemcitabine. The decision should be individualized and take into account different toxicity profiles, previous exposure, patient preferences and breast cancer subtype.	I/A	75%
In patients pre-treated (in the adjuvant and/or metastatic setting) with an anthracycline and a taxane, single agent capecitabine, vinorelbine or gemcitabine are the preferred choices. Additional choices include platinum agents, a different taxane, liposomal anthracyclines or eribulin. The decision should be individualised and take into account different toxicity profiles, previous exposure, patient preferences, and country availability. *Liposomal anthracyclines, albumin-bound taxane and eribulin are Medsafe-approved but not Pharmac-funded (as of July 2025).*	I/A	89%
If given in the adjuvant setting, provided that maximum cumulative dose has not been achieved and that there are no cardiac contra-indications, anthracyclines can be re-used in ABC, particularly if there has been at least one year of disease-free survival.	I/B	85%

Section V. ER-positive/HER2-negative (luminal-like) ABC

Guideline statement	LoE / GoR	NZ Consensus
Endocrine therapy is the preferred option for hormone receptor positive disease, even in the presence of visceral disease, unless there is visceral crisis, for pre- and perimenopausal women with OFS/OFA, men (preferably with an LHRH agonist) and postmenopausal women.	I/A	100%
Many trials in ER+ ABC have not included ***pre-menopausal*** women. Despite this, young women with ER+ ABC should have adequate ovarian function suppression or ablation (OFS/OFA) and then be treated in the same way as post-menopausal women, with endocrine therapies with and without targeted therapies.	Expert opinion/A	100%
Future trials exploring new endocrine-based strategies should be designed to allow for enrolment of both pre- and post-menopausal women, and men.	Expert opinion/A	100%
For pre-menopausal women, for whom endocrine therapy was decided, ovarian suppression/ablation combined with additional endocrine-based therapy is the preferred choice.	I/A	89%
Ovarian ablation by laparoscopic bilateral oophorectomy ensures definitive estrogen suppression and contraception, avoids potential initial tumour flare with LHRH agonist, and may increase eligibility for clinical trials. Patients should be informed on the options of OFS/OFA and decision should be made on a case-by-case basis.	Expert opinion/C	90%
Single agent tamoxifen is the only available endocrine option for pre-menopausal women who decline ovarian suppression or ablation (OFS/OFA) but the panel believes it is a less effective option.	I/D	95%

A CDK4/6 inhibitor combined with endocrine therapy is the standard of care for patients with ER+/HER2 -ABC, since it very substantially increases OS, as well as PFS and either maintains or *improves QoL*. The CDK4/6 inhibitor can be combined with an AI or with fulvestrant, in de novo or recurrent ABC, in 1st or 2nd line, and in cases of primary or secondary resistance (as defined per ABC guidelines). This recommendation applies to post-menopausal women, to pre- and perimenopausal women in combination with an LHRH agonist, and to men preferably in combination with a *LHRH agonist.* *Currently there are three CDK4/6 inhibitors available: palbociclib, ribociclib and abemaciclib.* *All three are Medsafe-approved; only palbociclib and ribociclib are Pharmac-funded (as of September 2025).*	I/A	100%
ER positive / HER2 negative ABC CDK4/6 inhibitors The SONIA trial attempted to answer the question whether a CDK4/6 inhibitor (90% palbociclib) combined with endocrine therapy should be given as 1st or 2nd line therapy for ER+/HER2 neg ABC. No statistically significant differences were seen in PFS 2 (primary endpoint) nor OS nor QoL, at 37 months follow-up. It is currently unknown if the results would be the same with ribociclib or abemaciclib. Based on these results, it may be an acceptable option to use ET alone as 1st line therapy for selected patients (e.g. low volume of disease, long DFI, patient preferences, accessibility constraints) with ER+/HER2 neg ABC. However, in view of the totality of data (OS benefit and different 2nd line options), the panel still favors the use of a CDK4/6i + ET as 1st line therapy for the majority of patients with this ABC subtype.	I/A	100%
ER positive / HER2 negative ABC CDK4/6 inhibitors There are no data comparing a combination of CDK4/6 inhibitor and ET vs. ET alone as maintenance therapy after chemotherapy. Both options are acceptable. Note: CDK 4/6 inhibitor maintenance therapy is technically currently not an option in NZ as SA criteria for palbociclib and ribociclib require that either 1) the disease has relapsed or progressed during prior endocrine therapy, or 2) patient has not received prior systemic treatment for metastatic disease.	II/B	63%

ER positive / HER2 negative ABC The use of a CDK4/6 inhibitor + ET after disease progression on a CDK4/6 inhibitor (i.e. beyond progression) has been evaluated in small phase 2 trials, with conflicting results and is not recommended for routine clinical practice, outside a clinical trial*. *MAINTAIN and post-MONARCH trials. Post-Monarch is a phase III trial, showing PFS improvement with abemaciclib+ fulvestrant in 2nd line. This can now be considered a treatment option. PACE and PALMIRA using palbo after progression on palbo, are negative. Palbociclib is Medsafe registered and Pharmac funded.	Expert opinion/D	75%
At present, no validated predictive biomarkers other than hormone receptor status exist to identify patients who will/will not benefit from the addition of a CDK4/6 inhibitor or an mTOR inhibitor to endocrine therapy and none of the studied biomarkers is ready for use in clinical practice. Research efforts must continue.	I/E	100%
The optimal sequence of endocrine-based therapy is uncertain. It depends on which agents were previously used in (neo)-adjuvant settings, duration of response to those agents, burden of disease, patient's preference and availability. Available options for 1st line include AI/Tamoxifen+LHRH agonist (in pre-/perimenopausal) + CDK4/6 inhibitor. For 2nd line: AI/tamoxifen/fulvestrant + CDK4/6 inhibitor (only if not used in 1st line) or + everolimus, fulvestrant + alpelisib (for PIK3CA mutant), AI, tamoxifen, fulvestrant. *For pre and perimenopausal with OFS/OFA, men (preferably with LHRH agonist) and post-menopausal women.	I/A	95%
Options for treatment of ER+ disease beyond second line include single agents not previously used (non-steroidal and steroidal AI, tamoxifen, fulvestrant, megesterol acetate, low dose estrogen).	II/B	89%
Challenging a patient with an agent on which the disease previously progressed, after an initial response, is occasionally considered, but there are no robust data to support *this approach.*	Expert opinion/B	100%
Concomitant CT + ET has not shown a survival benefit and should not be performed outside a clinical trial.	II/D	100%

Endocrine treatment after CT (maintenance ET) to maintain benefit is a reasonable option, though it has not been properly assessed in randomised trials.	III/B	100%
ER positive / HER2 negative ABC Trials comparing the different combinations of endocrine + targeted agents with single agent CT, in the 1st and later lines settings, are ongoing and some have been reported. In the PEARL trial, despite several trial limitations, ET + palbociclib versus Capecitabine yielded similar efficacy, while toxicity profiles were different, in favour of ET+palbociclib. In Young-PEARL, for premenopausal women, ET + palbociclib was superior to capecitabine in terms of PFS. In view of the substantial survival benefit seen with ET + CDK4/6 inhibitors in 1st line, never seen before with chemotherapy, this combination should be considered the standard of care for 1st line therapy of ER+/HER2 negative ABC. For pre and perimenopausal women with OFS/OFA, men (preferably with LHRH agonist) and post-menopausal women.	I/A	100%
The addition of the mTOR inhibitor everolimus to an aromatase inhibitor (AI) is a valid option for some patients previously exposed to or naïve of (in case CDK4/6i are not available) endocrine therapy, since it significantly prolongs PFS, albeit without evidence of significant OS benefit. Tamoxifen or fulvestrant can also be combined with everolimus. Adequate prevention with steroid mouthwashes, close monitoring and proactive treatment of adverse events is needed, particularly in older patients treated with everolimus, due to the increased incidence of toxic deaths reported in the Bolero-2 trial. Everolimus is not Pharmac-funded (as of September 2025), and not Medsafe-approved for advanced breast cancer. *For pre and perimenopausal with OFS/OFA, men (preferably with LHRH agonist) and post-menopausal women. ESMO-MCBS: 2	Expert opinion/C I/B	100%

ER positive / HER2 negative ABC: Alpelisib Aleplisib with fulvestrant is a treatment option for patients with PIK3CA-mutant tumours (in exons 9 or 20), previously exposed to an AI and with appropriate HbA1C levels, since it provided about 5 months benefit in median PFS, without statistically significant OS benefit. The decision to give alpelisib should take into consideration the inclusion/exclusion criteria in the SOLAR-1 trial (i.e: pre-existing diabetes & baseline HbA1c), as well as the toxicity profile of alpelisib. *Alpelisib or other PI3K inhibitors are not Pharmac-funded (as of September 2025), but is Medsafe-approved.* MCBS: 3 For pre and perimenopausal women with OFS/OFA, men (preferably with LHRH agonist) and post-menopausal women.	I/A	100%
ER positive / HER2 negative ABC: Alpelisib Few patients previously treated with a CDK4/6i were included in the SOLAR-1 trial. However, a non-randomized cohort study (ByLieve) seems to indicate that alpelisib retains its efficacy if used after a CDK4/6i. In view of the magnitude of OS benefit seen with ET + CDK4/6i, this approach is considered the standard of care for 1st line therapy and ET (fulvestrant or AI) + alpelisib should be reserved for the 2nd line setting in cases of PIK3CA-mutant tumours. *Alpelisib or other PI3K inhibitors are not Pharmac-funded (as of September 2025) but is Medsafe-approved.* ESMO-MCBS: 3 For pre and perimenopausal with OFS/OFA, men (preferably with LHRH agonist) and post-menopausal women.	I/B	95%
ER positive / HER2 negative ABC: Alpelisib Patients receiving alpelisib in combination with endocrine therapy for PIK3CA mutated ABC should be instructed to take non-sedating antihistamines daily to prevent rash at start of therapy. Antihistamines can be discontinued after 4 weeks, as the risk for rash is primarily in the first 2 weeks of therapy. *Alpelisib or other PI3K inhibitors are not Pharmac-funded (as of September 2025) but is Medsafe-approved.*	I/B	100%

ER positive / HER2 negative ABC Elacestrant, an oral SERD, has been approved by the US FDA as 2nd/3rd line therapy for patients with ER+/HER2 negative ABC with an ESR1 mutation, based on a randomized phase III trial demonstrating 1.9 months median PFS advantage (HR: 0.546). This advantage was most notable in patients who were previously treated with a CDK4/6 inhibitor for more than 6 months. Where available, Elacestrant is an option for patients in 2nd/3rd line setting with an ESR1 mutation. *Elacestrant is not MEDSAFE registered and not Pharmac listed.*	I/C	94%
ER positive / HER2 negative ABC Capivasertib, an AKT inhibitor, combined with fulvestrant was compared to placebo plus fulvestrant, in patients with ER+/HER2 negative ABC, with 1 or 2 lines of previous ET and none or 1 line of chemotherapy for metastatic disease; recurrence or progression while on or <12 months from end of adjuvant AI, or progression while on prior AI for ABC was required; about 70% of pts received prior CDK4/6i The results showed a 3.6 month benefit in median PFS (HR: 0.60) in the overall population and a 4.2 ms median PFS benefit (HR: 0.50) in the AKT pathway-altered population (i.e. PIK3CA and/or PTEN and /or AKT1 alteration). OS results are still immature. GI side effects, mainly diarrhea (72%), were seen. Based on these results, where approved, capivasertib added to fulvestrant may be used as a treatment option in endocrine resistant ER+/HER2 neg ABC with an AKT pathway-altered (i.e. PIK3CA and/or PTEN and / or AKT1 alteration). It is unknown what is the efficacy of capivasertib after an ADC such as T-Dxd or SG or how it compares with everolimus or alpelisib. *Capivasertib is not MEDSAFE registered and not Pharmac listed.*	I/B	88%

ER positive / HER2 negative ABC	I/B	94%
Sacituzumab govitecan was compared with chemotherapy of physician's choice, in patients with ER+/HER2 negative ABC, previously treated with at least 1 line of ET, taxane, and CDK4/6 inhibitor in any setting and at least 2, but no more than 4, lines of CT for metastatic disease (60% of pts had received 3 or more lines of CT). Results showed a 1.5 month improvement in median PFS and 3.2 months median OS, both in HER2 low and HER2 zero. No new safety signals were seen. Education, prophylaxis and early management of side effects, in particular diarrhea and nausea/vomiting, remain important. The OS benefit seen in this heavily pretreated population makes sacituzumab govitecan a treatment option for this patient population. *Sacituzimab is MEDSAFE registered for this indication, but not Pharmac listed (as of September 2025).*		

ER positive / HER2 negative ABC		
In the RIGHT Choice trial, the combination of ribociclib + aromatase inhibitor (+ LHRH agonist in pre-menopausal women) was compared to combination chemotherapy (docetaxel + capecitabine, paclitaxel + gemcitabine or capecitabine + vinorelbine) as 1st line therapy for pre/peri-menopausal women with ER+/HER2 neg ABC with "clinically aggressive disease" defined as: symptomatic visceral metastases, rapid disease progression or impending visceral compromise, markedly symptomatic non-visceral disease, but with bilirubin <1.5 (therefore not in liver visceral crisis as defined by the ABC guidelines). The ET + CDK4/6i arm yielded a 12 ms benefit in PFS, with similar ORR and similar time to onset of response in both arms, but substantially better toxicity profile for the ET-based arm.		
These results reinforce the place of ET + CDK4/6 inhibitors as standard of care for 1st line therapy for the majority of patients with ER+/HER2 negative ABC, including those with "clinically aggressive disease".	I/A	88%
Although the trial was run in pre/peri-menopausal women, this panel believes the results also apply to post-menopausal women and men with the same disease characteristics.	Expert opinion/B	88%

Section VI. HER2 low ABC

Guideline statement	LoE / GoR	NZ Consensus
ER positive / HER2 low ABC Trastuzumab Deruxtecan (T-Dxd) was compared to chemotherapy of physician's choice, in patients with HR positive HER2 low ABC, treated with 1-2 lines of chemotherapy in the metastatic setting and ER+ disease considered endocrine refractory, and yielded a 6.4 months benefit in median OS and 4.7 months in median PFS, making it a preferred treatment option in this setting (Destiny Breast 04). Trastuzumab-deruxtecan was also compared with chemotherapy of physician's choice in patients with HR positive HER2 low ABC, who had received one or more lines of endocrine therapy, but no chemotherapy for metastatic disease. For the HER2 low group it yielded a 5.1 month benefit in median PFS. Overall survival data are still immature (Destiny-Breast 06). Treatment with T-Dxd was associated with ILD/pneumonitis (including toxic deaths), increased GI toxicity and fatigue. ILD/ Pneumonitis can be fatal and requires active imaging surveillance with non-contrast CT scans, and proper management. Nausea and vomiting require adequate prophylaxis. *Trastuzumab-deruxtecan is MEDSAFE approved, but not PHARMAC listed for this indication (as of September 2025).*	I/A	88%
ER positive / HER2 low ABC There are very few data regarding the best sequence of administration of ADCs for ER+/HER2 low ABC. Note: INT ABC panel voted on the following statement, which has been removed from NZ version: In view of the populations treated and results of the trials of T-Dxd and sacituzumab govitecan, the panel believes that T-Dxd should be used earlier than sacituzimab govetican.	Expert opinion/B	88%

Triple negative / HER2 low ABC Trastuzumab Deruxtecan (T-Dxd) was compared to treatment of physician's choice, in 58 patients with triple negative/ HER2 low ABC, treated with 1-2 lines of chemotherapy in the metastatic setting. In this small population the results in terms of PFS and OS were similar to the overall Destiny Breast-04 study population and T-Dxd may therefore be considered a treatment option for patients with the same characteristics of those enrolled in Destiny Breast 04. ILD/Pneumonitis can be fatal and requires active imaging surveillance with non-contrast CT scans, and proper management. Nausea and vomiting require adequate prophylaxis.	I/B	81%
Triple negative / HER2 low ABC There are very few data regarding the best sequence of administration of ADCs for ER negative/HER2 low ABC. In view of the results of the trials of T-Dxd and sacituzumab govitecan in this patient population, the panel believes that sacituzumab govitecan should be used earlier than T-Dxd.	II/A	69%

Section VII. HER2-positive ABC

Guideline statement	LoE / GoR	NZ Consensus
Anti-HER2 therapy should be offered early (as 1st line) to all patients with HER2+ ABC, except in the presence of contra-indications to the use of such therapy.	I/A	95%
The optimal duration of anti-HER2 therapy for ABC (i.e. when to stop these agents) is currently unknown.	Expert opinion/C	100%
In patients achieving a complete remission, the optimal duration of maintenance anti-HER2 therapy is unknown and needs to be balanced against treatment toxicity, logistical burden and cost. Stopping anti-HER2 therapy, after several years of sustained complete remission, may be considered in some patients, particularly if treatment re-challenge is available in case of progression.	Expert opinion/C	100%
*New Zealand funding criteria do not allow for the HER2 targeted therapies trastuzumab and pertuzumab to be continued when the disease progresses on treatment. *An exception to this rule is for patients who develop brain metastases on trastuzumab +/- pertuzumab, while their extracerebral disease is still well controlled. * Trastuzumab and pertuzumab are large molecules that normally don't cross the blood-brain barrier. * In this scenario, when local therapy could be offered to treat the brain metastases, these HER2 targeted therapies could be continued to control the extracerebral metastatic disease.		100%

ER + / HER2+ ABC For patients with ER+/HER2+ ABC, for whom CT + anti-HER2 therapy was chosen as 1st line therapy and provided a benefit, it is reasonable to use ET + anti-HER2 therapy as maintenance therapy, after stopping CT, although this strategy has not been studied in randomised trials. Duration of maintenance therapy should be until progression, unacceptable toxicity or patient request, and needs to be evaluated in clinical trials. There are no data to decide between single agent anti-HER2 or dual blockade, to combine with maintenance ET after stopping CT, in ER+/HER2+ ABC. Note: In Cleopatra, maintenance was done with dual blockade alone (without ET)	NA/A	100%
The standard 1st line therapy for patients previously untreated with anti-HER2 therapy is the combination of CT + trastuzumab and pertuzumab, because it has proven to be superior to CT + trastuzumab in terms of OS in this population.	I/A	100%
HER2-positive ABC CT agents to combine with a dual blockade of trastuzumab + pertuzumab are docetaxel or paclitaxel. Also possible are vinorelbine, nab-paclitaxel and capecitabine. *Nab-paclitaxel is Medsafe-approved but not Pharmac-funded (as of September 2025).*	I/A I/B II/A, II/B II/A	89%
HER2-positive ABC Regarding the CT component of HER2-positive ABC treatment: When pertuzumab is not given, 1st line regimens for HER2+ ABC can include trastuzumab combined with vinorelbine* or a taxane. Differences in toxicity between these regimens should be considered and discussed with the patient in making a final decision. Other CT agents can be administered with trastuzumab but are not as well studied and are not preferred. * Single agent vinorelbine in association with anti-HER2 therapy has shown superior or equal efficacy compared to taxanes and has a better tolerability.	I/A	100%

HER2-positive ABC: 1st line For patients previously treated (in the (neo)adjuvant setting) with anti-HER2 therapy, the combination of CT + trastuzumab and pertuzumab is the preferred option for 1st line therapy. Few (N=88; 10%) of patients in Cleopatra trial received prior trastuzumab in (neo-) adjuvant setting and all with trastuzumab-free interval > 12 months. ESMO-MCBS: 4	I/A	100%
HER2-positive ABC: 2nd line and beyond Trastuzumab deruxtecan (T-Dxd) showed substantial PFS (HR: 0.28, absolute benefit not yet reached) and an initial trend for OS benefit when compared to T-DM1, in pretreated patients with HER2+ ABC. About 50% of patients received the treatment as 1st or 2nd line and the other 50% in later lines. Where approved, trastuzumab deruxtecan (T-Dxd) is the preferred treatment option in the 2nd line setting, after exposure to trastuzumab and pertuzumab (DESTINY-03 trial). Pulmonary toxicity (ILD*/Pneumonitis) is rare but can be fatal and requires active surveillance and proper management. Nausea and vomiting require adequate prophylaxis. If not used in the 2nd line setting, trastuzumab deruxtecan (T-Dxd) is the preferred treatment option in later lines of therapy, including in heavily pretreated patients with HER2+ ABC (median lines of therapy: 6). ESMO-MCBS: pending	I/A	95%
HER2-positive ABC: 2nd line and beyond For patients without access to or with contra-indications for T-Dxd, T-DM1 remains the preferred 2nd line therapy, since it has proven superior efficacy (in terms of OS) relative to other HER2-based therapies in the 2nd line (vs. lapatinib + capecitabine) and beyond (vs. treatment of physician's choice). *Trastuzumab-emtansine (T-DM1) is Pharmac-funded after progression on trastuzumab+/- pertuzumab in 1st line. Lapatinib is Medsafe-approved but not Pharmac-funded as a second line therapy after progression on trastuzumab.* ESMO-MCBS: 3	I/A	95%

HER2-positive ABC: 2nd line and beyond Dual blockade with tucatinib + trastuzumab + capecitabine showed a benefit in median PFS (2 months) and median OS (4 months), over trastuzumab + capecitabine, in patients previously treated with trastuzumab, pertuzumab and T-DM1, including patients with stable or active brain metastases. Toxicity needs education and early intervention (i.e. diarrhoea). Where approved, it is a treatment option in this setting. *Tucatinib is not Pharmac-funded (as of September 2025) or Medsafe-approved.* *Trastuzumab is not Pharmac-funded (as of September 2025) for continuation beyond progression.* ESMO-MCBS: 3	I/A	95%
HER2-positive ABC For later lines of therapy, trastuzumab can be administered with several CT agents, including but not limited to, vinorelbine (if not given in 1st line), taxanes (if not given in 1st line), capecitabine, liposomal anthracyclines, platinum, gemcitabine, or metronomic CM. *Trastuzumab is not Pharmac-funded (as of September 2025) for continuation beyond progression.* *Liposomal anthracyclines are Medsafe-approved but not Pharmac-funded (as of September 2025).* The decision should be individualized and take into account different toxicity profiles, previous exposure, patient preferences, and country availability.	II/A	84%

Section VIII. Triple Negative ABC

Guideline statement	LoE / GoR	NZ Consensus
In triple negative ABC patients (regardless of BRCA status), previously treated with anthracyclines with or without taxanes in the (neo)adjuvant setting, carboplatin demonstrated comparable efficacy and a more favorable toxicity profile, compared to docetaxel, and is therefore an important treatment option.	I/A	100%
For non-BRCA-associated triple negative ABC, there are no data supporting different or specific CT recommendations, besides platinum. Therefore, all CT recommendations for HER2 negative disease also apply for triple negative ABC.	I/A	100%
Immunotherapy for triple negative ABC Checkpoint inhibitors + chemotherapy (pembrolizumab + taxane or carboplatin/gemcitabine) is the preferred treatment option for 1st line therapy for most patients with PD-L1+* triple negative ABC, either de novo or diagnosed at least 6 months from (neo)adjuvant chemotherapy. *Nab-paclitaxel is Medsafe-approved but not Pharmac-funded (as of September 2025).* * CPS score ≥10. ESMO-MCBS: 4	I/A	100%
Immunotherapy for triple negative ABC Atezolizumab in combination with nab-paclitaxel may be an option for 1st line therapy of patients with PD-L1+* triple negative ABC. *Atezoluzimab is Medsafe-approved but not Pharmac-funded (as of September 2025).* *Nab-paclitaxel is Medsafe-approved but not Pharmac-funded (as of September 2025).* * PD-L1 score ≥1% (SP142 PD-L1 IHC). ESMO-MCBS:3	II/B	85%

Checkpoint inhibitor monotherapy in later lines for triple negative ABC is not recommended, due to low response rates.	I/E	84%
Immunotherapy for other ABC subtypes Several ongoing trials are evaluating the role of this type of treatment in other ABC subtypes (non-TNBC) and, for the moment, it is not recommended outside clinical trials. * For PD-L1 testing, see Precision Medicine Statements.	NA/E	100%
Sacituzumab govitecan for triple negative ABC Sacituzumab govitecan is the preferred treatment option for patients with triple negative ABC, treated with ≥ 2 lines (at least one of them in the metastatic setting), since it demonstrated a 5.5 months benefit in OS and a 4 months benefit in PFS. Education, prophylaxis and early management of side effects, in particular diarrhoea and nausea/vomiting, are important. *Sacituzumab govitecan is not Pharmac-funded or Medsafe-approved (as of September 2025).* ESMO-MCBS: 4	I/A	90%

Section IX. Hereditary ABC

Guideline statement	LoE / GoR	NZ Consensus
For ABC patients, results from germline genetic testing have therapeutic implications and testing should therefore be performed as early as possible. Appropriate counselling should be provided, to patients and their families, if a pathogenic germline mutation is found.	I/A	89%
At present only germline mutations in BRCA 1/2 have proven clinical utility and therapeutic impact.	I/A	79%
Testing for other additional moderate-to high-penetrance genes may be considered, if deemed appropriate by the geneticist/genetic counsellor, in particular because they may have implications for family members. However, it must be clarified to the patient that at present, a mutation in another moderate-high penetrance gene has no direct clinical implications for the patients themselves, in the setting of ABC.	Expert opinion/C	84%
In patients with gBRCA-associated triple negative or endocrine-resistant HER2- ABC, previously treated with an anthracycline +/- a taxane (in adjuvant and/or metastatic setting), a platinum regimen is the preferred chemotherapy option, if not previously administered. All other chemotherapy recommendations are similar to those for sporadic ABC.	I/A	84%
Hereditary ABC - PARP Inhibitors For patients with a gBRCA mutation single agent PARP inhibitor (olaparib or talazoparib) is one of the preferred treatment options for those with basal-like ABC, since they are associated with a PFS benefit, improvement in QoL and a favorable toxicity profile. *Olaparib and talazoparib are not Pharmac-funded (as of September 2025), both are Medsafe-approved for treatment of germline BRCA-mutated HER2 negative ABC.*	I/A	100%

Hereditary ABC - PARP Inhibitors Data from a small phase 2 trial demonstrated a benefit from olaparib for individuals with a somatic BRCA1/2 mutation or a germline PALB2 mutation. It is acceptable to offer this treatment to these patients, acknowledging the limitation of data, since it is unlikely that large trials will be run. *Olaparib is not Pharmac-funded (as of September 2025), but is Medsafe-approved for treatment of germline BRCA-mutated HER2 negative ABC after prior treatment with chemotherapy.*	II/B	95%
Hereditary ABC - PARP Inhibitors It is unknown how single agent olaparib or talazoparib compare with platinum compounds in this setting, as well as to the optimal use with platinum (combined or sequential), and their efficacy in tumours progressing after platinum. *Olaparib and talazoparib are not Pharmac-funded (as of September 2025), but both are Medsafe-approved.*	II/B	95%
Hereditary ABC - PARP Inhibitors In ER+ gBRCA-associated ABC, the optimal sequence between PARPi and ET+ CDK4/6i was not formally tested. However, given the OS benefit seen with CDK4/6i, the panel considers them the standard of care for 1st line therapy and recommends their use before a PARPi.	Expert opinion/A	90%
Hereditary ABC - PARP Inhibitors In triple negative PD-L1+ and gBRCA-associated ABC, the optimal sequence between PARPi and CT + immune-checkpoint inhibitors was not formally tested. However, given the OS benefit seen with immunotherapy, the panel considers it the preferred option for 1st line therapy, for the majority of the patients. More research is needed to answer questions related to treatment sequencing and other disease subtypes, i.e., HER2+ disease in the context of BRCA1/2 mutations. *Immune checkpoint inhibitors are Medsafe-approved but not Pharmac-funded (as of September 2025) for treatment of ABC. PARPi are Medsafe-approved but not Pharmac-funded (as of September 2025) for treatment of gBRCA- associated ABC.*	Expert opinion/B	89%

Hereditary ABC - PARP Inhibitors BROCADE3 was the first phase 3 trial testing a PARP inhibitor (veliparib) in gBRCA ABC that included platinum. Initial presentation of results showed a small benefit in PFS (1.9 ms). However, durable PFS at 3 years was seen in a significant minority (1/4 patients) during veliparib maintenance, which could provide patients lacking other maintenance treatment options, with chemotherapy-free time. Mature OS data are needed before this regimen can be recommended for routine clinical practice. *Veliparib is not Medsafe-approved or Pharmac-funded (as of September 2025).*	I/D	90%

Section X. Precision Medicine

Guideline statement	LoE / GoR	NZ Consensus
Multigene panels, such as those obtained using next generation sequencing (NGS) or other technology on tumour DNA have not yet proven beneficial in clinical trials for ABC, their impact on outcome remains undefined and should not be used in routine clinical practice.	I/D	
For patients who are suitable to participate in clinical trials of novel therapies and readily able/motivated to attend a centre with relevant clinical trials, NGS testing may be used in the context of prospective molecular triage programs to select patients for therapeutic trials.		83%
Specific tests (as distinguished from broad mutation profiles) are useful and discussed in separate statements; others may play a role in the future as the medicines they are linked with, achieve regulatory approval.		
NGS is not publicly funded in NZ.		
In patients with advanced/recurrent TNBC, TILs should be quantified (using light microscopy from a recent metastatic biopsy or from their primary).	I/B	63%
In patients with advanced/recurrent TNBC, PD-L1 status (assays SP142 Ventana assay >1% or more) should be assessed as well.	I/B	78%
Combined positive score (CPS) ≥10) as pre-existing immune response is associated with higher benefit from checkpoint blockade with CT.		
Circulating tumour DNA (ctDNA) assessment is not recommended for demonstration of disease progression at this stage.	I/D	100%
Circulating tumour DNA (ctDNA) assessment is an option for the detection of PIK3CA mutations, for selection of patients eligible for alpelisib.	II/A	100%

PIK3CA mutation status If treatment with PI3K inhibitor alpelisib is accessible, patients should be tested for PIK3CA mutation (in exon 9 and 20) in a tissue (metastasis or primary) and/or by ctDNA testing in blood. Patients who do not have an available archival tissue sample and have an uninformative result using the liquid biopsy test could consider undergoing a tumour biopsy for PIK3CA mutation testing. *Testing for PIK3CA mutation is available in NZ but is not publicly funded.*	I/B	100%
ESR1 mutation status Where ESR1 mutation status is available, in the presence of an ESR1 mutation, treatment with an aromatase inhibitor is not the optimal strategy. Acquired ESR1 mutations occur commonly in case of disease progression under treatment with an AI +/- a targeted agent (i.e. CDK4/6 inhibitor). For the next line of therapy, a non-AI-based option may therefore be a better option.	II/B	90%
ESR1 mutation status Treatment should not be changed based on ESR1 mutation status alone and confirmation of disease progression is mandatory. Availability of ESR1 mutation status is not mandatory for the adequate management of ER+/ HER2 negative ABC.	II/D	90%
PD-L1 status for ABC PD-L1 status should be tested in cases of 1st line triple negative ABC, if treatment with immune checkpoint inhibitors is accessible available, preferably in a metastatic tumour sample.	I/A	100%

PD-L1 status for ABC PD-L1 status is the companion test for the use of the combination of pembrolizumab and CT, as 1st line therapy for triple negative ABC, using PD-L1 IHC with a Combined Positive Score or CPS ≥ 10 (CPS score: number of PD-L1 staining cells (tumour cells, lymphocytes, macrophages) divided by the total number of viable tumour cells, multiplied by 100).	I/A	100%
PD-L1 status for ABC PD-L1 status is the companion test for the use of the combination of atezolizumab and nab-paclitaxel, as 1st line therapy for triple negative ABC, using IHC with the SP142 antibody (Ventana), and a cut-off of 1% of positive staining on immune cells.	I/A	90%
Patients with low (1-10%) ER positive (and PR positive), HER2 negative ABC should not be considered for endocrine therapy exclusively. Patients with low (1-10%) ER positive (and PR positive), HER2 negative ABC can be considered as patients with triple negative ABC for clinical trials.	III/B	100%

Section XI. Specific sites of metastases: Bone/Brain/Liver/Pleural Effusion/Chest Wall Recurrences

Guideline statement	LoE / GoR	NZ Consensus
Bone metastases: Radiological assessments are required in patients with persistent and localised pain due to bone metastases to determine whether there are impending or actual pathological fractures. If a fracture of a long bone or vertebrae is likely or has occurred, an orthopaedic assessment is required as the treatment of choice may be surgical stabilisation which is generally followed by radiotherapy. In the absence of a clear fracture risk, radiotherapy is the treatment of choice.	I/A	100%
For palliative radiation of an uncomplicated* symptomatic bone metastasis, a single 8 Gy fraction is recommended. *Uncomplicated is no impending fracture or no spinal canal involvement and without significant neuropathic involvement.		74%
Neurological symptoms and signs which suggest the possibility of spinal cord compression must be investigated as a matter of urgency. This requires a full radiological assessment of the potentially affected area as well as adjacent areas of the spine. MRI is the method of choice. An emergency surgical opinion (neurosurgical or orthopaedic) may be required for surgical decompression. If no decompression/stabilisation is feasible and indicated, emergency radiotherapy is the treatment of choice and vertebroplasty is also an option.	I/B	100%

Bone metastases Regarding the use of bone targeted agents (bisphosphonate, denosumab), the ABC panel endorses the ESMO Guidelines related to this subject. *Denosumab is not Pharmac-funded (as of September 2022) and not Medsafe-approved.*	I/A	100%
Brain metastases Patients with a single or a small number of potentially resectable brain metastases should be treated with surgery or radiosurgery. Radiosurgery is also an option for some unresectable brain metastases.	I/B	95%
If surgery/radiosurgery is performed it may be followed by whole brain radiotherapy but this should be discussed in detail with the patient, balancing the longer duration of intracranial disease control and the risk of neurocognitive effects.	I/C	89%
HER2-positive ABC and brain metastases Because patients with HER2+ ABC and brain metastases can live for several years, consideration of long-term toxicity is important and less toxic local therapy options (e.g. stereotactic radiotherapy) should be preferred to whole brain radiotherapy, when available and appropriate (e.g. in the setting of a limited number of brain metastases).	I/A	100%
Brain metastases from HER2+ ABC Trastuzumab Deruxtecan (T-Dxd) has shown activity against brain metastases from HER2+ ABC, previously treated or untreated with local therapy, and can be considered a treatment option.	II/B	94%
In patients with HER2 positive ABC who develop brain metastases with stable extracranial disease, systemic therapy should not be changed.	I/D	84%

HER2-positive ABC & brain metastases For patients with HER2 positive ABC where brain metastases are the only site of recurrence and for whom stereotactic radiotherapy is feasible and accessible, the addition of chemotherapy to local therapy is not known to alter the course of the disease and is not recommended.	I/D	100%
HER2-positive ABC & brain metastases Patients who received localized treatments for brain metastases from HER2-positive ABC and who have well-controlled systemic disease, should continue anti-HER2 therapy. It is recommended to re-start the anti-HER2 therapy (trastuzumab) if this had been stopped.	II/B	95%
HER2-positive ABC & brain metastases A possible alternative is the usage of tucatinib + trastuzumab + capecitabine, although this option may also be reserved for progression of the disease after local therapy. *Tucatinib is not Medsafe-approved or Pharmac-funded (as of September 2025).* *Trastuzumab is not Pharmac-funded (as of September 2025) to be continued beyond progression.*	I/A	100%
HER2-positive ABC & brain metastases TDM-1 has also shown activity against active brain metastases in one prospective single arm study (KAMILLA) and is therefore a treatment option.	II/A	95%

HER2-positive ABC & brain metastases For patients with HER2 positive ABC with progressive brain metastases as the predominant site of disease burden and no local therapy option available, treatment with tucatinib + trastuzumab + capecitabine is the best available option. *Tucatinib is not Medsafe-approved or Pharmac-funded (as of September 2025).* *Trastuzumab is not Pharmac-funded (as of September 2025) to be continued beyond progression.*	I/A	86%
If this treatment is not accessible and/or if no further relevant local therapy options are available, a change in systemic therapy is a reasonable option.	II/B	100%
Brain metastases Radio-necrosis after stereotactic radiotherapy for brain metastases is an uncommon complication that may occur especially with longer survival and follow-up, and in particular in cases of re-irradiation. Differential diagnosis with tumour progression is often difficult.		
A course of high-dose steroids is the first treatment of choice for symptomatic patients. Surgery may also be considered.	III/B	76%
Where a steroid-sparing option is essential and/or other options have failed, bevacizumab may be used to decrease the surrounding oedema, usually at a dose of 7.5 mg/kg every 2 weeks, for a median of four cycles. Prospective randomized trials are needed to validate further this option. *Bevacizumab is not Pharmac-funded (as of September 2025) and is not Medsafe-approved.*	III/B	

Liver metastases Prospective randomised clinical trials of local therapy for breast cancer liver metastases are urgently needed, since available evidence comes only from series in highly selected patients. Since there are no randomised data supporting the effect of local therapy on survival, every patient must be informed of this when discussing a potential local therapy technique. Local therapy should only be proposed in very selected cases of good performance status, with limited liver involvement, no extra-hepatic lesions, after adequate systemic therapy has demonstrated control of the disease. Currently, there are no data to select the best technique for the individual patient (surgery, stereotactic RT, TACE, intra-hepatic Chemotherapy).	Expert opinion/C	100%
Malignant pleural effusions Use of an intrapleural catheter and consideration of pleurodesis with intrapleural administration of talc or drugs (e.g. bleomycin, biological response modifiers) after successful thoracocentesis when the lung is fully expanded (not useful in case of a trapped lung or extensive pleural thickening), can be helpful to reduce the likelihood of rapid re- accumulation of pleural fluid.	III/B	89%
Systemic therapy to treat the underlying malignant pleural disease should be considered.	III/A	95%
Chest wall or regional (nodal) recurrences Due to the high risk of concomitant distant metastases, patients with chest wall or regional (nodal) recurrence should undergo full restaging, including assessment of chest, abdomen and bone.	Expert opinion/A	100%
Chest wall and regional recurrences should be treated with surgical excision when feasible with limited risk of morbidity.	II/A	100%
Locoregional radiotherapy is indicated for patients not previously irradiated.	II/A	
For patients previously irradiated, re-irradiation of all or part of the chest wall may be considered in selected cases.	Expert opinion/C	

In addition to local therapy (surgery and/or RT), in the absence of distant metastases, the use of systemic therapy (CT, ET and/or anti-HER2 therapy) should be considered.	I/B	100%
Chemotherapy after first local or regional recurrence improves long term outcomes in ER negative disease and can be used.	I/B	100%
Endocrine therapy in this setting improves long term outcomes for ER positive disease and should be used.	I/B	95%
The choice of systemic treatment depends on tumour biology, previous treatments, length of disease free interval, and patient-related factors (co-morbidities, preferences, etc).	Expert opinion/A	100%
Chest wall and regional (nodal) recurrences In patients with disease not amenable to radical local treatment, the choice of palliative systemic therapy should be made according to principles previously defined for metastatic disease. These patients may still be considered for palliative local therapy.	Expert opinion/B	100%

Section XII. Specific populations

Guideline statement	LoE / GoR	NZ Consensus
Male patients with ABC Male patients with ABC should be offered genetic counselling and testing.	II/A	100%
Male patients with ABC For ER positive male ABC, which represents the majority of the cases, ET is the preferred option, unless there is visceral crisis or rapidly progressive disease needing a fast response.	III/A	100%
Male patients with ABC For ER positive male ABC tamoxifen is the preferred option.	IV/B	95%
Male patients with ABC For male patients with ABC who need to receive an aromatase inhibitor (AI), a concomitant LHRH agonist or orchidectomy is the preferred option.	IV/B	89%
Male patients with ABC Male patients with ER+ ABC should be treated with the same options as female patients, including access to targeted agents such as CDK4/6, mTOR and PIK3CA inhibitors. *mTORi and PIK3CAi are not Pharmac-funded (as of September 2022), mTORi are not Medsafe-approved but a PIK3CAi is.*	II/A	95%

Older frail patients with ABC When no specific note is made, all ABC guidelines are to be implemented independently of the age of the patient.	Expert opinion/A	100%
Older frail patients with ABC Independant of age, all patients should be involved in the treatment decision making process if they wish to do so, and their preferences should be taken into account.	Expert opinion/A	100%
Older frail patients with ABC Independent of age, all eligible patients should be informed about potential clinical trials and provided with adequate information and informed consent to be able to decide if they wish to participate.	Expert opinion/A	100%
Older frail patients with ABC What determines the possibility to use a specific anticancer agent is not age by itself but the existence of comorbidities with associated impact in adequate organ function such as liver, renal, cardiac, and/or neurological functions as well as bone marrow reserve.	I/A	100%
Older frail patients with ABC For treatment decision making, careful evaluation of comorbidities, performance status and geriatric assessment are crucial and more relevant than chronological age. A geriatric prescreening tool such as G8 assessment should be used initially, and a full geriatric assessment be performed if clinical frailty is suspected on pre-screening (e.g. if low G8 scores are found). G8 scoring tool	I/A	95%

Older frail patients with ABC Special attention should be given to potential drug interactions, in view of the common use of comedication/ polypharmacy by older patients.	I/A	100%
Older frail patients with ABC The ABC Guidelines endorse the *EUSOMA-SIOG* guidelines for the management of older patient with breast cancer, namely the following statement: Regarding systemic treatment for metastatic disease: different treatment schedules, dose reductions, or stepwise dose-escalation before reaching standard recommended dose might be required in older patients and reduce the risk of adverse outcomes.	Expert opinion/A	95%
Older frail patients with ER positive / HER2 negative ABC In view of the substantial survival benefit seen with ET + CDK4/6 inhibitors in 1st line, this combination is considered the standard of care for 1st line therapy for the majority of patients with ER+/HER2 negative ABC, independently of the patient's age.	I/A	100%
Older frail patients with ER positive / HER2 negative ABC Real world data suggest that ET+CDK4/6 inhibitors can be beneficial also in unfit older patients.	III/B	83%
Older frail patients with ER positive / HER2 negative ABC In unfit patients and very elderly (80+) patients, testing a reduced starting dose of the CDK4/6 inhibitor is a reasonable but not sufficiently studied strategy.	Expert opinion/B	89%

Older frail patients with ER positive / HER2 negative ABC If no absolute cardiac contra-indications exist, older patients with HER2 positive ABC should have access to anti-HER2 agents.	I/A	94%
Older frail patients with ER positive / HER2 negative ABC Certain anti-HER2 agents such as TKIs and ADCs, which are usually associated with more side effects, may need a lower starting dose, careful monitoring and dose adjustments according to toxicity in older frail patients.	Expert opinion/A	100%

Section XIII. How to treat tough issues in ABC

ABC and pregnancy

Guideline statement	LoE / GoR	NZ Consensus
ABC, contraception and pregnancy All persons of reproductive age with ABC should be counselled about use of non-hormonal contraception (independent of the tumour subtype) and the risks of conceiving while receiving treatment for ABC.	II/A	95%
ABC, contraception and pregnancy Special attention should be given to persons of reproductive age with ABC being treated without OFS/OFA since several therapies used for ABC have a low gonadotoxic effect and will not induce menopause.	II/A	100%
ABC and pregnancy Management of a pregnant patient with ABC is a complex and delicate situation that requires multidisciplinary discussion and experienced care. Advice should be sought from experts in the field such as the International Advisory Board of CIP (Cancer in Pregnancy) (www.ab-cip.org)	Expert opinion/A	100%
ABC and pregnancy Management of a pregnant patient with ABC is a complex and delicate situation that requires multidisciplinary discussion and experienced care. The preferences of the patient and of whomever the patient wishes to be involved must always be taken into account, after appropriate and transparent sharing of information about all management options and their potential impact on the patient's survival, fetal health and the future of the child.	Expert opinion/A	100%

ABC and pregnancy Management of a pregnant patient with ABC is a complex and delicate situation that requires multidisciplinary discussion and experienced care. The preferences of the patient and of whomever the patient wishes to be involved must always be taken into account, after appropriate and transparent sharing of information about all management options and their potential impact on the patient's survival, fetal health and the future of the child.	Expert opinion/B	84%
ABC and pregnancy Among all available systemic therapies, only chemotherapy can be safely administered during pregnancy and only in the 2nd and 3rd trimesters.	II/A	89%
ABC and pregnancy The most complex situation relates to HER2+ disease diagnosed in the 1st and 2nd trimester, because anti-HER2 therapy is critical for optimal disease control but cannot be administered during the entire pregnancy.	Expert opinion/A	95%
ABC and pregnancy Termination of pregnancy is a major consideration in some circumstances and should be available for patients who decide in favor of it*. Note: This statement has been altered for NZ. The INT panel voted for the following statement: Termination of pregnancy is a major consideration in some circumstances and should be available for patients who decide in favor of it, *within the first 12 weeks of pregnancy.*	Expert opinion/A	89%

Inflammatory (IBC) locally advanced breast cancer (LABC)

Guideline statement – For the purpose of these recommendations LABC means inoperable, non-metastatic locally advanced breast cancer	LoE / GoR	NZ Consensus
Inflammatory BC (IBC): definition IBC is a clinicopathological diagnosis that requires an interprofessional approach for diagnosis. IBC is designated as T4d or stage IV in case of metastatic disease at presentation. All of the following criteria must be met for a diagnosis of IBC: a) rapid onset of breast erythema, edema and/or peau d'orange, and/or warm breast, with or without an underlying palpable mass; b) duration of history no more than six months; c) erythema occupying at least one-third of the breast; d) pathologic confirmation of invasive carcinoma. A skin punch biopsy may help in the diagnosis, but it is not indispensable. Skin ulcerations are rare in IBC and more common in non-inflammatory LABC.	I/A	100%
Inoperable LABC or IBC and metastatic IBC BEFORE starting any therapy, at least one core biopsy providing histological type, grade and biomarker expression is indispensable to guide treatment decisions: Biomarkers include: a) For inoperable LABC and inoperable IBC : ER, PR, HER2 b) For metastatic IBC: ER, HER2, PD-L1 if TNBC For a) and b), patients should also have germline BRCA1, BRCA2 and PALB2 testing, but this result is not necessary prior to starting treatment. If germline testing is negative, BRCA1/2 somatic testing can be done as it may impact treatment.	I/A	81%

LABC and IBC Since LABC and IBC patients have a substantial risk of metastatic disease, a full staging workup, including a complete history, physical examination, lab tests and imaging of chest and abdomen and bone, before initiation of systemic therapy is highly recommended.	I/A	100%
For non-lobular invasive breast cancers PET-CT, if available, is preferred instead of and not in addition to CT-scans and bone scan. For most invasive lobular breast cancers CT-scans and bone scans or whole-body MRI are preferred. Note: FAPI-PET for staging of invasive lobular breast cancer is available in NZ as part of the Lumina study.	II/A	69%
Inoperable LABC HR positive Options for HR+ LABC include an anthracycline- and taxane-based primary chemotherapy regimen, or endocrine-based therapy (i.e. ET + CDK4/6 inhibitor).	I/A	88%
Inoperable LABC HR positive The choice of CT versus ET + CDK4/6 inhibitor, as initial treatment, depends on tumour characteristics (grade, biomarker expression, burden of disease,) and patient considerations (performance status, associated symptoms, comorbidities, preferences).	Expert opinion/A	88%
Inoperable IBC HR positive If chemotherapy is chosen, an anthracycline- and taxane-based primary chemotherapy regimen is recommended, followed by an endocrine-based therapy (ET + CDK4/6 inhibitor) post-operatively.	I/A	95%

Inoperable LABC or metastatic IBC TNBC Anthracycline- and taxane + platinum-based primary chemotherapy is recommended as initial treatment. Note: this recommendation might change as taxane+/- platinum without use of anthracycline might be recommended as first line treatment.	I/A	94%
Inoperable LABC or metastatic IBC TNBC Pembrolizumab should also be added, independently of PD-L1 status if non-metastatic disease and in PD-L1+ metastatic disease. Pembrolizumab is Medsafe approved and Pharmac listed for metastatic triple negative PD-L1+ ABC (BSIG has submitted request for non-resectable PD-L1+ LABC TN BC to be included in SA criteria.)	I/A	81%
Inoperable LABC and IBC HER2 positive Anthracycline-based primary chemotherapy should be incorporated in the treatment regimen.	I/B	50%
Inoperable LABC and IBC gBRCA mut Olaparib should be included in the treatment of IBC or inoperable LABC in gBRCAmut as this is a potentially curable situation and fits with the results from the OLYMPIA study. It is currently unknown how to optimally integrate the use of Olaparib with post-operative capecitabine or pembrolizumab, in gBRCA mut triple negative initially inoperable LABC or IBC, with residual disease after surgery. However, there are safety data allowing for the concomitant use of olaparib and pembrolizumab, and the panel prefers this option to the combination of capecitabine + pembrolizumab for these patients. *Olaparib is Medsafe approved, but not Pharmac listed for this indication (as of Oct 24)*	III/B	75%

Inoperable LABC and IBC gBRCA mut It is also currently unknown how to optimally integrate the use of Olaparib with post-operative abemaciclib, in gBRCA mut ER+/HER2 neg initially inoperable LABC or IBC. It is not possible to administer concomitantly olaparib and a CDK4/6i (safety concerns); since there are data allowing for a later start of abemaciclib in the adjuvant setting, it can be envisioned to administer olaparib first and then abemaciclib *Abemaciclib is Medsafe approved but not Pharmac listed (as of Oct 24).*	III/B	63%

Section XIV. How to optimally treat a patient with ABC in visceral crisis

Visceral crisis is defined as severe organ dysfunction as assessed by signs and symptoms, laboratory studies and rapid progression of disease.

- Visceral crisis is NOT the mere presence of visceral metastases, but implies important ORGAN COMPROMISE, leading to a clinical indication of the most efficacious therapy.

Examples

- Liver visceral crisis: rapidly increasing bilirubin >1.5 ULN, in the absence of Gilbert syndrome or biliary obstruction.
- Lung visceral crisis: Rapidly increasing dyspnoea at rest, not alleviated by drainage of pleural effusion

Guideline statement	LoE / GoR	NZ Consensus
Management of visceral crisis Therapeutic options for patients with visceral crisis are limited and evidence is scarce since these patients are almost always excluded from clinical trials. In ER+/HER2 negative ABC with visceral crisis, ET + CDK4/6 inhibitor are not contraindicated and may be a better option than chemotherapy.	II/B	69%
Therapeutic options for patients with visceral crisis are limited and evidence is scarce since these patients are almost always excluded from clinical trials. In HER2+ ABC with visceral crisis, the use of anti-HER2 agents is crucial and feasible.	II/A	81%
In situations of liver visceral crisis, options are further limited by the severe liver function impairment. Weekly regimens and lower doses are recommended.	IV/B	81%

For bone marrow infiltration, weekly reduced dose paclitaxel or capecitabine or ET + CDK4/6i (in case of ER+/HER2 neg disease) are among the best options.	IV/B	81%
In some situations, urgent surgery and/or radiation therapy and/or other interventional techniques (i.e. laser therapy for bronchial obstruction) may be needed.	IV/B	88%
Admission to ICU should not be denied if there is a possibility of reversing the clinical situation, after careful discussion with the patient and family, and always respecting (but not necessarily agreeing with) the patient's wishes (if they are unrealistic).	Expert opinion/NA	81%

Section XV. Management of leptomeningeal disease (LMD) of ABC

Guideline statement	LoE / GoR	NZ Consensus
Leptomeningeal disease (LMD) There is no accepted standard of care for breast cancer LMD. It is crucial that patients with LMD are included in clinical trials, namely in trials evaluating therapies for CNS disease.	Expert opinion/A	83%
The choice of treatment (radiotherapy, intra-CSF therapy, systemic therapy, supportive care) should consider prognostic evaluation, multidisciplinary discussion and always an in-depth discussion with the patient and the caregivers.	Expert opinion/A	78%
Staging of patients with LMD should include brain and full spine imaging with MRI with gadolinium to assess the full extent of the disease. Imaging should focus on sites of symptomatic disease if full cranio-spinal axis treatment (RT) is not recommended.	Expert opinion/A	78%
Focal RT to symptomatic lesions in brain and/or cranio-spinal axis, should be considered for circumscribed, particularly symptomatic lesions.	III/B	88%
Whole Brain RT can be considered for extensive nodular or symptomatic linear LMD.	III/B	78%
Leptomeningeal disease (LMD) A ventriculoperitoneal shunt may be placed to palliate symptoms of increased intracranial pressure or symptomatic hydrocephalus.	Expert opinion/B	78%

Leptomeningeal disease (LMD) Intra-CSF chemotherapy has not been proven to improve OS nor QoL but may palliate symptoms in some cases, although significant toxicity may also occur. It can be considered in select cases, in centres with experience if systemic disease is stable.	III/C	61%
The choice of systemic therapy for LMD should take into account the breast cancer subtype and previous treatments.	II/A	89%
Albeit in very small case series, there are some efficacy data in LMD for capecitabine monotherapy, the combination capecitabine + trastuzumab + tucatinib, and for T-Dxd.	V/B	72%

Section XVI. Management of patient with HIV and ABC

NZ PANEL HAS NOT VOTED ON THESE STATEMENTS

These are the international consensus statements. They are included for reference, for the benefit of New Zealand patients and clinicians. They were not voted on by local clinicians due to the lack of experience with breast cancer in this patient group.

Guideline statement	LoE / GoR
Prevalence of HIV comorbidity in ABC patients depends on HIV endemicity (varies 6 - 26%). Patients living with HIV who develop breast cancer have consistently worse survival, both in early and metastatic settings. HIV+ breast cancer patients have worse toxicity, especially myelotoxicity and infections. Data on how to manage ABC in a patient living with HIV is scarce, especially concerning new anticancer agents. Breast cancer in patients living with HIV should be co-managed by an oncologist and HIV specialist working in a multidisciplinary way.	Expert opinion/A
Prevalence of HIV comorbidity in ABC patients depends on HIV endemicity (varies 6 - 26%). Patients living with HIV who develop breast cancer have consistently worse survival, both in early and metastatic settings. HIV+ breast cancer patients have worse toxicity, especially myelotoxicity and infections. Data on how to manage ABC in a patient living with HIV is scarce, especially concerning new anticancer agents. People living with HIV have a higher incidence of other diseases such as tuberculosis and hepatitis. Before starting anticancer treatment, these diseases should be looked for and if diagnosed, treatment should be initiated.	Expert opinion/B

In general, the same ABC guidelines apply to HIV+ and HIV neg patients with ABC. However, careful consideration should be given to dose reductions and/or increased intervals (G-CSF recommended for myelotoxic CT agents).	Expert opinion/A
Most cytotoxic agents can be safely initiated if viral load is undetectable and CD4+T-count is at least 200 under modern ART regimens.	IV/B
HIV therapy should be initiated or continued during cancer therapy.	Expert opinion/A
In anti-retroviral naïve patients, it is recommended to initiate ART and wait for about 2 weeks before starting anticancer therapies, if clinically possible.	Expert opinion/B
Potential drug-drug interactions must always be checked. If interactions are a concern, it is recommended to check the viral load more often. For drugs that cause lymphopenia, CD4+ T-cell counts should be monitored more frequently.	Expert opinion/B

Section XVII. Supportive and palliative care

Guideline statement	NZ Consensus
Supportive care allowing safer and more tolerable delivery of appropriate treatments should always be part of the treatment plan.	87%
Introduction of expert palliative care early in the ABC journey, for effective control of symptoms such as pain, should be a priority.	93%
Access to effective pain treatment is necessary for all patients in need of pain relief.	100%
Optimally, discussions about patient preferences at the end of life should begin early in the course of metastatic disease. However, when active treatment no longer is able to control widespread and life-threatening disease, and the toxicities of remaining options outweigh the benefits, physicians and other members of the healthcare team should initiate discussions with the patient (and whānau/family members/friends, if the patient agrees) about end-of-life care.	93%
Cancer-related fatigue is frequently experienced by patients with ABC, exerts a deleterious impact on QoL and limits physical, functional, psychological and social wellbeing. The aetiology of this fatigue is complex, therefore effective management needs to be multidimensional. It is important to assess cancer-related fatigue using appropriate patient-reported outcome (PRO) measures before implementing various nonpharmacological (such as exercise) and if needed pharmacological interventions.	87%
Management of dyspnea: Treatable causes like pleural effusion, pulmonary emboli, cardiac insufficiency, anemia, drug toxicity must be ruled out. Patient support is essential. Oxygen is of no use in non-hypoxic patients. Opioids are the drugs of choice in the palliation of dyspnea.	93%
Benzodiazepines can be used in patients experiencing anxiety.	93%

	LoE / GoR	NZ Consensus
Steroids can be effective in dyspnea caused by lymphangitis carcinomatosis, radiation or drug-induced pneumonitis, superior vena cava syndrome, an inflammatory component, or in (cancer-induced) obstruction of the airways (in which case laser/stent is to be considered).		93%
Management of cancer and treatment-related cognitive impairment (CRCI), aka "Onco-brain" Cognitive dysfunction associated with cancer diagnosis and treatment has been increasingly reported by breast cancer patients, in the early and advanced settings, who did not have localised treatment to the brain nor other cognitive disorders. Poor performance in neuropsychological tests and of structural changes in brain imaging (i.e. volume reduction in grey matter, less connectivity and activation) are findings of this effect. However self reports of cognitive dysfunction are more prevalent than objective findings, probably due to the multidimensionality of this complaint. Imaging studies should only be used to rule out CNS disease. The exact mechanisms of CRCI are not clear, probably multifactorial and is frequently associated with other cancer related symptoms such as fatigue, anxiety, depression, pain, distress and sleep disorders.	III/NA	98%
Management of cancer and treatment-related cognitive impairment (CRCI), aka "Onco-brain" Routine assessment of clinical symptoms of cognitive dysfunction and awareness/education.	II/A	91%
Routine physical activity is recommended (weekly: 150–300 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity) in view of its association with neurogenesis in brain areas related to memory.	II/A	89%

Management of cancer and treatment-related cognitive impairment (CRCI), aka "Onco-brain"	II/A	91%
Screening for potential reversible factors and corrective measures when possible. [Such factors include: medications and their side effects, emotional distress, depression/anxiety, symptom burden (specially pain, fatigue and sleep disturbance), comorbidities, use of alcohol and other agents that may alter cognition, new-onset vitamin deficiencies and endocrinopathies (eg, TSH, B12)].		
If important impact on self-reported QoL: Refer to neuropsychological assessment and cognitive rehabilitation	III/A	96%

Relevant drug interactions	100%
Special attention should be given to potential interactions between targeted agents and common medications for comorbidities, due to the risk of interference with efficacy and/or safety. Examples: • Tamoxifen and ribociclib – increased risk of QTC prolongation • PPI and ribociclib/palbociclib/abemaciclib – decreased efficacy due to shared metabolism • Corticosteroids and checkpoint inhibitors – possible decreased efficacy due to competing mechanisms of action (i.e. immunosuppression) • Antibiotics and checkpoint inhibitors – decreased efficacy due to possible interference with microbiota	

Alternative therapies (i.e. therapies used instead of scientifically evidence based medicines) are not recommended in any phase or stage of cancer treatment.	100%

Complementary and integrative medicine: Some complementary therapies have the potential to reduce disease symptom burden and/or side effects of anticancer therapies, and therefore improve the QoL of ABC patients.	100%

Integrative medicine brings conventional and complementary approaches together in a coordinated way. It emphasises a holistic, patientfocused approach to health care and wellness – often including mental, emotional, functional, spiritual, social, and community. It aims for wellcoordinated care between different providers and institutions.	80%

Evidence suggests beneficial effects of the following methods, which can therefore be used: Physical exercise/sport (equivalent to 3–5 hrs of moderate walking per week) improves QoL, cardio-respiratory fitness, physical performance and fatigue, and it may also improve DFS and OS; MBSR (Mindfulness-based stress reduction) programs, hypnosis and yoga may improve QoL and fatigue, and help reduce anxiety, distress and some side effects of anti-cancer therapies; Acupuncture may help against CT-induced nausea and vomiting, fatigue and hot flashes.	100%
The following methods of alternative medicine are **not recommended** in ABC since available evidence shows no effect at best, or even association with worse outcome: Antioxidant supplements; Drugs outside the approved indication (e.g. methadone); Herbs including Chinese herbal medicine; Orthomolecular substances (selenium, zinc, etc.); Oxygen and ozone therapy; Proteolytic enzymes, thymic peptides; Phytoestrogens (soy-food, isoflavones); High-dose vitamins (vitamin C, D, E, carotenoids, etc.); L-carnitine, laetrile.	87%
In 2018, the American Society of Clinical Oncology (ASCO) Expert Panel endorsed the Society of Integrative Oncology guideline on the use of integrative therapies during and after breast cancer treatment. The panel deemed the guideline to be clear, thorough, and based on the most relevant scientific evidence, and endorsed it with added discussion points. Key recommendations include the following: Music therapy, meditation, stress management, and yoga are recommended for anxiety/stress reduction; Meditation, relaxation, yoga, massage, and music therapy are recommended for depression/mood disorders; Meditation and yoga are recommended to improve quality of life; Acupressure and acupuncture are recommended for reducing chemotherapy-induced nausea and vomiting; Acetyl-L-carnitine is not recommended to prevent chemotherapy-induced peripheral neuropathy because of a possibility of harm; No strong evidence supports the use of ingested dietary supplements to manage breast cancer treatment–related adverse effects. Clinicians should consider referring ABC patients to the guidelines. Additional information is available at: www.asco.org/supportive-care-guidelines	93%

Breast cancer centres/units/departments should be aware that the majority of their patients would like to be informed about complementary and integrative medicine and that many of them are using it. Physicians should actively ask for information about its use, in view of the potential deleterious interactions with specific anti-cancer therapies.	100%
Clinicians should consider providing patients with a list of registered local practitioners of complementary therapies that have the potential to reduce disease symptom burden and/or side effects of anticancer therapies. Such professionals could include NZASA-registered acupuncturists, MNZ-registered massage therapists, CEPNZ-registered exercise physiologists.	80%

Levels of Evidence Grading System

Levels of evidence

I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials *without heterogeneity.*
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with *demonstrated heterogeneity.*
III	Prospective *cohort studies*.
IV	Retrospective cohort studies or *case–control studies*.
V	Studies without control group, case reports, *experts' opinions*.

Levels of Evidence Grading System

Grades of recommendation

A	Strong evidence for efficacy with a substantial clinical benefit, *strongly recommended.*
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, *generally recommended.*
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, ...), *optional.*
D	Moderate evidence against efficacy or for adverse outcome, generally *not recommended.*
E	Strong evidence against efficacy or for adverse outcome, *never recommended.*