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Management of Early and Metastatic Breast Cancer

Insights from the Asia Pacific region on risk assessment and treatment modalities

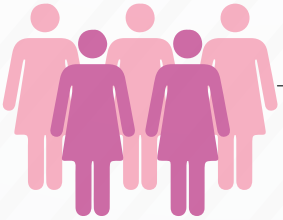
Breast cancer (BC) is one of the leading causes of cancer-related morbidity and mortality worldwide[1]

BC remains the most common cancer among Asian women, accounting for 45.3% of cases worldwide[2]

Asian women present approximately 10 years earlier than women from Western countries[2]

~2–25% of Asian patients present with locally advanced and *de novo* metastatic disease compared with 3–10% of patients in the Western countries[3]

Significant regional variations have been reported in the prevalence of BC and associated mortality[2]



Variables

- Healthcare systems
- Reimbursement strategies
- Healthcare access
- Drug availability and cost
- Screening and diagnosis

Risk factors in Asian women[2,3]

Older age

Family history of BC

Early menarche

Late menopause

High body mass index

Obesity or overweight

Exposure to tobacco smoke

High dietary intake of fatty foods

Treatment modalities and therapeutics[4]

Locoregional treatment	Systemic treatments	Targeted treatments
• Breast-conserving surgery • Lymph node dissection • Mastectomy and breast reconstruction • Ablation therapy • Radiotherapy	• Endocrine therapy (ET): selective oestrogen receptor modulators (SERMs), selective oestrogen receptor degraders (SERDs), aromatase inhibitors (AIs) • Chemotherapy • Cyclin-dependent kinase (CDK) 4/6 inhibitors: palbociclib and abemaciclib	• Phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR) inhibitors: alpelisib, inavolisib/capivasertib/everolimus • Poly (ADP-ribose) polymerase (PARP) inhibitors: olaparib and talazoparib
Antibody-drug conjugates (ADCs)		**Immune checkpoint inhibitors (ICIs)**

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Pan-Asian treatment guidelines based on expert consensus[2,3,4]

China, Indonesia, India, Japan, Korea, Malaysia, the Philippines, Singapore, Taiwan, and Thailand

Early breast cancer (EBC)[2]

Screening, diagnosis, pathology, and molecular biology	Staging and risk assessment
• Mammography every 2 years in women aged 45–69 years • Screening in women with pathogenic variants and a strong family history • Clinical examination and ultrasound imaging • Magnetic resonance imaging in high-risk or inconclusive cases • Screening for distant metastases in symptomatic patients with a high-risk of recurrence • Biopsy and histological assessment and grading • Biomarker evaluation: ER, progesterone receptor and human epidermal growth factor receptor 2 (HER2), proliferation marker and Ki67 • Tumour-infiltrating lymphocytes • Germline testing and genetic counselling	• Tumour-Node-Metastasis staging of tumour sample • Blood work-up • Computed tomography (CT) scan of the chest and abdomen in high-risk patients with suspected metastasis • Family history and menopausal status evaluation • [18F]2-fluoro-2-deoxy-D-glucose (FDG)–positron emission tomography (PET)–CT scanning for high-risk patients

Management

Locoregional treatment

- Neoadjuvant radiotherapy (RT)
- Surgery
- Postoperative RT
- Mastectomy and reconstruction
- Post-mastectomy and nodal RT for high-risk EBC
- Tegafur-gimeracil-oteracil potassium is approved in Taiwan for early BC with a certain risk of recurrence

Triple-negative breast cancer (TNBC)	HER2-positive EBC	Hormone receptor (HR)-positive/ HER2-negative EBC
• Chemotherapy with or without an ICI • Adjuvant olaparib in high-risk patients • Adjuvant ICI with capecitabine may be considered for residual disease	• Neoadjuvant systemic chemotherapy • Anti-HER2 therapy comprising trastuzumab–pertuzumab • Trastuzumab emtansine is also indicated	• ET • Adjuvant chemotherapy in high-risk EBC • Tamoxifen or AIs • Adjuvant olaparib or abemaciclib • Bisphosphonates in post-menopausal high-risk patients

Metastatic BC (MBC)[3]

Diagnosis, pathology, and molecular biology	• Biopsy and histological assessment	• Re-assessment of biomarker status and tumour biology	• Genomic profiling	• Circulating tumour DNA
Staging and risk assessment	• CT scan of the chest and abdomen, and bone scintigraphy	• F-FDG PET-CT	• Brain imaging in symptomatic patients	• Fracture risk assessment

Management

HR-positive, HER2-negative BC	HER2-positive BC	TNBC	Hereditary BC
• CDK4/6 inhibitor combined with ET • Ovarian function suppression/ovarian ablation in premenopausal women receiving ET • PI3K inhibitors • PARP inhibitors • Chemotherapy in ET-resistant patients	• Pertuzumab–trastuzumab –docetaxel • ET maintenance • Second-line therapy: trastuzumab deruxtecan • Third-line therapy: tucatinib–capecitabine–trastuzumab	• Chemotherapy in combination with an ICI	• PARP inhibitor

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Adverse effects of BC treatments[4,5,6,7]

ETs

SERMs

Treatment
- Tamoxifen
- Elacestrant

Unique side effects
- Irregular menses, vaginal discharge, mood changes, venous thromboembolism (VTE), and endometrial carcinoma

Common side effects
- Hot flashes
- Arthralgias
- Sexual dysfunction

SERDs

Treatment
- Fulvestrant
- Elacestrant

Unique side effects
- Nausea, vomiting, and diarrhoea

AIs

Treatment
- Letrozole
- Anastrozole
- Exemestane

Unique side effects
- Osteoporosis, fractures, and cardiovascular events

Immunotherapy

Treatment
- Programmed death-1
- Pembrolizumab
- Programmed death ligand-1
- Durvalumab
- Atezolizumab

Common side effects
- Rash
- Pruritus

PARP inhibitors

Treatment
- Olaparib

Common side effects
- Erythema nodosum
- Photosensitivity

Treatment
- Talazoparib

Common side effects
- Hypotension
- Thrombocytopenia

Targeted therapies

CDK4/6 inhibitors

Treatment
- Palbociclib
- Abemaciclib
- Ribociclib

Unique side effects
- Alopecia, elevated liver enzymes, VTE, and infections

Common side effects
- Diarrhoea
- Vomiting
- Nausea
- Cytopenias
- Rash
- Fatigue
- Nausea
- Stomatitis

mTOR inhibitor

Treatment
- Everolimus

Unique side effects
- Anaemia, infections, pneumonitis, and hyperglycaemia

PI3K inhibitors

Treatment
- Alpelisib
- Inavolisib

Unique side effects
- Anaemia, hypokalaemia, pneumonitis, and hyperglycaemia

AKT inhibitor

Treatment
- Capivasertib

Unique side effects
- Hyperglycaemia

ADCs

Treatment
- HER2 (trastuzumab deruxtecan)

Common side effects
- Alopecia
- Stomatitis
- Rash
- Pruritus
- Hyperpigmentation
- All-grade interstitial lung disease in 10–15% of patients

Treatment
- Trophoblast cell-surface antigen 2 (sacituzumab govitecan) and datopotamab deruxtecan

Common side effects
- Alopecia
- Rash
- Stomatitis

Management strategies to mitigate adverse effects[4,5,6]

- Systemic and topical corticosteroids
- Non-steroidal anti-inflammatory drugs
- Antibiotic treatments
- Dose reduction
- Anticoagulant therapies for VTE
- Blood glucose monitoring
- Oral antihistamines and retinoids
- Oral care

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BC treatments and associated side effects can significantly impair patients' quality of life[4,8]

A multidisciplinary team and collaborative approach are crucial to personalise treatment and improve patient care[2,3,8]

- Locoregional and systemic treatment
- Surgical reconstruction
- Bone metastases and orthopaedic evaluation
- Cardiotoxicity
- Endocrinology
- Dermatology
- Reproductive planning
- Psychological support

Treatment considerations[2]

Tumour burden: size, location, number of lesions, and extent of lymph node involvement

Menopausal status

Patient age

General health and comorbidities

Tumour biology: pathology and molecular biomarkers

Patient preference

Fertility preservation in younger premenopausal patients

Breast reconstruction

Patient involvement and shared decision-making[2,3,4,8]

Patient education about diagnosis and treatment options

Recommend patient-centred websites and reliable sources of information

Provide accessible reproductive care, including pregnancy counselling, contraception, and fertility preservation

Encourage and support participation in clinical trials

Offer psychological and social support

Discuss the risks and benefits of breast reconstruction

Encourage a healthy lifestyle to lower the risk of complications and recurrence

Recommend regular follow-up and screening

Digital health and telerehabilitation

Key message

A multidisciplinary and patient-centred approach can enable accurate diagnosis, systematic treatment planning, monitoring, and timely management of adverse effects, thereby improving the outcomes and quality of life of patients with EBC or MBC

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