June 26th 2018
HONG KONG BREAST CANCER FOUNDATION
ANNUAL SCIENTIFIC MEETING 2018

Summary of Session 3

Current standards of care for patients with hormone-responsive recurrent breast cancer

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Approximately 75% of postmenopausal patients have hormone-responsive breast cancer.[1] The third edition of the Advanced Breast Cancer (ABC 3) guidelines published by ESMO recommend endocrine therapy (ET) as first-line treatment for patients with metastatic disease in the absence of visceral crisis and endocrine resistance.[2] In such patients, ET is preferable to first-line chemotherapy.[3]

In oestrogen receptor-positive (ER+) postmenopausal patients, first-line ET options include a selective ER modulator (SERM; eg, tamoxifen), a selective ER down-regulator (SERD; eg, fulvestrant), an aromatase inhibitor (AI) alone, combination AI and SERD, or combination ET and targeted drugs such as cyclin-dependent kinase (CDK) inhibitors.[2]

Fulvestrant versus AI therapy for patients with ET-sensitive breast cancer

Fulvestrant monotherapy is more effective than anastrozole in an ET-naive population of patients with breast cancer.[4,5] However, superiority of fulvestrant in combination with a non-steroidal AI compared with an AI alone as a first-line therapy in postmenopausal patients could not be confirmed in two randomized studies.[2]

Combination ET and targeted drug treatment options for patients with ET-sensitive and AI-resistant breast cancer

Despite the established effectiveness of AIs for inhibiting tumour progression, AI resistance may be observed in patients who relapse.[1] Primary (or *de novo*) resistance occurs in patients who have relapsed during the first 2 years of adjuvant ET, or whose disease has progressed within the first 6 months of first-line ET for metastatic disease.[2] Secondary (or acquired) resistance occurs in patients who relapse while receiving ET for more than 2 years or within 12 months of completing adjuvant ET, or while receiving ET and experiencing disease progression after 6 months of initiating first-line therapy for metastatic disease.[2]

To delay the development of AI resistance inevitable in prolonged first-line AI treatment, combination regimens that include an AI with a mammalian target of rapamycin (mTOR) inhibitor, such as everolimus, are effective in patients with disease progression following treatment with a non-steroidal AI.[6] Median progression-free survival (PFS) was 21.7 months (95% confidence interval [CI], 18.1–23.9) and objective response rate (ORR) was 43.6% in patients treated with first-line everolimus in combination with exemestane.[6] Median overall survival has not yet been reached after a median duration of follow-up of 23.5 months.[6]

Alternatively, an AI in combination with a CDK inhibitor is also effective as first-line therapy for AI-sensitive patients.[7] Palbociclib, ribociclib and abemaciclib, in combination with an AI, significantly prolonged median PFS and generated a significantly higher ORR compared with an AI alone in phase

3 studies of AI-sensitive patients.[7,8] Moreover, in patients with AI-resistance, fulvestrant in combination with a CDK inhibitor significantly prolonged median PFS compared with fulvestrant alone.[8]

Summary

Patients with hormone-responsive breast cancer should receive ET as first-line therapy instead of chemotherapy. While ET is an effective treatment, resistance to AIs is observed in some patients, and the use of mTOR or CDK inhibitors in combination with an AI should be administered as first-line therapy. For AI-resistant patients, a mTOR inhibitor in combination with a steroidal AI, or a CDK inhibitor in combination with fulvestrant, are effective strategies for circumventing AI resistance.

Panel Discussion

Dr Stephanie HY Lau
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A 64-year-old patient with a complex medical history and multiple comorbidities, including metabolic and cardiovascular disease (CVD), presented with bilateral breast cancer with no distant metastases. She underwent a bilateral modified radical mastectomy (MRM). Pathological findings revealed an invasive ductal carcinoma in the left breast which was ER+, progesterone receptor-positive (PR+), human epidermal growth factor receptor 2-negative (HER2-) and Ki-67 18%. The deep surgical margin was close. Adjuvant docetaxel–cisplatin combination chemotherapy and letrozole were administered in light of her comorbidities. She also received locoregional radiotherapy (RT). One year later, the patient was diagnosed with recurrent disease and had several sclerotic spinal lesions consistent with metastasis; she was administered palliative RT to the spine and continued letrozole therapy.

The case study concluded with contributions from other members of the meeting who agreed with Dr Lau's treatment plan and suggested trying a combination of fulvestrant and a CDK4/6 inhibitor or combining an alternative AI with everolimus.

Dr Joanne W Chiu
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AI-associated bone loss is common in postmenopausal patients with hormone-responsive breast cancer, and its real-world prevalence is underestimated in randomized controlled trials.[9] Administering bisphosphonate therapy to postmenopausal patients with breast cancer reduces the risk of bone recurrence, the incidence of fracture and mortality.[9] Accordingly, several organizations have published guidelines for administering adjuvant bisphosphonates and other bone-modifying agents in patients with breast cancer. Based on her ongoing research, Dr Chiu emphasized that the standard of care for patients should include assessing risk factors for bone loss, such as body mass index, previous history of fracture and steroid use, prior to administering AI therapy.

Dr Peter Choi
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A 56-year-old patient underwent a MRM of the right breast for a grade 2 invasive ductal carcinoma not otherwise specified, with extensive lymphovascular invasion. The tumour was ER+, PR-, HER2- and Ki-67 60%. The patient received adjuvant chemotherapy with cyclophosphamide, methotrexate and 5-fluorouracil (CMF) for six cycles, and tamoxifen therapy for 2 years before she made the decision to cease treatment. Unfortunately, 2 years later, she experienced extensive chest wall recurrence with positive right axillary lymph nodes, which she attempted to treat with traditional Chinese medicine, and was unsuccessful. A positron emission tomography and computerized tomography (PET/CT) scan showed diffuse chest recurrence with multiple skin nodules and chest wall infiltration, along with level I–III lymph nodes in her right axilla, supraclavicular fossa, level I lymph nodes in her left axilla and metastases in the ilium and pubic bone**.** Additionally, her tumour marker carcinoma antigen (CA) 15-3 was 68.7 U/mL. A chest wall biopsy confirmed a metastatic carcinoma of the primary breast tissue (ER+, PR+ and HER2-) and the patient subsequently began treatment with palbociclib (125 mg) for 21 days with one week of rest in each cycle, in combination with letrozole. She demonstrated a good partial response, but required frequent treatment delays and dose reductions due to developing grade 2/3 thrombocytopenia and leukopenia. She also developed grade 3 mucositis of the lips and oral mucosa, which caused eating difficulties and resulted in substantial weight loss. After 1 year of treatment, the patient is currently on palbociclib 75 mg (one week on/one week off). A PET/CT scan in June 2018 showed all the patients' active lesions became metabolically quiescent.

References

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