Palbociclib: Safe and Effective in an 85-Year-Old Female with Metastatic Bilateral Breast Cancer

Sir,

Hormone receptor (HR)-positive breast cancer represents the largest subtype of breast cancer, accounting for the majority of malignant neoplasms of the breast. For many years, treatment of HR-positive disease has been focused on targeting the estrogen receptor signalling pathway.[1] However, both new and acquired resistance to hormonal blockade occurs in a large subset of this particular cancer. The cyclin-dependent kinases (CDKs) are a large family of serine–threonine kinases that play an important role in regulating cell-cycle progression. Palbociclib, a small-molecule CDK4 and CDK6 inhibitor, has shown its ability to preferentially inhibit the growth of estrogen receptor-positive breast cancer cells, act synergistically with antiestrogens, and reverse endocrine resistance.[2] In the PALOMA-2 trial, first-line Palbociclib plus Letrozole versus Letrozole plus Placebo significantly prolonged median progression-free survival (PFS) in women with estrogen receptor-positive/HER2-negative metastatic breast cancer.[3,4]

An 85-year-old hypertensive female, with a family history of breast cancer, presented with progressively enlarging left breast mass for 4 months. On examination, a mobile left breast mass was palpable in the upper inner quadrant of the breast. The rest of the physical examination was unremarkable. Mammogram showed an ill-defined, soft tissue density area with spiculations in the upper quadrant of the left breast in its central part measuring 2.5 x 2 cm and a small, ill-defined soft tissue density area with spiculated margins in the upper outer quadrant of the right breast, BIRAD V. Benign-looking lymph nodes were seen in bilateral axillae. These findings were concordant with ultrasound as well. CT scan revealed well-defined hypo-attenuating soft tissue mass lesion with slight lobulated margins in the upper half of the left breast measuring 1.8 x 2.6 x 2.1 cm in size along with sub-centimeter enhancing axillary lymph nodes, largest level I node measured 6.7 mm on the left side. Another ill-defined soft tissue density was seen in the right breast measuring 8.0 x 5.0 mm along with a few sub-centimetre enhancing right axillary nodes, largest measuring 7 mm in the short axis. In addition, sub-centimetre mediastinal lymph nodes were noted, the largest pre-carinal node measured 8.0 mm in the short axis. Bone scan revealed a mildly increased tracer uptake in D11, suspicious of metastatic deposit. Furthermore, an MRI of lumber spine showed, well defined hypo-intense lesion in the D11 vertebral body on the left side with minimal post-contrast enhancement measuring 1.6 x 1.2 cm in the CC and AP dimensions suggestive of metastatic deposit. A biopsy of the left breast revealed infiltrating ductal carcinoma Grade I, estrogen and progesterone receptors, strong positive, and HER2-negative and Ki 67 of 5-10% and biopsy of the right breast revealed infiltrating ductal carcinoma Grade II, estrogen and progesterone receptors, strong positive, and HER2-negative and Ki 67 of 30-35%. Further evaluation with PET CT scan revealed left breast mass 2.2x 1.5 cm with SUV 2.49, multiple sub-centimetre FDG-avid lymph nodes in the right supraclavicular region medially and extending up to level VI with SUV of 3.91, and multiple lymph nodes in the mediastinum, pre-tracheal, para-tracheal, and along the arch of aorta with size 1.1cm with SUV of 5.67 and two sub-centimetre, non-FDG-avid nodules in the right middle lobe of the lung with no skeletal metastasis. Later, she was started on a combination of CDK 4/6 inhibitor, Palbociclib, 100 mg a day, orally in 4-week cycles (3 weeks of treatment followed by 1 week off), Letrazole, 2.5 mg continuously and zoledronic acid, 4 mg, intravenous once in 6 months as part of systemic therapy.

An interim PET CT scan for response evaluation revealed stable disease. She was continued on the same treatment regimen until four months later, when she experienced Grade 2 neutropenia and thrombocytopenia leading to the treatment interruptions. Hence, the dose of Palbociclib was reduced to 75 mg a day. Three months later, PET CT scan revealed a reduction in both breast masses' sizes and their metabolic activity and interval resolution of multiple sub-centimetre FDG-avid lymph nodes in supraclavicular and mediastinal locations. She was continued on the same treatment regimen without treatment interruption.

A recent PET CT scan in June 2023 revealed interval stable disease. Therefore, the same treatment will be continued until disease progression or Grade 3 to 4 adverse effects. It has been over two years after the initial diagnosis, the patient had a good quality of life, tolerated the treatment, and the systemic disease was well-controlled on the initial treatment regimen.

Palbociclib, plus an aromatase inhibitor (AI) specifically showed an overall survival benefit and real-world PFS benefit in metastatic breast cancer patients, with and without visceral metastases or bone-only disease, and among subgroups of patients not well represented in breast cancer clinical trials, including black patients and patients aged ≥75 years. Real world PFS was significant in age >75 years (HR 0.77 (95% confidence interval: 0.61-0.97) favouring Palbociclib plus AI *vs.* AI alone.[5] Haematological toxicities may lead to delay in treatment, dose reductions or even stoppage of the treatment.[6]

PATIENTS' CONSENT:
Informed consent was taken from the patient who participated in the study.

COMPETING INTEREST:
The author declared no conflict of interest.

AUTHOR'S CONTRIBUTION:
AHO: Conceived the idea, performed literature search, and drafted the manuscript.

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