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IN BRIEF

Abemaciclib (*Verzenio*) for Early Breast Cancer

The oral cyclin-dependent kinase (CDK) 4/6 inhibitor abemaciclib (*Verzenio* – Lilly), which was approved by the FDA in 2017 for treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, has now been approved for use in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for adjuvant treatment of patients with HR-positive, HER2-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score $\geq 20\%$.¹

HR-POSITIVE, HER2-NEGATIVE BREAST CANCER –

About 70% of all breast cancers are HR-positive and HER2-negative. Standard treatment (a combination of surgery, radiation, and adjuvant/neoadjuvant chemotherapy plus adjuvant endocrine therapy) is effective for HR-positive, HER2-negative early breast cancer, but recurrence is common.² Ki-67 is a prognostic biomarker for tumor proliferation; a score $\geq 20\%$ is associated with early recurrence and poor prognosis.^{3,4}

MECHANISM OF ACTION – CDKs 4 and 6 regulate the G1/S phase transition within the cell cycle; they are often overexpressed in HR-positive breast cancer, leading to cell cycle progression and cell proliferation. Inhibition of CDK 4/6 results in cell cycle arrest, senescence, and apoptosis.

CLINICAL STUDIES – FDA approval of abemaciclib for the new indication was based on the results of an open-label trial (monarchE) in 5637 women and men with HR-positive, HER2-negative, node-positive, resected, early breast cancer at high risk of recurrence (≥ 4 positive pathologic axillary lymph nodes or 1-3 positive axillary lymph nodes and at least one of the following: tumor size ≥ 5 cm, histologic grade 3, or Ki-67 score $\geq 20\%$). Patients were randomized to receive abemaciclib 150 mg twice daily for

2 years plus adjuvant endocrine therapy or endocrine therapy alone. Invasive disease-free survival (IDFS) at 2 years was 92.2% with combination therapy versus 88.7% with endocrine therapy alone, a statistically significant difference.⁵ IDFS at 3 years was 88.8% with combination therapy and 83.4% with endocrine therapy alone.⁶ Data beyond 3 years are not available.

Another CDK 4/6 Inhibitor – In a trial (Penelope-B) in 1250 women with HR-positive, HER2-negative early breast cancer at high risk of relapse, addition of the oral CDK 4/6 inhibitor **palbociclib** (*Ibrance*) 125 mg once daily for 13 cycles (21 days on, 7 days off) to adjuvant endocrine therapy did not improve IDFS compared to endocrine therapy alone.⁷

ADVERSE EFFECTS – The most common adverse effects (frequency $\geq 20\%$) of abemaciclib in the monarchE trial were diarrhea, infections, neutropenia, fatigue, leukopenia, nausea, anemia, and headache. Severe (grade ≥ 3) adverse events occurred in 46% of patients in the abemaciclib group and in 13% of those in the placebo group. About 17% of patients in monarchE stopped taking abemaciclib because of adverse effects.

DOSAGE, ADMINISTRATION, AND COST – The recommended starting dosage of abemaciclib for the new indication is 150 mg twice daily taken in combination with tamoxifen or an aromatase inhibitor. The drug should be taken for a total of 2 years or until disease recurrence or unacceptable toxicity occurs. A 30-day supply of *Verzenio* costs about \$13,870.⁸

CONCLUSION – Addition of the oral CDK 4/6 inhibitor abemaciclib (*Verzenio*) to adjuvant endocrine therapy improved invasive disease-free survival at 3 years in women and men with HR-positive, HER2-negative, node-positive, resected, early breast cancer at high risk of recurrence. No data are available on the durability of this effect beyond 3 years. Severe (grade ≥ 3) adverse events were reported in about 50% of patients. ■

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8. Approximate. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. November 5, 2021. Reprinted with permission by First Databank, Inc. All rights reserved. ©2021. www.fdbhealth.com/policies/drug-pricing-policy.

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