Palbociclib: Will the race against endocrine resistance end?

Sir,

Nearly, 80% of the breast cancers express estrogen receptors (ERs), progesterone receptors, or both. Endocrine therapies remain the backbone of the systemic treatment for hormone receptor positive cancers by substantially reducing the risk of relapse.[1] Many women still relapse during or after completing adjuvant therapy. Further systemic therapy remains considerably challenging for these patients. Fulvestrant, a selective ER modulator has modest activity in these patients[2,3] and the development of effective therapies that can reverse resistance to endocrine therapy, is of clinical importance.

Palbociclib (IBRANCE, developed by Pfizer) is an oral, reversible, selective, small-molecule inhibitor of cyclin-dependent kinases (CDK) 4, and CDK 6. CDKs are important modulators of cell cycle entry and progression in response to growth signals, and inhibition of these kinases with palbociclib could enhance the activity of other anticancer drugs in tolerable regimens.[4] On February 03, 2015, the USA Food and Drug Administration granted accelerated approval to palbociclib (IBRANCE, Pfizer, Inc.) for use in combination with letrozole for the treatment of postmenopausal women with ER-positive, human epidermal growth factor receptor 2 (HER-2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease.[5] This approval was based on encouraging results found in Phase III study PALOMA3. This Phase III randomized controlled study involved 521 patients with advanced hormone-receptor-positive, HER-2 neu negative breast cancer that had relapsed or progressed during prior endocrine therapy. Patients in a 2:1 ratio received palbociclib and fulvestrant or placebo and fulvestrant. The primary endpoint was progression-free survival and secondary endpoints were overall survival, objective response; patient reported outcomes and safety. A preplanned interim analysis demonstrated that median progression-free survival was in favor of palbociclib arm (9.2 months vs. 3.8 months hazard ratio for disease progression or death, 0.42; 95% confidence interval: 0.32–0.56; $P < 0.001$). The most common Grade 3 or 4 adverse events in the palbociclib-fulvestrant group were neutropenia (62.0%, vs. 0.6% in the placebo-fulvestrant group), leukopenia (25.2% vs. 0.6%), and anemia (2.6% vs. 1.7%), thrombocytopenia (2.3% vs. 0%), and fatigue (2.0% vs. 1.2%). Febrile neutropenia was reported in 0.6% of the palbociclib-treated patients and 0.6% of the placebo-treated patients. The rate of discontinuation due to adverse events was 2.6% with palbociclib and 1.7% with placebo.[6]

The recommended dose of palbociclib is a 125 mg capsule taken orally once daily for 21 consecutive days, followed by 7 days off treatment to comprise a complete cycle of 28 days. The common side effects are neutropenia, fatigue, anemia, nausea, stomatitis, alopecia, diarrhea, thrombocytopenia, decreased appetite, vomiting, asthenia, peripheral neuropathy, and epistaxis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Saurabh Samdariya, Puneet Kumar Bagri, Puneet Pareek, Ruchi Kumawat

Department of Radiation Oncology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

Correspondence to: Dr. Saurabh Samdariya, Room No. 311, Resident Hostel, All India Institute of Medical Sciences Residential Complex, Basni Phase-II, Jodhpur - 342 005, Rajasthan, India.
E-mail: drsaurabh.onco@gmail.com

REFERENCES

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: An overview of the randomised trials. Lancet 2005;365:1687-717.
2. Di Leo A, Jerusalem G, Petruzelka L, Torres R, Bondarenko IN, Khasanov R, *et al.* Results of the CONFIRM phase III trial comparing fulvestrant 250 mg with fulvestrant 500 mg in postmenopausal women with estrogen receptor-positive advanced breast cancer. J Clin Oncol 2010;28:4594-600.
3. Di Leo A, Jerusalem G, Petruzelka L, Torres R, Bondarenko IN,

Khasanov R, *et al.* Final overall survival: Fulvestrant 500 mg vs 250 mg in the randomized CONFIRM trial. J Natl Cancer Inst 2014;106:djt337.
4. Dhillon S. Palbociclib: First global approval. Drugs 2015;75:543-51.
5. Available from: http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm432886.htm. [Last accessed on 2015 Jul 14].
6. Turner NC, Ro J, André F, Loi S, Verma S, Iwata H, *et al.* Palbociclib in hormone-receptor-positive advanced breast cancer. N Engl J Med 2015;373:209-19.

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.167861

Cite this article as: Samdariya S, Bagri PK, Pareek P, Kumawat R. Palbociclib: Will the race against endocrine resistance end?. Clin Cancer Investig J 2015;4:775-6.