Sorscher. Int J Cancer Clin Res 2016, 3:069
Volume 3 | Issue 5
ISSN: 2378-3419

International Journal of
Cancer and Clinical Research

Case Report: Open Access

A First Case of Male Breast Cancer Responding to Combined Aromatase Inhibitor/Palbociclib Therapy

Steven Sorscher*

Department of Oncology, Wake Forest Medical School, USA

***Corresponding author:** *Steven Sorscher, MD, Professor of Medicine, Department of Oncology, Wake Forest Medical School, Medical Center Blvd, Winston-Salem, NC 27104, Tel: 336-716-0230, E-mail: ssorsche@wakehealth.edu*

Abstract

For men with metastatic breast adenocarcinoma standard therapies typically involve the same therapies used for woman. Recently the FDA approved the aromatase inhibitor letrozole combined with the inhibitor of cyclin dependent kinase 4/6 (CDK4/6) palbociclib as first line therapy for women with metastatic breast cancer [1]. Here we report a first case of a man with metastatic breast cancer whose tumor responded to palbociclib and letrozole. This combination might be effective for other men with metastatic breast cancer as well.

Introduction

Male breast cancer is far rarer and less studied than female breast cancer. Tamoxifen is considered both standard adjuvant therapy and treatment for metastatic breast cancer [2,3].

Several reports have highlighted clinical differences between male and female breast cancers. For example, as adjuvant therapy Eggemann, et al. demonstrated in a large retrospective study that the overall survival in male breast cancer was significantly better for those treated with adjuvant tamoxifen compared to those treated with an aromatase inhibitor [4].

Grief et al reported statistically significant better 5-year overall survival for women compared to men with stages 0, 1 and 2 breast cancers [5]. Abreu et al reported that survival from time to recurrence was less long in men compared to women [6]. Nilsson also showed both median and relative survival were inferior in male breast cancer patients compared to female breast cancer patients [7].

In what was described as the "first pooled analysis of the literature synthesizing all available data coming from case reports/case series" the authors noted a complete response (CR) rate of 5.7%, partial response (PR) of 23.8%, and concluded that the aromatase inhibitors in men with metastatic breast cancer are an effective and safe treatment option for hormone receptor-positive metastatic male breast cancer patients [8].

Palbociclib is a kinase inhibitor indicated in combination with letrozole for the treatment of postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor 2 (HER-2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease, but is not FDA approved for the treatment of male breast cancer, based primarily on a clinical trial showing roughly a doubling of progression free survival (PFS) compared to treatment with letrozole alone in this group of patients (20.2 versus 10.2 months) [1].

Palbociclib is an oral inhibitor of CDK 4/6 activity. It appears to inhibit progression of cancer cells in G1-S phase by mitigating the hyperphosphorylation and thereby activating the retinoblastoma tumor suppressor gene product. In cancer cell lines, aromatase inhibitors are synergistic with palbociclib in inhibiting proliferation [1,9]. Compared to aromatase inhibitor therapy (letrozole) alone, the combination of letrozole with pabloclib resulted in a 10 month progression-free survival benefit and a 55.4% versus 39.4% response rate as first line therapy for metastatic hormonal receptor positive, HER2 negative breast cancer and pabloclib is now FDA approved in this setting and when combined with fulvestrant as second line therapy for women with tumors as well [1,10].

Case Report

RR was a 64-year-old male when he underwent a left mastectomy for Stage IIIB (T4N1M0) invasive breast adenocarcinoma in early 2006. The records do not reflect whether the patient was offered neoadjuvant systemic therapy. The patient had no personal or family history of breast cancer or ovarian cancer or known risk factors for developing breast cancer.

The tumor was ER positive and HER2 negative (IHC = 0). No germline mutation in BRCA1 or BRCA2 was identified (Myriad Genetics Laboratories, Salt Lake City, UT 84108). He received 5 years of adjuvant tamoxifen therapy followed by 2.5 years of extended adjuvant therapy with letrozole, although adjuvant aromatase inhibitor therapy is not considered "standard of care" for men with breast cancer.

In September 2013 he presented with dyspnea and a CT scan showed mediastinal adenopathy and a large right pleural effusion. He underwent talc pleurodesis and a pleural biopsy which confirmed ER positive (IHC = 100%) HER2 negative (IHC = 0) recurrent breast adenocarcinoma. He was receiving adjuvant letrozole therapy at the time of recurrence.

Systemic therapies since that time have included paclitaxel, liposomal doxorubicin, fulvestrant with progression and/or intolerance of each. On 3-1-2016 a CT C/A/P demonstrated pro-

ClinMed International Library

Citation: Sorscher S (2016) A First Case of Male Breast Cancer Responding to Combined Aromatase Inhibitor/Palbociclib Therapy. Int J Cancer Clin Res 3:069

Received: September 25, 2016: **Accepted:** October 17, 2016: **Published:** October 19, 2016

gressive mediastinal lymphadenopathy and pleural soft tissue nodularity while receiving nab-paclitaxel. Therapy was changed to letrozole (2.5 mg poqD) and pablociclib (125 mg poqD x 21 days) q28 days. On 5-1-2016, a repeat CT C/A/P showed "stable nodularity and no change in mediastinal lymphadenopathy". On 7-16-2016 a repeat CT C/A/P demonstrated "interval decrease in the size of multiple right epiphrenic lymph nodes".

Discussion

Responses to aromatase inhibitors have been reported in men with metastatic breast cancer [8,11]. Years after aromatase inhibitor therapy became standard first line therapy for metastatic disease in woman, Finn et al reported a near doubling of progression free survival for patients receiving palbociclib, a CDK4/6 inhibitor combined with letrozole compared to letrozole alone (20.2 vs. 10.2 months) and the FDA approved this combination for women with hormone receptor positive, HER2 negative disease [1]. It has been felt that targeting both the hormone receptor pathway and simultaneously the CDK 4/6 pathway, which is part of the PIK3CAsignaling pathway, was successful in part because PIK3CA is the most commonly mutated gene in hormone receptor positive breast cancer. While not as common in male as female breast cancers, PIK3CA is also the most commonly mutated gene in male breast cancer [12].

At the time of recurrence it is unlikely RR's cancer responded to letrozole alone because his progressive disease was diagnosed while on adjuvant letrozole therapy. It seems more likely that the combination of the letrozole with the palbociclib induced the radiographic response. Given the usual modest toxicities of each of these drugs, further reports of aromatase inhibitor/palbociclib use might show responses, leading to this combination being seen as an option to be considered in men with breast cancer.

Conflict of Issue Disclosure

Speaker's Bureaus for Celgene and Pfizer Pharmaceutical Companies.

References

1. Richard S Finn, Prof John P Crown, Istvan Lang, Katalin Boer, Prof Igor M Bondarenko, et al. (2015) The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol 16: 25-35.
2. Gradishar WJ, Anderson BO, Balassanian R, Blair SL, Burstein HJ, et al. (2016) Invasive Breast Cancer Version 1.2016, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 14: 324-354.
3. White J, Kearins O, Dodwell D, Horgan K, Hanby AM, et al. (2011) Male breast carcinoma: increased awareness needed. Breast Cancer Res 13: 219.
4. Eggemann H, Ignatov A, Smith BJ, Altmann U, von Minckwitz G, et al. (2013) Adjuvant therapy with tamoxifen compared to aromatase inhibitors for 257 male breast cancer patients. Breast Cancer Res Treat 137: 465-470.
5. Greif JM, Pezzi CM, Klimberg VS, Bailey L, Zuraek M (2012) Gender differences in breast cancer: analysis of 13,000 breast cancers in men from the National Cancer Data Base. Ann Surg Oncol 19: 3199-3204.
6. Henriques Abreu M, Henriques Abreu P, Afonso N, Pereira D, Henrique R, et al. (2016) Patterns of recurrence and treatment in male breast cancer: A clue to prognosis? Int J Cancer 139: 1715-1720.
7. Nilsson C, Holmqvist M, Bergkvist L, Hedenfalk I, Lambe M, et al. (2011) Similarities and differences in the characteristics and primary treatment of breast cancer in men and women - a population based study (Sweden). Acta Oncol 50: 1083-1088.
8. Zagouri F, Sergentanis TN, Azim HA Jr, Chrysikos D, Dimopoulos MA, et al. (2015) Aromatase inhibitors in male breast cancer: a pooled analysis. Breast Cancer Res Treat 151: 141-147.
9. Finn RS, Dering J, Conklin D, Kalous O, Cohen DJ, et al. (2009) PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro. Breast Cancer Res 11: R77-R77.
10. Turner NC, Ro J, André F, Loi S, Verma S, et al. (2015) Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. N Engl J Med 373: 209-219.
11. Kuba S, Ishida M, Oikawa M, Nakamura Y, Yamanouchi K, et al. (2016) Aromatase inhibitors with or without luteinizing hormone–releasing hormone agonist for metastatic male breast cancer: report of four cases and review of the literature. Breast Cancer 23: 945-949.
12. Piscuoglio S, Ng CK, Murray MP, Guerini-Rocco E, Martelotto LG, et al. (2016) The Genomic Landscape of Male Breast Cancers. Clin Cancer Res 22: 4045-4056.