Reduced incidence of breast cancer in women adherent to testosterone or testosterone-anastrozole hormone therapy: updated interim analysis

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Objectives

A 10-year prospective IRB study, approved March of 2008, was designed to follow pre and postmenopausal women with symptoms of hormone deficiency, treated with testosterone (T) or testosterone combined with anastrozole (T + A) subcutaneous implants for the occurrence of breast cancer (BCA).
In January 2015, an 82-month interim analysis was performed in patients who remained adherent to therapy, updating a previous 5-year analysis, which showed a reduced incidence of BCA in women on T therapy in the intent to treat group and more-so in patients adherent to T therapy compared to age-matched controls, historical controls and age-matched Surveillance, Epidemiology and End Results (SEER) incidence rates[1].

Methods

A web-based application using Microsoft Active Server Pages with a MySQL database backend system was custom developed to follow and track patients, T dosing information along with 'person-days' of therapy.
T pellets are implanted every 3 months on average. The program identifies women who have not returned for therapy within a pre-set time frame of 240 days, the maximum duration of T implant therapy[1]. **Adherent** patients are defined as women who receive T or T + A pellet implants at less than 240 day (regular) intervals. Any participant not seen for 240 days was contacted and BCA status documented.
The incidence rates of BCA in this analysis are reported as an unadjusted, un-weighted value of diagnosed cases divided by the sum of person-years of observation in adherent patients, i.e., patients compliant with T therapy. This value is compared to our previous results, including our control group, and current, SEER 2007-2011 US invasive BCA expected age-matched incidence rates[2].
4-8 mg of anastrozole (A), an aromatase inhibitor, is combined with T in the pellet implant and is prescribed to women who show signs or symptoms of estrogen excess[1].

Indications for aromatase inhibitor therapy

- Increased risk for BCA: ADH, ALH, Family history
- Severe fibrocystic breast disease, breast pain
- Endometriosis, fibroids, dysfunctional uterine bleeding
- Moderate to severe PMS, anxiety, irritability
- Menstrual or migraine headaches
- Insulin resistance, metabolic syndrome, abdominal obesity
- Fluid retention, edema, bloating

Results

1388 women were enrolled in the study from March 2008 - March 2013. As of 15 January 2015, the mean age of 471 patients who remained adherent to therapy was 58.2 ± 8.72 y, range 34.6-90.7 (Figure 1). The mean duration of therapy was 6.05 ± 1.74 y, range 2.07-9.16 (Figure 2). 40-50% of women are currently treated with the combination T + A. There have been 4 cases of invasive BCA (1 additional since March 2013) diagnosed in women adherent T or T + A therapy per 5231 person-years (p-y) of therapy. This translates to an incidence of 76/100 000 p-y, which is substantially lower than current SEER age-matched incidence rates (297/100 000) and our control group (390/100 000), and remains consistent with our previously reported 5-year adherent group (73/100 000). This translates to a RR of 0.26 compared to SEER expected incidence rates.
The invasive BCA was a 4mm DCIS with a 1.2 mm area of microinvasion, ER-. Two cases of DCIS were diagnosed, both < 15mm, one ER- and one ER+.

Figure 1

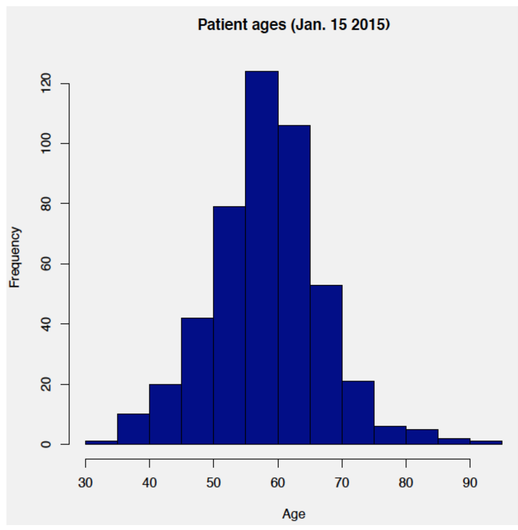
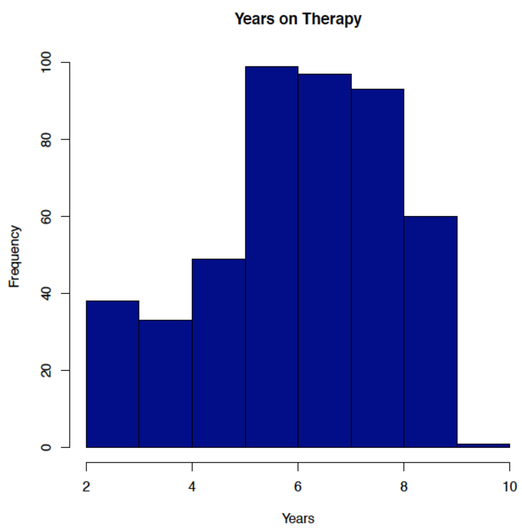


Figure 2



Conclusion

At 82 months, continuous T and T + A hormone therapy, delivered as a subcutaneous implant, continued to be breast protective as evidenced by the reduced incidence of breast cancer in women adherent to therapy.
Further studies should be done on T and T combined with A, an aromatase inhibitor, for hormone therapy as well as for prevention and therapy of breast cancer.

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Bibliography

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2. Howlader N, et.al. SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/, based on November 2013 SEER data submission, posted to the SEER web site, April 2014.

ABBV: ADH, atypical ductal hyperplasia; ALH, atypical lobular hyperplasia; DCIS, ductal carcinoma in situ; RR, relative risk; ER, estrogen receptor

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