

5<sup>th</sup> World Congress on

# BREAST CANCER

June 15-17, 2017 London, UK

## Contralateral prophylactic mastectomy with reconstruction increases health care utilization and cost

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**Background:** Rates of contralateral prophylactic mastectomy in women with unilateral breast cancer continue to rise, especially in women undergoing immediate breast reconstruction (IBR).

**Methods:** We utilized administrative claims data from a large U.S. commercial insurance database (OptumLabs) to identify women age 18+ years who underwent IBR 1/2004-12/2013. We compared 2-year total costs of care and unadjusted utilization rates between unilateral mastectomy (UM) and bilateral mastectomy (BM) for implant-based and autologous reconstruction. Comparisons were tested using t-test and differences in cost were estimated with Wilcoxon rank sum test.

**Results:** 11,728 women undergoing mastectomy with IBR were identified; 7,693 with implant reconstruction (2,090, 27% UM and 5,603, 73% BM) and 4,035 with autologous reconstruction (1,754, 43% UM and 2,281, 57% BM). Mean hospital length of stay at initial surgery and overall rate of office visits was similar between BM+IBR and UM+IBR, however rate of A&E visits was higher for BM+IBR (34.2 per 100 women vs. 30.2,  $p < 0.0001$ ). For implant reconstruction total 2-year cost of care was higher for BM+IBR than UM+IBR for commercial insurance (\$106,469 vs. \$96,689,  $p < 0.001$ ) however it was not significantly different for medicare advantage. For autologous reconstruction, total medicare advantage 2-year cost of care was higher for BM+IBR (\$57,602 vs \$37,713,  $p = 0.027$ ) with even greater differences seen in commercial insurance.

**Conclusion:** BM+IBR (autologous or implant) was associated with increased A and E visits and higher total cost of care over 2-years compared to UM+IBR. Patients considering contralateral prophylactic mastectomy should be counseled on the additional risks and costs associated with BM+IBR.

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## GT198 and Her2 double positivity as an improved therapeutic marker for herceptin treatment in human breast cancer

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Breast cancer is a lethal cancer in women. It is urgent to identify new therapeutic biomarkers to facilitate the treatment. Therapeutic drug Herceptin (trastuzumab) is effective in Her2-positive breast cancer treatment, however, there is inconsistency to distinguish responders versus non-responders using Her2 as a sole biomarker. The human *GT198* gene is a breast and ovarian cancer gene at chromosome 17q12, 2.9 Mb proximal from the *ERBB2* gene encoding Her2. Both germline mutations and high frequency somatic mutations in *GT198* are present in breast and ovarian cancer. In breast and ovarian tumors, somatic mutations are present in tumor stromal stem cells. Gene copy number increase of *GT198* has also been found in breast cancer. Here we find that Her2 and *GT198* proteins are co-expressed in breast tumor stromal cells carrying *GT198* mutations, suggesting that Herceptin may in fact also target *GT198*-positive tumor stromal cells. Her2 gene amplicons generally encompass large genomic regions, thus the two adjacent genes may co-amplify and result in coexpression. Our finding suggests that *GT198*/Her2 double positivity is potentially a more specific therapeutic marker for Herceptin. In particular, positive tumor stroma, in addition to tumor, deserves more attention in clinical decisions. Since herceptin is extensively used in the treatment of breast cancer and *GT198* is a causative breast cancer gene, this study provides insights into novel mechanisms associated with herceptin efficacy and reveals new biomarker using *GT198* for improved targeted therapy.

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