7N Invited

Local therapy options in BRCA1/2 carriers with operable breast cancer: the importance of adjuvant chemotherapy

L. Pierce[1], K. Phillips[2], K. Griffith[1], S. Buys[3], D. Gaffney[3], M. Moran[4], B. Haffty[5], M.K.B. Ben-David[6], J. Garber[7], S. Merajver[1], J. Balmaña[8], A. Meirovitz[9], S. Domchek[10]. *[1]University of Michigan, Ann Arbor, US; [2]Peter MacCallum Cancer Center, Victoria, Australia; [3]University of Utah, Salt Lake City, Utah, US; [4]Yale University, New Haven, US; [5]UMDNJ-Robert Wood Johnson Medical School, New Brunswick, New York, US; [6]Sheba Medical Center, Ramat Gan, Israel; [7]Dana-Farber Cancer Center, Boston, US; [8]Hospital d'Hebron, Barcelona, Spain; [9]Hadassah Medical Organization, Jerusalem, Israel; [10]University of Pennsylvania, Philadelphia, US*

Background: Women with inherited germline BRCA1/2 mutations have a 55−85% cumulative risk of developing breast cancer (BC) by age 70. Carriers with breast cancer must choose between breast conservation (BCT) and mastectomy (M) yet data on outcomes are limited.

Methods: 655 women with deleterious BRCA1/2 mutations diagnosed with operable BC and treated with BCT or M were identified and underwent follow-up to assess local, regional and systemic rates of recurrence. Cox regression models were constructed to detect significant associations between patient and clinical characteristics and time-to-event endpoints.

Results: Local component as first failure was significantly more likely in those treated with BCT compared to M, with cumulative estimated risks of 23.5% vs. 5.5%, respectively, at 15 years ($p < 0.0001$). Lack of chemotherapy use was associated with a significantly increased rate of ipsilateral in-breast events, HR 5.4, $p = 0.0001$. Conversely, 15-year estimates in carriers treated with BCT and chemotherapy was 11.9% ($p = 0.08$ when compared to M). Most events appeared to be second primary cancers rather than failure to control the primary tumor. The risk of contralateral breast cancer (CBC) exceeded 40% in all groups but was not significantly different by use of adjuvant radiotherapy (RT) or not. No significant differences were observed in rates of systemic recurrence, breast cancer-specific or overall survival between the BCT and M groups.

Conclusions: BRCA1/2 mutation carriers with breast cancer have similar overall survival whether treated with M or BCT. However, women undergoing BCT have an elevated risk of a second in-breast event that is significantly reduced in the presence of chemotherapy. Rates of CBC events are high and do not appear to be significantly increased by scatter RT.

8N Invited

Similar outcome in a randomized phase III trial comparing docetaxel versus vinorelbine both combined with trastuzumab as first line treatment for metastatic or locally advanced human epidermal growth factor receptor 2 (HER2) positive breast cancer

M. Andersson[1], E. Lidbrink[2], E. Wist[3], K. Enevoldsen[4], A.B. Jensen[5], P.G. Sørensen[6], K. Bjerre[7], S. Møller[7], J. Bergh[2], S.T. Langkjer[4]. *[1]Copenhagen University Hospital Rigshospitalet, Department of Oncology, Copenhagen, Denmark; [2]Karolinska University Hospital & Karolinska Institutet, Department of Oncology, Stockholm, Sweden; [3]Ullevaal Hospital, Department of Oncology, Oslo, Norway; [4]Vejle Hospital, Department of Oncology, Vejle, Denmark; [5]Århus Kommunehospital, Department of Oncology, Århus, Denmark; [6]Roskilde Hospital, Department of Oncology, Roskilde, Denmark; [7]Danish Breast Cancer Cooperative Group, Secretariat, Copenhagen, Denmark*

Background: Taxanes combined with trastuzumab are registered for treatment of HER2 positive metastatic breast cancer. However, phase II data indicate that vinorelbine with trastuzumab has high efficacy and less toxicity.

Methods: Patients with HER2 positive locally advanced or metastatic breast cancer naïve to chemotherapy for disseminated disease and for trastuzumab within 12 months with normal organ function including cardiac function and good performance status were randomized to receive either docetaxel 100 mg/m^2 day 1 or vinorelbine 30−35 mg/m^2 i.v. days 1+8 both combined with trastuzumab 8 mg/kg loading dose and thereafter 6 mg/kg day 1 q 3 weeks until progression or unacceptable toxicity. Tumor assessments were conducted every 9 weeks. Analyses of measures of efficacy were conducted according to intent-to-treat.

Results: During 05/2004−08/2008 143 patients were randomized to docetaxel and 141 to vinorelbine at 27 institutions. Groups were well balanced with regard to demographic and prognostic factors including age (median 56 vs 57 years), prior adjuvant chemotherapy (43% vs 52%, hereof anthracycline 33% vs 41% and taxane 1% vs 2%) and trastuzumab (1% vs 0%), stage (locally advanced 9% vs 9%), hormone receptor positive status (53% vs 60%), liver metastases (40% vs 40%), and measurable disease (86% vs 84%), With a median potential follow-up of 34 months, 178 patients have progressed, 114 have died and 39 are still on treatment. The median number of chemotherapy cycles administered was 8 for docetaxel and 10 for vinorelbine. Median dose intensity of chemotherapy was 0.86 vs 0.93. More patients had grade III-IV toxicity with docetaxel than with vinorelbine, 81% vs 51% ($p < 0.0001$) including febrile neutropenia, 34% vs 10% ($p < 0.0001$) and stopped chemotherapy because of toxicity, 20% vs 7% ($p < 0.001$). Median time to treatment failure for chemotherapy was 6.3 vs 8.4 months ($p < 0.0001$). Median time to progression was 12.5 vs 13.6 months ($p = 0.57$). Response rate (pts. with measurable disease, %): CR: 12 vs 9, PR: 38 vs 38, CR+PR: 50 vs 48 SD: 22 vs 25, PD: 8 vs 4, NE: 20 vs 23 ($p = 0.64$). Median overall survival time was 36.1 vs 39.1 months ($p = 0.57$).

Conclusion: The outcome was similar for first line treatment with vinorelbine and docetaxel both combined with trastuzumab but vinorelbine could be administered for a longer time and had a more favorable toxicity profile. It should therefore be considered as a potentially better first line alternative.