442 Poster

Are There Any Differences of Biomarker Changes in Short Term Neoadjuvant Ais (Exemestane Vs. Letrozole)?

D. Miura[1], M. Hanaoka[1], A. Shimomura[1], T. Iwatani[1], H. Kawabata[1], T. Fujii[2]. [1]*Toranomon Hospital, Department of Breast and Endocrine Surgery, Tokyo, Japan;* [2]*Toranomon Hospital, Department of Pathology, Tokyo, Japan*

Background: Current approaches of neoadjuvant endocrine therapy are focusing on biomarker analysis of the diagnostic specimens. One of the important things is to treat patients with an endocrine agent for several months before surgery to identify tumors that are responsive to treatment. Little is known about the biomarker changes in specific agents and whether the changes affect following treatment. A pilot study was conducted to investigate the differences of biomarker changes in short term neoadjuvant endocrine therapy (exemestane vs. letrozole) and also to investigate the difference in treatment durations of each AI.

Materials and Methods: Tumors from 60 postmenopausal women with confirmed ER positive stage 1−3 breast cancers in neoadjuvant endocrine therapy, which compared exemestane and letrozole for at least 10 days (10 days to 6 weeks) before surgery, were analyzed for pre- and post-treatment mRNA expression of ERα, ERβ, PR, HER2, and Ki67 from FFPE samples using with QuantiGene Assay. We also compared these biomarker changes in treatment duration, less than 3weeks (group S) vs. 3−7 weeks (group M). Statistical tests were two-sided. Totally 126 samples from 60 women, 31 took exemestane 25 mg daily and 29 did letrozole 2.5 mg daily until the surgery, were analyzed. Median treatment durations of exemestane and letrozole were 23 and 25 days. The group S and group M consisted of 14 and 16 patients in exemestane and 12 and 17 in letrozole. Any other clinical characteristics were well balanced between the two treatment arms.

Results: Statistical significant decreases of PR and Ki67 and increase of ERβ were found in both exemestane and letrozole arms compared to baseline. These biomarkers had almost similar trends in both treatments irrespective of treatment duration (group S and M). ERα significantly decreased in letrozole (−35%) compared to exemestane (−16%). Although statistical significance of mean % decreases of Ki67 was found in both treatments in any duration (group S and M, −59% and −44% in exemestane, −30% and −44% in letrozole), no significant was found in each AI. Mean % decreases of ERα were −21% (group S) and −11% (group M) in exemestane and −18% (group S) and −46% (group M) in letrozole. This difference was statistically significance (−11% vs.−46%, p = 0.02). Interestingly a significant change of HER2 was only found in group M of exemestane (mean % change +67%, p = 0.04) compare to letrozole (+6%).

Conclusions: Neoadjuvant exemestane and letrozole treatment for short duration had both significantly decreased Ki67 mRNA level irrespective of treatment duration. Longer duration of AI treatment may change in ER and HER2 status and affect the responsiveness of the following treatment.

443 Poster

The German Cohort of the TEAM Trial: Does Prior Chemotherapy Affect the Efficacy of Endocrine Therapy?

M. Bossart[1], P. Hadji[2], D. Kieback[3], A. Hasenburg[1]. [1]*University Medical Center Freiburg, Obstetrics and Gynecology, Freiburg, Germany;* [2]*University Hospital of Giessen and Marburg, Obstetrics and Gynecology, Marburg, Germany;* [3]*Elblandkliniken, Obstetrics and Gynecology, Meissen, Germany*

Background: The Tamoxifen Exemestane Adjuvant Multinational (TEAM) trial was a large, multinational, randomized, open-label phase III trial evaluating the efficacy and safety of 5 years of exemestane 25 mg daily versus tamoxifen 20 mg daily for 2.5−3 years followed by exemestane for 2−2.5 years.

Material and Methods: We performed a retrospective analysis of patients who were enrolled in the TEAM trial in Germany (n = 1502) to assess the effect of different chemotherapies on the efficacy of endocrine therapy.

Results: In the total evaluable patient population there was no significant difference in overall survival (OS) between patients who had received prior chemotherapy and those who had not (P = 0.02836). However, disease free survival (DFS) and distant recurrence free survival (DRFS) were significantly better in patients who had not received prior chemotherapy versus those who had received chemotherapy (P = 0.0308 and P = 0.0001). DFS and DRFS were significantly different in this patient population dependent on the prior chemotherapy regime used (P = 0.0018 and P = 0.0001, respectively). There was a trend towards poorer DFS and an increased incidence of distant recurrence in patients who had received prior chemotherapy with anthracycline compared with those who had not received anthracycline chemotherapy. Baseline characteristics indicated that patients who underwent anthracycline chemotherapy were more likely to have undergone mastectomy (P = 0.00003) and had a worse prognosis (P < 0.00001 for each aspect of TNM classification) than those who did not.

In exemestane monotherapy-treated patients, there were no significant differences in OS and DFS according to prior chemotherapy use. Exemestane monotherapy-treated patients who had received no prior chemotherapy had significantly better DRFS compared with those who had received prior anthracyclines ($P = 0.0029$). There was no significant difference in DRFS for other chemotherapy regimens (CMF or other) versus no chemotherapy in this group.

Conclusion: Patients with endocrine therapy without chemotherapy had significantly improved DFS and DRFS compared to those who had received both. This is probably due to the advanced disease stage of patients requiring chemotherapy. Interestingly in Exemestan monotherapy-treated patients only anthracyclines were inferior to no chemotherapy concerning DRFS.

445 Poster

PrefHer: a Clinical Trial to Evaluate Patient Preference for Trastuzumab Administered Subcutaneously or Intravenously in Patients with HER2-positive Early Breast Cancer

X. Pivot[1], A. Knoop[2], G. Curigliano[3], P. Barrett-Lee[4], M. Lichinitser[5], V. Mueller[6], C. Camci[7], J. Gligorov[8], N. Scotto[9], L. Fallowfield[10]. [1]*CHU Jean Minjoz, Besançon, France;* [2]*Odense University Hospital, Odense, Denmark;* [3]*European Institute of Oncology, Milan, Italy;* [4]*Cardiff University and Velindre Cancer Centre, Cardiff, United Kingdom;* [5]*N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation;* [6]*University Medical Center, Hamburg, Germany;* [7]*University of Gaziantep, Gaziantep, Turkey;* [8]*APHP Tenon, University of Paris VI, Paris, France;* [9]*F. Hoffmann-La Roche Ltd, Basel, Switzerland;* [10]*Sussex Health Outcomes Research & Education in Cancer (SHORE-C), University of Sussex, Sussex, United Kingdom*

Background: One year of trastuzumab (Herceptin®)-based therapy, consisting of eighteen 3-weekly cycles, is standard of care for HER2-positive early breast cancer (EBC). Trastuzumab is administered intravenously (IV) over 30−90 minutes. A subcutaneous (SC) formulation of trastuzumab has been developed, which is rapid to administer (within 5 minutes), potentially improving convenience for patients and reducing administration costs.

The recent Phase III HannaH study (NCT00950300) compared the pharmacokinetics, efficacy and safety of the trastuzumab SC formulation and the trastuzumab IV formulation in 596 patients receiving (neo)adjuvant therapy for HER2-positive EBC. In this pivotal study, the trastuzumab SC formulation demonstrated pharmacokinetics (C_{trough}) and pathological complete response rate non-inferior to that of trastuzumab IV, with a safety profile consistent with the known safety profile of trastuzumab IV.

The PrefHer study is designed to evaluate patient preference for SC administration of trastuzumab.

Methods: PrefHer is a randomised, multicentre, international, Phase II cross-over trial (NCT01401166). The primary endpoint is the proportion of patients indicating an overall preference for SC or IV administration of trastuzumab. Secondary endpoints include event-free survival, immunogenicity, safety and healthcare professional satisfaction with SC administration of trastuzumab. Patients who have completed (neo)adjuvant chemotherapy for invasive HER2-positive EBC are randomised 1:1 to receive 4 cycles of trastuzumab SC (600 mg) administered using a single-use injection device, followed by 4 cycles of trastuzumab IV (8 mg/kg–>6 mg/kg), or the reverse sequence. Patients are interviewed by telephone before randomisation, and again after they have experienced both methods of trastuzumab administration. Interviews are conducted by experienced interviewers using a structured schedule translated into the relevant languages. Enrolment began in October 2011, with the aim of recruiting 200 patients by the end of Q1, 2012. A sub-study will also be performed in parallel at selected participating centres to evaluate medical resource utilisation ('time and motion study').