496 Poster

Endometrial safety of cross-over treatment with tamoxifen followed by exemestane

D.G. Kieback[1], N. Harbeck[2], W. Bauer[3], P. Hadji[4], G. Weyer[5], A. Hasenburg[6]. *[1]Helios Medical Center, Gynecology, Aue, Germany; [2]Technical University, Gynecology, Munich, Germany; [3]Community Hospital, Gynecology, Villingen-Schwenningen, Germany; [4]University Hospital, Gynecology, Marburg, Germany; [5]Independent Clinical Research Consulting, Biometrics, Berlin, Germany; [6]University of Freiburg, Gynecology, Freiburg, Germany*

Background: A prospective open label randomized multicenter substudy was performed in the German TEAM Trial Group to evaluate the effects of the irreversible aromatase antagonist Exemestane (EXE) and the ER agonist/antagonist Tamoxifen (TAM) on the endometrium during adjuvant treatment for postmenopausal estrogen receptor positive breast cancer with regard to the risk of endometrial cancer.

Methods: Transvaginal Ultrasound Scans (TVS) were performed at baseline, 6 and 12 months of treatment if no proliferation >5 mm was present, and in 3 months intervals if endometrial thickness exceeded 5 mm. Intent-to-treat analysis was performed based on 158 patients. Primary endpoint was the time interval from randomization to the earliest occurrence of endometrial hyperplasia >10 mm. Secondary endpoints were the time from randomization to endometrial hyperplasia >5 mm and the time interval from randomization to vaginal bleeding. Analysis of Time to Event Curves was performed by Kaplan–Meier method, analysis of differences between treatments by two-sided Logrank test and Cox Proportional Hazards. Differences in frequency were compared by Fisher's Exact Test.

Results: 65 patients were available for analysis in the TAM arm, 78 in the EXE arm. Both groups were comparable regarding age, height, tumor grade, and stage. Median follow-up was 727 (EXE) and 526 days (TAM). In this time period, there were no (EXE) vs. 11 (TAM) cases of endometrial hyperplasia >10 mm ($p < 0.0001$), 11 (EXE) vs. 34 (TAM) patients with hyperplasia >5 mm ($p < 0.006$). In total, endometrial hyperplasia was observed 11 times in the EXE arm vs. 45 times in the TAM arm ($p < 0.0001$). Time to endometrial hyperplasia was significantly longer in the EXE group ($p < 0.0001$); HR was 0.160 indicating an 84% risk reduction of hyperplasia in the EXE group. Increase in endometrial thickness from baseline to 6mo. was 2.94 mm (EXE) vs. 5.41 mm (TAM), from baseline to 12 mo 2.64 mm vs. 6.0 mm respectively ($p < 0.0006$). Only 1 patient underwent histological sampling in the EXE group (no hyperplasia) vs. 18 in the TAM subset.

Conclusion: Irreversible inactivation of aromatase by EXE resulted in significantly less endometrial proliferation than TAM. While during the TAM treatment phase there were significantly more interventions to obtain endometrial histology, n precancerous or cancerous lesions were observed. The cross-over approach of TAM followed by EXE was safe in regard to endometrial cancerogenesis.

497 Poster

A randomized phase II study of aprepitant, ondansetron and dexamethasone for chemotherapy-induced nausea and vomiting in Chinese breast cancer patients receiving moderately emetogenic chemotherapy

W. Yeo[1], F.K.F. Mo[1], J.J.S. Suen[1], W.M. Ho[1], S.L. Chan[1], W.K. Yeung[1], W. Lau[1], K.K.C. Lee[2], W.H. Kwan[1], B. Zee[1]. *[1]Prince of Wales Hospital, Clinical Oncology, Hong Kong SAR, China; [2]Prince of Wales Hospital, Pharmacy, Hong Kong SAR, China*

Objectives: This is a single center, randomized phase II, double-blind placebo-controlled study to evaluate the NK(1)-receptor antagonist, aprepitant, in Chinese breast cancer patients. The primary objective was to compare the efficacy of aprepitant-based antiemetic regimen and standard antiemetic regimen for the prevention of chemotherapy-induced nausea and vomiting (CINV) in patients who received moderately emetogenic chemotherapy. The secondary objective was to compare the patient-reported quality of life in these two groups of patients.

Patients and Methods: Eligible breast cancer patients were chemotherapy-naive and treated with adjuvant AC chemotherapy (i.e. cyclophosphamide 600 mg/m^2 and doxorubicin 60 mg/m^2). Patients were randomly assigned to either an aprepitant-based regimen (day 1, aprepitant 125 mg, ondansetron 8 mg, and dexamethasone 12 mg before chemotherapy and ondansetron 8 mg 8 hours later; days 2 through 3, aprepitant 80 qd) or a control arm which consisted of standard regimen (day 1, ondansetron 8 mg and dexamethasone 20 mg before chemotherapy and ondansetron 8 mg 8 hours later; days 2 through 3, ondansetron 8 mg bid). Data on nausea, vomiting, and use of rescue medication were collected with a self-report diary, patients quality of life were assessed by self-administered Functional Living Index-Emesis (FLIE).

Results: Of 127 patients randomized, 124 were assessable. For CINV in Cycle 1 AC, there was no significant difference in proportion of patients with reported complete response, complete protection, total control, 'no vomiting', 'no significant nausea' and 'no nausea'. The requirement of rescue medication appears to be lesser in patients treated with the aprepitant-based regimen those with the standard regimen (11% v 20%; $P = 0.06$). Assessment of FLIE revealed that while there was no difference in the nausea domain and the total score between the two groups of patients; however, patients receiving standard antiemetic regimen had significantly worse quality of life in the vomiting domain (mean score $\pm$SD = 23.99$\pm$30.79) when compared with those who received the aprepitant-based regimen (mean score $\pm$SD = 3.40$\pm$13.18) ($p < 0.05$). Both treatments were generally well tolerated.

Conclusion: The aprepitant regimen appears to reduce requirement of rescue medication when compared with the control regimen for prevention of CINV in patients receiving both an anthracycline and cyclophosphamide, and is associated with a better quality of life during adjuvant AC chemotherapy.

Acknowledgement: This study has been supported by an educational grant from Merck Sharpe & Dohme (Asia) Ltd.

498 Poster

The effects of breast cancer treatment on cognitive functions

E. Hedayati[1], A. Schedin[1], M. Albertsson[1], H. Nyman[2], B. Nilsson[1]. *[1]Karolinska Institutet, Oncology, Stockholm, Sweden; [2]Karolinska Institutet, Clinical neuroscience, Stockholm, Sweden*

Background: We have started a longitudinal study to investigate a) if the effects of being given a breast cancer diagnosis may affect cognitive functions in women, b) if adjuvant therapy may have detrimental effects on cognition, c) if subjects with substantial cognitive impairment after therapy may benefit from a cognitive training program.

Materials and Methods: The study is dimensioned for 140 subjects. The subjects are recruited consecutively and prospectively from the mammography-screening program at Södersjukhuset, Stockholm. According to the results of the diagnostic process the patients are divided in two main groups by "biological" randomization; healthy subjects and women with breast cancer (n = 70 in each group). All participants are examined by a web-based battery of neuropsychological tests at four times: at inclusion and before diagnosis, after diagnosis and/or operation (two months), after treatment (six months), and follow-up after an additional three months. Subjects who score one standard deviation below the mean compared to baseline, in any of four cognitive domains (Response speed, Processing speed, Memory and Attention) after treatment will be offered to participate in a randomized trial of cognitive training versus control.

Results: We have so far included 65 subjects. 30 have completed the third test session. Preliminary results show that patients with a recent breast cancer diagnosis and subsequent surgery demonstrate a tendency toward a cognitive decline in attention. There is a significant cognitive decline in memory in the breast cancer group after treatment $p = 0.029$ (repeated measures ANOVA) and inclination of mild impairment in processing speed. Conclusions: The preliminary results may be interpreted to suggest that receiving a breast cancer diagnosis and/or surgery may be associated to a substantial cognitive decline in a subgroup of patients. After six months of treatment a subgroups of patients have a significant decline in memory, which is not dependent on other cognitive functions, depression or anxiety.

Women with breast cancer receiving adjuvant chemotherapy often report difficulties with memory, attention and concentration difficulties. We believe that the fact that breast cancer is the most common cancer among women and specially among women of working age in Sweden may, in itself, motivate a study of cognitive effects of its treatment.