Title

Biomarker Profiles and Cytoplasmic Vacuolization as Predictors of Progression-Free Survival and Clinical Response to Neoadjuvant Chemotherapy in Patients with Epithelial Ovarian Cancer

Journal

Gynecologic Oncology, 107(2)

ISSN

0090-8258

Authors

Mahdavi, A
Chopra, S
Hunter, M
et al.

Publication Date

2007-11-01

DOI

10.1016/j.ygyno.2007.08.053

Conclusions. Despite more aggressive use of growth factors and reduced initial CT doses, only 54% of pts completed 4 or more cycles and a large proportion terminated CT due to toxicity. Further studies into the pharmacokinetics of adjuvant CT in elderly patients and appropriate agent, dose and schedule selection are required.

doi:10.1016/j.ygyno.2007.08.052

43

Biomarker Profiles and Cytoplasmic Vacuolization as Predictors of Progression-Free Survival and Clinical Response to Neoadjuvant Chemotherapy in Patients with Epithelial Ovarian Cancer

A. Mahdavi, S. Chopra, M. Hunter, W. Brewster, I. Ramzy, K.S. Tewari
Division of Gynecologic Oncology, University of California Irvine School of Medicine, Orange, CA

Objective. To determine if immunohistochemical (IHC) staining patterns and morphologic features are correlated with clinical response, and progression-free survival (PFS) in patients with epithelial ovarian cancer (EOC) who had undergone neoadjuvant chemotherapy (NC).

Methods. Tissues were obtained from interval cytoreduction of 21 consecutive patients with EOC treated with NC. They were studied by IHC for HER-2/neu, p53, Ki-67 and CA-125 expression and examined for morphologic changes induced by chemotherapy. Pathologists were blinded to clinical outcome measures. Response was measured according to RECIST criteria. Kaplan–Meier survival analysis was stratified by pathologic variables in univariate analysis.

Results. The median age was 62 yrs (range, 35–88 yrs). 95.2% were FIGO stage IIIC-IV. Following 3–4 cycles of NC, 19% achieved a complete and 57% a partial clinical response. The median time to CA-125 nadir for the entire study group was 9.0 months (range, 3–21). The median PFS was 7.4 months (range, 0–50). The median overall survival (OS) has not been reached. Tumor grade and degenerative cytoplasmic vacuolization correlated with clinical response ($p=0.0476$). Time to CA-125 nadir (24 vs. 9 months, $p<0.001$) and high p53 IHC positivity (35 vs. 18 months, $p=0.03$) were associated with a favorable PFS, while both increased HER-2/neu (5 vs. 17 months, $p=0.007$) and Ki67 IHC ($p=0.03$) immuno-reactivity were inversely correlated with PFS.

Conclusions. Biomarker profiles, specifically p53, HER-2-neu and Ki67 following NC may be indicative of impending response to therapy. The presence of cytoplasmic vacuolization and high tumor grade may also be predictive of subsequent PFS. This information may be used in tailoring further management of these patients. Further studies with larger sample size may be warranted.

doi:10.1016/j.ygyno.2007.08.053

44

A Retrospective Review of Short Term Outcomes in the Use of Seprafilm® in Patients with Gynecologic Malignancies

A. Tan, R. Ramirez, R. Bliss, M. Geller
Department of Obstetrics, Gynecology, and Women's Health, Division of Gynecologic Oncology, University of Minnesota, Minneapolis, MN

Objectives. 1) To determine if the use of Seprafilm® adhesion barrier affects disease free and overall survival in patients with epithelial ovarian, fallopian tube, and primary peritoneal cancer. 2) To determine if the rates of immediate complications were increased with the use of Seprafilm®.

Background. Seprafilm® is a bioresorbable membrane composed of chemically modified hyaluronate-carboxymethylcellulose that has been proven to prevent adhesion formation between adjacent tissues in randomized controlled studies. However, there are concerns regarding its use in surgery for malignancy. *In vitro* studies in a colorectal cancer model demonstrated enhanced metastatic potential of tumors on sodium hyaluronate. Although prospective studies to date in colorectal cancers have not shown a difference in cancer outcomes in patients receiving Seprafilm®, these data are still immature. The safety of Seprafilm®, specifically in gynecologic malignancies, has yet to be investigated. To address these concerns, we performed a retrospective review to assess the effects of Seprafilm® on the disease free and overall survival in patients that had surgical staging procedures for ovarian, fallopian tube, and primary peritoneal cancer.

Materials and methods. Following IRB approval, 141 patients with epithelial ovarian, fallopian tube, and primary peritoneal cancers who underwent initial staging or interval debulking from January 2001 to December 2004 at the University of Minnesota were identified. Medical records were reviewed and information on patient demographics, medical history, surgical procedure, post-operative complications, disease stage, histology, adjuvant therapy, disease free (DF) and overall survival (OS) was collected. Two-sample *t*-tests were used to compare BMI, initial CA125, and EBL between groups. Exact chi-square tests were used to compare patient characteristics, medical history, surgical procedures, adjuvant treatments, and complication rates. DF and OS curves were constructed using Kaplan–Meier estimation and compared using the log-rank test to determine statistical significance to a p-value of 0.05.

Results. Of the 141 patients, 55 received Seprafilm® and 86 did not. Patient clinical and pathologic characteristics were overall comparable between the two groups, except for clear cell histology. The Seprafilm® group contained a statistically significant greater number of patients diagnosed with clear cell histology (p-value$=0.048$). The surgical procedures and immediate post-operative complication rates between the two groups were equivalent. No statistically significant differences in DF or OS were detected. The 5 year DF was 23.6 vs. 33.3 months and OS was 48.8 vs. 56.7 months, log-rank p-value$=0.8$, Seprafilm® vs. no Seprafilm®, respectively.