



## The potential benefit of 6 vs. 3 cycles of chemotherapy in subsets of women with early-stage high-risk epithelial ovarian cancer: An exploratory analysis of a Gynecologic Oncology Group study

John K. Chan <sup>a,\*</sup>, Chunqiao Tian <sup>b</sup>, Gini F. Fleming <sup>c</sup>, Bradley J. Monk <sup>d</sup>, Thomas J. Herzog <sup>e</sup>, Daniel S. Kapp <sup>f</sup>, Jeffrey Bell <sup>g</sup>

<sup>a</sup> Division of Gynecologic Oncology, Department of Obstetrics, Gynecology, & Reproductive Sciences, University of California, San Francisco School of Medicine, UCSF Helen Diller Family Comprehensive Cancer Center, 1600 Divisadero St. Box 1702, San Francisco, CA 94143-1702, USA

<sup>b</sup> GOG Statistical & Data Center, Roswell Park Cancer Institute, Buffalo, NY 14263, USA

<sup>c</sup> University of Chicago, Chicago, IL 60637, USA

<sup>d</sup> University of California, Irvine Medical Center, Chao Family Comprehensive Cancer Center, Orange, CA 92868, USA

<sup>e</sup> Columbia University, New York, NY 10032, USA

<sup>f</sup> Stanford University School of Medicine, Stanford Cancer Center, Stanford, CA 94305, USA

<sup>g</sup> OhioState University, Riverside Methodist Hospital, Columbus, OH 43214, USA

### ARTICLE INFO

#### Article history:

Received 17 July 2009

Revised 20 October 2009

Accepted 23 October 2009

Available online 28 November 2009

#### Keywords:

Early stage epithelial ovarian cancer cycles chemotherapy

### ABSTRACT

**Objectives.** A prior clinical trial on early-stage high risk ovarian cancer showed a lower recurrence rate in those treated with six vs. three cycles of chemotherapy. We proposed to identify subsets of patients who may benefit from more cycles of chemotherapy.

**Methods.** Outcomes of patients who underwent six vs. three cycles of chemotherapy were analyzed based on clinico-pathologic factors. Kaplan–Meier estimates and Cox Regression Model were used for analyses.

**Results.** Of 427 patients (median age: 55 years), 69% had stage I disease, 30% had clear cell, 25% endometrioid, 23% serous, 7% mucinous, and 15% had other cell types. The risk of recurrence in those who had six vs. three cycles of chemotherapy was not different based on age, performance status, stage, grade of disease, presence of ascites, tumor rupture, or positive cytology. However, those with serous tumors had a significantly lower risk of recurrence after six vs. three cycles of chemotherapy (HR = 0.33, CI = 0.14–0.77;  $p = 0.04$ ) in contrast to non-serous tumors (HR = 0.94, CI = 0.60–1.49). Nevertheless, a test of homogeneity did not show a difference in treatment effects across cell types ( $p = 0.285$ ). Of those with serous tumors, the 5-year recurrence-free survival was 83% and 60% in those who received six vs. three cycles of chemotherapy, respectively ( $p = 0.007$ ).

**Conclusions.** In this exploratory analysis of early-stage high risk ovarian cancer, our data suggest that six rather than three cycles of chemotherapy may decrease the recurrence of patients with serous tumors. Further studies are needed to confirm these findings.

© 2009 Elsevier Inc. All rights reserved.

### Introduction

Of the estimated 21,550 new epithelial ovarian cancers (EOC) diagnosed in the United State in 2009, approximately one third had (International Federation of Obstetrics and Gynecology) FIGO stage I and II disease. Although the survival of early-stage disease is significantly higher than those with advanced cancers, approximately 20–30% of patients with early-stage cancers will succumb to their

disease [1–7]. Previous reports have shown that age, stage, tumor rupture, cell type, tumor grade, large volume ascites, and dense adhesions are important clinico-pathological prognostic factors [8–17]. Although women with thoroughly staged IA or IB disease and favorable histology have excellent survivals, those with higher risk disease, defined as stage I, grade 3; stage IC, stage II, or clear cell, have a significant risk for recurrence ranging from 25% to 45% and are generally treated with adjuvant chemotherapy.

The optimal duration of adjuvant chemotherapy in early stage ovarian cancer is unclear. Although the European Organisation for Research and Treatment of Cancer–Adjuvant Chemo Therapy in Ovarian Neoplasm (EORTC-ACTION) and International Collaborative Ovarian Neoplasm (ICON) trials have used four and six cycles, respectively, the Gynecologic Oncology Group (GOG) has historically

\* Corresponding author. Division of Gynecologic Oncology, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco School of Medicine, UCSF Helen Diller Family Comprehensive Cancer Center, 1600 Divisadero St. Box 1702, San Francisco, CA 94143-1702, USA. Fax: +1 415 885 3586.

E-mail address: [chanjohn@obgyn.ucsf.edu](mailto:chanjohn@obgyn.ucsf.edu) (J.K. Chan).