



## Single agent carboplatin versus carboplatin plus pegylated liposomal doxorubicin in recurrent ovarian cancer: Final survival results of a SWOG (S0200) phase 3 randomized trial

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### ABSTRACT

**Objectives.** Randomized phase 3 trials have demonstrated the utility of a regimen of carboplatin plus pegylated liposomal doxorubicin (PLD) in recurrent ovarian cancer, and have provided provocative data suggesting a substantially lower risk of carboplatin-associated hypersensitivity if PLD is delivered in combination with the platinum agent.

**Methods.** To further examine both of these clinically-relevant issues, the survival outcome (with longer follow-up) and hypersensitivity reaction profile of a previously reported phase 3 trial that compared single agent carboplatin (AUC 5) to carboplatin (AUC 5) plus PLD (30 mg/m<sup>2</sup>) delivered on an every 4-week schedule in recurrent ovarian cancer (SWOG 0200) were re-analyzed.

**Results.** In the limited number of patients ( $n=61$ ) entered into this phase 3 study before closure by the SWOG Data Safety and Monitoring Committee due to insufficient accrual, there was an initially reported improvement in outcome associated with the combination regimen. With longer follow-up and additional events there is still a statistically-significant improved progression-free survival (median: 12 versus 8 months,  $p=0.02$ ), but the previously observed impact of the two-drug regimen on overall survival is no longer apparent (median: 31 versus 18 months;  $p=0.2$ ). While no hypersensitivity reactions were reported in the carboplatin plus PLD arm (0/31), 9 of 30 patients (30%) of women randomized to single agent carboplatin experienced an allergic episode ( $p=0.0008$ ), with 5 being >grade 2 in severity.

**Conclusion.** Despite a favorable impact of carboplatin and PLD on progression-free survival in this trial, the effect on overall survival is not statistically significant. For currently unknown reasons, administering PLD with carboplatin appears to substantially reduce the incidence of platinum-associated hypersensitivity reactions.

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### Introduction

The results of both previously published, and more recently presented, phase 3 randomized trials have provided clinically-relevant data that can assist clinicians in their determination of optimal management for women experiencing recurrence of epithelial ovarian cancer [1–5]. In particular, two phase 3 studies have demonstrated the superiority of the delivery of a platinum agent plus paclitaxel or carboplatin plus gemcitabine, compared to the admin-

istration of a non-paclitaxel containing platinum regimen or single agent carboplatin, respectively, in this clinical setting [1,2].

An additional phase 3 trial (Southwest Oncology Group study S0200) that compared single agent carboplatin to a regimen of carboplatin plus pegylated liposomal doxorubicin (PLD), that was unfortunately discontinued early due to inadequate accrual, also revealed a provocative improvement in progression-free survival associated with the 2-drug regimen (12 months versus 8 months;  $p=0.03$ ), despite very limited patient numbers [4]. Further, at the time the results of this underpowered study were reported, there was an observed statistically-significant improvement in overall survival (26 months versus 18 months;  $p=0.02$ ) [4].

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