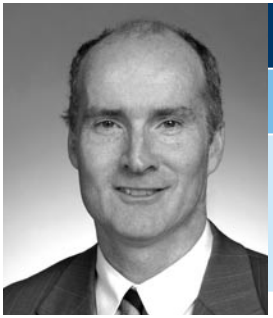


INTERVIEW

## Thomas J Herzog, MD

Dr Herzog is Director of Gynecologic Oncology and Physicians and Surgeons Alumni Professor of Clinical Gynecology and Obstetrics at Columbia University Medical Center in New York, New York.

### Tracks 1-12



## Select Excerpts from the Interview

### Tracks 2-3

**DR LOVE:** What is your approach to intraperitoneal (IP) chemotherapy in ovarian cancer?

**DR HERZOG:** I believe it is crucial for patients to complete therapy without significantly deviating from the schedule and doses that were administered in the GOG-0172 trial, which reported a large overall survival difference (Armstrong 2006; [1.1]).

The only initial change I make is to shorten the 24-hour paclitaxel infusion on day one to a three-hour infusion for convenience. After the first or second

cycle, I consider how the patients are faring. Only if they are not tolerating therapy am I willing to lower the dose.

Choosing the correct patient for IP therapy is key. IP therapy should be avoided for patients with significant comorbidities, elderly patients and those with impaired performance statuses.

**DR LOVE:** What supportive care is necessary when administering IP chemotherapy?

**DR HERZOG:** I consider hydration to be vital. I have had one patient and have seen reports of others who sustained severe renal damage when not adequately hydrated, so this is an extremely important issue.

It is also important to understand that these patients must know that if they go home and are not tolerating oral intake well, that is an emergency and they need to call their doctors immediately.

We also use growth factors liberally in terms of white blood cell support. The rate of febrile neutropenia warrants consideration of prophylactic growth factors for all of these patients.

**1.1**

**GOG-0172: A Phase III Trial of Intraperitoneal versus Intravenous Chemotherapy for Stage III Ovarian Cancer**

| | Intravenous therapy group | Intraperitoneal therapy group | Relative risk | *p*-value |
|---|---|---|---|---|
| Progression-free survival | 18.3 months | 23.8 months | 0.80 | 0.05 |
| Overall survival | 49.7 months | 65.6 months | 0.75 | 0.03 |

Armstrong DK et al. *N Engl J Med* 2006;354(1):34–43.

## Track 5

**DR LOVE:** What are your thoughts on the results presented at ASCO of the GOG-0218 trial evaluating bevacizumab with chemotherapy after debulking surgery?

**DR HERZOG:** On the basis of the safety and efficacy data presented at the ASCO plenary session (Burger 2010; [3.2, 3.3]), it is reasonable to say that up-front concomitant bevacizumab/chemotherapy followed by maintenance bevacizumab is an option in the initial management of ovarian cancer.

The median progression-free survival (PFS) improved from 10.3 months to 14.1 months, and although I would have preferred a larger difference, this patient population had poorer prognoses overall and the hazard ratio looks good.

The survival data are not mature yet, and before bevacizumab is considered the standard approach for the initial management of ovarian cancer we need to see mature survival data from the GOG-0218 trial.

## Tracks 8-10

**DR LOVE:** How do you approach recurrent ovarian cancer?

**DR HERZOG:** The approach to treatment of recurrent ovarian cancer is different depending on whether the disease is considered to be platinum resistant or platinum sensitive.

The difference between these two groups is defined by the treatment-free interval after initial platinum-containing chemotherapy. Disease that recurs within six months of initial platinum-containing therapy is deemed platinum resistant, and that which recurs after six months of such therapy is considered platinum sensitive.

Platinum-resistant ovarian cancer is usually treated with single-agent chemotherapy. Liposomal doxorubicin is the most common drug in my practice in this setting because of the convenient schedule and reasonable toxicity profile. Other options include topotecan, which can be administered on either the FDA-approved schedule of daily times five or the weekly schedule. Additional single-agent options to consider in this setting are docetaxel, etoposide, gemcitabine and bevacizumab.

Among patients with platinum-sensitive, symptomatic disease or those who have experienced recurrence beyond one year of initial therapy, I consider platinum/paclitaxel or platinum/gemcitabine. Another regimen combining a platinum agent and pegylated liposomal doxorubicin has demonstrated improved PFS in comparison to carboplatin/paclitaxel in this setting (Pujade-Lauraine 2009; [1.2]).

The toxicity profiles were different, with patients in the pegylated liposomal doxorubicin group experiencing fewer hypersensitivity reactions. So this is a third option that should be considered when selecting a platinum-containing doublet for platinum-sensitive ovarian cancer.

Another option I consider for patients with platinum-sensitive disease and fewer than 18 months of initial treatment is using something other than a taxane, as they received six cycles of a taxane in the initial regimen.

We know that we can likely replace the nonplatinum agent in the doublet without compromising efficacy, and we have a different toxicity profile when using a nontaxane. Additional benefit may also be gained — perhaps a different mechanism of action with the hope of overcoming the initial resistance.

All of these factors compel me to use a platinum and gemcitabine most commonly and sometimes to consider a platinum and pegylated liposomal doxorubicin for patients with platinum-sensitive disease.

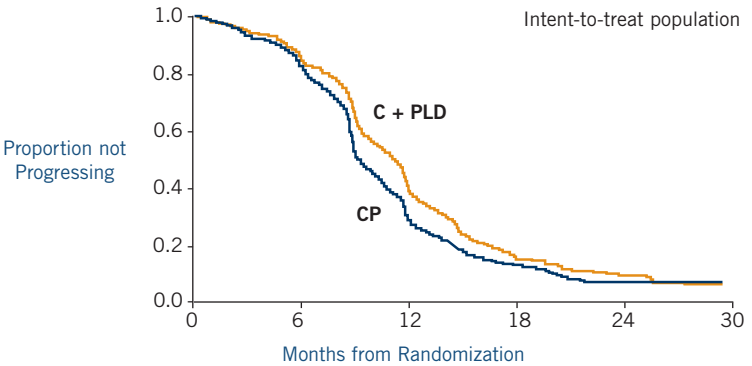
**DR LOVE:** What is your experience with the side effects and tolerability of platinum/gemcitabine or platinum/liposomal doxorubicin in ovarian cancer?

**DR HERZOG:** Platinum/gemcitabine is well tolerated overall. One issue is the day-eight dosing. Approximately half of patients require some dose reduction on day eight. When you reach the correct dose for the patient, it is tolerated well.

I have administered the platinum/liposomal doxorubicin combination to probably 10 or 15 patients. One needs to be mindful of myelosuppression. However, patients like the 28-day schedule, which was used in the CALYPSO trial. I have not seen much hand-foot syndrome with this regimen either. ■

**1.2**

**CALYPSO: Progression-Free Survival (PFS) with Carboplatin (C) and Pegylated Liposomal Doxorubicin (PLD) versus Carboplatin and Paclitaxel (P) in Relapsed Platinum-Sensitive Ovarian Cancer**




In PLD/C arm, PLD dose was 30 mg/m$^2$

| | C + PLD | CP | *p*-value (superiority) | *p*-value (inferiority) |
|---|---|---|---|---|
| Median PFS, mo | 11.3 | 9.4 | 0.005 | <0.001 |

With permission from Pujade-Lauraine E et al. *Proc ASCO* 2009;**Abstract LBA5509**.

## SELECT PUBLICATIONS


Armstrong DK et al. **Intraperitoneal cisplatin and paclitaxel in ovarian cancer.** *N Engl J Med* 2006;354(1):34-43.

Burger RA et al. **Phase III trial of bevacizumab in the primary treatment of advanced epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer: A Gynecologic Oncology Group study.** *Proc ASCO* 2010;**Abstract LBA1**.

Kose MF et al. **A phase II study of gemcitabine plus carboplatin in platinum-sensitive, recurrent ovarian carcinoma.** *Gynecol Oncol* 2005;96(2):374-80.

Pujade-Lauraine E et al. **A randomized phase III study of carboplatin and pegylated liposomal doxorubicin versus carboplatin and paclitaxel in relapsed platinum-sensitive ovarian cancer (OC): CALYPSO study of the Gynecologic Cancer Intergroup (GCIG).** *Proc ASCO* 2009;**Abstract LBA5509**.