OCU | 2008 VOL 1 | ISSUE 2

Ovarian Cancer™ UPDATE

Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

EDITOR

Neil Love, MD

INTERVIEWS

Deborah K Armstrong, MD

David R Spriggs, MD

Robert L Coleman, MD

CME Certified

Subscribe to Podcasts or download MP3s of this program at OvarianCancerUpdate.com

Ovarian Cancer Update
A Continuing Medical Education Audio Series

STATEMENT OF NEED/TARGET AUDIENCE

Optimal oncologic management of ovarian cancer begins with intensive surgical staging and cytoreduction, followed by primary chemotherapy and, for most patients, subsequent medical management when platinum-resistant disease recurrence prevails. Although many single-agent and combination cytotoxic recurrence regimens have been studied, only recently has the advent of antibody and small-molecule growth-inhibitory targeted agents been integrated into the ovarian cancer research milieu. It is hoped that the results from these trials will lead to the emergence of new therapeutic agents and changes or enhancements in the indications for existing treatment strategies, ultimately improving the duration and quality of life for patients with recurrent ovarian cancer. In order to offer optimal oncology care to the ovarian cancer population — including the option of clinical trial participation — practicing medical and gynecologic oncologists must be well informed of these advances. To bridge the gap between research and patient care, *Ovarian Cancer Update* uses one-on-one discussions with leading oncology investigators. By providing access to the latest research developments and expert perspectives, this CME program will assist medical and gynecologic oncologists in the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Manage localized, locally advanced and metastatic ovarian cancer based on an understanding of the pathophysiology of the disease and the clinical presentation.
- Appropriately utilize surgical staging for the prognosis and subsequent medical management of epithelial ovarian cancer, based on the NCCN guidelines.
- Evaluate the risks and benefits of primary chemotherapy when devising management strategies for ovarian cancer, including intraperitoneal and intravenous regimens for patients with Stage II and Stage III optimally debulked disease and taxane-based chemotherapy regimens.
- Consider the use of biologic agents and/or regimens based on relevant clinical trial data when treating recurrent platinum-sensitive and platinum-resistant ovarian cancer.
- Select therapies for patients with ovarian cancer, with an understanding of the relevance of the distinct mechanisms of action of novel targeted signal transduction inhibitors.
- Develop an algorithm for monitoring patients in remission, including radiographic studies and CA125 levels.
- Utilize maintenance chemotherapy for patients with ovarian cancer who are in remission, as appropriate.
- Consider the relative efficacy and adverse effects of acceptable treatment modalities when managing primary, metastatic or recurrent disease.
- Counsel appropriately selected patients about the availability of ongoing clinical trials.

PURPOSE OF THIS ISSUE OF *OVARIAN CANCER UPDATE*

The purpose of Issue 2 of *Ovarian Cancer Update* is to support the learning objectives by offering the perspectives of Drs Armstrong, Spriggs and Coleman on the integration of emerging clinical research data into the management of ovarian cancer.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this educational activity for a maximum of 3 *AMA PRA Category 1 Credit(s)™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY

This CME activity contains both audio and print components. To receive credit, the participant should listen to the CDs, review the monograph and complete the Post-test and Educational Assessment and Credit Form located in the back of this monograph or on our website. This monograph contains edited comments, clinical trial schemas, graphics and references that supplement the audio program. **OvarianCancerUpdate.com** includes an easy-to-use, interactive version of this monograph with links to relevant full-text articles, abstracts, trial information and other web resources indicated here in **blue underlined text**.

This program is supported by educational grants from Centocor Ortho Biotech Services, Eli Lilly and Company and Genentech BioOncology.

TABLE OF CONTENTS

(Special thanks to Herbert Kotz, MD, a medical oncologist at the National Cancer Institute, who collaborated with us in planning the interviews in this program.)

If you would like to discontinue your complimentary subscription to *Ovarian Cancer Update*, please email us at **Info@ResearchToPractice.com**, call us at (800) 648-8654 or fax us at (305) 377-9998. Please include your full name and address, and we will remove you from the mailing list.

KEY PUBLICATIONS DISCUSSED IN THIS PROGRAM

Burger RA et al. **Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: A Gynecologic Oncology Group study.** *J Clin Oncol* 2007;25(33):5165-71. **Abstract**

Coleman RL et al. **Early changes in CA125 after treatment with pegylated liposomal doxorubicin or topotecan do not always reflect best response in recurrent ovarian cancer patients.** *Oncologist* 2007;12(1):72-8. **Abstract**

Ferrandina G et al. **Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer.** *J Clin Oncol* 2008;26(6):890-6. **Abstract**

Gordon AN et al. **Recurrent epithelial ovarian carcinoma: A randomized phase III study of pegylated liposomal doxorubicin versus topotecan.** *J Clin Oncol* 2001;19(14):3312-22. **Abstract**

Han ES et al. **Relationship of angiogenesis biomarkers and clinical response to bevacizumab (Bev) in persistent or recurrent epithelial ovarian cancer (EOC) and primary peritoneal cancer (PPC) patients treated in a Phase II Gynecologic Oncology Group study.** *Proc ASCO* 2007;**Abstract 21021**.

Konner JA et al. **A phase II study of intravenous (IV) and intraperitoneal (IP) paclitaxel (Tax), IP cisplatin (Cis), and IV bevacizumab (Bev) as first-line chemotherapy for optimal stage II or III ovarian, primary peritoneal, and fallopian tube cancer.** *Proc ASCO* 2007;**Abstract 5523**.

Markman M et al. **Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: A Gynecologic Oncology Group study.** *Gynecol Oncol* 2006;101(3):436-40. **Abstract**

Orlando M et al. **Randomized trials of combination chemotherapy (combo) versus monotherapy (mono) in relapsed ovarian carcinoma (ROC): A meta-analysis of published data.** *Proc ASCO* 2007;**Abstract 5524**.

Pfisterer J et al. **Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: An intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG.** *J Clin Oncol* 2006;24(29):4699-707. **Abstract**

Wright JD et al. **A multi-institutional evaluation of the safety and efficacy of bevacizumab for recurrent, platinum-resistant ovarian cancer.** *Proc ASCO* 2006;**Abstract 5019**.

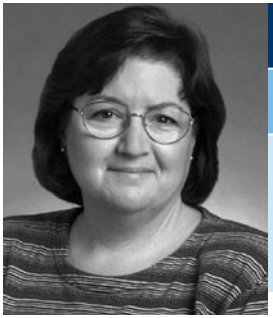
CONTENT VALIDATION AND DISCLOSURES

Research To Practice is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the Research To Practice scientific staff and an external, independent reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Armstrong** — Advisory Committee: Bayer Pharmaceuticals Corporation, Biogen Idec, Cephalon Inc, Genentech BioOncology, Onyx Pharmaceuticals Inc. **Dr Spriggs** — Advisory Committee: Abraxis BioScience, Merck and Company Inc, Ortho Biotech Products LP; Consulting Agreements: Bristol-Myers Squibb Company, Eli Lilly and Company, Genentech BioOncology, Roche Laboratories Inc; Data Safety and Monitoring Board: GlaxoSmithKline; Paid Research: Eli Lilly and Company, Genentech BioOncology. **Dr Coleman** — Consulting Agreements: Abraxis BioScience, Eli Lilly and Company, Genentech BioOncology, GlaxoSmithKline, Ortho Biotech Products LP; Paid Research: Abraxis BioScience; Speakers Bureau: Eli Lilly and Company, GlaxoSmithKline, Ortho Biotech Products LP.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.



INTERVIEW

Deborah K Armstrong, MD

Dr Armstrong is Associate Professor of Oncology and Associate Professor of Gynecology and Obstetrics at The Sidney Kimmel Comprehensive Cancer Center at The Johns Hopkins University in Baltimore, Maryland.

Tracks 1-22

Select Excerpts from the Interview

Track 1

DR LOVE: Would you discuss some of the important ongoing clinical trials in ovarian cancer?

DR ARMSTRONG: Probably the most provocative and interesting ongoing studies are incorporating bevacizumab. It is interesting that unlike the diseases for which bevacizumab has FDA approval — lung, colorectal and breast cancer — bevacizumab has strikingly significant single-agent activity in ovarian cancer.

I believe that in renal cell cancer, the response rate with bevacizumab may be nine or 10 percent, but in the single-agent study by the Gynecologic Oncology Group (GOG) in ovarian cancer, the response rate was 21 percent (Burger 2007; [1.1]).

1.1

GOG-170-D: A Phase II Trial of Bevacizumab Monotherapy in Persistent or Recurrent Epithelial Ovarian Cancer or Primary Peritoneal Cancer (N = 62)

Efficacy data

Response rate	21% (90% CI: 12.9-31.3%)
Complete response	4.8%
Partial response	12.9%
Median duration of response	10.3 months
Stable disease	51.6%
Progression-free survival (PFS) ≥ 6 months	40.3% (90% CI: 29.8-53.6%)

Conclusions

"In the second and third line treatment setting, patients with recurrent epithelial ovarian and primary peritoneal cancer, single agent bevacizumab:

- *Well tolerated at the dose and schedule of 15 mg/kg q21 days*
- *Active by clinical response and PFS"*

CI = confidence interval

SOURCE: Burger RA et al. *J Clin Oncol* 2007;25(33):5165-71. **Abstract**

If we obtain the same results that we've seen in some of the other diseases, in which bevacizumab seems to make chemotherapy more effective, we may be able to extend the current limits of treatment for ovarian cancer.

The GOG-0218 trial for patients with newly diagnosed ovarian cancer is a randomized study evaluating paclitaxel/carboplatin alone, paclitaxel/carboplatin with bevacizumab and paclitaxel/carboplatin with bevacizumab and bevacizumab consolidation.

All three arms of the trial have patients coming in every three weeks after the completion of chemotherapy to receive either placebo or bevacizumab (1.2).

In ovarian cancer, we have the fortunate situation that even with bulky disease, most patients respond to chemotherapy. If bevacizumab performs as it does in other diseases, we might be changing the paradigm for treatment of this disease.

1.2

GOG-0218: A Phase III Randomized Study of Carboplatin and Paclitaxel versus Carboplatin, Paclitaxel and Concurrent Bevacizumab with or without Extended Bevacizumab

Protocol IDs: GOG-0218, NCT00262847; Target Accrual: 2,000 (Open)

Eligibility

- Histologically confirmed Stage III with any gross residual disease OR Stage IV ovarian epithelial or primary peritoneal cancer
- No prior chemotherapy for abdominal or pelvic cancer
- At least four weeks since major surgical procedure or open biopsy

[1] Chemotherapy = (paclitaxel 175 mg/m^2 + carboplatin AUC 6 mg/mL x min) every 21 days x 6 cycles

[2] Bevacizumab = 15 mg/kg every 21 days (beginning cycle 2)

SOURCE: NCI Physician Data Query, May 2008.

Track 12

DR LOVE: What do we know about response rates and disease control with the available treatment options for patients who experience a recurrence within six months after receiving initial therapy with a platinum agent and a taxane? What is the role of re-treating with a platinum agent?

DR ARMSTRONG: For clinical trials, we have used recurrence within six months as our cutoff to define platinum-resistant and platinum-sensitive disease. Unfortunately, that has probably led to the magical thinking that something unique and wonderful happens at six months, but actually it's a continuum.

If you evaluate any of the available strategies — topotecan, liposomal doxorubicin, re-treatment with a platinum or a taxane — the farther out the patient is from the initial therapy, the greater the sensitivity and the higher the response rate. The time from completion of initial therapy is a measure of potential chemotherapy sensitivity.

We don't see huge response rates with almost anything used in the first six months. Obtaining another complete response is difficult when the patient experiences a recurrence within the first six to 12 months. It happens, but it's not common. The longer someone is out from the initial therapy, the more likely we are to obtain a complete response.

Two large randomized studies have evaluated a platinum agent alone versus platinum-based combinations for patients with late relapses — after six to 12 months. ICON-4 compared paclitaxel/carboplatin or cisplatin to carboplatin or cisplatin alone (Parmar 2003), and the AGO trial evaluated carboplatin versus gemcitabine/carboplatin (Pfisterer 2006a; [1.3]).

Both of those trials showed an improvement in progression-free survival with combination therapy. The gemcitabine/carboplatin versus carboplatin study was not powered to detect differences in overall survival, and it didn't show any difference.

It's nice to have more than one platinum-based combination to offer patients. I believe both of these studies have led to a paradigm shift. For patients whose disease recurs more than six to 12 months after initial therapy, most of us will reuse a platinum-based doublet.

DR LOVE: For a patient who experiences a recurrence at six months, what would you most likely consider?

DR ARMSTRONG: At six months, especially with measurable disease, I would use sequential single agents. I would start with a nonplatinum agent.

1.3

Gemcitabine with Carboplatin versus Carboplatin Alone for Patients with Platinum-Sensitive Recurrent Ovarian Cancer

"This study clearly demonstrates that gemcitabine plus carboplatin is superior to carboplatin in terms of progression-free survival and response rate. Finally, relative to therapy with taxanes, gemcitabine plus carboplatin exhibited a preferable toxicity profile as evidenced by greatly diminished neuropathy and alopecia, which are of importance for the affected women. Therefore, gemcitabine plus carboplatin represents a new treatment option for patients with platinum-sensitive recurrent ovarian cancer."

SOURCE: Pfisterer J et al. *J Clin Oncol* 2006a;24(29):4699-707. **Abstract**

Track 13

DR LOVE: What's the role of consolidation therapy?

DR ARMSTRONG: SWOG-9701/GOG-178 evaluated every four-week paclitaxel for 12 or three cycles in patients with ovarian cancer who had received five or six cycles of a platinum agent and a taxane and achieved a clinical complete response.

The Data Safety Monitoring Board stopped the study at approximately half the projected accrual because an improvement in progression-free survival was evident for the patients who received 12 months of paclitaxel (Markman 2006b; [1.4]).

No survival advantage was observed. Is that because the trial was stopped early?

No one knows. Is the standard now almost 18 months of chemotherapy?

I believe that doctors should discuss it with the patient and make a decision about whether to continue with maintenance therapy. People have argued that it may be just as effective to wait until clinical relapse and then use the drugs. I tend not to use consolidation therapy with a taxane.

We have conducted two similar types of studies with a short duration of topotecan therapy, and neither has shown a benefit (Pfisterer 2006b; De Placido 2004). However, those trials used three months of therapy, which was the control arm in the paclitaxel study. Perhaps if we'd used a longer duration of therapy with topotecan, we would have observed some benefit.

I believe this is a situation in which the biologic agents will play a role instead of more chemotherapy. They would have less toxicity. It would be lovely if we had the equivalent of hormonal therapy in breast cancer. Most patients reach remission, but it doesn't last.

1.4

SWOG-9701/GOG-178: A Phase III Randomized Trial of 12 versus Three Months of Consolidation Paclitaxel After a Complete Response to Platinum- or Paclitaxel-Based Chemotherapy

	Twelve cycles of paclitaxel (n = 150)	Three cycles of paclitaxel (n = 146)	*p*-value
Median progression-free survival	22 months	14 months	0.01
Median overall survival	53 months	46 months	0.27

SOURCE: Markman M et al. *Proc ASCO* 2006b;**Abstract 5005**.

Track 14

DR LOVE: Here's a quick case question for you: What do you say to a patient who is asymptomatic with a stable CT after six cycles of pegylated liposomal doxorubicin as second-line therapy?

DR ARMSTRONG: I tell patients, "We will keep you on this therapy. We will stop it for either of two reasons. One is if your disease progresses. The other is if you develop intolerable toxicities."

The bigger question is, if we stop the therapy and the patient hasn't experienced a complete response, what is the chance that the tumor will grow quickly? If the tumor starts to grow, what is the chance that reintroducing the drug will induce a response again?

DR LOVE: What do you think about continuing liposomal doxorubicin at the same dose but perhaps for a longer interval?

DR ARMSTRONG: Most of our patients tell us that the last week before they

come in for chemotherapy is the week when they feel best. So you can argue that by increasing the time between treatments, you will provide patients with the best quality of life. I certainly have done that with patients for whom I had concerns about nonhematologic toxicities for which you don't necessarily have to hold treatment. ■

SELECT PUBLICATIONS

Burger RA et al. **Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: A Gynecologic Oncology Group study.** *J Clin Oncol* 2007;25(33):5165-71. **Abstract**

Burger RA et al. **Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer (EOC) or primary peritoneal cancer (PPC): A Gynecologic Oncology Group (GOG) study.** *Proc ASCO* 2005;**Abstract 5009**.

Cannistra SA et al. **Phase II study of bevacizumab in patients with platinum-resistant ovarian cancer or peritoneal serous cancer.** *J Clin Oncol* 2007;25(33):5180-6. **Abstract**

De Placido S et al. **Topotecan compared with no therapy after response to surgery and carboplatin/paclitaxel in patients with ovarian cancer: Multicenter Italian Trials in Ovarian Cancer (MITO-1) randomized study.** *J Clin Oncol* 2004;22(13):2635-42. **Abstract**

Diaz JP et al. **The safety and efficacy of bevacizumab therapy in recurrent ovarian carcinoma.** *Proc ASCO* 2008;**Abstract 16528**.

Kaye SB. **Bevacizumab for the treatment of epithelial ovarian cancer: Will this be its finest hour?** *J Clin Oncol* 2007;25(33):5150-2. No abstract available

Markman M et al. **Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: A Gynecologic Oncology Group study.** *Gynecol Oncol* 2006a;101(3):436-40. **Abstract**

Markman M et al. **Survival (S) of ovarian cancer (OC) patients (pts) treated on SWOG9701/GOG178: 12 versus (v) 3 cycles (C) of monthly single-agent paclitaxel (PAC) following attainment of a clinically-defined complete response (CR) to platinum (PLAT)/PAC.** *Proc ASCO* 2006b;**Abstract 5005**.

Markman M et al. **Phase III randomized trial of 12 versus 3 months of maintenance paclitaxel in patients with advanced ovarian cancer after complete response to platinum and paclitaxel-based chemotherapy: A Southwest Oncology Group and Gynecologic Oncology Group trial.** *J Clin Oncol* 2003;21(13):2460-5. **Abstract**

McGonigle KF et al. **Phase II prospective study of weekly topotecan and bevacizumab in platinum refractory ovarian cancer or peritoneal cancer (OC).** *Proc ASCO* 2008;**Abstract 5551**.

Miller DS et al. **A phase II evaluation of pemetrexed (LY231514, IND #40061) in the treatment of recurrent or persistent platinum-resistant ovarian or primary peritoneal carcinoma: A study of the Gynecologic Oncology Group.** *Proc ASCO* 2008;**Abstract 5524**.

Parmar MK et al. **Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: The ICON4/AGO-OVAR-2.2 trial.** *Lancet* 2003;361(9375):2099-106. **Abstract**

Pfisterer J et al. **Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: An intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG.** *J Clin Oncol* 2006a;24(29):4699-707. **Abstract**

Pfisterer J et al. **Randomized phase III trial of topotecan following carboplatin and paclitaxel in first-line treatment of advanced ovarian cancer: A gynecologic cancer intergroup trial of the AGO-OVAR and GINECO.** *J Natl Cancer Inst* 2006b;98(15):1036-45. **Abstract**

Rose PG et al. **A phase II study of docetaxel in paclitaxel-resistant ovarian and peritoneal carcinoma: A Gynecologic Oncology Group study.** *Gynecol Oncol* 2003;88(2):130-5. **Abstract**

INTERVIEW

David R Spriggs, MD

Dr Spriggs is Head of the Division of Solid Tumor Oncology and is the Winthrop Rockefeller Chair of Medical Oncology at Memorial Sloan-Kettering Cancer Center in New York, New York.

Tracks 1-19

Select Excerpts from the Interview

Tracks 1, 5-7, 11-12

DR LOVE: What was the rationale behind the Phase II trial combining intraperitoneal chemotherapy and systemic bevacizumab as first-line treatment for optimal Stage II or Stage III ovarian cancer (2.1)?

DR SPRIGGS: Memorial Sloan-Kettering has been committed to identifying ways to enhance the delivery of intraperitoneal chemotherapy for almost 20 years, and the evolution of the field has been quite extraordinary. In the past 10 to 12 years, three consecutive Phase III studies have demonstrated a substantial survival advantage for patients receiving intraperitoneal chemotherapy for ovarian cancer (Alberts 1996; Markman 2001; Armstrong 2002).

The peritoneal cavity is lined by a mesothelium that expresses mesothelin, a documented target and presumed ligand for the CA125/MUC16 molecule. We believe that because so many cases of ovarian cancer express CA125/MUC16, it has a propensity to bind to these tissues, and indeed, a predominance of ovarian cancer occurs in the peritoneal cavity. Therefore, delivering systemic therapy to the cavity is a rational approach.

We added bevacizumab systemically because it has significant activity in ovarian cancer. A series of reports have suggested that single-agent bevacizumab is potent in inhibiting tumor growth and even in shrinking ovarian tumors (Han 2007).

DR LOVE: What was the rationale for the trial design?

2.1 **Phase II Study of Intravenous (IV) and Intraperitoneal (IP) Paclitaxel (Tax), IP Cisplatin and IV Bevacizumab (Bev)**

Protocol IDs: 06-064, NCT00588237; Accrual: 41 (Open)

Eligibility

- Optimal Stage II or Stage III ovarian, epithelial ovarian, primary peritoneal or fallopian tube cancer
- No prior chemotherapy for any abdominal or pelvic tumor
- No prior radiation therapy to any portion of the abdominal cavity or pelvis

Treatment protocol → **IV paclitaxel + IV bev* day 1, IP cisplatin day 2, IP paclitaxel day 8**

Interim safety and efficacy data (n = 8):
"All 31 planned doses of chemotherapy have been administered in full. One dose of IP Tax was delayed for 2 days due to abdominal pain. One patient had her first dose of Bev delayed for 1 cycle due to surgical wound infection. There have been no toxicities > grade 3....

Grade 3 toxicities per patient: fatigue (12.5%); hyponatremia (25%); hypokalemia (25%); hypertension (12.5%); abdominal pain (12.5%); and neutropenia (12.5%). Of the 5 patients with pretreatment CA125 >35 Units/mL, 4 normalized their value after 1 cycle of chemotherapy and 1 patient normalized after 2 cycles."

* Bev begins day 1, cycle 2. Patients receive up to six cycles of therapy or until disease progression or unacceptable toxicity.

SOURCES: Konner JA et al. *Proc ASCO* 2007;**Abstract 5523**; NCI Physician Data Query, May 2008.

DR SPRIGGS: We know that a huge difference in toxicity exists between 75 and 100 mg/m^2 of cisplatin and, based on the intravenous cisplatin data, we believe 50 is as effective as 100 mg/m^2. By decreasing the intraperitoneal dose to 75 mg/m^2, we felt we could ensure that approximately two thirds, or 50 mg/m^2, of the cisplatin would get into the circulation, which is reported to be equivalent to 100 mg/m^2 (McGuire 1995).

We knew that paclitaxel stays in the peritoneal cavity for a long time and felt the sustained exposure was probably important in the success of GOG-172, so we elected to use intraperitoneal paclitaxel (Armstrong 2002). Also, we chose to administer paclitaxel and cisplatin on separate days to avoid the neuropathy associated with combining these agents. So far, the level of neurotoxicity has been acceptable.

DR LOVE: What have you observed with this regimen with regard to tolerability?

DR SPRIGGS: We've found that patients can tolerate the regimen. The dropout rate is not high, and the toxicities are modest (Konner 2007; [2.1]).

Bevacizumab is a remarkably well-tolerated drug. Understanding the physiology of the kidney and how VEGF works, it's not surprising that some proteinuria occurs and that bleeding and clotting problems can occur, although the frequency is low. While hypertension is fairly common, none of these side effects are deal breakers.

The difficulty is that the first-line treatment of ovarian cancer includes an aggressive surgical procedure. We need to ensure that we are not promoting the formation of new blood clots, heart attacks or strokes in these patients. We also have the concern that bevacizumab might interfere with new blood vessel formation during wound healing.

Based on the colorectal cancer experience, our patients do not receive bevacizumab for six to eight weeks after surgery, and we have found that to be safe. The other issue is bowel perforation, which has been reported as a side effect of bevacizumab in patients treated for ovarian cancer (Cannistra 2007).

DR LOVE: How do you use bevacizumab in your practice off study?

DR SPRIGGS: Bevacizumab has single-agent effectiveness of 15 to 20 percent (1.1, page 4), which is comparable to gemcitabine, topotecan and vinorelbine, among other agents, so it's a reasonable choice for patients who have received pegylated liposomal doxorubicin and gemcitabine as single agents for platinum-resistant disease. Bevacizumab has relatively few chronic side effects, but it does have some rare serious side effects, so we need to have a careful discussion with patients regarding the benefits and risks.

Tracks 13-14

DR LOVE: What is your algorithm for first-line therapy after surgery?

DR SPRIGGS: At Memorial Sloan-Kettering, we first try to enroll patients in a clinical trial. In our up-front program, patients whose disease is optimally debulked are entered in the Phase II trial of intravenous and intraperitoneal paclitaxel with intraperitoneal cisplatin and intravenous bevacizumab. If the patient can't receive bevacizumab but is a candidate for intraperitoneal therapy, we administer the same regimen but without bevacizumab off study.

Patients whose disease is suboptimally debulked are enrolled on GOG-0218 comparing carboplatin/paclitaxel to carboplatin/paclitaxel/bevacizumab with or without extended bevacizumab (1.2, page 5). Patients who cannot receive bevacizumab receive carboplatin and paclitaxel off study.

DR LOVE: Once the disease progresses, how do you treat?

DR SPRIGGS: Most patients achieve a partial, if not a complete, remission with their primary therapy. Those who do not, but rather experience disease progression while receiving chemotherapy, represent an adverse group. Outside of a clinical trial, I would use pegylated liposomal doxorubicin, understanding that despite therapy, these patients still do not have a good prognosis.

For the patients who do achieve a remission but then experience recurrence, we use the platinum-sensitivity mark that Markman put forward, by which patients whose disease recurs within six months represent the platinum resistant, and they are most likely to receive either an investigational agent in a Phase II trial or pegylated liposomal doxorubicin as the alternative (Markman 1992).

Track 15

DR LOVE: How does the efficacy of pegylated liposomal doxorubicin compare to gemcitabine?

DR SPRIGGS: A recent publication in the *JCO* suggests that pegylated liposomal doxorubicin is similar, not inferior, to gemcitabine in efficacy (Ferrandina 2008; [2.2]). However, it is important to remember that pegylated liposomal doxorubicin has a slow onset of action, and for a patient with rapidly progressive disease, we may not have time to wait for it to begin to work. In that setting, a topoisomerase inhibitor or gemcitabine is probably a better choice.

Otherwise, pegylated liposomal doxorubicin has many advantages. We administer it once every four weeks, rather than every three, and our starting dose is 40 mg/m^2 because we find that's more tolerable than 50 mg/m^2.

DR LOVE: What is the toxicity profile?

DR SPRIGGS: Some say they have never seen a true case of pegylated liposomal doxorubicin-related cardiotoxicity, but I have. The conservative approach is to order echocardiograms as you go beyond two or three cycles, and when you get to a maximum total doxorubicin dose in the 400- to 450-mg range, you should carefully weigh the benefit and risks. We don't know exactly how much pegylated liposomal doxorubicin is enough. ■

2.2 Phase III Trial of Gemcitabine (GEM) versus Pegylated Liposomal Doxorubicin (PLD) in Progressive or Recurrent Ovarian Cancer (N = 153)

"Grade 3 or 4 neutropenia was more frequent in GEM-treated patients versus PLD-treated patients (P = .007). Grade 3 or 4 palmar-plantar erythrodysesthesia was documented in a higher proportion of PLD patients (6%) versus GEM patients (0%; P = .061). The overall response rate was 16% in the PLD arm compared with 29% in the GEM arm (P = .056). No statistically significant difference in time to progression (TTP) curves according to treatment allocation was documented (P = .411). However, a trend for more favorable overall survival was documented in the PLD arm compared with the GEM arm, although the P value was of borderline statistical significance (P = .048). Statistically significantly higher global QOL [quality of life] scores were found in PLD-treated patients at the first and second postbaseline QOL assessments.

Conclusion: GEM does not provide an advantage compared with PLD in terms of TTP in ovarian cancer patients who experience recurrence within 12 months after primary treatment but should be considered in the spectrum of drugs to be possibly used in the salvage setting."

SOURCE: Ferrandina G et al. *J Clin Oncol* 2008;26(6):890-6. **Abstract**

SELECT PUBLICATIONS

Alberts DS et al. **Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer.** *N Engl J Med* 1996;335(26):1950-5. **Abstract**

Armstrong DK et al. **Randomized phase III study of intravenous (IV) paclitaxel and cisplatin versus IV paclitaxel, intraperitoneal (IP) cisplatin and IP paclitaxel in optimal stage III epithelial ovarian cancer (OC): A Gynecologic Oncology Group trial (GOG 172).** *Proc ASCO* 2002;**Abstract 803**.

Cannistra SA et al. **Phase II study of bevacizumab in patients with platinum-resistant ovarian cancer or peritoneal serous cancer.** *J Clin Oncol* 2007;25(33):5180-6. **Abstract**

Ferrandina G et al. **Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer.** *J Clin Oncol* 2008;26(6):890-6. **Abstract**

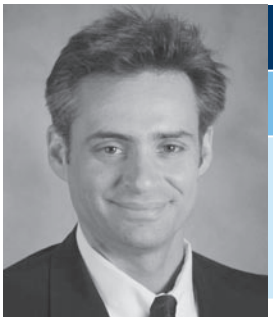
Han ES et al. **Relationship of angiogenesis biomarkers and clinical response to bevacizumab (Bev) in persistent or recurrent epithelial ovarian cancer (EOC) and primary peritoneal cancer (PPC) patients treated in a Phase II Gynecologic Oncology Group study.** *Proc ASCO* 2007;**Abstract 21021**.

Konner JA et al. **A phase II study of intravenous (IV) and intraperitoneal (IP) paclitaxel (Tax), IP cisplatin (Cis), and IV bevacizumab (Bev) as first-line chemotherapy for optimal stage II or III ovarian, primary peritoneal, and fallopian tube cancer.** *Proc ASCO* 2007;**Abstract 5523**.

Markman M et al. **Phase III trial of standard-dose intravenous cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: An intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group.** *J Clin Oncol* 2001;19(4):1001-7. **Abstract**

Markman M, Hoskins W. **Responses to salvage chemotherapy in ovarian cancer: A critical need for precise definitions of the treated population.** *J Clin Oncol* 1992;10(4):513-4. No abstract available

McGuire WP et al. **Assessment of dose-intensive therapy in suboptimally debulked ovarian cancer: A Gynecologic Oncology Group study.** *J Clin Oncol* 1995;13(7):1589-99. **Abstract**



INTERVIEW

Robert L Coleman, MD

Dr Coleman is Professor and Director of Clinical Research in the Department of Gynecologic Oncology at The University of Texas MD Anderson Cancer Center in Houston, Texas.

Tracks 1-13

Select Excerpts from the Interview

Tracks 4-5

DR LOVE: Would you discuss the GOG-0213 study?

DR COLEMAN: GOG-0213 will examine two key issues: surgery in recurrent disease and the role of adding biologic agents to standard chemotherapy in the recurrent setting (3.1). The trial will enroll patients with platinum-sensitive recurrent ovarian cancer treated with a prior regimen for recurrence, although the patients could have received maintenance therapy as part of the primary treatment. This trial also allows for prior exposure to biologic agents.

Recently, we amended the trial to allow patients who have a biological recurrence, which has been defined as an elevation in CA125 to twice the upper

limit of normal or greater than 100 u/mL after it normalizes. Platinum sensitivity in this trial is evaluated by traditional parameters at six months. We made the important decision to evaluate patients at six to 12 months and after 12 months in both the chemotherapy and the surgery arms. Some information suggests that patients with longer disease-free intervals may benefit more from surgery.

DR LOVE: What's the trial design?

DR COLEMAN: The first randomization has to do with whether the patient is considered to be a surgical candidate. This was a particularly difficult parameter to develop because surgeons have different criteria for what they consider operable in the recurrent setting.

In prior retrospective and prospective nonrandomized reports, the only consistent observation was that patients with no visible residual disease after surgery seemed to benefit the most from this procedure. We defined surgical eligibility based on that endpoint. If an investigator felt that all of a patient's disease could be removed, the patient was eligible to enter the surgical randomization.

After this randomization, or if patients are not surgical candidates, they go on to the chemotherapy randomization, which compares paclitaxel/carboplatin in the standard treatment arm to paclitaxel/carboplatin and bevacizumab, followed by bevacizumab maintenance, in the experimental arm.

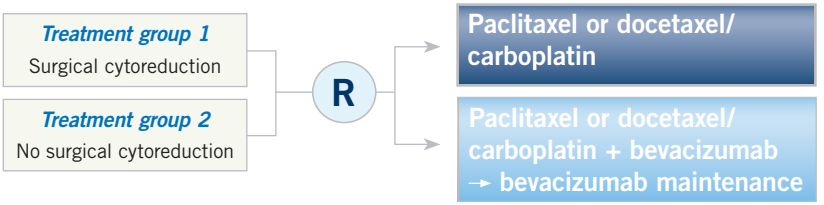
3.1

GOG-0213: A Phase III Study of Carboplatin and Paclitaxel with or without Bevacizumab After Surgery for Patients with Recurrent Ovarian Epithelial Cancer, Primary Peritoneal Cavity Cancer or Fallopian Tube Cancer

Protocol IDs: GOG-0213, NCT00565851; Target Accrual: 660 (Open)

Eligibility

- Recurrent ovarian, peritoneal cavity or fallopian tube cancer; CA125 > 2 times upper limit of normal or histologic confirmation of recurrence; ≥6 months after completion of front-line biologic therapy



Study Contact

Gynecologic Oncology Group
Robert Coleman, MD
Tel: 713-745-3357; 800-392-1611

SOURCES: NCI Physician Data Query, May 2008; **www.clinicaltrials.gov**, May 2008.

Track 9

DR LOVE: Would you discuss the findings of your recent paper on CA125?

DR COLEMAN: We evaluated a data set from the pegylated liposomal doxorubicin registration trial (Gordon 2001), which provided a unique window into the short period during the first two cycles of therapy. We wanted to examine how CA125 performed among the responders and nonresponders in that cohort.

We observed a large number of responders with rising CA125 levels after they began therapy (Coleman 2007; [3.2]). Because of the reliance on CA125 in the community, I was afraid that people were abandoning the drugs early in therapy because of these effects in CA125 levels.

It's important to realize that you can observe a rise in CA125 early on in treatment. Don't have a knee-jerk reaction and assume that the patients will not benefit from therapy.

3.2

Early Changes in CA125 Level After Treatment with Pegylated Liposomal Doxorubicin (PLD) or Topotecan Do Not Always Reflect Best Response in Recurrent Ovarian Cancer

"The results of this analysis demonstrate that PLD- and topotecan-treated patients who achieve an objective response may have increasing CA125 values after the first cycle of therapy and that 15% of PLD-treated patients will have CA125 values, increased from baseline after two cycles of therapy.

Although most responders were ultimately observed to have decreasing CA125 values, 6% of topotecan-treated patients and 10% of PLD-treated patients were found to have a rise of greater than 25% from baseline following cycle 2. This is an important observation in that in the absence of findings on physical examination or radiographic imaging, a decision to continue a chemotherapeutic is based almost entirely on the trends in biomarker values...

This study demonstrates that early changes in CA125 values may not reflect the ultimate clinical response as determined by radiographic measures."

SOURCE: Coleman RL et al. *Oncologist* 2007;12(1):72-8. **Abstract**

Track 13

DR LOVE: What is your approach to systemic therapy of platinum-sensitive recurrent disease?

DR COLEMAN: Traditionally, platinum sensitivity describes the time during which patients who have received a platinum again would likely have a response, which is approximately six months (Blackledge 1989; Markman 1991). We expect the phenotype of platinum sensitivity to extend across all drugs in that most drugs perform better in patients with longer treatment-free intervals. A near linear relationship exists between those two.

Having said that, we tend to treat platinum-sensitive disease with combination therapy. Both paclitaxel/carboplatin and newly approved gemcitabine/carboplatin are important combinations to consider in that setting. A meta-analysis presented at ASCO suggests that these combinations tend to help patients in the short term (Orlando 2007).

The major question is whether sequencing the same agents will yield the same endpoint. That's the focus of a trial run by Dr Angeles Alvarez Secord at Duke, who's evaluating docetaxel and carboplatin administered either in combination or as sequential therapy (NCT00090610). We may find that the combination of these agents adds toxicity and short-term gains but adds nothing in terms of long-term survival.

DR LOVE: How do you approach treatment for these patients in the clinical setting?

DR COLEMAN: I tend to offer patients the most aggressive therapy that I feel is safe. If these patients are good candidates for surgery, with resectable disease, I consider them for surgery.

Off protocol and without surgery considerations, if the toxicities are not too high, I recommend reinduction with a taxane/platinum regimen or with gemcitabine/carboplatin, particularly for patients with neurotoxicity from their first-line therapy.

DR LOVE: What have you observed with gemcitabine/carboplatin in terms of tolerance and antitumor effects?

DR COLEMAN: It's quite tolerable. Gemcitabine is approved for weekly administration. To make that administration safe, we use a lower dose of the carboplatin. Gemcitabine/cisplatin is also a reasonable strategy for this tumor type.

One modification we've made for patients who are intolerant to gemcitabine/carboplatin or gemcitabine/cisplatin on the traditional schedule is to break it up and administer both the platinum agent and the gemcitabine every 14 days. That's well tolerated, and we've seen impressive responses. ■

SELECT PUBLICATIONS

Blackledge G et al. **Response of patients in phase II studies of chemotherapy in ovarian cancer: Implications for patient treatment and design of phase II trials.** *Br J Cancer* 1989;59(4):650-3. **Abstract**

Coleman RL et al. **Early changes in CA125 after treatment with pegylated liposomal doxorubicin or topotecan do not always reflect best response in recurrent ovarian cancer patients.** *Oncologist* 2007;12(1):72-8. **Abstract**

Gordon AN et al. **Recurrent epithelial ovarian carcinoma: A randomized phase III study of pegylated liposomal doxorubicin versus topotecan.** *J Clin Oncol* 2001;19(14):3312-22. **Abstract**

Markman M et al. **Second-line platinum therapy in patients with ovarian cancer previously treated with cisplatin.** *J Clin Oncol* 1991;9(3):389-93. **Abstract**

Orlando M et al. **Randomized trials of combination chemotherapy (combo) versus monotherapy (mono) in relapsed ovarian carcinoma (ROC): A meta-analysis of published data.** *Proc ASCO* 2007;**Abstract 5524**.

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The response rate with bevacizumab monotherapy for patients with ovarian cancer is approximately _____.**
   a. 40 percent
   b. 20 percent
   c. 10 percent
   d. Five percent

2. **GOG-0218 will evaluate the role of _____ in combination with paclitaxel/carboplatin for women with newly diagnosed Stage III or IV ovarian cancer.**
   a. Bevacizumab
   b. Pertuzumab
   c. Trastuzumab
   d. Gemcitabine
   e. None of the above

3. **Which of the following platinum-based combinations have been found to improve progression-free survival for patients with relapsed platinum-sensitive ovarian cancer?**
   a. Paclitaxel/carboplatin
   b. Gemcitabine/carboplatin
   c. Topotecan/carboplatin
   d. Both a and b
   e. All of the above

4. **In the safety data from the Phase II trial of intravenous and intraperitoneal paclitaxel, intraperitoneal cisplatin and intravenous bevacizumab presented at ASCO 2007, which of the following were reported?**
   a. Grade IV hypertension
   b. Grade IV wound dehiscence
   c. Grade IV proteinuria
   d. No Grade IV toxicities

5. **Bevacizumab-associated bowel perforation has been reported in the treatment of patients with _____ cancer.**
   a. Colon
   b. Ovarian
   c. Both a and b
   d. None of the above

6. **In data published by Ferrandina and colleagues, gemcitabine _____ demonstrate a significant improvement in time to progression when compared to pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer.**
   a. Did
   b. Did not

7. **GOG-0213 will examine _____.**
   a. Surgical cytoreduction versus no surgery in surgical candidates
   b. Paclitaxel/carboplatin versus paclitaxel/carboplatin and bevacizumab → bevacizumab maintenance
   c. Both a and b
   d. None of the above

8. **Among patients with recurrent ovarian cancer, a strong linear correlation exists between early changes in CA125 level and best response to treatment with pegylated liposomal doxorubicin or topotecan.**
   a. True
   b. False

9. **The primary side effect of pegylated liposomal doxorubicin in patients with ovarian cancer who have progressive disease is _____.**
   a. Hand-foot syndrome
   b. Neurotoxicity
   c. Myelosuppression
   d. Stomatitis

10. **In clinical trials, the cutoff used to determine platinum-sensitive versus platinum-resistant disease after receiving initial therapy is _____.**
    a. Three months
    b. Six months
    c. 12 months

Post-test answer key: 1b, 2a, 3d, 4d, 5c, 6b, 7c, 8b, 9a, 10b

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Ovarian Cancer Update — Issue 2, 2008

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART ONE — Please tell us about your experience with this educational activity

BEFORE completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

- **Activity and clinical use of gemcitabine/carboplatin in the treatment of platinum-sensitive disease** 4 3 2 1
- **Value of CA125 in monitoring response to pegylated liposomal doxorubicin or topotecan in recurrent ovarian or primary peritoneal cancer** 4 3 2 1
- **Intraperitoneal versus intravenous chemotherapy in ovarian and primary peritoneal cancer** 4 3 2 1
- **GOG-0213 trial of adjuvant carboplatin/paclitaxel with or without bevacizumab and/or secondary cytoreduction surgery in platinum-sensitive disease** 4 3 2 1

AFTER completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

- **Activity and clinical use of gemcitabine/carboplatin in the treatment of platinum-sensitive disease** 4 3 2 1
- **Value of CA125 in monitoring response to pegylated liposomal doxorubicin or topotecan in recurrent ovarian or primary peritoneal cancer** 4 3 2 1
- **Intraperitoneal versus intravenous chemotherapy in ovarian and primary peritoneal cancer** 4 3 2 1
- **GOG-0213 trial of adjuvant carboplatin/paclitaxel with or without bevacizumab and/or secondary cytoreduction surgery in platinum-sensitive disease** 4 3 2 1

Was the activity evidence based, fair, balanced and free from commercial bias?

☐ Yes ☐ No

Please explain: . . . . . .

Will this activity help you improve patient care?

☐ Yes ☐ No ☐ Not applicable

If no, please explain: . . . . . .

Did the activity meet your educational needs and expectations?

☐ Yes ☐ No

If no, please explain: . . . . . .

Please respond to the following LEARNER statements by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = Learning objective not met N/A = Not applicable

As a result of this activity, I will:

- Manage localized, locally advanced and metastatic ovarian cancer based on an understanding of the pathophysiology of the disease and the clinical presentation. . . . . 4 3 2 1 N/M N/A
- Appropriately utilize surgical staging for the prognosis and subsequent medical management of epithelial ovarian cancer, based on the NCCN guidelines. . . . . 4 3 2 1 N/M N/A
- Evaluate the risks and benefits of primary chemotherapy when devising management strategies for ovarian cancer, including intraperitoneal and intravenous regimens for patients with Stage II and Stage III optimally debulked disease and taxane-based chemotherapy regimens. . . . . 4 3 2 1 N/M N/A
- Consider the use of biologic agents and/or regimens based on relevant clinical trial data when treating recurrent platinum-sensitive and platinum-resistant ovarian cancer. . . 4 3 2 1 N/M N/A
- Select therapies for patients with ovarian cancer, with an understanding of the relevance of the distinct mechanisms of action of novel targeted signal transduction inhibitors. . . . . 4 3 2 1 N/M N/A
- Develop an algorithm for monitoring patients in remission, including radiographic studies and CA125 levels. . . . . 4 3 2 1 N/M N/A
- Utilize maintenance chemotherapy for patients with ovarian cancer who are in remission, as appropriate. . . . . 4 3 2 1 N/M N/A
- Consider the relative efficacy and adverse effects of acceptable treatment modalities when managing primary, metastatic or recurrent disease. . . . . 4 3 2 1 N/M N/A
- Counsel appropriately selected patients about the availability of ongoing clinical trials. . . . . 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

What other practice changes will you make or consider making as a result of this activity?

.....

What additional information or training do you need on the activity topics or other oncology-related topics?

.....

Additional comments about this activity:

.....

.....

May we include you in future assessments to evaluate the effectiveness of this activity?

☐ Yes ☐ No

PART TWO — Please tell us about the faculty for this educational activity

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

Faculty	Knowledge of subject matter	Effectiveness as an educator
Deborah K Armstrong, MD	4 3 2 1	4 3 2 1
David R Spriggs, MD	4 3 2 1	4 3 2 1
Robert L Coleman, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty for this activity:

.....

REQUEST FOR CREDIT — Please print clearly

Name: ..... Specialty: .....

Degree:

☐ MD ☐ DO ☐ PharmD ☐ NP ☐ BS ☐ RN ☐ PA ☐ Other .....

Medical License/ME Number: ..... Last 4 Digits of SSN (required): .....

Street Address: ..... Box/Suite: .....

City, State, Zip: .....

Telephone: ..... Fax: .....

Email: .....

Research To Practice designates this educational activity for a maximum of 3 *AMA PRA Category 1 Credit(s)™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

I certify my actual time spent to complete this educational activity to be _____ hour(s).

Signature: ..... Date: .....

To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.OvarianCancerUpdate.com/CME.

OCU208

Ovarian Cancer™

U P D A T E

Editor	Neil Love, MD
Managing Editor	Kathryn Ault Ziel, PhD
Scientific Director	Richard Kaderman, PhD
Senior Director, Medical Affairs	Aviva Asnis-Alibozek, PA-C, MPAS
Writers	Lilliam Sklaver Poltorack, PharmD Douglas Paley Anne Jacobson, MPH
Continuing Education Administrator for Nursing	Sally Bogert, RNC, WHCNP
Content Validation	Margaret Peng Erin Wall Clayton Campbell
Director, Creative and Copy Editing	Aura Herrmann
Creative Manager	Fernando Rendina
Graphic Designers	Jessica Benitez Jason Cunnius Tamara Dabney Shantia Daniel Claudia Munoz
Senior Production Editor	Alexis Oneca
Traffic Manager	Tere Sosa
Copy Editors	Dave Amber Margo Harris David Hill Rosemary Hulce Kirsten Miller Pat Morrissey/Havlin Carol Peschke Susan Petrone
Production Manager	Tracy Potter
Audio Production	Frank Cesarano
Web Master	John Ribeiro
Faculty Relations Manager	Melissa Vives
CME Director/CPD Director	Isabelle Tate
Contact Information	Neil Love, MD Research To Practice One Biscayne Tower 2 South Biscayne Boulevard, Suite 3600 Miami, FL 33131 Fax: (305) 377-9998 Email: DrNeilLove@ResearchToPractice.com
For CME/CNE Information	Email: CE@ResearchToPractice.com

Copyright © 2008 Research To Practice. All rights reserved.

The compact discs, Internet content and accompanying printed material are protected by copyright. No part of this program may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording or utilizing any information storage and retrieval system, without written permission from the copyright owner.

The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management.

Any procedures, medications or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use, review of any applicable manufacturer's product information and comparison with recommendations of other authorities.

Ovarian Cancer™

U P D A T E

Copyright © 2008 Research To Practice.
This program is supported by educational grants from Centocor Ortho Biotech Services, Eli Lilly and Company and Genentech BioOncology.

Research
To Practice®

Sponsored by Research To Practice.

Last review date: June 2008
Release date: June 2008
Expiration date: June 2009
Estimated time to complete: 3 hours