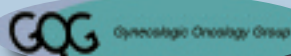


# Newsletter

SPRING 2009

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## Chairman's Corner

Philip J. DiSaia, MD

A summary of the CTEP/Cooperative Groups chairs conference call held on January 27, 2009 will be the subject of this report. Many subjects were discussed and this report will highlight those that I believe are most pertinent to the Group at large.

We began the meeting by discussing a new central IRB process, which probably will take place beginning May 1, 2009. In this new process, protocols will be submitted from the Philadelphia office to the central IRB and simultaneously to the multiple institutional IRBs for simultaneous approval. Those institutional IRBs who wish to await central IRB decision and are, at this juncture, accepting of the central IRB decision, will continue as in the past. Those institutional IRBs who have insisted upon a review process of their own, formally following the central IRB review, will be allowed to proceed with their institutional review process immediately without CIRB approval needed. We expect that occasionally there will be some wording differences on the consent form but that is commonplace and should not present a problem. I hasten to add that amendments to protocols will not follow the same process but amendments will go first to the central IRB and will not be sent to the institutional IRBs until they have been approved by the central IRB. However, we have been promised that the central IRB will process these amendments in 2-5 days.

Another important issue that was discussed at this rather productive meeting was a new type of Sub Committee H



Philip J. DiSaia, MD - Group Chair

review. Several of the Chairs have suggested in the past that the site visits and "reverse" site visits done prior to approval of a reapplication for Group funding are expensive and probably unnecessary. It is estimated that the rehearsals, personnel time, etc. associated with these site visits cost the Groups at least \$300,000. Obviously this money could be used in many other ways. To CTEPs credit it has taken this matter under serious consideration and is considering limiting "reverse" site visits to a limited number of individuals appearing before Subcommittee H after submission of the written document and upon receipt by the Group Chairman of questions from Committee H. This might mean that the Chairman, Vice Chairman, Vice Chairman for Science, Group Statistician and Executive Director might go to Washington to answer questions emanating from a review of the written document by Subcommittee H. Obviously this would make site visit rehearsals etc.

**CHAIR** continued on Page 3

## Remembering a friend

I lost a good friend last month and so did GOG. Dr. Steve Williams, Director of the Indiana University Melvin and Bren Simon Cancer Center, passed away due to cancer on February 15, 2009. Steve was a Medical Oncologist who had a long dedication to GOG. Initially, he chaired several rare ovarian studies, Protocols 44, 45, 78, 90, and 116. In recognition of his expertise, knowledge, and commitment, he was named Co-chair of the Ovarian Committee and later Chair of this important body. When IU decided to apply for a Cancer Center grant, Steve was the impetus behind the effort. Under his direction the Cancer Center research funding exceeded \$75 million.

The medical and research tributes that could be made are extensive and well-

deserved. However, what I will always remember is the person. No matter how high his professional stature rose, he was always the same "good old Steve." He was an absolute joy to be with. I always looked forward to his trips to the SDC for Study Chair reviews. The work was professionally accomplished, but never without enjoyable moments. Once he arrived at my house on a Saturday night which also was Halloween. Within ten minutes of arriving, he and I were on our hands and knees in the garage crawling through my daughter's haunted house. On another occasion, we went to a Buffalo Bill's game (the Colts were still in Baltimore and Steve had never been to a professional game before). We went to the stadium early, and went down near the sideline. Steve's

jaw dropped and he marveled: "I've never seen the band this close before!" After the game, my brother, a sportscaster, took Steve into the locker room during interviews. Steve was bug eyed! That night we had to watch the interviews on all three stations. Subsequently, when the Colts moved to Indianapolis and were in the AFC East, Steve became a season ticket holder, and I went to numerous Bills-Colts games in Indianapolis with him. He still retained the same wide-eyed enthusiasm.

In recent years, Steve was less involved in GOG due to his Cancer Center responsibilities. However, whenever I was at IU we would always visit. He was one of those people that retained the closeness of the relationship even when opportunities to visit were infrequent. I was fortunate to know him. We all were!

## CPC celebrates 15th anniversary with GOG

The Cancer Prevention and Control (CPC) Committee is celebrating its 15<sup>th</sup> anniversary in the GOG. It was developed in 1994 and has focused on the design of Cancer Prevention and Control which utilize the scientific and clinical resources of the GOG membership. The CPC Committee goals include:

1. Developing effective cancer prevention and/or control research trials that deal with relevant issues, behaviors, and practices affecting women.
2. Developing mechanisms to improve the scientific knowledge associated with gynecologic oncology and the well-being of women affected by genital malignancies.
3. Promoting effective management of cancer patients by determining appropriate instruments for assessment of treatment effects and treatments to eliminate or prevent adverse therapeutic effects.
4. Establishing scientifically viable

mechanisms for the early detection and prevention of gynecologic cancers.

With these goals in mind we would like to share some information about our currently open and upcoming trials with the broader GOG membership and encourage you to participate in these protocols. Currently the CPC has 6 open studies.

**GOG-0207** "A Randomized Double-Blind Phase II Trial of Celecoxib in the Treatment of Patients with Cervical Intraepithelial Neoplasia 2/3 or 3" is now very near accrual and we look forward to the interpretation of the results.

**GOG-0215** is a study evaluating the effect of zoledronic acid on bone mineral density in premenopausal women who have undergone surgery to have both ovaries removed. This study is nearing the half point of accrual and the committee is pushing hard to complete accrual over the next nine months.

**GOG-0236** goal is to compare the effec-

tiveness of the Flexitouch® System to standard home lymphedema therapy in the maintenance of lower extremity lymphedema in women with a history of a gynecologic malignancy. As with many of the studies done in the CPC committee, there is a quality of life component.

**GOG-0224** is a randomized, controlled phase II evaluation of megestrol in different doses and sequence in the treatment of endometrial intraepithelial neoplasia. This study seeks to determine the frequency of complete remission of a community biopsy diagnosis of AEH or EIN in patients treated for 12 weeks with continuous versus interrupted progestin therapy (oral megestrol 40 mg/twice daily or oral megestrol 80 mg/twice daily for 2 weeks on then 2 weeks off for a total of 12 weeks) versus patients who receive no progestin treatment.

**GOG-0214** "Phase II Double Blind Randomized Trial Evaluating the Biologic

*CPC continued on page 7*

## Office for Human Research Protections (OHRP) Updates

The Office of Management and Budget has renewed its approval of the information collected on the form entitled *Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption (Common Rule)*. The renewal was conducted under the Paperwork Reduction Act and will last through January 31, 2012.

This form, OMB No. 0990-0263, can be used to certify IRB review and

approval to the Department or Agency in accordance with the Common Rule. The form can be accessed at:

<http://www.hhs.gov/ohrp/human-subjects/assurance/OF310.rtf>

OHRP has also posted on its website a finalized guidance document entitled *Guidance on Engagement of Institutions in Human Subjects Research*. The finalized guidance can be accessed at:

<http://www.hhs.gov/ohrp/human-subjects/guidance/engage08.html>

This new guidance document replaces two prior OHRP guidance documents on the engagement of institutions in human subjects research. They include the January 26, 1999 document “*Engagement of Institutions in Research*,” and the December 23, 1999 document “*Engagement of Pharmaceutical Companies in HHS Supported Research*.”

### CHAIR *continued from Page 1*

unnecessary and result in a large cost savings. The majority of the Group Chairs encourage proceeding with this type of modification.

Additionally, the funding for collection of biospecimens was announced; however, only when

these specimens are collected in conjunction with pharmacogenetic research protocols. Requests for such limited funding will be granted on a first come first serve basis and is limited to Phase III trials. Headquarters will be distributing additional information as we obtain further clarification of this funding opportunity but Group

members interested in this resource should be on alert.

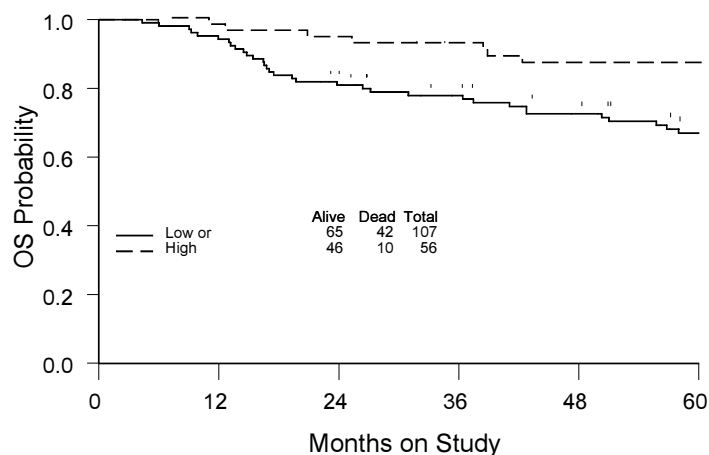
The importance of international trials was emphasized with the hope of accelerating accrual primarily to Phase III trials. Guidelines for adopting wider use of international trials will be forthcoming. This effort is spearheaded by Dr. Ted Trimble.

<b>Abraxis Oncology</b>	 <p><b>GOG Industry Collaboration Team</b></p>	<b>Morphotek, Inc.</b>
<b>Advaxis</b>		<b>Novartis Pharmaceuticals</b>
<b>Amgen, Inc.</b>		<b>Ortho Biotech Products, LP</b>
<b>Bayer/Onyx Pharmaceuticals</b>		<b>OSI Oncology</b>
<b>BD Diagnostics-TriPath</b>		<b>Pfizer, Inc.</b>
<b>Bristol-Myers Squibb</b>		<b>Ponaird Pharmaceuticals</b>
<b>Caris/MPI</b>		<b>Precision Therapeutics, Inc.</b>
<b>Celegene Corporation</b>		<b>Regeneron Pharmaceuticals</b>
<b>Cell Therapeutics, Inc.</b>		<b>Sanofi-Aventis Pharmaceuticals</b>
<b>Eli Lilly &amp; Company</b>		<b>Exiqon Dx</b>
		<b>Genentech BioOncology</b>
		<b>Genzyme Biosurgery</b>
		<b>GlaxoSmithKline</b>
		<b>ImClone Systems, Inc.</b>
	<b>Merck</b>	

## GOG helps clarify role of Hypoxia and Angiogenesis in Cervical Carcinoma

One of the fundamental differences between normal and tumor tissue is the tumor vasculature. As a solid tumor expands, the rate of cancer cell proliferation surpasses the ability of the existing vasculature to supply growth factors, nutrients, and oxygen. A critical hallmark of solid tumors is low oxygen tension, or hypoxia. Because the vasculature cannot sustain the demands of the cancer cells, solid tumors are invariably less well oxygenated compared to the normal tissue of origin. In an attempt to overcome the deficiencies of the existing vasculature and stimulate their own growth, tumors induce the expression of pro-angiogenic factors to increase their blood supply. As a result of the hypoxia inherently associated with tumor expansion, tumors induce blood vessel growth (angiogenesis) by secreting various growth factors (e.g. Vascular Endothelial Growth Factor or VEGF). Angiogenesis is also required for the spread of a tumor, or metastasis. Single cancer cells can break away from an established solid tumor, enter the blood vessel, and be carried to a distant site, where they can implant and begin the growth of a secondary tumor. Evidence now suggests that the blood vessel in a given solid tumor may in fact be a mosaic of normal and abnormal vessels, composed of both endothelial cells and tumor cells. This mosaic allows for intermittent shedding of tumor cells into the vasculature. Because a substantial portion of the new vasculature is immature and dysfunctional, angiogenesis often exacerbates focal tumor hypoxia leading to increased resistance to radiation (RT) and chemotherapy.

The GOG has recently evaluated the prognostic significance of markers of angiogenesis among women with high-risk, early-stage cervical cancer treated on GOG protocol 0109 (Randall LM et al *Gynecol Oncol*. 2008 Dec 23. [Epub ahead of print]). This trial randomized women after radical hysterectomy with positive margins, parametrial spread, or positive nodes to pelvic RT versus pelvic RT and cisplatin based chemotherapy. One hundred seventy-three tumor specimens were analyzed by semi-quantitative immunohistochemical (IHC) staining for vascular endothelial growth factor (VEGF, pro-angiogenesis factor), thrombospondin-1 (TSP-1, anti-angiogenesis factor), CD31 (non-specific endothelial marker of micro-vessel density [MVD]), and CD105 (tumor-specific endothelial marker). TSP-1 expression was observed in 65% of cases while 66% expressed high VEGF, 34% exhibited high CD31 and 66% displayed high CD105. In univariate analyses, CD31 MVD, but not tumor TSP-1, was associated with improved PFS (HR=0.37; 95% CI=0.18-0.76; p=0.007) and OS (HR=0.37; 95% CI=0.17-0.79; p=0.010). After adjusting



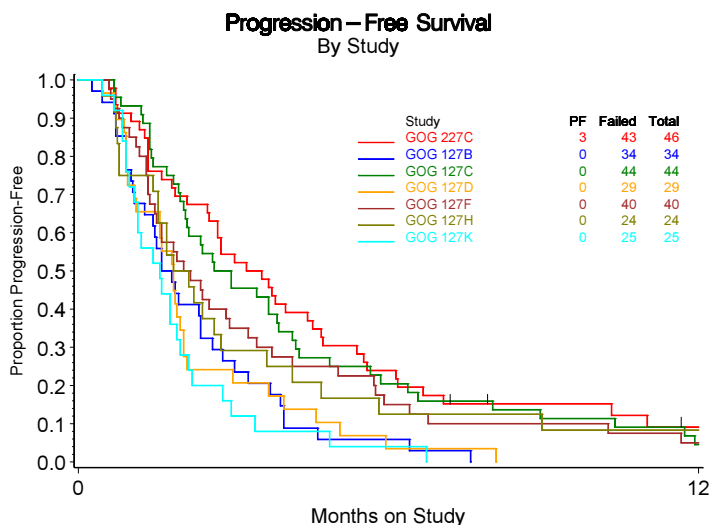
**Figure 1.** Kaplan-Meier plot of overall survival for women categorized by CD31 MVD entered on GOG Protocol 0109

for prognostic clinical covariates, high CD31 MVD, but not TSP-1, VEGF or CD105 MVD, was an independent prognostic factor for PFS (HR=0.36; 95% CI=0.17-0.75; p=0.006) and OS (HR=0.36; 95% CI=0.17-0.79; p=0.010). This study confirmed the hypothesis that tumor angiogenesis as measured by CD31 MVD is an independent prognostic factor for both PFS and OS in high-risk, early-stage cervical cancer. The authors hypothesized that this finding may be explained by improved treatment response in well-vascularized, well-oxygenated tumors (Figure 1).

More recently, at the 40<sup>th</sup> Annual Meeting of the Society of Gynecologic Oncologists (Abstract 28), Liao et al evaluated the same cohort of patients by analyzing CAIX. CAIX is a marker of hypoxia since its expression is controlled by the transcription factor, hypoxia inducible factor-1 and is up-regulated in hypoxic regions of tumor tissues. They showed that tumor hypoxia as measured by IHC expression of CA-IX was also an independent prognostic factor for both PFS and OS in this group of patients enrolled on GOG protocol 0109.

Importantly, women who had tumors with high CD31-MVD (high angiogenesis) and low CA-IX (low hypoxia) had the best PFS and OS whereas those with low CD31-MVD (low angiogenesis) and low CA-IX (low hypoxia) had intermediate PFS and OS and those with low CD31-MVD (low angiogenesis) and high CA-IX (high hypoxia) had the worst PFS and OS. Adjusted Cox regression modeling demonstrated that CA-IX and CD31-MVD were each independent prognostic factors for PFS and OS. Taken together, these findings support the hypothesis that im-

*GOG continued on next page*



**Figure 2.** Comparison of progression-free survival (PFS) from historical studies in the 0127 queue compared to the PFS from GOG 0227-C with bevacizumab

*GOG continued from previous page*

proved treatment response is observed in the well-vascularized and well-oxygenated cervical cancers with high CD31-MVD and low CA-IX expression. These findings will now be prospectively evaluated in tumor tissue from patients enrolled on GOG 0191 and 0219.

Moving towards the therapeutic intervention of hypoxic tumors, the highest scientific priority of the GOG Cervical Cancer Committee is the successful completion of GOG protocol 0219. This randomized phase III trials investigates the addition of the novel hypoxic cell cytotoxin, tirapazamine (TPZ), to pelvic RT and cisplatin in women with bulky or locally advanced cervical cancer (IB2, IIA >4cm, IIB, IIIB, or IVA). After a small initial phase I dose escalation study outside the GOG, the GOG activated protocol 0219 with an interim analysis for safety planned after the first 30 patients on the experimental arm completed therapy. This safety evaluation showed an unacceptable rate of grade 3 and 4 leukopenia and metabolic abnormalities above the pre-set threshold of 20% leading to a dose reduction of TPZ to 220 mg/m<sup>2</sup> (max = 385 mg) on days 1, 15, 29 with Cisplatin 60 mg/m<sup>2</sup> (max = 105 mg) and TPZ 220 mg/m<sup>2</sup> (max = 385 mg) alone on days 8, 10, 12, 22, 24, 26. There were no treatment related deaths and the impact of the toxicities seen in the first 30 patients enrolled on the TPZ arm of 0219 did not appear to have great clinical significance when assessing treatment compliance (cycles of therapy and treatment window). Finally, a second safety analysis of GOG 0219 has recently been performed and determined the reduced doses on the TPZ arm to be acceptable (below the pre-set threshold of 20%) and tolerable.

Hypoxia and angiogenesis are also being investigated in

**Eligibility:**

- Primary Stage IVB or recurrent/persistent carcinoma of the cervix
- Measurable disease
- GOG performance status 0-1

**Randomize to One of the Four Regimens:**

**Primary Endpoints:**

- Overall survival (OS)
- Frequency and severity of toxicity

**Secondary Endpoints:**

- Progression-free survival (PFS)

**Regimen I**  
 Paclitaxel 135 mg/m<sup>2</sup> IV over 24 hrs on day 1  
 Cisplatin 50 mg/m<sup>2</sup> IV on day 2 **OR**  
 Paclitaxel 175 mg/m<sup>2</sup> IV over 3 hrs on day 1  
 Cisplatin 50 mg/m<sup>2</sup> IV on day 2 **OR**  
 Paclitaxel 175 mg/m<sup>2</sup> IV over 3 hrs on day 1  
 Cisplatin 50 mg/m<sup>2</sup> IV on day 1

Cycles repeated q21 days to progression/toxicity\*\*

**Regimen II**  
 Paclitaxel 135 mg/m<sup>2</sup> IV over 24 hrs on day 1  
 Cisplatin 50 mg/m<sup>2</sup> IV on day 2  
 Bevacizumab 15 mg/kg IV day 2 **OR**  
 Paclitaxel 175 mg/m<sup>2</sup> IV over 3 hrs on day 1  
 Cisplatin 50 mg/m<sup>2</sup> IV on day 2  
 Bevacizumab 15 mg/kg IV day 2 **OR**  
 Paclitaxel 175 mg/m<sup>2</sup> IV over 3 hrs on day 1  
 Cisplatin 50 mg/m<sup>2</sup> IV on day 1  
 Bevacizumab 15 mg/kg IV day 1

Cycles repeated q21 days to progression/toxicity\*\*

**Regimen III**  
 Paclitaxel 175 mg/m<sup>2</sup> over 3 hrs on day 1  
 Topotecan 0.75 mg/m<sup>2</sup> over 30 mins days 1-3  
 Cycles repeated q21 days to progression/toxicity\*\*

**Regimen IV**  
 Paclitaxel 175 mg/m<sup>2</sup> over 3 hrs on day 1  
 Topotecan 0.75 mg/m<sup>2</sup> over 30 mins days 1-3  
 Bevacizumab 15 mg/kg IV day 1  
 Cycles repeated q21 days to progression/toxicity\*\*

**Figure 3.** Schema for GOG protocol 0240

advanced (stage IVB) and recurrent cervical cancer. The GOG recently reported the results of protocol 0227-C (Monk et al J Clin Oncol. 2009 Jan 12. [Epub ahead of print]). This phase II trial evaluated the single agent activity of bevacizumab, a recombinant humanized anti-vascular endothelial growth factor monoclonal antibody at 15 mg/kg intravenously every 21 days until disease progression or prohibitive toxicity. Eleven patients (23.9%; two-sided 90% CI, 14% to 37%) survived progression free for at least 6 months, and five patients (10.9%; two-sided 90% CI, 4% to 22%) had partial responses. The median response duration was 6.21 months (range, 2.83 to 8.28 months). The median PFS and overall survival times were 3.40 months (95% CI, 2.53 to 4.53 months) and 7.29 months (95% CI, 6.11 to 10.41 months), respectively. This compared favorably with historical phase II GOG trials in this setting (Figure 2) and will be studied prospectively in the soon to be activated trial, protocol 0240 (Figure 3).

Hypoxia and angiogenesis appear to be pivotal to tumor progression and prognosis in cervical cancer. The GOG is investigating novel agents to combat these interrelated processes in both newly diagnosed and recurrent lesions. Only through translational research and clinical trial enrollment will the challenges of treating cervical cancer be overcome.

*Bradley J Monk, MD, is Associate Professor and Director of Research for the Gynecologic Oncology Department at Chao Family Comprehensive Cancer Center, University of California Irvine Medical Center. He is also Chair of the GOG Cervical Cancer Committee.*

## Carboplatin dose calculation and creatinine measurement standards

Paul Sabbatini MD, Franco Muggia, MD, and Michael Bookman, MD, were kind enough to provide this article for the Spring newsletter on behalf of the GOG Medical Oncology Committee.

### Background Information

A variety of approaches have been used historically to measure serum creatinine including alkaline picrate methods, enzymatic or partially enzymatic assays, and HPLC methods. The National Kidney Disease Education Program (NKDEP) Laboratory Working Group in collaboration with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the European Communities Confederations of Clinical Chemistry (EC4) recently reviewed the variability related to serum creatinine measurements and made recommendations to standardize and improve creatinine measurement. The key recommendation was that serum creatinine determination be done using an Isotope Dilution Mass Spectrometry Method (IDMS) using an IDMS traceable standard reagent.

It is important to note that the impetus for this change was *not* related to the evaluation of serum creatinine for the purpose of drug dosage calculation, but rather to standardize the measurement of creatinine and subsequent GFR calculation for the early detection of chronic kidney disease so that appropriate treatments can be implemented. The majority of commercial laboratories have already converted to this standard and many hospitals have done so or are in the process of changing.

The key points with regards to the newer IDMS traceable versus non-IDMS traceable creatinine values are as follows:

1. The serum creatinine normal reference range decreases when laboratories convert to IDMS determined creatinine values. There is an approximately systematic 12% reduction in creatinine values when determined by the IDMS standardized method. It is recommended by the NKDEP that IDMS standardized creatinine determination methods are reported to two decimal places for clarity regarding method used (0.92 mg/dl rather than 0.9 md/dl).
2. The IDMS method has only been evaluated with a Modification of Diet in Renal disease Formula (MDRD4) to calculate GFR. The IDMS creatinine has not been validated with the Jelliffe or Cockcroft-Gault (C-G) formulas for the calculation for creatinine clearance to be used in clinical trials involving drug dosing. Furthermore, the MDRD formula was historically used to assess patients for chronic kidney disease and there is little data regarding its use for the calculation of drug dosages particularly with anti-neoplastic agents.
3. Without adjusting for the IDMS creatinine, the calculations of the estimated creatinine clearance to define drug dosages will be affected by the change. The calculated creatinine clearance based on a reduced creatinine will be higher and subsequent calculated drug doses will be increased.

4. Therefore, a “back calculation” of IDMS to non-IDMS creatinine values is required if one is to input the value in the more commonly utilized Jelliffe or Cockcroft-Gault (C-G) formulas for creatinine clearance determination. Several formulas have been proposed for this conversion of IDMS to non-IDMS creatinine such as the following:

$$\text{Corrected (non-IDMS) creatinine} = (\text{IDMS creatinine} * 1.065) + 0.067$$

5. The correct creatinine value is then used in the Jelliffe (as in most GOG protocols) or Cockcroft Gault formulas as usual to calculate the creatinine clearance.
6. Once the creatinine clearance is correctly determined, it is used in the usual manner in the Calvert formula for dose calculation:  
**Dose (mg) = Target AUC X (GFR [ml/min] + 25 [ml/min])**

Therefore the only change required is to provide a correction to the creatinine value if it is determined by the IDMS standard method and you wish to input it into the Jelliffe or Cockcroft-Gault formulas.

*For ease of calculation, the GOG carboplatin dose calculation tool on line has been modified and now allows one to choose whether an IDMS derived or non-IDMS derived creatinine is used and all other calculations are performed appropriately to derive the carboplatin dose:*

[https://gogmember.gog.org/GOG/CarboPlatin/CarboPlatin\\_new.asp](https://gogmember.gog.org/GOG/CarboPlatin/CarboPlatin_new.asp)

### What have we learned in trying to address this issue?

The process of laboratories converting methods and reporting results is evolving and not always straightforward. As noted, it has been recommended by the NKDEP that IDMS standardized creatinine determination methods are reported to two decimal places for clarity regarding method used (0.92 mg/dl rather than 0.9 md/dl, for example). However, it has come to our attention that a minority of hospital laboratories are not following this convention. Some are using the IDMS method but are reporting results in the “X.X” format to one decimal point to “avoid confusion”. One hospital laboratory was found that reported the value in the “X.XX” format but was not utilizing IDMS standards. Another hospital laboratory was deriving the creatinine value using non-IDMS methods but manually converting it to an IDMS “equivalent” value perhaps to avoid needed upgrades.

It is reasonable to assume that commercial laboratories such as Quest Diagnostics (converted to IDMS in 2008) and LabCorp already use IDMS determinations and no further investigation is required. If they offer a calculated creatinine clearance (or GFR) on the report, however, it will be utilizing the MDRD4 formula as discussed which was designed to estimate renal function for assessing chronic kidney disease and not for the

*Creatinine continued on next page*

# New Horizons GYN Cancer Research Fund

The GOG would like to thank the following individuals and families for their generous contributions to the **New Horizons GYN Cancer Research Fund**:

Debbie Miller  
Joanne Rutgers, MD  
Rodney Zahner

## **In Memory of Carol Reese**

Rebecca Reese  
Steve Schneberger  
Brian and Annette O'Harra  
John Donbet

Jim Simon  
Carol L. Reese Memorial Fund  
Maureen Delaney  
Rosemarie Perillo  
Martha Hicks  
Patricia Usifer  
Terri Cron  
Sandy Weishaupt  
George Michael  
Sue Walker

## **In Memory of Connie Tayler**

Ms. Traci Tayler Kelly  
( Friends and family)

## **In Memory of Jan Kellner**

Kathleen Couling

## **In Honor of Janice Gause**

Adrienne & David Watford  
Bonnie Ackerman  
Caroline Crocker  
Ebbie & Bill Mitchell  
Marie Lambert  
Maureen Rush

Violet Long- Sunday School  
Kensington Elementary School,  
Koala Club Members

## **In Memory of Melissa Moore**

Nancy Johnson

*CPC continued from page 2*

Effect of Levonorgestrel on the Ovarian Epithelium in Women at High Risk for Ovarian Cancer" which is primarily a biomarkers study that will determine the impact of levonorgestrel on the relative frequency of apoptosis, proliferation, and TGF-beta expression in the ovarian epithelium and fallopian tubes from women with a high risk of ovarian cancer.

**GOG-0237** which was activated in February of 2009. The study is a comparative analysis of CA-IX, p16, proliferative markers and human papillomavirus in the diagnosis of significant cervical lesions in patients with a cytologic diagnosis of atypical glandular cells. This study will build on the results from GOG-0171.

Upcoming studies which we hope will be activated in the

next six months include two very exciting projects. One that will study the epidemiology of lymphedema and one that will look at how exercise and diet can effect the recurrence of ovarian cancer.

**GOG-0244** - Prospective evaluation of lower extremity lymphedema in women undergoing radical surgery for gynecologic malignancy.

**GOG-0225** - Can Diet and Physical Activity Modulate Ovarian Cancer Progression Free Survival?

At the semiannual GOG meetings the CPC is also hosting a CPC table where we provide information about all of our open and upcoming studies. I encourage you to stop by and see what we have to offer during the July 2009 meeting. If you have any questions about any of our protocols please contact Mary Clouser at [mclouser@u.arizona.edu](mailto:mclouser@u.arizona.edu).

*Creatinine continued from previous page*

purpose of drug dosing until more data is available.

### **How should you proceed?**

1. The best way to ascertain the method used is to ask your hospital laboratory whether a standard IDMS traceable creatinine determination method is being employed. Calculations of GFR for the purpose of carboplatin dosing should be based on using the appropriate formula (IDMS or non IDMS).
2. Commercial laboratories (Quest, LabCorp) utilize IDMS creatinine determinations.
3. The GOG online calculator should be used to verify dosing for each patient. It allows you to select which creatinine method is utilized, and it is recommended that a copy of the on-line calculation be retained in the research chart to provide documentation of how the calculation was performed in the event of any question during review or audit.
4. For new patients enrolling in a study utilizing carboplatin, the correct dose of carboplatin should be calculated using the correct formula based on the creatinine determination method used.

5. If a patient has already initiated therapy, and the incorrect formula was utilized for GFR estimation, it is recommended (but not required) that the GFR and carboplatin dose be recalculated utilizing the appropriate formula (IDMS or non-IDMS). In general, if a change is required, this will result in a small dose reduction.

### **For more information:**

Wade, WE and Spruill. New Serum Creatinine Assay Standardization: Implications for Drug Dosing. *Ann of Pharmacotherapy* 41: 475 – 480, 2007.

Spruill WJ, Wade WE, Cobb HH. Estimating Glomerular Filtration Rate with a Modification of Diet in Renal Disease Equation: Implications for Pharmacy. *Am J Health-Sys Pharm* 64(6): 652-660, 2007.

Myers GL and the National Kidney Disease Education Program Laboratory working Group. Recommendations for Improving Serum Creatinine Measurement: A Report from the laboratory working group of the national kidney disease education program. *Clin Chem* 52: 5-18, 2006.

[http://www.nkdep.nih.gov/labprofessionals/creatinine\\_standardization.htm](http://www.nkdep.nih.gov/labprofessionals/creatinine_standardization.htm)

# BALTIMORE 2009

*79th Annual Meeting*

## Gynecologic Oncology Group

Baltimore Marriott  
Waterfront Hotel  
*Baltimore, MD*

July 16-19, 2009  
*Symposium – July 16*

For more  
information, visit the  
GOG website at  
[www.gog.org](http://www.gog.org)



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