Addressing GOG’s concern with new NCI director

Editor’s Note: In light of recent policy events surrounding the possible merger of cooperative groups, the Gynecologic Oncology Group is publishing a recent letter written by GOG’s Group Chair, Dr. Philip J. DiSaia, to Dr. Harold-Varmus, Director, National Cancer Institute. Dr. DiSaia’s letter is taking the place of the normal “Chair’s Corner” article.

Harold Varmus, M.D.  
Director of NCI  
National Cancer Institute

Dear Dr. Varmus,

I am writing to you as the Chair of the Gynecologic Oncology Group: one of the ten Cooperative Groups supported by the National Cancer Institute. My comments are the collective opinion of the Group Leaders and the Board of Directors. Our concern revolves around the new policies being developed in response to the Institute of Medicine (IOM) report suggesting a merger of the ten Cooperative Groups into a smaller number of Groups. The Division of Cancer Treatment and Diagnosis has suggested that there be four Groups (three of which would be composed primarily of existing Medical Oncology Groups) and that the remaining Groups e.g. the Gynecologic Oncology Group (GOG), the National Surgical Adjuvant Breast and Bowel Project (NSABBP) and the American College of Radiology Imaging Network (ACRIN) be coalesced into a fourth group.

The GOG would like to thank its newsletter sponsors

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The GOG is the only Group studying malignancies of the female genital tract. The success of the GOG rests primarily on the enthusiasm of the gynecologic oncologist in the United States, most of whom accrue patients to the GOG studies. Attempts by other Groups to study gynecological malignancies have failed because they could not enlist the cooperation of our nation’s gynecologic oncologists. The merger of Groups as different as RTOG, NSABP and ACRIN will result in a loss of the “esprit de corps” among gynecologic oncologists and a loss of the accrual momentum we’ve established over the last forty years. We respectfully request that the Gynecologic Oncology Group be viewed in a light similar to the Children’s Oncology Group in that we are functioning with specific interests and in the area of specific diseases such as ovarian cancer and that the
Updated FAQ’s for dosing of Carboplatin

In early October 2010, NCI/CTEP issued an action letter to alert investigators of a modification in dosing of carboplatin in studies they sponsored. In response to the action letter GOG prepared an appendix for all trials that included carboplatin. The appendix was originally posted to the website in October 2010. It was subsequently updated in February 2011 in response to the questions that were raised following the original broadcast. The following FAQ are provided here for your reference:

Q: If a patient is currently being treated on a GOG protocol and is not experiencing problems, should the dose be changed?
A: If patient’s dose was calculated with a creatinine of less than 0.7 or she has a BMI of 25 or higher, she must have dose recalculated with the next treatment. This is to ensure patient safety.

Q: Should sites use the Carboplatin dosing appendix in a specific protocol or the updated appendix?
A: If a protocol was not amended yet to include the updated appendix the updated appendix should be used instead of the protocol appendix.

Q: Has the carboplatin calculator on the GOG website been updated?
A: Yes, the carboplatin calculator on the Website has been updated. The new online calculator is an important and useful tool to help eliminate dosing errors. Feedback from the Group has been extremely positive and we urge you to access the calculator on the Website under “Tools.”


Q: If patient’s BMI is 25 or higher requiring the need for the adjusted weight, and subsequently the patient loses weight which brings the BMI below 25, does site use the actual or adjusted weight?
A: If the weight changes by 10% or more, Carboplatin needs to be recalculated. If the 10% change puts patient’s BMI below 25, the site should use the actual weight.

The language in the updated appendix follows:

Carboplatin dose calculation instructions
1) The Cockcroft-Gault formula will be used in GOG trials (not the Jelliffe formula).
2) Conversion of IDMS creatinine levels to “non-IDMS” values will not be permitted.
3) The carboplatin calculation tool on the GOG website has been updated. A legacy carboplatin calculator (using the Jelliffe formula and IDMS to “non-IDMS” conversion) is also available, if needed for dose modifications (see below).

Dosing of Carboplatin
1) The carboplatin dose will be calculated to reach a target area under the curve (AUC) according to the Calvert formula using an estimated glomerular filtration rate (GFR) from the Cockcroft-Gault formula.
2) The initial dose of carboplatin must be calculated using GFR. In the absence of renal toxicity greater than or equal to CTCAE Grade 2 (serum creatinine >1.5 x ULN) or toxicity requiring dose modification, the dose of carboplatin will not need to be recalculated for subsequent cycles, but will be subject to dose modification for toxicity as noted in the protocol.
3) Carboplatin doses will be based on the subject’s weight at baseline and will remain the same throughout the study. However, the doses will be recalculated if the patient has a weight change of greater than or equal to 10% from baseline.
4) In patients with abnormally low serum creatinine (less than 0.7 mg/dl), the creatinine clearance should be estimated using a minimum value of 0.7 mg/dl. If a patient is currently being dosed using a creatinine value less than 0.7 mg/dl, adjust dose with next planned treatment.
5) For trials where patients enter and are treated within less than or equal to 12 weeks of surgery: If a more appropriate (higher) baseline creatinine value is available from the pre-operative period (within 4 weeks of surgery date), that value may also be used for the initial estimation of GFR.

Calvert formula
Carboplatin dose (mg) = target AUC x (GFR + 25)
(Note: the GFR used in the Calvert formula should not exceed 125 ml/min.)

Maximum carboplatin dose (mg) = target AUC (mg/ml x min) x 150 ml/min.

The maximum allowed doses of carboplatin are:
AUC 6 = 900 mg
AUC 5 = 750 mg
AUC 4 = 600 mg

For the purposes of this protocol, the GFR is considered to be equivalent to the estimated creatinine clearance. The estimated creatinine clearance (ml/min) is calculated by the

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In Memorium: Donald Gallup

GOG remembers friend and colleague, Dr. Donald Gallup

We are deeply saddened to report the death of longtime Gynecologic Oncology Group member and leader, Dr. Donald Gallup, on Saturday, January 8, 2011. Born in Youngstown, Ohio on June 20, 1936, Dr. Gallup attended medical school at Emory University. He then served an internship at Greenville General Hospital, Greenville, S.C., completing his residency in Obstetrics and Gynecology at the Naval Hospital in San Diego, Calif. Dr. Gallup completed his fellowship in Gynecologic Oncology at the University of Michigan Medical Center, Ann Harbor, Mich., with his mentor and colleague, Dr. George Morley.

Don was a good friend and respected colleague to many of us in the GOG. His accomplishments within the group and elsewhere were many and varied. He was a veteran of the United States Navy, retiring after more than 20 years of dedicated service at the rank of Captain. During that time, he was awarded medals for National Defense, Vietnam Service, Vietnam Campaign and Navy Meritorious Service. Dr. Gallup practiced at several institutions during his career, including his most recent position at Mercer University School of Medicine as Professor of Obstetrics and Gynecology and Chair of the Obstetrics and Gynecology Department. He also served as Director of Gynecologic Oncology and Program Director of the Residency Program of Obstetrics and Gynecology at Memorial Health University Medical Center.

Dr. Gallup was very involved in several national, state and institutional organizations, participating in a leadership capacity in many of them, most notably SGO and the GOG. We at GOG know Don best for his many years of service as inaugural Chairman and subsequently co-Chairman of the Quality of Life Committee. In that role, Don was a passionate advocate for the patient, and for the best quality science we could bring to the committee and the group. Over 15 years, he elevated the Quality of Life Committee from a start-up collection of interested colleagues to a committee respected by his peers for producing the very best in quality of life measurement science.

Along with his family, friends, patients and colleagues, we will miss Don. We’ll miss more than his dedication and loyal service; we’ll miss his decency, his integrity, his friendship and his raucous laughter.

CHAIR from Page 1

GOG be permitted to continue as an independent Group. In our reading of the IOM report, there is no specific number of Groups specified and there is no clear mandate to have four Groups versus five.

We are very concerned that the wonderful progress we have achieved in the last forty years in the field of gynecological cancers will not continue as a separate entity. We are particularly concerned about our studies in the area of ovarian cancer where the gynecologic oncologist is in a unique position for obtaining tissue at surgery and following through with post operative treatments as designed in group protocols. Cooperative Groups composed of mostly Medical Oncologists will not have access to this tissue and the patients needed to do the research.

Should you wish to discuss the opinion of our Group Leaders further, please contact me pjdisaia@uci.edu or 714-456-5220 and I will arrange to come to Washington or participate in a conference call as you wish. We are very concerned that a merger with other unrelated groups will cause our Group to dissipate and the excellent science in our subspecialty will also be lost.

Sincerely,

Philip J. DiSaia, MD, Chair
Gynecologic Oncology Group
FDA Final Rule: IND Safety Reporting Requirements

The Food and Drug Administration is issuing final regulations addressing the safety reporting requirements for investigational new drug applications (INDs) found in 21 CFR part 312 and for bioavailability and bioequivalence studies found in 21 CFR part 320.

This final rule is expected to improve the quality of safety reports submitted to FDA, thereby enhancing the safety of patients in clinical trials. The final rule lays out clear, internationally harmonized definitions and standards so that critical safety information about investigational new drugs will be accurately and rapidly reported to the agency, minimizing uninformative reports and enhancing reporting of meaningful, interpretable information.

This regulation requires changes to expedited (immediate) serious adverse event reporting requirements for investigators to IND sponsors such as NCI/CTEP, GOG and industry.

NCI/CTEP plans to implement these new requirements and revised reporting tables prospectively for all new studies/protocols and those that are “in review” as of March 28, 2011.

Additional information regarding the Final Rule can be found on the FDA website at:


Please refer to the weekly electronic mailing for additional information regarding changes to SAE reporting guidelines as it becomes available.

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method of Cockcroft-Gault using the following formula:

\[
\text{Creatinine Clearance (mL/min)} = \frac{[140 - \text{Age (years)}] \times \text{Weight (kg)} \times 0.85}{72 \times \text{serum creatinine (mg/dl)}}
\]

Notes:
1) Weight in kilograms (kg):
   a. Body Mass Index (BMI) should be calculated for each patient. A BMI calculator is available at the following link: http://www.nhlbisupport.com/bmi/
   b. Actual weight should be used for estimation of GFR for patients with BMI of less than 25.
   c. Adjusted weight should be used for estimation of GFR for patients with BMI of greater than or equal to 25.
   d. Adjusted weight calculation:
      Ideal weight (kg) = (((Height (cm)/2.54) – 60) x 2.3) + 45.5
      Adjusted weight (kg) = ((Actual weight – Ideal weight) x 0.40) + Ideal weight
   e. If a patient with BMI of greater than or equal to 25 is currently being dosed using actual weight, adjust dose with next planned treatment.

2) The Cockcroft-Gault formula above is specifically for women (it includes the 0.85 factor).

At the time of a dose modification for toxicity:
1) If the creatinine at the time of a dose modification is lower than the creatinine used to calculate the previous dose, use the previous (higher) creatinine; if the creatinine at the time of a dose modification is higher than the creatinine used to calculate the previous dose, use the current (higher) creatinine. This will ensure that the patient is actually receiving a dose reduction.

2) If the dose of carboplatin (mg) at the time of dose modification, is higher than the previous dose due to the use of the Cockcroft-Gault formula [when the previous dose was calculated using the Jelliffe formula and IDMS to “non-IDMS” conversion (if applicable)], use the same method that was used to calculate the previous dose [Jelliffe formula and IDMS to “non-IDMS” conversion (if applicable)], to calculate the dose of carboplatin (mg) at the time of dose reduction. A legacy carboplatin calculator is available on the GOG website for this purpose. This will ensure that the patient is actually receiving a dose reduction.
AGO-OVAR 12/LUME-Ovar 1 is a multicentre, randomized, double-blind Phase III trial to investigate the efficacy and safety of BIF 1120® in combination with carboplatin and paclitaxel compared with placebo plus carboplatin and paclitaxel in patients with advanced ovarian cancer.

AGO-OVAR 12 is a joint collaboration between several participating Academic Study Groups led by the Arbeitsgemeinschaft Gynäkologische Onkologie, Studiengruppe Ovarialkarzinom (AGO-OVAR). The Coordinating Investigator is Prof. Dr. Andrea du Bois (Meibaden, Germany).

**OBJECTIVE**

To investigate the efficacy and safety of BIF 1120® plus chemotherapy as compared with placebo plus chemotherapy in patients with advanced ovarian cancer.

**SELECTED ELIGIBILITY CRITERIA**

1. First diagnosis of histologically confirmed epithelial ovarian, fallopian tube or primary peritoneal cancer (U-1300)
2. FIGO stages IIB-IV
3. Females aged 218 years
4. Life expectancy of at least 6 months
5. Eastern Cooperative Oncology Group performance status 0, 1 or 2
6. Prior surgery
7. Planned application of first dose of chemotherapy after wound healing, but no later than 10 weeks after surgery

**STRATIFICATION**

- No macroscopic residual tumour (<1 cm) vs. macroscopic residual tumour (>1 cm) post surgery
- FIGO stage IIB-III vs. IVA
- Carboplatin dose (AUC 5 vs. AUC 6 mg/mL x min)

**ENDPOINTS**

Primary endpoint: PFS (investigator's assessment)

Secondary endpoints (efficacy): PFS (radiological assessment); overall survival; time to tumour marker progression (CA-125); objective response

Other important endpoints: incidence and intensity of adverse events; changes in safety laboratory parameters; patient-reported outcome; health-related quality of life

For more information about AGO-OVAR 12/LUME-Ovar 1, including eligibility criteria, please visit: www.clinicaltrials.gov

*BIF 1120® is an investigational agent and is not approved for the treatment of ovarian cancer. Its efficacy and safety have not been established.
San Diego meeting highlighted by satellite symposium

Matthew H. Weeks, MA
Institute for Medical Education & Research, Inc.

At the 2011 GOG Semi-Annual Meeting in San Diego, California, IMER conducted a CME satellite symposium titled, Current and Emerging Research in Ovarian Cancer: Integrating Results Into Future Research and Practice. This activity was chaired by Bradley J. Monk, MD, FACOG, FACS, from the Creighton University School of Medicine at St. Joseph’s Hospital and Medical Center. Other faculty members included Robert L. Coleman, MD, FACOG, FACS, from The University of Texas M. D. Anderson Cancer Center, Angeles A. Secord, MD, from Duke University School of Medicine, and Thomas J. Herzog, MD, from Columbia University Medical Center. The activity, which featured interactive discussions on the GOG 218 and ICON7 trials, was well received with a diversified audience (See Figure 1).IMER is pleased to make the slide deck from the symposium available for download. Please visit www.IMERonline.com/GOG640 to access the slide deck and other resources in gynecologic malignancies.
New Horizons GYN Cancer Research Fund

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

- Jack and Jan Kellner Memorial Fund
  - Philip J. DiSaia, MD
  - Joel Sorosky, MD

- In Memory of Kay Kiesner
  - Jay and Mary Beth Coonan

- In Memory of Barbara LoMenzo
  - William C. McGuire

- In Memory of Janice Elaine Lamber Gause
  - The Pluff Mudd Supper Club and Committee

- In Memory of Carol Reese
  - Emily and Paul Porensky

- In Honor of The Gilday Foundation
  - Joseph Campbell

- In Honor of Dr. Philip J. DiSaia, MD
  - Larry Copeland, MD

- General Donation
  - Bucks County Planning Commission

San Diego 2011

Young Investigators awarded at 2011 Semi-Annual Meeting in San Diego

The Gynecologic Oncology Group announced its two winners of the 2011 Young Investigators Award during the January 2011 Semi-Annual Meeting in San Diego, Calif. Dr. Philip DiSaia congratulated Kristy K. Ward, MD and Whitney Graybill, MD, MS (both pictured with Dr. DiSaia, above, left to right) during the opening ceremonies on January 17, 2011.

“Chasing the Cure”
5K Run/5K Pump and Run/1 Mile Fun Run

September 17, 2011
Doyle Community Center, Sturgis, MI

Race starts at 9 a.m.

For more information and registration, visit chasingthecure.net

Proceeds benefit the New Horizons GYN Cancer Research Fund.

GOG awards bracelets to participants of 2010 Ovarian Cancer Awareness Run/Walk

GOG Patient Advocate Debbie Miller, center, pictured with cancer survivors and “Steppin’ Out” charm recipients (left to right): Wendy Barkett, Dianne Blankenstein, Elaine Hilderbrand and Linda Bezner

The Gynecologic Oncology Group recently had the opportunity to show its own support for an event that helped to raise Ovarian Cancer awareness. The GOG donated four of its own “Steppin’ Out” charms to participants of the National Ovarian Cancer Coalition, Dallas/Ft. Worth Chapter’s 10th Anniversary Run/Walk to Break the Silence on Ovarian Cancer. The event benefits the National Ovarian Cancer Coalition education and benefit programs nationwide. This particular event took place on September 25, 2010.

The GOG, with specific help from Patient Advocate Debbie Miller, was proud to award the four charms to event participants and cancer survivors: Wendy Barkett, Dianne Blankenstein, Elaine Hilderbrand and Linda Bezner.

“These ladies were so excited about receiving the charms,” said Miller. “Thanks GOG for supporting the event.”
Friday, July 15, 2011

A 90-minute complimentary CME-certified Luncheon Satellite Symposium to be held in conjunction with the GOG’s Semi-Annual Meeting, 12:00 – 1:30 pm, immediately following the GOG General Session.

Please check www.GOG.org in the coming weeks for more information and registration.

This activity is not part of the Official GOG Semi-Annual Meeting.