8. **Ship the Plasma to the GOG Tissue Bank**. Ship the frozen plasma to the GOG Tissue Bank as described in Section IX.

# VII. Preparing Whole Blood for GOG-0213

## A. Requirement

An amendment has been approved to collect a whole blood specimen from new patients on GOG-0213 as well as women who have already been enrolled on GOG-0213 regardless of randomization and treatment. Patients already enrolled on GOG-0213 will need to be re-consented. Blood must only be collected from women who give permission for their blood to be submitted and used for this research study.

If the patient gives permission, 10 ml blood will need to be drawn into a purple-top Vacutainer® tubes with the anti-coagulant EDTA at one time point. The whole blood will need to be collected as described in Section VII-D and shipped to the GOG Tissue Bank as described in Section IX.

Patients may participate in this treatment protocol even if they don't give permission for their blood to be used for research or if the submitting institution is a Non-US site and submission of blood is logistically infeasible. **If blood cannot be submitted for GOG-0213, please indicate the reason in item 5 on the SP Form, such as patient refused, tried but not able to draw blood, or Non-US site logistically infeasible.**

## B. Time Point

Whole blood will need to be collected prior to or after starting treatment on this phase III trial or at any time during follow up. Although the collection time point is flexible, we encourage sites to try and collect the blood as soon as possible to remove this requirement from your patient's form schedule. If you need to get an extension for submitting the whole blood specimen, please contact a Translational Research Scientist at 716-845-5702.

## C. Purpose

The translational research objective of this protocol is to bank DNA from whole blood for research and evaluate the association between single nucleotide polymorphisms (SNPs) and measures of clinical outcome including overall survival, progression-free survival and adverse events.

## D. Instructions for Preparing Whole Blood

1. **Label the Purple-Top Vacutainer® Tube.** Label the 10-ml Purple-Top Vacutainer® tube with EDTA for this protocol with the GOG protocol number (GOG-0213), GOG Bank ID Number (####-##-G###), the Specimen Code (WB01 for whole blood), and the collection date (mm/dd/yyyy).
2. **Draw Blood**. Draw 10 ml of blood into the Purple-Top Vacutainer® tube with EDTA until the vacuum is exhausted.
   * **For GOG-0213, do not collect blood the day before a holiday** as staff will not be available at the Bank to receive or process the blood.
3. **Mix Blood with the EDTA**. Mix the blood with the anticoagulant (EDTA) by gently inverting the tube 5-10 times.
4. **Store the Blood at Room Temperature.** Store the blood at room temperature until the specimen can be shipped to the GOG Tissue Bank.
5. **Complete the Form SP**. Complete the GOG Specimen Form (Form SP) online using SEDES as specified in Section VIII. Submit a copy of Form SP with the specimen when it is shipped to the GOG Tissue Bank, and retain a copy in your files.
   * ***Please remember to indicate the Specimen Type is "Whole blood" in item 8, the Items Shipped is "Tube/Vial" in item 9, the quantity shipped is "1" in Item 10, the "Storage Type" is "Room Temperature", the "Type of blood collection tube" is "EDTA", and "Platelet count required" is "No".***

6. **Ship the Blood.** Ship the blood for a given GOG-0213 patient the day the blood is drawn to the GOG Tissue Bank as described in Section IX.
   * ***Please note that the blood specimen must be shipped the day the blood is drawn for delivery the next morning as this specimen must undergo immediate processing upon receipt to extract high quality DNA.***

# VIII. Submitting Form SP for GOG-0213

## A. Form SP Requirements for Each GOG-0213 Patient

One Form SP must be completed and electronically submitted to the GOG Statistical and Data Center (SDC) ***for each specimen*** required for the protocol regardless of the specimen submission status using the SDC Electronic Data Entry System (SEDES). Specific instructions for completing Form SP are available via SEDES by scrolling down to the SP Forms for GOG-0213.

## B. Instructions for Submitting Form SP Online

Form SP must be submitted to the GOG SDC online using SEDES which is available on the GOG Web Menu under *Registration/Data Entry*. To access Form SP for online submission, log onto the GOG Web Menu and use SEDES to electronically enter Form SP data. Any questions about access or problems should be directed to the User Support Department at the GOG Statistical and Data Center at support@gogstats.org or by phoning 716-845-7767. Retain a printout of the completed form for your records and include a copy of the completed form when the specimen is shipped to the GOG Tissue Bank. It is not necessary to send a completed Form SP to the GOG Tissue Bank when the specimens are not submitted.

# IX. Shipping Specimens for GOG-0213

**A. All** specimens will be shipped to the GOG Tissue Bank at the following address:

**GOG Tissue Bank – Protocol GOG-0213**
**Nationwide Children's Hospital**
**700 Children's Drive, WA1340**
**Columbus, OH 43205**
**Phone: (614) 722-2865**
**Fax: (614) 722-2897**
**E-mail:** gogbank@nationwidechildrens.org

## B. Archival Primary or Metastatic Tumor - Block or Sections (Mandatory Specimen)

An archival primary or metastatic tumor specimen (FT01) either a block or unstained sections must be shipped to the GOG Tissue Bank within 8 weeks of study enrollment **using your own shipping container** at the address provided using the US Postal Mail at your own expense. If shipping slides, please pack slides in a plastic slide cassette labeled with the GOG protocol code, Bank ID, specimen code and collection date. Tape the slide cassette shut and wrap in bubble wrap in bubble wrap or another type of padded material before shipment. This specimen may also be included in the dual chamber Specimen Kit for GOG-0213 if it was available when the recurrent tumor, pre-op serum and/or normal tissue are ready to be shipped to the GOG Tissue Bank.

## C. Fixed Recurrent Tumor and Frozen Recurrent (Mandatory Specimens) as well as the Pre-Op Serum, Pre-Op Plasma, Formalin-Fixed Normal Tissue and Frozen Normal Tissue (Optional but High Priority Specimens)

To satisfy the specimen requirement(s) for patients who are enrolled at GOG or CTSU Institutions, are randomized to have secondary cytoreductive surgery and give permission for their serum and/or tissue to be used for this research study, the mandatory fixed recurrent tumor (FR01) and frozen recurrent tumor (RR01) specimens and any of the optional specimens (pre-op serum – SB01, pre-op plasma – PB01, fixed normal tissue – FN01 and frozen normal tissue – RN01) will need to be shipped to the GOG Tissue Bank **using the dual-chamber Specimen Kit** within 3 days of surgery when possible. If this is not possible, please ship them to the GOG Tissue Bank at your earliest convenience. The SP Forms for these specimens, however, must be received at the GOG Statistical and Data Center within 7 days of surgery.

**Instructions for Shipping Fixed and Frozen Specimens**

1. **Bag the Fixed Tissue Specimens.** Transfer the fixed recurrent tumor and/or normal tissue in a jar(s) of formalin or embedded in a paraffin block(s) into a plastic biohazard secondary envelope containing absorbent material, and then put the secondary envelope into the Tyvek envelope. Expel as much air as possible before sealing both envelopes.
2. **Pack the Fixed Tissue Specimens into the Kit.** Place the Tyvek envelope containing the fixed tissue specimens into one chamber of the Dual-Chamber Specimen Kit.
3. **Pre-Fill Kit with Dry Ice.** Layer dry ice into the other chamber of the Dual-Chamber Specimen Kit until it is about 1/3 full.
4. **Transfer Frozen Specimens into Individual Zip-Lock Bags.** Transfer the frozen recurrent tumor, frozen normal tissue, cryotubes of frozen serum and/or cryotubes of frozen plasma from each patient into individual zip-lock bags. Expel as much air as possible before sealing the bag.
5. **Transfer the Bags of Frozen Specimens into a Secondary Envelope and a Tyvek Envelope.** Transfer the zip-lock bags with the frozen recurrent tumor tissue, frozen normal tissue, the cryotubes of frozen serum and/or the cryotubes of frozen plasma into a plastic biohazard secondary envelope containing absorbent material, and then put the secondary envelope into the Tyvek envelope. Expel as much air as possible before sealing both envelopes.
6. **Pack Specimens and Dry Ice into the Specimen Kit .** Place the Tyvek envelope containing the frozen specimens into the chamber and then fill the kit to the top with dry ice.
7. **Insert SP Forms.** Insert a copy of the SP Forms for each specimen packed in this Specimen Kit in the space between internal chambers and the outside plastic holder.
8. **Seal Kit Securely.** Place the styrofoam cover on top of the Kit and then seal the kit securely with filament or other durable sealing tape.
9. **Print and Attach Shipping Label**. Access the GOG Tissue Bank's Kit Management application via the GOG Web Menu to obtain a shipping label. Once in the application select "Shipping Label" from the tool bar at the top of the screen in order to print a Federal Express shipping label.
10. **Complete and Attach Other Labels**. After completing the Dry Ice Label (UN1845), attach the Dry Ice Label and an Exempt Human Specimen Sticker to the side of the box.
11. **Arrange for Pick-Up**. Make arrangements for Federal Express pick-up through your usual institutional procedure or by calling 1-800-238-5355.
12. **Ship Specimens.** Ship the fixed and frozen specimens with the accompanying SP Forms to the GOG Tissue Ban k via Federal Express Priority Overnight delivery Please ship specimens Monday through Thursday for a Tuesday through Friday delivery.

## D. Submission of Whole Blood for GOG-0213.

A whole blood specimen will be required for all patients who give permission for their blood to be submitted and used for this research study.

Although the GOG Tissue Bank will not provide a specimen kit for shipping this whole blood specimens to the GOG Tissue Bank for GOG-0213, your institution will still be required to comply with International Air Transportation Association (IATA) standards (www.iata.org).

To ship whole blood specimens to the GOG Tissue Bank at ambient temperature you will need the following: (1) sturdy shipping container (e.g., a FedEx Box or another type of cardboard or Styrofoam

box), (2) biohazard bag with absorbent material, (3) puncture and pressure resistant envelope (e.g. Tyvek envelope), (4) Exempt Human Specimen Sticker, and (5) blank *FedEx Express US Airbill.*

If you do not have these materials available at your Institution, you may order them from any supplier.

Biohazard bag and absorbent material can be ordered from Saf-T-Pak (Phone: 800-814-7484; Website: www.saftpak.com).

- STP-710 Disposable 2-Part Secondary Pressure Vessel, Medium (i.e., secondary shipping envelope)
- STP-151 100 mL Absorbent Strip – 6 inches (i.e., absorbent material)

Cardboard FedEx shipping boxes are available from FedEx at no charge. If you do not have a FedEx pick-up and supply center at your Institution, you can request that your Driver bring extra boxes to you at your next pick-up. FedEx Customer Service can be reached at 800-Go-FedEx (800-463-3339).

If your Institution has a small number of patients on GOG trials or has limited funding to purchase supplies, please consider "cost sharing" with other GOG institutions or your parent institution.

**Instructions for Shipping Whole Blood Specimens For DNA Extraction Using Your Own Shipping Container**

***Special reminder***: The whole blood specimens for this protocol must be shipped to the GOG Tissue Bank at ambient (room) temperature the day the blood is drawn. These blood specimens must be drawn in a 10-ml purple-top (EDTA) tube and can be shipped on a Monday through Friday schedule for Tuesday through Saturday morning delivery. Bank staff will be available for immediate processing of the blood specimens upon receipt. Bank staff do not work holidays and will not be available to process the blood so d**o not collect blood for GOG-0213 the day before a holiday.** Please make other arrangements to collect this blood specimen on a different day. **Please note that you can place up to 4 different blood specimens in one biohazard bag.**

1. **Place the Whole Blood Tube(s) into a Biohazard Bag with Absorbent Material.** Place the whole blood specimen labeled with the protocol code, Bank ID, specimen code (WB01) and collection data into a biohazard bag with an absorbent strip. Expel as much air as possible before sealing the bag.
2. **Place the Blood Tube(s) into a Tyvek Envelope.** Next place the blood wrapped in padding into a Tyvek envelope. Expel as much air as possible before sealing the envelope.
3. **Place the Tyvek Envelope into a Sturdy Cardboard Box and include Bubble Wrap or Other Padding as Needed.** Place the Tyvek envelope containing up to 4 whole blood specimens into a sturdy cardboard box like the smallest cardboard FedEx box. If you are using a larger cardboard box, you can batch ship blood in more than one Tyvek envelope each containing up to 4 tubes of blood. Include bubble wrap or other padding as needed to secure the Tyvek envelope(s) inside the box.
4. **Place the SP Form(s) into the Cardboard Box.** Insert a print out of the SP Form(s) for the whole blood specimen(s) into the cardboard box.
5. **Tape the Cardboard Box.** Seal the cardboard box with filament or other durable sealing tape.
6. **Print and Attach a Shipping Label.** Access the GOG Tissue Bank's Kit Management application via the GOG Web Menu to obtain a shipping label. Once in the application select "Shipping Label" from the tool bar at the top of the screen in order to print a Federal Express shipping label. If blood is collected on a Friday, please select "*Saturday Delivery*". Saturday delivery is **only available** for the shipment of whole blood.
7. **Complete and Attach Other Labels.** Attach the Exempt Human Specimen Sticker to the side of the cardboard box.
8. **Arrange for Federal Express Pick-Up.** Make arrangements for Federal Express pick-up through your usual institution procedure or by calling 1-800-238-5355.

9. **Ship the Specimens to the GOG Tissue Bank.** Ship the whole blood specimen(s) and the SP Form(s) at ambient temperature to the GOG Tissue Bank at the address provided above on a Monday through Friday schedule for a Tuesday through Saturday morning delivery.

# X. Banking Specimens for GOG-0213

The GOG Tissue Bank staff will be responsible for all of the general activities associated with receiving, banking and distributing the clinical specimens submitted for GOG-0213. The Bank staff will also be responsible for preparing and distributing Dual-Chamber Specimen Kits with the materials specified in Section III for this protocol. The cost of shipping the GOG-0213 specimens from the GOG participating institutions to the GOG Tissue Bank will be billed to the GOG Tissue Bank Federal Express account.

Upon receipt of any shipments containing specimens for GOG-0213, the GOG Tissue Bank staff will immediately assess the type, quantity, and condition of the specimens received; complete the appropriate fields in the GOG Specimen Form; enter the specimens into their database system; and store the specimens under the appropriate conditions. The GOG Tissue Bank staff will complete the bottom part of Form SP for each specimen and submit the data to the GOG Statistical and Data Center electronically within 3 business days of receiving any clinical specimens for this protocol. A copy of the completed Form SP for each specimen will be retained in the files kept at the GOG Tissue Bank. In addition, the GOG Tissue Bank will work with the GOG Statistical and Data Center to reconcile specimen identifiers, information, condition, and quality as needed.

## A. Archival Formalin-Fixed and Paraffin-Embedded Tumor and Normal Tissue

Archival or formalin-fixed tissue will be received as a paraffin block, sections (sixteen unstained sections, 5 micrometer in thickness, on charged slides suitable for standard immunohistochemistry assays) or in a formalin-jar. Staff at the GOG Tissue Bank will make sure that each block, slide or formalin-jar is labeled with the GOG protocol number (GOG-0213), GOG Bank ID, the appropriate specimen code and the collection date. FT01 will be used for archival primary or metastatic tumor. If both are submitted, ideally FT01 will be used for archival primary tumor and FT02 will be used for archival metastatic tumor. If this is not the case, the staff at the GOG Tissue Bank should not relabel these specimens. Formalin-fixed recurrent tumor should be labeled with the specimen code FR01 whereas formalin-fixed normal tissue should be labeled with the specimen code FN01. When research specimens undergo pathology review, if the type of tissue in the research specimen does not match up with the electronic data in item 22 on the SP Form (type of tissue), staff at the GOG Tissue Bank will need to inform the GOG Statistical and Data Center and the GOG Institution so that item 22 on Form SP can be amended.

1. **Block**. If a paraffin block is received, each block will be stored under vacuum and protected from light until sections need to be prepared and/or blocks need to be cored to prepare tissue microarrays (TMAs) for this protocol.

   a. **Unstained Sections**.

      Just before distribution of these specimens for laboratory testing, sections will be prepared as needed based on the type of testing to be performed. Individual slides will be labeled with the identifiers indicated above. The slides will then distributed wax-dipped, stored under vacuum, and protected from light.

   b. **Tissue Microarrays (TMAs)**.
      The GOG Tissue Bank will collaborate with the GOG Statistical and Data Center and the GOG Tissue Utilization Subcommittee to design and create a series of TMAs for GOG-0213 to study markers of recurrence, survival and treatment response or resistance. The specific types of the TMAs that can be created will depend on the paraffin block submissions for this protocol and the clinical outcomes observed for these cases. For example, one TMA could contain matched cores

of tumor collected prior to initiating first line and second-line therapy with adjacent normal tissue from secondary cytoreductive surgery whereas another TMA could represent tumor cores from patients who experienced short survival, intermediate survival or long survival or include tumor cores from patients treated on a specific treatment arm who experienced short, intermediate or long progression-free survival. Ideally, each TMA will contain 250 cores with 200 individual cases and 50 controls. Since three to four cores from the same paraffin block are needed to reflect staining in a conventional tissue section, each of GOG-0213 TMAs will be generated in quadruplicate. Each quadruplicate TMA block will contain 200 independent cases with the same 50 controls. This will allow one set to be used for screening or exploratory analyses and the other for validation. The controls will include: 15 human cell lines with known molecular profiles, 20 gynecologic tissues [normal and cancer], and 15 non-gynecologic tissue [normal and cancer]. Incorporation of the same controls on each of these TMAs will allow investigators to evaluate the performance of the individual arrays and allow inferences to be drawn across arrays when certain criteria are satisfied. The Bank will position the cores in fixed positions in the quadruplicate blocks. Each core will be 1 mm in diameter and 2 mm in depth whenever possible. In cases where lesion size is a limitation, 0.8 mm x 2 mm cores will be obtained. Core loss during sectioning will increase with the number of sections into the block and statistical sections will build in an average estimated loss of 15%. GOG pathologists will identify the highest quality cases for inclusion on the TMA, select the exact sites within a block to be cored for the TMA, and evaluate the quality of the TMA sections generated including a light microscopic examination of core integrity and loss as well as neoplastic cellularity. Immunohistochemical staining for markers that are sensitive to fixation conditions and oxidation including p27 and androgen receptor may be used to identify tissues suitable for coring. Each TMA section will be wax dipped, vacuum sealed and protected from light to protect the antigenicity of the tissue prior to distribution for laboratory testing.

2. **Unstained Sections**. When tissue specimens are received as unstained sections, the slides will be wax-dipped, stored under vacuum, and protected from light.

3. **Pieces of Tissue in a Formalin-Jar**. When tissue specimens are received in a formalin-jar, the tissue will undergo standard histologic processing and be embedded in a paraffin block. The blocks will be stored under vacuum, and protected from light until sections need to be prepared and/or blocks need to be cored to prepare tissue microarrays (TMAs) for this protocol.

**B. Frozen Recurrent Tumor and Normal Tissue Specimens**

Frozen recurrent tumor and normal tissue will be received snap frozen or OCT-embedded and frozen. Staff at the GOG Tissue Bank will make sure the tumor specimen (actually the zip-lock bag and/or the OCT mold) is labeled with the GOG protocol number (GOG-0213), GOG Bank ID, the appropriate specimen code (RR01 for recurrent tumor and RN01 for normal tissue) and the collection date. The frozen tissue specimen will be stored at the Bank in an ultra-cold freezer (≤ -70°C) or in a liquid nitrogen storage tank.

**C. Pre-Op Serum**

Frozen pre-op serum will be received as aliquots in up to 10 screw-cap cryogenic vials. Staff at the GOG Tissue Bank will make sure that each aliquot of pre-op serum is labeled with the GOG protocol number (GOG-0213), GOG Bank ID, the appropriate specimen code (SB01) and the collection date. These aliquots will be stored at the Bank in an ultra-cold freezer (≤ -70°C) or in a liquid nitrogen storage tank. In order for serum to be considered as satisfactory for GOG-0213, the processing time in Item 11 on Form SP should be "< 4 hours", the type of storage condition in Item 12 on Form SP should be "Ultracold freezer/liquidN2/dry ice", the type of type of blood collection in Item 16 on the SP Form should be "Red top", and the serum should arrive at the Bank frozen solid in contact with visible dry ice.

**D. Pre-Op Plasma**

Frozen pre-op plasma will be received as aliquots in up to 10 screw-cap cryogenic vials. Staff at the GOG Tissue Bank will make sure that each aliquot of pre-op plasma is labeled with the GOG protocol number

(GOG-0213), GOG Bank ID, the appropriate specimen code (PB01) and the collection date. These aliquots will be stored at the Bank in an ultra-cold freezer (≤ -70°C) or in a liquid nitrogen storage tank. In order for plasma to be considered as satisfactory for GOG-0213, the processing time in Item 11 on Form SP should be "< 4 hours", the type of storage condition in Item 12 on Form SP should be "Ultracold freezer/liquidN2/dry ice", the type of type of blood collection in Item 16 on the SP Form should be "EDTA", and the plasma should arrive at the Bank frozen solid in contact with visible dry ice.

**E. Whole Blood**

Each whole blood specimen will need to be processed immediately upon receipt to extract DNA, assess the DNA concentration and quality, and then to store the DNA in an ultra-cold freezer in aliquots labeled with the GOG protocol code, Bank ID, specimen code (WB01-DNA) and collection date. Ideally the blood will be received in a liquid state in a purple-top Vacutainer® tube with EDTA. Staff at the GOG Tissue Bank will need to document the date of DNA extraction using the format mm/dd/yyyy, DNA concentration in [brackets] and 260/280 ratio in (parenthesis) in item 30 on Form SP and to note comments regarding specimen condition in item 31 on Form SP.

# XI. Distributing Specimens for Laboratory Testing for GOG-0213

Chairs of the GOG Committee for Experimental Medicine and the GOG Tissue Utilization Subcommittee will coordinate to make decisions regarding when specimens will be distributed to approved-investigators for approved laboratory testing. The GOG Statistical and Data Center and the GOG Tissue Bank will work together to coordinate the physical distribution of the specific specimens for select patients to the approved investigators for laboratory testing. Specimen selection will be based on information regarding specimen procurement and condition as well as patient eligibility, evaluation criteria, statistical considerations, and relevant clinical information.

For each shipment, the GOG Tissue Bank staff will need to e-mail the investigator and the GOG Statistical and Data Center an electronic file that includes an inventory of all specimens included in the shipment with the specimen specific identifiers as well as quantity and condition of the specimens being shipped. The GOG Statistical and Data Center will email the investigator an electronic file containing the specimen identifiers with relevant information regarding specimen condition, suitability for testing, eligibility/evaluability for a given component of the research study, and fields for the laboratory data. The investigator will need to use the specimen identifiers in the electronic file from the GOG Statistical and Data Center to avoid having to enter these identifiers thus reducing redundant data entry and minimizing the chance for errors when connecting the laboratory testing data to the clinical information for the GOG participating institutions.

The investigators performing the laboratory testing on any GOG-0213 specimens will not be given access to any personal identifiers. The investigators will be responsible for the direct supervision and oversight of the laboratory testing performed on these specimens. The individuals at the respective laboratories will be responsible for keeping accurate records of all laboratory testing performed on the GOG-0213 specimens, ensuring that the laboratory testing results are linked to the appropriate specimen-specific identifiers and transferring relevant laboratory data to the GOG Statistical and Data Center for analysis. The study chair will coordinate with the study co-chairs, scientific collaborators and the GOG Statistical and Data Center to analyze, report, and publish the study results.

**A. Archival and Formalin-Fixed Tissue Specimens (Primary, Metastatic and/or Recurrent Tumor as well as Adjacent Normal Tissue)**

When appropriate, the GOG Tissue Bank staff will be responsible for shipping a specified number of unstained sections from conventional paraffin blocks and/or the GOG-0213 TMAs to Dr. Michael Birrer at MGH Cancer Center and/or a CEM-approved investigator for biomarker, proteomic and genomic analyses. Laser-capture microdissection will be performed as need to examine cell type-specific expression profiles. The exact choice of the biomarkers and profiles to be evaluated and the assays to be performed in this specimen will be reevaluated based on evolving data in the field.

**B. Frozen Recurrent Tumor and Normal Tissue**

When appropriate, the GOG Tissue Bank staff will be responsible for shipping a specific quantity of frozen tumor tissue, frozen sections and/or scrolls from select GOG-0213 patients to Dr. Michael Birrer at MGH Cancer Center and/or a CEM-approved investigator for biomarker, proteomic and genomic analyses. Laser-capture microdissection will be performed as need to examine cell type-specific expression profiles. The exact choice of the biomarkers and profiles to be evaluated and the assays to be performed in these specimens will be reevaluated based on evolving data in the field.

**C. Pre-Op Serum and Pre-Op Plasma**

When appropriate, the GOG Tissue Bank staff will be responsible for shipping an aliquot of satisfactory pre-op serum and pre-op plasma from select GOG-0213 patients to Dr. Michael Birrer at MGH Cancer Center and/or a CEM-approved investigator for biomarker and proteomic analyses. The exact choice of the biomarkers and proteomic profiles to be evaluated and the assays to be performed in these specimens will be reevaluated based on evolving data in the field.

D. **DNA from Whole Blood**

When appropriate, the GOG Tissue Bank staff will be responsible for shipping an appropriate quantity of DNA with corresponding Q/C data to Dr. Michael Birrer at MGH Cancer Center and/or a CEM-approved investigator for whole genome SNP-associations studies and/or evaluation of individual SNPs.

# XII. Distributing Specimens for Future Research

All of the residual tumor, tissue, serum and plasma specimens still remaining after completion of GOG-0213 and any whole blood collected from women on GOG-0213 will be banked in the GOG Tissue Bank and made available as needed for approved cancer or non-cancer research projects based on GOG Tissue Bank - Specimen Distribution Policies if the following condition is satisfied: Each study patient in question must have provided permission for the use of her specimens for cancer and/or non-cancer research. These responses (choices) will be documented on the informed consent document that the patient signs for the protocol and electronically when the staff at the treating GOG institution enters the patient's choices online using the Specimen Consent Application available on the GOG website.

The Specimen Consent Application also captures the patient's decision regarding (1) the use of her clinical information collected by the GOG as part of her participation in this trial for future research that uses her specimens, (2) the use of her specimens to be used for future research to study changes in genetic material (those passed on in families or that are not passed on in families but are either natural changes or influenced by environment and lifestyle), and (3) for someone at your institution such as a doctor or nurse to contact her in the future to ask her to take part in more research.

**The specimens will be used for research purposes only until they are used up or until the patient changes her mind.** The staff at the GOG treating institutions will use the Specimen Consent Application to amend the patient's choice(s) regarding the future use of her specimens if the patient changes her mind. This application

shares information with the GOG Statistical and Data Center and the GOG Tissue Bank and has management, reporting, confirmation and validation features. If the patient does not give permission for the use of her specimens for future cancer or non-cancer research, the GOG Tissue Bank will be instructed to destroy (incinerate) any remaining specimens to insure that the patient's wishes are honored.

Chairs of the GOG Committee for Experimental Medicine and the GOG Tissue Utilization Subcommittee will coordinate to make decisions regarding when specimens will be distributed to approved investigators for approved laboratory testing. The GOG Statistical and Data Center and the GOG Tissue Bank will work together to coordinate the physical distribution of the specific specimens for select patients to the approved investigators for laboratory testing. Specimen selection will be based on information regarding specimen procurement and condition as well as patient eligibility, evaluation criteria, statistical considerations, and relevant clinical information. The GOG Statistical and Data Center will email the investigator an electronic file containing the specimen identifiers with relevant information regarding specimen condition, suitability for testing, eligibility/evaluability for a given component of the research study, and fields for the laboratory data if appropriate. For each shipment, the GOG Tissue Bank staff will e-mail the investigator and the GOG Statistical and Data Center an electronic file that includes an inventory of all specimens included in the shipment with the specimen specific identifiers as well as quantity and condition of the specimens being shipped.

The investigators performing approved research on any GOG-0213 specimens will not be given access to any personal identifiers. The investigators will be responsible for the direct supervision and oversight of the laboratory testing performed on these specimens. The individuals at the respective laboratories will be responsible for keeping accurate records of all laboratory testing performed in the GOG specimens, ensuring that the laboratory testing results are linked to the appropriate specimen-specific identifiers and transferring relevant laboratory data to the GOG Statistical and Data Center for analysis. The approved principal investigator (PI) will coordinate with co-PIs, scientific collaborators and the GOG Statistical and Data Center to analyze, report, and publish the research results. Any presentation or publication will comply with the GOG Publications Policy and acknowledge the National Cancer Institute grants to the GOG Administrative Office (CA 27469), the GOG Tissue Bank (CA 27469 and CA 11479) and the GOG Statistical and Data Center (CA 37517).

APPENDIX IV

**NCI Standard Protocol Language (as of March 26, 1998) Standard Language to Be Incorporated into All Protocols Involving Agent(s) Covered by a Clinical Trials Agreement (CTA) or a Cooperative Research and Development Agreement (CRADA):**

The agents (hereinafter referred to as "Agent"), **Bevacizumab and Erlotinib**, used in this protocol are provided to the NCI under a Clinical Trials Agreement (CTA) or a Cooperative Research and Development Agreement (CRADA) between **Genentech, Inc.** (hereinafter referred to as "Collaborator") and the NCI Division of Cancer Treatment, Diagnosis. Therefore, the following obligations/guidelines apply to the use of the Agent in this study:

1. Agent may not be used outside the scope of this protocol, nor can Agent be transferred or licensed to any party not participating in the clinical study. Collaborator data for Agent are confidential and proprietary to Collaborator and should be maintained as such by the investigators.

2. For a clinical protocol where there is an investigational Agent used in combination with (an)other investigational Agent(s), each the subject of different CTAs or CRADAs, the access to and use of data by each Collaborator shall be as follows (data pertaining to such combination use shall hereinafter be referred to as "Multi-Party Data."):

a. NCI must provide all Collaborators with written notice regarding the existence and nature of any agreements governing their collaboration with NIH, the design of the proposed combination protocol, and the existence of any obligations which would tend to restrict NCI's participation in the proposed combination protocol.

b. Each Collaborator shall agree to permit use of the Multi-Party Data from the clinical trial by any other Collaborator to the extent necessary to allow said other Collaborator to develop, obtain regulatory approval or commercialize its own investigational Agent.

c. Any Collaborator having the right to use the Multi-Party Data from these trials must agree in writing prior to the commencement of the trials that it will use the Multi-Party Data solely for development, regulatory approval, and commercialization of its own investigational Agent.

3. The NCI encourages investigators to make data from clinical trials fully available to Collaborator for review at the appropriate time (see #5). Clinical trial data developed under a CTA or CRADA will be made available exclusively to Collaborator, the NCI, and the FDA, as appropriate.

4. When a Collaborator wishes to initiate a data request, the request should first be sent to the NCI, who will then notify the appropriate investigators (Group Chair for cooperative group studies, or PI for other studies) of Collaborator's wish to contact them.

5. Any data provided to the Collaborator must be in accordance with the guidelines and policies of the responsible Data Monitoring Committee (DMC), if there is a DMC for this clinical trial.

6. Any manuscripts reporting the results of this clinical trial should be provided to CTEP for immediate delivery to Collaborator for advisory review and comment prior to submission for publication. Collaborator will have 30 days from the date of receipt for review. An additional 30 days may be requested in order to ensure that confidential and proprietary data, in addition to Collaborator's intellectual property rights, are protected. Copies of abstracts should be provided to Collaborator for courtesy review following submission, but prior to presentation at the meeting or publication in the proceedings. Copies of any manuscript and/or abstract should be sent to:

Regulatory Affairs Branch, CTEP, DCTD, NCI
Executive Plaza North, Room 7111
Bethesda, Maryland 20892
FAX: (301) 402-1584

The Regulatory Affairs Branch will then distribute them to the Collaborator.

APPENDIX V

**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 an 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 method of Cockcroft-Gault using the following formula:

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

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.

# プロトコル文書

# 日本語版

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送付元： KIA NEFF
PROTOCOL SECTION

日付： 2014年9月29日

RE： PROTOCOL GOG-0213－REVISION #12

**試験タイトル**：“プラチナ感受性の再発卵巣癌、原発性腹膜癌および卵管癌に対する二次的腫瘍減量手術の有効性、およびカルボプラチンとパクリタキセル（またはゲムシタビン）の併用療法にベバシズマブを併用維持療法として使用した場合の有効性を検討するランダム化第Ⅲ相比較臨床試験　NCIによる薬剤提供：ベバシズマブ（NSC#704865,IND#113912）”

NCI Version June 23, 2014

スタディチェア：Robert L. Coleman, M.D., (713) 745-3357; email: rcoleman@mdanderson.org

IRB審査の推奨：

（　）　審査不要
（X）　迅速審査；ただし、施設IRBの要求を優先する
（　）　説明文書変更のため、審査を推奨

***ベバシズマブにおけるリスク情報が改訂されたが、追加されたリスクは旧版のCAEPRにすでに含まれていたものと非常に似通っている、もしくは関連のあるものであり、患者も同意書（ICD）ですでに目にしているものである。**今回の場合でいうと、（1）流涙はアレルギー性鼻炎に関連する；（2）創合併症は創離開を含み、より一般的な用語である；（3）脱水は、その他の有害事象である大腸炎、悪心および嘔吐に関連する；（4）感染、その他（壊疽性筋膜炎）は既にリスクとして特定されている感染のタイプのひとつである；（5）好中球数減少の頻度が増し「Less likely」から「Likely」へ移行したが、このリスクは既に特定されている；（6）血小板数減少の頻度が増し、「因果関係は不明だが報告されているリスク」から「Less likely」に移動したが、既に反映した好中球数減少の頻度増加の骨髄抑制に関連するリスクである；

同意書にこれらの変更（すなわち、リスク関連情報の表記方法の変更や追記）があった場合、IRB により改訂された同意書が審査、承認されるまでの間、新規の患者登録を中断する必要はない。このような同意書の改訂では、患者登録は IRB 審議、承認前も継続可能だが、IRB 承認が得られるまで改訂同意書を使用することはできない。アクションレターは発行されないことに注意されたい。

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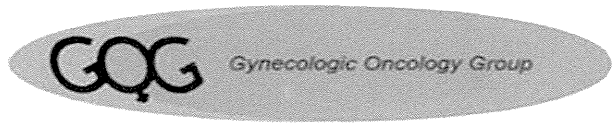


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# 変更概要

The following changes are being submitted in response to an RA from Dr. Helen Chen (Helen.chen@nih.gov):
For Protocol Amendment #12 to:

NCI Protocol #: GOG-0213
Local Protocol #: GOG-0213

NCI Version Date: June 23, 2014
Protocol Date: June 23, 2014

| # | セクション | ページ | 変更 |
|---|---|---|---|
| 1 | タイトルページ | 1 | NCT# 00565851が追加された。<br>NCI version dateが更新された。<br>Revision #1-12を含む。<br>Lead InstitutionおよびParticipating Organizationsが追加された。<br>トランスレーショナルリサーチ研究代表者がKathereen Darcyから Heather Lankesに変更された。 |
| 2 | 4.36 | 24-28 | 改訂版CAEPR(Versionn2.3, 2013/8/1)が追加された。<br>（本文参照） |
| 3 | 5.1 | 33 | OPENによる患者の組み入れおよび登録に伴い変更された。 |
| 4 | 10.1-10.3 | 53-59 | プロトコルにおいての参照元AdEERSはCTEP-AERSへと変更された。 |
| 5 | ICD | | 説明同意文書に追加の変更を行った。 |

# GOG-0213　試験実施計画書

プラチナ感受性の再発卵巣癌、原発性腹膜癌および卵管癌に対する二次的腫瘍減量手術の有効性、およびカルボプラチンとパクリタキセル（またはゲムシタビン）の併用療法にベバシズマブを併用維持療法として使用した場合の有効性を検討するランダム化第Ⅲ相比較臨床試験

NCIによる薬剤提供：ベバシズマブ（NSC#704865,IND#113912）**(12/19/2011)（10/01/2012）NCT# 00565851**

NCI Version 06/23/2014

（改訂#1～12 を含む）

ポイント:

一症例あたり - 14

メンバーシップ - 6、さらに手術適応に関するランダム化割付が行われる場合は 6 ポイント追加

Lead Institution: NRG/NRG Oncology

**Participating Organizations**
**ALLIANCE** / Alliance for Clinical Trials in Oncology
**ECOG-ACRIN** / ECOG-ACRIN Cancer Research Group
**SWOG** / SWOG


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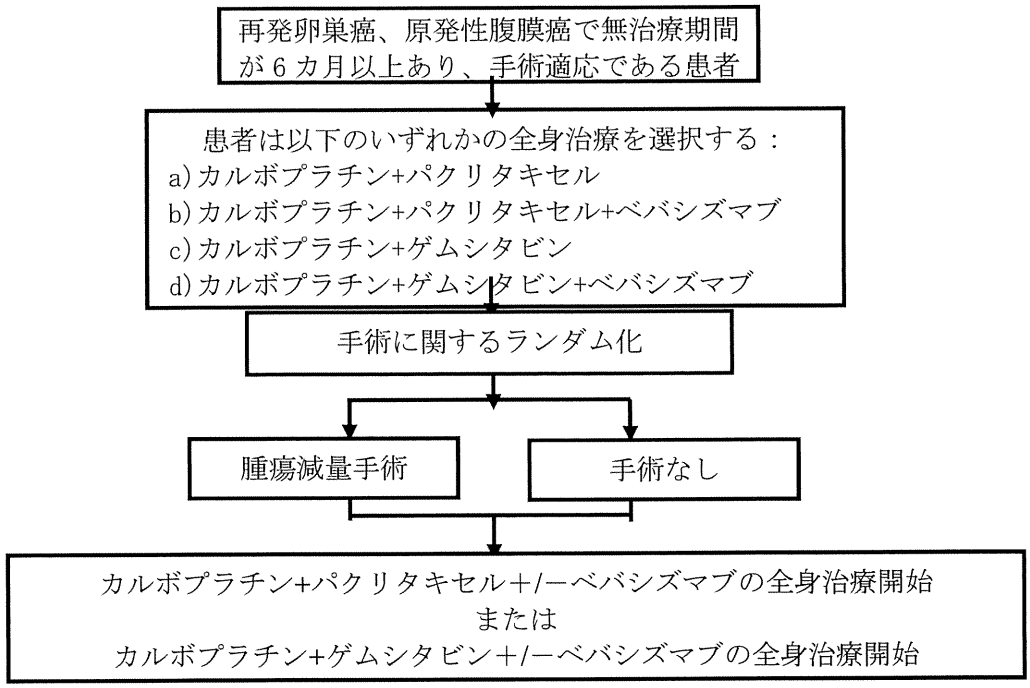
**GOG**：患者登録開始 12/06/2007
改訂 08/4/2008
改訂 06/22/2009
改訂 03/15/2010
改訂 08/23/2010
改訂 01/03/2011
改訂 08/29/2011
改訂 09/26/2011
改訂 12/19/2011
改訂 10/01/2012
改訂 08/19/2013
改訂 09/29/2014

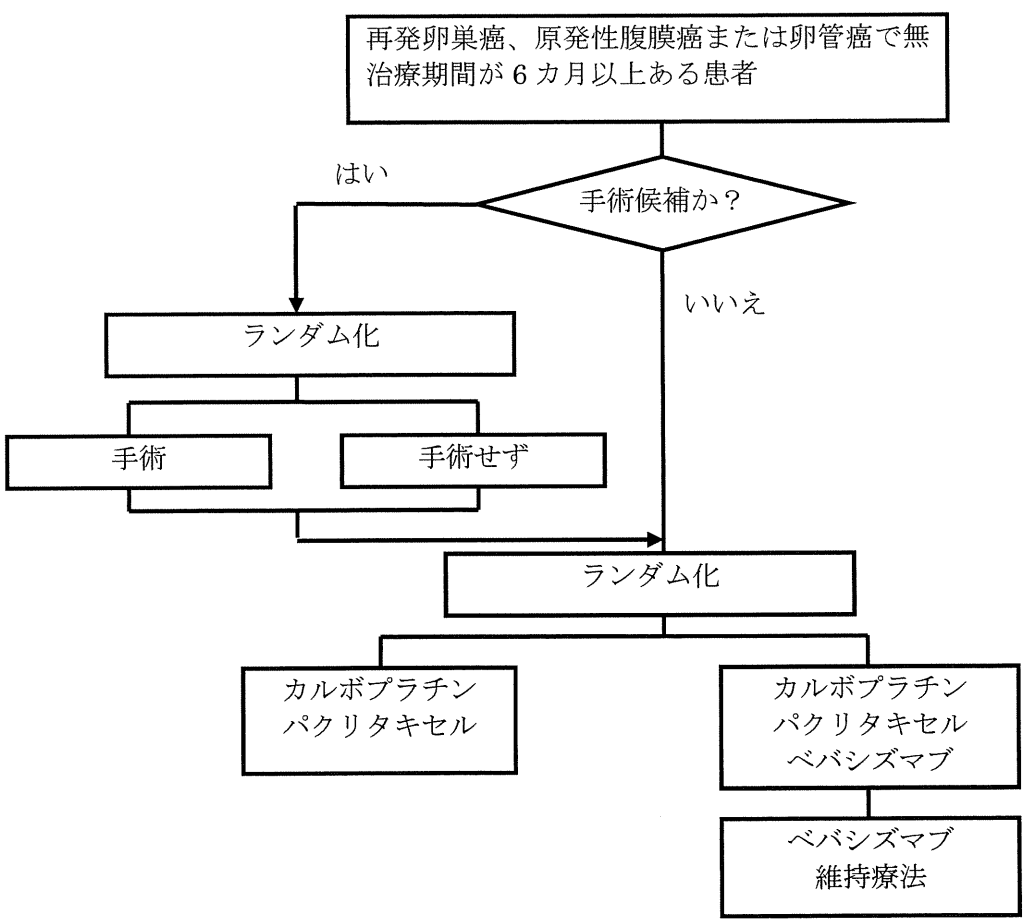
**GOG-Japan：作成 08/28/2009 Ver.1.0**
**改訂 04/02/2010 Ver.2.0**
**改訂 09/24/2010 Ver.3.0**
**改訂 01/21/2011 Ver.3.1**
**改訂 08/12/2011 Ver.6.1**
**改訂 09/06/2011 Ver.7.0**
**改訂 10/06/2011 Ver.8.0**
**改訂 01/18/2012 Ver.9.0**
**改訂 10/22/2012 Ver.10.0**
**改訂 09/06/2013 Ver.11.0**
**改訂 10/17/2014 Ver.12.0**
**改訂 11/14/2014 Ver.12.01**

8/29/2011 からのシェーマ（**08/29/11**）**(12/19/11)** （**10/01/2012**）




下記のシェーマは、12/6/2007 から 8/28/2011 までの間のものである。化学療法レジメンは目標症例登録数に達したためランダム化から削除し、手術に関するランダム化割付のみとする。（上記シェーマ参照）
**（08/29/11）(12/19/11)**

シェーマ（**06/22/09**）



本プロトコルにおける検体の必要条件および基礎的研究に関する詳細については、Section 7.32 および AppendixⅢ（検体の手続き）を参照のこと。手術群にランダム化割付がされ、かつ、今回の調査研究に検体が提供され使用されることを承諾する患者からは、二次的腫瘍減量術で採取する保存用の腫瘍組織検体および試験管 2 本分の血液（血清および血漿用）の提出を求めることになっているが、本プロトコルには検体の必要条件が新たに一つ追加された。既に GOG-0213 に登録済みの患者を含め、ランダム化および治療にかかわらず、同意が得られるすべての患者を対象として全血採取を行うことである。GOG-0213 に登録済みの患者に対しては、改めて全採血の承諾を求める必要がある。患者の承諾が得られない場合は、「患者は、血液が今回の調査研究への提供・使用目的で採取されることを承諾しましたか」という質問に対してオンライン検体同意書で「いいえ」を選択し、検体が採取／提供されなかった理由として全血（WB01）用の SP Form item 5 に「患者の承諾が得られない」と入力する。

手術のランダム化後の治療オプションには、カルボプラチンとの併用化学療法として、パクリタキセルもしくはゲムシタビンが含まれる。試験担当医師の判断で、どちらの化学療法もベバシズマブの投与が可能である。もしベバシズマブが選択された場合、疾患進行するか、容認できない有害事象が発生するまで、ベバシズマブの維持療法が行われる。**(10/01/2012)**

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