When patients seen in our Gynecologic Oncology clinic at the University of Wisconsin Hospital discuss treatment for their cancer, our physicians often consider enrolling them on clinical trials. In addition to the phase II and III clinical trials sponsored by the Gynecologic Oncology Group (GOG), the National Cancer Institute or Industry, there are also phase I studies. Gynecologic oncology patients are treated on two different types of phase I studies: GOG-sponsored, disease-specific studies and NCI- and Industry-sponsored non-disease specific studies.

Phase I studies vary considerably from a first-in-human testing of investigational agents to studies involving two standard agents being combined together. Phase I studies are characterized as studies focused on determining an optimum dose or doses of a novel agent or combination of agents in order to further test the agent or combination of agents in phase II or III clinical trials. They also frequently involve pharmacokinetic or biomarker sampling to better gauge how the body handles the agent(s) and to help determine optimum dosing for future testing.

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The more common phase I studies, which are non-disease specific, enroll patients with many different kinds of malignancy who do not have effective standard therapies available for treatment of their cancer. The University of Wisconsin Paul P. Carbone Comprehensive Cancer Center (UWCCC) Phase I program is one of the largest and most active programs in the United States with twenty (or more) phase I trials open at any one time. These studies include initial dose escalation studies of novel investigational agents (e.g. new VEGF inhibitors) to combination studies (e.g. paclitaxel + carboplatin + a novel signal transduction inhibitor).

Frequently patients with advanced, recurrent ovarian, endometrial or cervical cancer are treated on these studies at the UWCCC. The UWCCC Phase I program enrolls 125-150 patients every year on these studies.

As mentioned above, we also offer GOG Phase I studies to our patients. GOG phase I studies are usually disease specific and focus upon finding the optimum dosing combination of standard agents prior to phase II or III testing. Recent examples include combining whole abdominal radiotherapy with paclitaxel and cisplatin in advanced endometrial cancer or pelvic radiotherapy and cetuximab and cisplatin for cervical cancer. The patients treated on these studies are usually recently diagnosed and have not had prior therapy. These studies use known effective dosages and focus on slight changes in doses to improve tolerance or optimize effectiveness. Our current GOG Phase I studies available include GOG 9921 and GOG 9918 (see our current list of protocols for more information).
Our Feature Protocol:

GOG 9921: A Phase I Feasibility Trial of IP Cisplatin and IV Paclitaxel on Day 1 Followed by IP Paclitaxel on Day 8 Every 21 Days as Front-Line Treatment of Ovarian, Fallopian Tube and Primary Peritoneal Carcinoma

Women facing an ovarian cancer diagnosis must also face their mortality: approximately 30% of women diagnosed with advanced stage disease survive five years after diagnosis. We hope to change that figure with continued research and new treatment modalities. To date, the most promising research focused on improving survival rates for women with newly diagnosed advanced ovarian cancer was a trial utilizing intraperitoneal (IP) cisplatin and paclitaxel with concurrent intravenous (IV) paclitaxel. This protocol, GOG 172, reported the longest median survival of 65.6 months in optimally debulked stage III ovarian cancer. Despite these encouraging numbers, IP regimens have not been accepted as the current standard of care due to high toxicity.

Intraperitoneal chemotherapy is introduced into the patient’s peritoneal cavity via a catheter through a surgically-placed port. After infusion, the patient is asked to change position at certain time intervals to ensure adequate intra-abdominal distribution of the chemotherapy. No attempt is made to retrieve the infusate after infusion. Most often IP therapy is coupled with IV therapy to provide both local and systemic treatment.

At UW, we offer an IP/IV regimen as well as an IV regimen of platinum and taxane as standard of care, but often use the IV regimen due to the toxicity of IP therapy. In GOG 172, patients randomized to the IP therapy group reported significantly worse quality of life (QOL) measures during and shortly after treatment. However, there were no significant overall QOL differences between arms one year post-treatment. Differences in QOL are most likely due to toxicities associated with IP therapy. The challenge now is to modify the GOG 172 regimen to preserve survival advantage and make it tolerable for patients to receive a complete six cycles of chemotherapy without discontinuing due to distress and toxicity. GOG 9921 is a phase I feasibility study. Eligible subjects receive IV paclitaxel followed by IP cisplatin on day 1 and IP paclitaxel on day 8 of a 21-day cycle. Subjects will receive a total of six cycles unless they experience unacceptable toxicity or disease progression. Each cycle, participants will be evaluated for side effects by their doctor in the UW Gynecologic Oncology Clinic. A total of twenty women will be registered during the first phase of the study. Study researchers will analyze the toxicity assessments of this first cohort of twenty women and after statistical analysis determine if the regimen is feasible for a phase III study. An additional twenty women may be necessary to satisfy statistical requirements to evaluate for toxicity and therefore feasibility for further research of this regimen. It is our hope that this regimen will prove to be a less-toxic yet more effective standard of care for ovarian cancer and develop into renewed hope for women and families facing this difficult diagnosis.

Protocol Eligibility*

Key eligibility criteria:
- Histologic diagnosis of epithelial ovarian, primary peritoneal or fallopian tube carcinoma or carcinosarcoma
- Stage IIB, IIC, III or IV disease
- Appropriate surgical treatment for ovarian/fallopian/peritoneal primary cancer
- No prior chemotherapy or radiation therapy
- GOG performance status of 0-2
- Patients with unstable angina or history of myocardial infarction within six months

*select eligibility
**Our Current Protocols**

A complete listing of all clinical trials at the UW Carbone Cancer Center is also available on our website, www.cancer.wisc.edu.

### Ovarian / Primary Peritoneal / Fallopian Tube

- **GOG 186F**  A Phase II Evaluation of Docetaxel Plus Trabectedin With Growth Factor Support in the Third-Line Treatment of Recurrent or Persistent Ovarian, Fallopian Tube or Primary Peritoneal Cancer
- **GOG 212**  A Randomized Phase III Trial of Maintenance Chemotherapy Comparing Single Agent Paclitaxel or Xyotax (CT-2103) Versus No Treatment Until Documented Relapse in Women with Advanced Ovarian or Primary Peritoneal Cancer
- **GOG 213**  A Phase III Randomized Controlled Clinical Trial of Carboplatin and Paclitaxel, Alone or in Combination with Bevacizumab, followed by Bevacizumab And Secondary Cytoreductive Surgery in Platinum-Sensitive, Recurrent Ovarian, Peritoneal Primary and Fallopian Tube Cancer
- **GOG 218**  Phase III Trial of Carboplatin and Paclitaxel Plus Placebo Versus Carboplatin and Paclitaxel Plus Concurrent Bevacizumab in Women with Newly Diagnosed, Previously Untreated, Advanced Stage Epithelial Ovarian and Peritoneal Cancer
- **GOG 9921**  A Phase I Feasibility Trial of IP Cisplatin and IV Paclitaxel on Day 1 Followed by IP Paclitaxel on Day 8 Every 21 Days as Front-Line Treatment of Ovarian, Fallopian Tube and Primary Peritoneal Carcinoma
- **CO 07702**  A Phase III Randomized, Blinded, Placebo-controlled Trial of Carboplatin and Gemcitabine plus Bevacizumab in Patients with Platinum-Sensitive Recurrent Ovary, Primary Peritoneal, or Fallopian Tube Carcinoma
- **CO 08707**  A Non-Interventional Prospective Study of the Correlation of the Precision Therapeutics, Inc. Chemoresponse Assay with Progression-Free Survival in Patients with Recurrent Epithelial Ovarian, Peritoneal or Fallopian Tube Cancer

### Uterine

- **GOG 129Q**  A Phase II Evaluation of Gemcitabine in the Treatment of Recurrent or Persistent Endometrial Carcinoma
- **GOG229F**  A Phase II Evaluation of VEGF-Trap in the Treatment of Recurrent or Persistent Endometrial Cancer
- **GOG 232C**  A Phase II Evaluation of Paclitaxel, Carboplatin, and BSI-201 in the Treatment of Advanced, Persistent, or Recurrent Uterine Carinosarcoma
- **GOG 238**  A Randomized Trial of Pelvic Irradiation With or Without Concurrent Weekly Cisplatin in Patients with Pelvic-Only Recurrence of Carcinoma of the Uterine Corpus
- **GOG 248**  A Randomized Phase II Trial of Temsirolimus or the Combination of Hormonal Therapy Plus Temsirolimus in Women with Advanced, Persistent or Recurrent Endometrial Carcinoma
- **CC 06701**  Cytologic Analysis of Distention Media as a Screening Test for Endometrial Cancer

### Cervical

- **GOG 9918**  A Phase I Trial of Tailored Radiation Therapy with Concomitant Cetuximab and Cisplatin in the Treatment of Patients with Cervical Cancer
- **CO 09701**  A Phase III Randomized Clinical Trial of Laparoscopic or Robotic Radical Hysterectomy versus Abdominal Radical Hysterectomy in Patients with Early Stage Cervical Cancer

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**For more information about these clinical trials at the UW Carbone Cancer Center, contact Cancer Connect, (800) 622-8922 or (608) 262-5223 in the Madison area.**

**UW Gynecologic Oncology Research Staff:**

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Together We Can Save Lives
Learn More About UW Gynecologic Oncology

About 22,430 women in the United States will be told they have ovarian cancer this year.

President Barack Obama’s mother died of ovarian cancer.

Phase I trials are first to introduce new drugs into humans. They determine safe dosing of new therapies.

Phase II trials target new therapies at specific types of cancer. They determine the overall response of a small group of subjects, as well as side-effect information.

Phase III trials determine new treatment by comparing these treatments to the standard of care. Hundreds of subjects are required for these studies.

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