TO: NRG and NCORP Investigators

RE: Increasing Enrollment in GOG 0237 – A protocol designed to do comparative Analysis of CA-IX, p16, Proliferative Markers, and HPV in the diagnosis of significant cervical lesions in patients with a cytologic diagnosis of atypical glandular cells (AGC).

FROM: GOG 0237 Investigators

GOG 0237 is a cancer prevention study to evaluate biomarkers to identify women with atypical glandular cells on cervical cytology specimens at risk of having high grade epithelial lesions, especially adenocarcinoma in-situ. The eligibility for enrollment is as follows: Any woman age >18 year-old, no history of vaginal, cervical or endometrial cancer, no history of having received/receiving radiation/chemotherapy and having a cytologic diagnosis of atypical glandular cells (AGC) or histologic diagnosis of adenocarcinoma in-situ (AIS) can be enrolled into the study. All women enrolled into the study who have a positive H-HPV test are required to have a complete histologic examination of the cervix with cervical LEEP/cone biopsy.

Several amendments have recently been made to GOG 0237 (the follow-up to GOG 0171) to bring the 0237 protocol into alignment with current cervical cancer screening guidelines. Prior to the recent amendments, all patients with an AGC diagnosis had to agree to undergo a cone biopsy procedure regardless of their human papillomavirus (HPV) status. The amended protocol now allows North American study participants, whose cytology is found to be HPV negative, to discontinue study participation (with documentation of a negative HPV test result submitted to the NRG Statistical and Data Management Center). An additional amendment expands the eligibility criteria to include those participants diagnosed with adenocarcinoma in-situ.

GOG 0237 is the expansion of GOG0171 (closed).
Two important observations have been identified from the GOG 0171 study; (1) Carbonic Anhydrase IX (CAIX) + HPV testing was important in identifying patients with significant lesions (HSIL, In-situ and invasive carcinoma) who have received a cytologic diagnosis of AGC. However, the specificity is only 70% in the US and 44% in the Japanese cohorts, respectively; (2) In the Japanese cohort, there are special types of cervical cancer that are HPV negative and CAIX positive. Thus, the current cervical cancer screening guidelines applied for North American populations may not be suitable for the Japanese population.

The GOG 0237 study is being conducted in North America, Japan, and Korea with results from each population being analyzed separately.
Additional biomarkers have been added in order to test which subset (or combination) of markers will provide higher specificity in the diagnosis of cervical significant lesions in women with AGC cytologic diagnosis and provide higher sensitivity in the diagnosis of adenocarcinoma in-situ.
The Goal of GOG 0237
GOG 0237 is an important cervical cancer prevention study. The protocol is designed to not be limited to HPV and CAIX, but to also include other biomarkers. The goal of the study is to develop a panel of biomarkers to help clinicians and patients faced with the dilemma of how aggressively to treat/follow up a finding of AGC on cervical cytology. At the end of the study, it will also allow confirmation of the (Higher) incidence of HPV negative precancerous lesions in Japanese patients and evaluate the incidence of these lesions in a Korean population. These data will provide important information for devising optimal cervical cancer screening strategies regardless of ethnic origin.

We ask the site PI or Research Nurse at your institution to identify the physicians who manage women with abdominal Pap test results so they can be recruited. This will greatly aid us to complete the study by either enrolling more patients or participating in the study.

This trial is very straightforward to carry out:

(1) Identify the patient with an AGC cytologic diagnosis;
(2) Obtain a study liquid base cytology (LBC) specimen and ship to NRG;
(3) Proceed with a cervical biopsy, ECC, or EMC (age >35)

If results of #3 are **negative**, the patient may go off the study provided a negative HPV result is transmitted to NRG.

If results of #3 are **positive**, proceed with cervical cone biopsy and/or hysterectomy.

For patients with an AIS diagnosis made by cytology or ECC/biopsy:

(1) Obtain a study LBC; and
(2) Proceed with the standard treatment for AIS