GOG 286B: RANDOMIZED PHASE II/III STUDY OF PACLITAXEL/CARBOPLATIN/METFORMIN (NSC#91485) VERSUS PACLITAXEL/CARBOPLATIN/PLACEBO AS INITIAL THERAPY FOR MEASURABLE STAGE III OR IVA, STAGE IVB, OR RECURRENT ENDOMETRIAL CANCER

FAST FACTS

Supplied: *Metformin 850mg OR Placebo capsules*

PATIENT ELIGIBILITY
Eligible Patients

3.11 Patients must have measurable Stage III, measurable Stage IVA, Stage IVB (with or without measurable disease) or recurrent (with or without measurable disease) endometrial carcinoma. Histologic confirmation of the original primary tumor is required. Patients with the following histologic epithelial cell types are eligible: Endometrioid adenocarcinoma, serous adenocarcinoma, undifferentiated carcinoma, clear cell adenocarcinoma, mixed epithelial carcinoma, adenocarcinoma not otherwise specified (N.O.S.).

3.12 Measurable disease is defined by RECIST (version 1.1). Measurable disease is defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded). Each lesion must be □ 10 mm when measured by CT, MRI or caliper measurement by clinical exam; or □ 20 mm when measured by chest x-ray. Lymph nodes must be > 15 mm in short axis when measured by CT or MRI (See section 8).

3.13 Patients must have a GOG Performance Status of 0, 1, or 2.

3.14 Patients must have adequate:

a. Bone marrow function:
   - Absolute neutrophil count (ANC) greater than or equal to 1,500/mcl
   - Platelets greater than or equal to100,000/mcl.

b. Renal function:
   - Creatinine less than or equal to 1.5 x ULN

c. Hepatic function:
   - Bilirubin less than or equal to 1.5 x ULN
   - AST and ALT less than or equal to 3 x ULN
   - Alkaline phosphatase less than or equal to 2.5 x ULN

3.15 Prior Therapy:

Patients must **NOT** have received prior chemotherapy or targeted therapy, including chemotherapy used for radiation sensitization for treatment of endometrial carcinoma.

Patients may have received prior radiation therapy for treatment of endometrial carcinoma. Prior radiation therapy may have included pelvic radiation therapy, extended field pelvic/para-aortic radiation therapy, and/or intravaginal brachytherapy. All radiation therapy must be completed at least 4 weeks prior to the first date of study therapy.

Patients may have received prior hormonal therapy for treatment of endometrial carcinoma. All hormonal therapy must be discontinued at least one week prior to the first date of study therapy.

3.16 Patients must be able to swallow and retain orally-administered medication.

3.17 Patients must have signed an approved informed consent and authorization permitting release of personal health information. Individuals with impaired decision-making capacity are not eligible to participate on the study.

3.18 Patients must meet eligibility criteria as specified in section 7.0.

3.19 Patients must be 18 years or older.

Ineligible Patients

3.21 Patients must NOT be taking metformin or have been on metformin in the past 6 months.

3.22 Patients with a history of other invasive malignancies, with the exception of non-melanoma skin cancer are excluded if there is any evidence of other malignancy being present within the last three years.

3.23 Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.

3.24 Patients who are pregnant or nursing. If patients are of reproductive age and have not undergone hysterectomy, they must use an effective contraceptive method for the duration of this study.

3.25 Any condition associated with increased risk of metformin-associated lactic acidosis. (e.g. congestive heart failure defined as New York Heart Association {NYHA} Class III or IV functional status, history of acidosis of any type; habitual intake of 3 or more alcoholic beverages per day).

TREATMENT

- **Experimental: Arm I** (paclitaxel, carboplatin, metformin hydrochloride)

  Patients receive paclitaxel IV over 3 hours, carboplatin IV over 30 minutes on day 1, and metformin hydrochloride PO BID on days 1-21 (QD in course 1). Treatment repeats every 21 days for 6 courses in the absence of disease progression or unacceptable toxicity. Patients then receive maintenance therapy comprising metformin hydrochloride PO BID on days 1-21.
- **Active Comparator: Arm II** (paclitaxel, carboplatin, placebo)

  Patients receive paclitaxel IV and carboplatin IV as in Arm I. Patients also receive placebo PO BID on days 1-21 (QD in course 1). Treatment repeats every 21 days for 6 courses in the absence of disease progression or unacceptable toxicity. Patients then receive maintenance therapy comprising placebo PO BID on days 1-21.

PRE-STUDY PARAMETERS (refer section 7.0 for details)

- Physical examination and performance status
- Hip to waist ratio per section 7.5
- Adverse event assessment
- Concomitant medications
- Pregnancy test (serum or urine β-HCG)
- CBC and CMP
- Fasting glucose and insulin
- HgbA1C
- ECG
- Tumor measurements (CT scan or MRI)
- Chest x-ray or chest CT
- Patient Reported Outcomes
- Stained Pathology Slide Requirements for Central Review
- Optional blood and archived tissue samples