

SCRI GYN 19: A Randomized Phase II Study of Paclitaxel/Carboplatin with or without Sorafenib in the First –Line Treatment of Patients with Stage III/IV Epithelial Ovarian Cancer

Fast Facts

Sorafenib provided

Inclusion Criteria

1. Histologically confirmed, stage III or IV epithelial ovarian carcinoma
2. No previous treatment with chemotherapy or radiation therapy
3. All patients must have undergone cytoreductive surgery, with the following results:
 - a. No residual tumor nodule > 3cm
 - b. No residual tumor involvement of the bowel (ie. invasion into bowel wall)
 - c. No residual intestinal obstruction
4. Measurable or evaluable disease. Patients with elevated CA-125 levels and/or evaluable disease per RECIST criteria are eligible.
5. ECOG performance status 0 or 1 (See Appendix B).
6. ANC \geq 1500/ μ L, platelets \geq 100,000/ μ L, hemoglobin \geq 9.0 g/dL.
7. Total bilirubin \leq 1.5 x upper limits of normal (ULN), ALT and AST \leq 2.5 x ULN (\leq 5 x ULN for patients with liver metastases)
8. Serum creatinine \leq 1.5 x ULN
9. INR < 1.5 or a PT/PTT within normal limits. Patients receiving anti-coagulation treatment with an agent such as warfarin or heparin **may** be allowed to participate. For patients on warfarin, the INR may be > 1.5, and should be measured prior to initiation of sorafenib and monitored at least weekly until INR is stable in the desired therapeutic range.
10. Women of childbearing potential must have a negative serum pregnancy test performed within 7 days prior to start of treatment.
11. Patients must be able to understand the nature of this study and give written informed consent.

Exclusion Criteria

1. Age < 18 years
2. Active cardiac disease, including:
 - a. congestive heart failure > class II NYHA (Appendix H),
 - b. unstable angina or onset of angina within last 3 months,
 - c. myocardial infarction within 6 months
3. Cardiac ventricular arrhythmias requiring anti-arrhythmic therapy
4. Patients with CNS metastases. Patients with neurological symptoms must undergo a CT scan/MRI of the brain to exclude brain metastasis.
5. Uncontrolled hypertension defined as systolic blood pressure > 150mmHg or diastolic pressure > 90mmHg, despite optimal medical management
6. Known HIV, chronic hepatitis B or chronic hepatitis C infections
7. Women who are pregnant or lactating. Women of childbearing potential must agree to use adequate contraception from time of study entry until at least 3 months after the last administration of study drug.
8. Active clinically serious infection (> grade 2)
9. Thrombotic or embolic events such as cerebral vascular accident including transient ischemic attacks within the last 6 months.
10. Pulmonary hemorrhage/bleeding event \geq grade 2 within 4 weeks of starting treatment.
11. Any other hemorrhage/bleeding event \geq grade 3 within 4 weeks of starting treatment
12. Serious non-healing wound, ulcer, or bone fracture
13. Evidence of history of bleeding diathesis or coagulopathy
14. Major surgery, open biopsy, or significant traumatic injury within 4 weeks of starting treatment.
15. Any condition that impairs the ability to swallow whole pills
16. Patients with any type of malabsorption
17. Known or suspected allergy to any of the agents used in this treatment
18. Use of St. John's Wort or rifampin

Pre-Study Parameters

1. History and physical including weight, performance status, blood pressure
2. Labs including CBC with differential, CMP, LDH, uric acid, PT/PTT, CA-125, urinalysis, Beta HCG for women of child bearing potential.
3. Tumor measurement: CT chest/abdomen/pelvis, CT or MRI head if suggestive of neurologic symptoms

Treatment

Arm A – Cycle = 21 days

Drug	Dose	Route	Frequency
Paclitaxel	175 mg/m ²	IV	Day 1
Carboplatin	AUC 6	IV	Day 1
Sorafenib (provided)	400 mg	PO	BID starting day 1

Paclitaxel + carboplatin continue for a maximum of six cycles. Sorafenib may continue if pt has stable disease or objective response.

Arm B – Cycle = 21 days

Drug	Dose	Route	Frequency
Paclitaxel	175 mg/m ²	IV	Day 1
Carboplatin	AUC 6	IV	Day 1

Paclitaxel + carboplatin continue for a maximum of six cycles.