PATIENT ELIGIBILITY:

Important note: The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01). All clinical and laboratory data required for determining eligibility of a patient enrolled on this trial must be available in the patient’s medical research record which will serve as the source document for verification at the time of audit.

1. **Timing**
   Patients must be enrolled before treatment begins. The date protocol therapy is projected to start must be no later than five (5) calendar days after the date of study enrollment.

2. **Patients on the Low Risk arms must be enrolled within 6 weeks (42 days) of diagnostic biopsy or surgery.**

3. **Patients on the Standard Risk arms must be enrolled within 6 weeks (42 days) of diagnostic biopsy or surgery with the following exceptions:**
   - A patient who initially has Stage I disease, not enrolled on AGCT1531, and was under surveillance post-surgery off study. This patient may be enrolled on one of the Standard Risk arms at recurrence if all relevant eligibility criteria and criteria in Section 4.3.3 are met.
   - A patient who initially had a mature/immature teratoma, not enrolled on AGCT1531, and was under surveillance post-surgery off study. If this patient recurs with a malignant germ cell tumor per the criteria in Section 4.2.2, the patient may be enrolled on one of the Standard Risk arms at recurrence if all relevant eligibility criteria are met.

4. **For Low Risk patients, recommended imaging studies should be obtained within 8 weeks prior to enrollment (repeat the tumor imaging if clinically indicated). See Section 4.2.1 for Immature Teratoma imaging, Section 4.3.1 for Low Risk Non-Seminoma MGCT imaging, or Section 4.4.1 for Low Risk Seminoma MGCT imaging.**

5. **For Standard Risk patients, recommended imaging studies should be obtained within 14 days prior to enrollment (repeat tumor imaging if clinically indicated). See Section 4.5.1 for Standard Risk 1 patients or 4.11.2 for Standard Risk 2 patients.**

6. **All clinical and laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated in the eligibility section below.**

7. **The CIRB has determined that assent of children age 14 and older is a necessary condition for proceeding with the research.**

8. **Retrospective Central Pathology Review**
   Central pathology review is always required and material should be submitted within three (3) weeks of enrollment. Tissue must be submitted for permanent sections and immunohistochemical analysis (see Section 14).

9. **All clinical and laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated. Laboratory values used to assess eligibility must be no older than seven (7) days at the start of therapy. Laboratory tests need not be repeated if therapy starts within seven (7) days of obtaining labs to assess eligibility. If a post-enrollment lab value is outside the limits of eligibility, or laboratory values are > 7 days old, then the following laboratory evaluations must be re-checked within 48 hours prior to initiating therapy: CBC with differential, bilirubin, ALT (SGPT) and serum creatinine. If the recheck is outside the limits of eligibility, the patient may not receive protocol therapy and will be considered off protocol therapy. The recommended imaging studies, if applicable, must be obtained within 8 weeks prior to enrollment for Low Risk patients, and within 14 days prior to enrollment for Standard Risk patients (clinical judgement should be used to determine if repeating the tumor imaging is necessary).**

10. **Low Risk/Stage 1 Rapid Central Surgical Review**
    After enrollment on the low risk stratum, a central review will be performed by study surgeons and study chair within 7 days of enrollment. See Surgical Guidelines (Section 13) for detailed recommendations. The following must be submitted within 72 hours of enrollment via RAVE in order for central review to be completed within 7 days of enrollment:
    - Surgical checklist,
• Operative note,
• Pathology report,
• Imaging report,
• Cytology report, if applicable, and
• Stage I Verification CRF.

If the review concludes that incomplete staging has occurred or that the patient has evidence of a higher stage, the treating physician may decide to transfer the patient to the standard-risk stratum if all eligibility requirements are met. Treatment randomization for those patients who will transfer to a standard-risk stratum will be accomplished by completing the Late Randomization Callback in OPEN. The callback must be completed prior to initiation of chemotherapy.

11. Note: Patients initially enrolled on the low risk stratum may be able to transfer to a standard risk stratum in certain circumstances (see Section 3.1.6, 4.2.2 and 4.3.2). Treatment randomization for these patients will be accomplished by completing the Late Randomization Callback in OPEN. The callback must be completed prior to initiation of chemotherapy.

12. Age
   • There is no age limit for the Low Risk Stratum (Stage I Ovarian Immature Teratoma and Stage I Non-Seminoma or Seminoma Malignant GCT (all sites))
   • Standard Risk 1
     Patient must be < 11 years of age at enrollment.
   • Standard Risk 2
     Patients must be ≥ 11 and < 25 years of age at enrollment.

13. Diagnosis
    Patients enrolling on one of the Low Risk arms must be newly diagnosed with a Stage I germ cell tumor. For the Standard Risk arms, patients must be newly diagnosed with metastatic germ cell tumor (Stage II or higher). Histologic confirmation of a primary extracranial germ cell tumor in any of the categories outlined in the table below is required of all patients at enrollment except for those who were initially diagnosed with Stage I non-seminoma malignant GCT and later recur during observation post surgery off study (see Section 3.1.4). For these patients, if elevated tumor markers rise to > 5x ULN on at least 2 measurements taken at least 1 week apart, a diagnostic biopsy is not required for enrollment. Please refer to Section 4.2.2 (for immature teratoma) and Section 4.3.3 (for non-seminomatous malignant GCT) for complete details.

    For COG, FIGO, AJCC and IGCCC staging criteria see Appendix II, Appendix III, Appendix IV and Appendix V, respectively.

    NOTE: for low risk patients, materials for rapid surgical central review must be sent within 7 days of study enrollment. See Section 3.1.6.
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Site</th>
<th>Stage</th>
<th>Grade</th>
<th>Histology</th>
<th>Tumor Markers</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Risk Stage I Immature Teratoma (IT)</strong></td>
<td>Ovarian</td>
<td>COG Stage I</td>
<td>2 or 3</td>
<td>Pure immature teratoma (may contain microscopic foci of yolk sac tumor)</td>
<td>α-FP ≤ 1,000 ng/mL</td>
<td>All ages</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FIGO Stage IA and IB</td>
<td></td>
<td>Mixed immature and mature teratoma (no pathological evidence of MGCT)</td>
<td>β-HCG institutional normal</td>
<td></td>
</tr>
<tr>
<td><strong>Non-Seminoma MGCT</strong></td>
<td>Ovarian, Testicular, or Extragonadal</td>
<td>COG Stage I</td>
<td></td>
<td>Must contain at least one of the following:</td>
<td>N/A</td>
<td>All ages</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FIGO Stage IA and IB</td>
<td></td>
<td>- yolk sac tumor, embryonal carcinoma, or choriocarcinoma (pure or mixed)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>AJCC Testicular Stage IA IB, and IS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low Risk Stage I Seminoma-MGCT</strong></td>
<td>Testicular</td>
<td>COG Stage I</td>
<td></td>
<td>May contain</td>
<td>N/A</td>
<td>All ages</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AJCC Testicular Stage IA IB, and IS</td>
<td></td>
<td>immature/mature teratoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Standard Risk 1 (SR1)</strong></td>
<td>Ovarian, Testicular, or Extragonadal</td>
<td>COG Stage II – IV</td>
<td></td>
<td>May NOT contain</td>
<td>N/A</td>
<td>&lt; 11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FIGO Stage IC, FIGO Stages II – IV (IGCCC criteria DO NOT apply)</td>
<td></td>
<td>yolk sac tumor (see notes), embryonal carcinoma, or choriocarcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Standard Risk 2 (SR2)</strong></td>
<td>Ovarian</td>
<td>COG Stage II and III</td>
<td></td>
<td>Must contain at least one of the following:</td>
<td>N/A</td>
<td>≥ 11 and &lt; 25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FIGO Stage IC, II and III</td>
<td></td>
<td>yolk sac tumor (see notes), embryonal carcinoma, or choriocarcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Testicular</td>
<td>COG Stage II - IV</td>
<td></td>
<td>Must contain at least one of the following:</td>
<td>Must be IGCCC Good Risk. Post op:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>AJCC Stage II, III and IGCCC Good Risk (See Appendix V)</td>
<td></td>
<td>yolk sac tumor (see notes), embryonal carcinoma, or choriocarcinoma</td>
<td>α-FP &lt; 1,000 ng/mL, β-HCG &lt; 5,000 mIU/mL and LDH &lt; 3.0 x normal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extragonadal</td>
<td>COG Stage II</td>
<td></td>
<td>Must contain at least one of the following:</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>yolk sac tumor (see notes), embryonal carcinoma, or choriocarcinoma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes:
- IGCCC criteria only apply to SR2 patients with a testicular primary tumor.
- Use post-op tumor marker levels to determine IGCCC risk group.
- Stage 1 seminoma patients are not eligible for the Standard Risk arms of the study.
- For the Low Risk Stage I Non-Seminoma MGCT and the Standard Risk arms, components of yolk sac tumor, embryonal carcinoma, or choriocarcinoma can be mixed with other forms of GCT, such as seminoma or mature or immature teratoma. If yolk sac tumor is the only malignant component present, then it must be deemed by the pathologist to be greater than a “microscopic component” of yolk sac tumor.

--- 14. Performance Level
Patients must have a performance status corresponding to ECOG scores of 0, 1, 2 or 3. Use Karnofsky for patients > 16 years of age and Lansky for patients ≤ 16 years of age (see Appendix VI).

--- 15. Organ Function Requirements
Organ function requirements apply ONLY to patients who will receive chemotherapy (SR1 and SR2 patients).
- 3.2.4.1 Adequate renal function defined as:
  - Creatinine clearance or radioisotope GFR ≥ 70 mL/min/1.73 m² or
  - A serum creatinine based on age/gender as follows:
<table>
<thead>
<tr>
<th>Age</th>
<th>Maximum Serum Creatinine (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
</tr>
<tr>
<td>1 month to &lt; 6 months</td>
<td>0.4</td>
</tr>
<tr>
<td>6 months to &lt; 1 year</td>
<td>0.5</td>
</tr>
<tr>
<td>1 to &lt; 2 years</td>
<td>0.6</td>
</tr>
<tr>
<td>2 to &lt; 6 years</td>
<td>0.8</td>
</tr>
<tr>
<td>6 to &lt; 10 years</td>
<td>1</td>
</tr>
<tr>
<td>10 to &lt; 13 years</td>
<td>1.2</td>
</tr>
<tr>
<td>13 to &lt; 16 years</td>
<td>1.5</td>
</tr>
<tr>
<td>≥ 16 years</td>
<td>1.7</td>
</tr>
</tbody>
</table>

The threshold creatinine values in this Table were derived from the Schwartz formula for estimating GFR (Schwartz et al. J. Peds, 106:522, 1985) utilizing child length and stature data published by the CDC.

- Adequate liver function defined as:
  - Total bilirubin ≤ 1.5 x upper limit of normal (ULN) for age, and
  - SGOT (AST) or SGPT (ALT) < 2.5 x upper limit of normal (ULN) for age (for the purpose of this study, the ULN for SGPT is 45 U/L).

- Adequate Hematological Function defined as:
  - Peripheral absolute neutrophil count (ANC) ≥ 1,000/mm³, and
  - Platelet count ≥ 100,000/mm³

16. Patients enrolling on the standard risk arms must be medically fit to receive protocol treatment and with no contraindications to protocol treatment.

17. Eligibility Criteria to Participate in the Pilot Study of the AYA-Hears Instrument (PROs of Ototoxicity) – See Section 3.2.6
EXCLUSION CRITERIA:

___1. Patients with any diagnoses not listed in the table in Section 3.2.2 including:
   - Stage I testicular cancer patients who have undergone primary RPLNC (retroperitoneal lymph node dissection),
   - Pure dysgerminoma
   - Pure mature teratoma,
   - Pure immature teratoma COG Stage I, Grade I
   - Pure immature teratoma COG Stage I, Grade 2, 3 with AFP ≥ 1000 ng/mL,
   - Pure immature teratoma COG Stage II - IV or FIGO Stage IC to IV,
   - Poor risk disease (age ≥ 11 years old and COG Stage IV ovarian, COG Stage III or IV EG, or IGCCC (see Appendix V) intermediate or poor risk testicular), or
   - Primary CNS germ cell tumor.
   - Germ cell tumor with somatic malignant transformation
   - Spermatocytic seminoma

___2. Patients must have had no prior systemic therapy for the current cancer diagnosis.

___3. Patients must have had no prior radiation therapy with the exception of CNS irradiation of brain metastases. (This exception only applies to SR1 patients; any patients over age 11 with distant metastases to brain [Stage IV disease] would be considered poor risk and therefore not eligible for this trial.)

___4. Patients with significant, pre-existing co-morbid respiratory disease that contraindicate the use of bleomycin, are ineligible for the standard risk arms of the trial.

___5. Pregnancy and Breast Feeding
   These criteria apply ONLY to patients who will receive chemotherapy (SR1 and SR2 patients).
   - Female patients who are pregnant since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required for female patients of childbearing potential.
   - Lactating females who plan to breastfeed their infants.
   - Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation.

___6. Concomitant Therapy
   - Sodium Thiosulfate (STS) should not be administered to any patient on this trial.

REQUIRED OBSERVATIONS:

Low Risk Stage I Grade 2, 3 Ovarian Immature Teratoma
Required Observations at baseline

Required Studies to be Obtained
- History & physical exam with VS
- Performance status
- α-FP, β-HCG

Recommended Baseline Imaging to be Obtained
- Abdominal/Pelvic CT or MRI
- Chest CT
- CT or MRI of brain only if clinically indicated

Participation in Optional Banking Studies is strongly encouraged. See Section 15.0 and Appendix VIII for Optional Banking Specimen collection schedules.
Low Risk Stage I MGCT
Required and Optional Observations

Required Studies to be Obtained

- Performance status
- $\alpha$-FP, $\beta$-HCG, LDH
- Serum (see Section 15.1) Testes only

Recommended Baseline Imaging to be Obtained

- CT or MRI of primary site - Extragonadal
- Testicular ultrasound - Testes
- Abdominal/Pelvic CT or MRI – All patients
- Chest CT - All patients
- CT or MRI of brain - Only if clinically indicated

Participation in Optional Banking Studies is strongly encouraged. See Section 15.0 and Appendix VIII for Optional Banking Specimen collection schedules.

Low Risk Stage I Seminoma Testicular MGCT
Observations—Low Risk Stage I Seminoma Testicular MGCT, All Ages

All required baseline studies must be performed within 7 days prior to the date of enrollment unless otherwise indicated below.

Imaging performed up to 8 weeks prior to the date of enrollment does not need to be repeated.

Note: The imaging modes and schedules listed here are not intended to replace institutional guidelines and are recommendations, not requirements.

Collection of serum specimens for banking for future research is REQUIRED for seminoma patients enrolled on this trial. See Section 15.0 and Appendix VIII for the Required and Optional Specimen Banking collection schedules.

Required Studies and Specimens to be Obtained

- Performance status
- $\alpha$-FP, $\beta$-HCG, LDH
- Serum (see Section 15.1) ²

Recommended Baseline and Relapse Imaging to be Obtained

- CT or MRI of primary site
- Testicular ultrasound
- Abdominal/Pelvic CT or MRI
- Chest CT
- CT or MRI of brain (Only if clinically indicated)

Optional Banking Studies (see Section 15.2 for complete details)

- Tumor Tissue (At diagnostic surgery)

1 If available, please document all tumor markers recorded prior to enrollment in RAVE.
2 Serum specimens should ideally be drawn as specified within +/- 14 days of the requested timepoint.
Required and Optional Observations - Standard Risk 1: Arm CEb – Cycle 1

- History, physical exam, Ht, Wt
- Performance status
- CT or MRI of brain, if clinically indicated
- Chest CT
- CT or MRI of abdomen/pelvis (all primary sites)
- Imaging of the primary site:
  - If primary site is testicular: Ultrasound of testes
  - If primary site is extragonadal: CT or MRI of primary site
  - If primary is ovarian: CT or MRI of abdomen/pelvis
- CBC, differential, platelets
- Electrolytes including Ca, PO₄, Mg⁺⁺
- BUN, creatinine
- AST, ALT, alkaline phosphatase, bilirubin
- Total serum protein/albumin
- Urinalysis
- α-FP, β-HCG, LDH (see Section 4.4.4)
- Audiogram/BAER (submit for rapid central review; see Appendix X) may be obtained within 8 weeks prior to the start of therapy
- Pulmonary function tests
- Pregnancy test for all females of childbearing potential
- Discuss fertility preservation with both genders.
- Optional banking specimens (see Section 15.0 and Appendix VIII)*

* Only obtain in patients who have consented to participation in this component of the trial.
Required and Optional Observations– Standard Risk 1: Arm PEb – Cycle 1

- History, physical exam, Ht, Wt
- Performance status
- CT or MRI of brain, if clinically indicated
- Chest CT
- CT or MRI of abdomen/pelvis (all primary sites)
- Imaging of primary site:
  - If primary site is testicular: Ultrasound of testes
  - If primary site is extragonadal: CT or MRI of primary site
  - If primary is ovarian: CT or MRI of abdomen/pelvis
- CBC, differential, platelets
- Electrolytes including Ca, PO4, Mg++
- BUN, creatinine
- AST, ALT, alkaline phosphatase, bilirubin
- Total serum protein/albumin
- Urinalysis
- α-FP, β-HCG, LDH (see Section 4.7.4)
- Audiogram/BAER (submit for rapid central review, see Appendix X) may be obtained within 8 weeks prior to the start of therapy
- Pulmonary function tests
- Pregnancy test for all females of childbearing potential
- Discuss fertility preservation with both genders.
- Optional banking specimens (see Section 15.0 and Appendix VIII)

* Only obtain in patients who have consented to participation in this component of the trial.
Required and Optional Observations – Standard Risk 2: Arm BEC – Cycle 1

- History, physical exam, Ht, Wt
- Performance status
- CT or MRI of brain, if clinically indicated
- Chest CT
- CT or MRI of abdomen/pelvis (all primary sites)
- Imaging of primary site:
  - If primary site is testicular: Ultrasound of testes
  - If primary site is extragonadal: CT or MRI of primary site
  - If primary is ovarian: CT or MRI of abdomen/pelvis
- CBC, differential, platelets
- Electrolytes including Ca, PO₄, Mg⁺⁺
- BUN, creatinine
- AST, ALT, alkaline phosphatase, bilirubin
- Total serum protein/albumin
- Urinalysis
- α-FP, β-HCG, LDH (see Section 4.10.4)
- Audiogram/BAER (submit for rapid central review, see Appendix X) may be obtained within 8 weeks prior to the start of therapy
- Pulmonary function tests
- Pregnancy test for all females of childbearing potential
- Sperm banking for male patients prior to start of treatment (optional)
- Discuss fertility preservation with both genders.
- Optional banking specimens* (see Section 15.0 and Appendix VIII)
- PRO and QOL* (See Section 16.0)

* Only obtain in patients who have consented to participation in this component of the trial.

Required Observations and Optional– Standard Risk 2: Arm BEP – Cycle 1

- History, physical exam, Ht, Wt
- Performance status
- CT or MRI of brain, if clinically indicated
- Chest CT
- CT or MRI of abdomen/pelvis (all primary sites)
- Imaging of primary site:
  - If primary site is testicular: Ultrasound of testes
  - If primary site is extragonadal: CT or MRI of primary site
  - If primary is ovarian: CT or MRI of abdomen/pelvis
- CBC, differential, platelets
- Electrolytes including Ca, PO₄, Mg⁺⁺
- BUN, creatinine
- AST, ALT, alkaline phosphatase, bilirubin
- Total serum protein/albumin
- Urinalysis
- α-FP, β-HCG, LDH: Day 1, 8 and 15 (see Section 4.13.4)
- Audiogram/BAER (submit for rapid central review, see Appendix X) may be obtained within 8 weeks prior to the start of therapy
- Pulmonary function tests
- Pregnancy test for all females of childbearing potential
- Sperm banking for male patients prior to start of treatment (optional)
- Discuss fertility preservation with both genders.
- Optional banking specimens* (see Section 15.0 and Appendix VIII)
- PRO and QOL* (See Section 16.0)

* Only obtain in patients who have consented to participation in this component of the trial.
TREATMENT PLAN:

EXPERIMENTAL DESIGN SCHEMA: LOW RISK (LR)

*Post-op tumor markers need to be lower (falling) compared to pre-op tumor markers.
Note: IGCCC criteria DO NOT apply to Low Risk/Stage I patients
EXPERIMENTAL DESIGN SCHEMA: POST-SURGERY EVALUATIONS FOR STAGE I
GRADE 2, 3 OVARIAN IMMATURE TERATOMA

Post-Surgery Response Evaluation

- **Tumor Markers**
  - Normal*
  - Elevated
  - Rising
    - Follow according to Section 4.2.2 until normal or rising

- **Tumor Imaging**
  - Surveillance imaging to look for a mass

**New mass**
- Tumor Markers Elevated
  - Surgery
    - Immature Teratoma
      - Consider Enrollment on Standard Risk Arm
    - Malignant GCT

- Tumor Markers Normal*
  - Surgery
    - Mature Teratoma
    - Immature Teratoma
    - Mature Teratoma with somatic malignancy

**No mass**
- Tumor Markers Elevated
  - See Section 4.2.2

- Tumor Markers Normal*
  - Biochemical CR
  - Consider Enrollment on Standard Risk Arm

* Tumor markers are considered normal for this protocol if α-FP and β-HCG are less than 5 times the upper limit of institutional normal.
EXPERIMENTAL DESIGN SCHEMA: POST-SURGERY EVALUATIONS FOR STAGE I MALIGNANT GCT (SEMINOMA AND NON-SEMINOMA)

Post-Surgery Response Evaluation

Tumor Markers

Normal*  
Elevated*  
Rising

Follow (according to Section 4.3.3) until either normal or rising

Biochemical CR

Consider Enrollment on Standard Risk Arm
See Section 4.3.3 (Seminoma patients are not eligible)**

Tumor Markers Normal

Surgery

Teratoma

Pathologic CR

Tumor Markers Elevated

Tumor Markers > 5x ULN and Rising

New mass

Consider Enrollment on Standard Risk Arm
See Section 4.3.3 (Seminoma patients are not eligible)**

Viable Cancer

Rising

* Tumor markers are considered normal for this protocol if α-FP and β-HCG are less than 5 times the upper limit of institutional normal.
** If there is evidence of recurrence, seminoma patients are not eligible for the SR arms and should be treated at the discretion of the treating physician.
EXPERIMENTAL DESIGN SCHEMA: STANDARD RISK 1 (SR1)

Standard Risk 1 (SR1)
- Age 0 < 11 years
- Stage COG II - IV extracranial GCTs, all sites
- Malignant GCT (yolk sac tumor, embryonal carcinoma or choriocarcinoma)
- IGCCC criteria DO NOT APPLY to SR1 patients

Stage I Seminoma patients are not eligible for the SR arms of AGCT1531

Consent and Enrollment onto AGCT1531 → Randomization →

CEb → 4 cycles of therapy → See Post-Chemotherapy Evaluations Experimental Design Schema

PEb → 4 cycles of therapy

C = CARBOplatin
P = CISplatin
E = Etoposide
b = Bleomycin
**EXPERIMENTAL DESIGN SCHEMA: STANDARD RISK 2 (SR2)**

Standard Risk 2 (SR2)
- Age ≥ 11 to < 25 years
- Ovarian, COG Stage II – III, FIGO IC-III
- Extragonadal, COG Stage II
- Testicular, COG Stage II – IV and IGCCC Good Risk*
- Malignant GCT (yolk sac tumor, embryonal carcinoma or choriocarcinoma)

Stage I Seminoma patients are not eligible for the SR arms of AGCT1531

Consent and Enrollment onto AGCT1531 → Randomization →

**BEC**
- 3 cycles of therapy

**BEP**
- 3 cycles of therapy

See *Post-Chemotherapy Evaluations: Experimental Design Schema*

B = Bleomycin
E = Etoposide
C = CARBOplatin
P = CISplatin

*IGCCC: Use post-onc tumor marker levels to determine IGCCC risk category. IGCCC criteria apply ONLY to patients with a testicular primary tumor.
EXPERIMENTAL DESIGN SCHEMA: POST-CHEMOTHERAPY EVALUATIONS

* Tumor markers are considered normal for this protocol if α-FP and β-HCG are less than 5 times the upper limit of institutional normal.
**TOXICITIES AND DOSAGE MODIFICATIONS:**
See Section 5.0.

**SPECIMEN REQUIREMENTS:**
See Section 15.0 – Required and Optional Banking Studies

Tissue (if not enrolled on APEC14B1)
- Snap frozen tumor tissue from primary and any metastatic site
- A block or 20 unstained slides cut sequentially from one representative block

Blood* - 5 mL in EDTA

Serum* - 5mL in a red top, spin and freeze

Plasma* - 10mL in EDTA, spin and freeze

Urine* - 10mL

*standard risk patients

**Required Serum Specimens**

**Blood collection:** 5 mL of blood in a red top tube should be collected and processed into serum at baseline and as indicated in Section 15.1
- Allow to clot at room temperature for up to 60 minutes, spin at 1500g for 15 minutes at room temperature. Split serum into 2 cryovials per time point.
- Label and ship per guidelines in 15.1