

CHR# H7015-06457-15

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Appendix A

**Bone Marrow Biopsy, Peripheral Blood Stem Cell Harvest & Administration
Care During Myelosuppression**

¹³¹I-Labelled MIBG

**(Metaiodobenzylguanidine) Therapy for Metastatic
or Unresectable Pheochromocytoma and other Related Tumors**

A Phase II Study CHR#H7015-06457-15 CC# 03991

INVESTIGATORS

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Indication for Iliac Crest Bone Marrow Biopsy: Extensive bone metastases (≥ 4 areas of bone metastases of > 1 cm diameter).

Contraindication for Peripheral Blood Stem Cell Collection: Bone marrow involvement with tumor on iliac crest bone marrow biopsy.

Indications for Peripheral Blood Stem Cell Collection

- 1) Proposed dose of ¹³¹I-MIBG > 12 mCi/kg *or* **> 500 mCi.**
- 2) Significant anemia, thrombocytopenia, or leukopenia.
 - Significant anemia is defined as: HCT $< 30\%$, or Hgb < 10.4 gm/dL, or RBC $< 3.6 \times 10^6/\mu\text{L}$.
 - Significant thrombocytopenia is defined as: platelet count $< 100 \times 10^3/\mu\text{L}$.
 - Significant leukopenia is defined as: leukocyte count $< 2.5 \times 10^3/\mu\text{L}$.

Patient Eligibility Requirements For Peripheral Blood Stem Cell Collection

- 1) Karnofsky Performance Status \geq 60%.
- 2) No active infection.
- 3) No evidence of tumor involving the bone marrow based upon clinical absence of significant bone metastases on whole-body ^{123}I -MIBG scan and MRI/CT scan. Patients with significant bone metastases (\geq 4 areas of metastases to bone of $>$ 1 cm diameter) will require an iliac crest bone marrow aspirate and biopsy within one month of stem cell collection. Peripheral blood stem cell collection may be performed on selected patients with bone marrow involvement by tumor.
- 4) Neutrophil count over 1,500/ μg and platelet count over 140,000 μL documented within one week of peripheral blood stem cell collection.

Autologous Peripheral Blood Stem Cell Harvesting

- 1) G-CSF will be administered to stimulate stem cell production.
- 2) Peripheral blood stem cells will be harvested (after G-CSF stimulation) by leukapheresis of blood drawn from the patient via central venous catheter and then reinfused.

Goals for Peripheral Blood Stem Cell Collection

- 1) Target goal is a CD34+ cell dose \geq $2.5 \times 10^6/\text{kg}$ body mass.
- 2) Minimum collection for eligibility will be a CD34+ cell dose \geq $2.0 \times 10^6/\text{kg}$ body mass.

Indication for Administration of Cryopreserved Autologous Peripheral Blood Stem Cells:

Prolonged ($>$ 2 weeks) significant cytopenia (e.g., ANC $<$ 200/ μL , platelet count $<$ 20,000/ μL , or Hct $<$ 25%).

Reduced Dose of ^{131}I -MIBG Required for Patients Without Cryopreserved Autologous Peripheral Blood Stem Cells: \leq 12 mCi/kg *and* \leq 500 mCi.

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Supportive Care During Neutropenia May Include:

- 1) For absolute neutrophil count (ANC) < 500/ μ L, Filgrastim (GCSF) may be given at a dose of 5 μ g/kg sc daily until ANC rises above 5,000/ μ L.
- 2) Acyclovir to prevent reactivation of SHV, H2V.
- 3) Septra for pneumocystis prophylaxis.
- 4) Irradiated blood products - to prevent engraftment of unrelated lymphocytes in blood products.
- 5) IV Ig until B-cell function returns.

Supportive Care During Thrombocytopenia May Include:

- 1) Platelet transfusions for patients whose platelet count drops to < 10,000/ μ L or who develop significant bleeding with platelet counts < 40,000/ μ L. Use irradiated platelets in the presence of neutropenia.
- 2) Avoidance of anticoagulants such as heparin and coumadin; avoidance of drugs that inhibit platelet aggregation, including aspirin, dipyridamole, clopidogrel, and large doses of vitamin E.
- 3) Avoidance of drugs that can cause gastric ulceration, especially NSAIDs.

Supportive Care During Anemia May Include:

- 1) Erythropoietin (EPO): Use of epoetin or darbepoetin is permitted at the discretion of the treating physician for HCT \leq 25% or persistent anemia.
- 2) Packed RBC transfusions are permitted at the discretion of the treating physician for HCT \leq 25% or persistent anemia. Use irradiated blood in the presence of neutropenia.