

# 88-007

NAV1.954699.002

CLINICAL INVESTIGATION STUDY PROPOSAL

- I. Activity: Nuclear Medicine Branch, Radiology Department, Naval Hospital, NMCNCR, Bethesda. Maryland, 20814
  
- II. Title: Phase III Study of <sup>131</sup>I-meta-iodobenzlguanidine sulfate (<sup>131</sup>I-mIBG) for localization of the adrenal medullae of humans.
  
- III. Investigators:
  - A. Principal:  
 Naval Hospital, NMCNCR, Bethesda, MD  
 CDR Eugene D. Silverman, MC USN, Head, Nuclear Medicine Division,  
 Radiology Department  
 Telephone: 295-4982  
  
 2% of time required for study  
 Projected rotation date: July 1989
  - B. Associates:  
 Naval Hospital, NMCNCR, Bethesda, MD  
 LCDR Aaron Micheal Kistler, MC USN  
 Resident in Nuclear Medicine  
 Telephone: 295 4960  
  
 2% of time required for the study  
 Projected rotation date: SEP 1989
  - C. Naval Hospital, NMCNCR, Bethesda, MD  
 Howard Stoops, RPh, CNPh  
 Nuclear Pharmacist  
 Radiology Department  
 Telephone: 295-~~6000~~ 4985  
  
 2% of time required for the study
  - D. Estimated Duration of Study: 5 years
  
- IV. Identification of Drug and Devices to be Used in the Study:  
<sup>131</sup>Iodine-meta-iodobenzylquanidine sulfate(<sup>131</sup>I-mIBG) for its localization in adrenal medullae of humans (no trade name).
  
- V. Manufacturing Information:
  - A. Source of the drug: Nuclear Pharmacy  
 University of Michigan Hospitals  
 University Hospital B1G412/0028  
 1500 East Medical Center Drive  
 Ann Arbor, MI 48109/0028
  - B. Dosage Form: <sup>131</sup>I-mIBG, intravenous Injection.
  - C. FDA Forms - FD1571, 1572, 1573: See enclosed forms.

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ENCLOSURE (2)

D. Cost to CIP for drugs and devices:

Outside of incidental lab supplies such as needles and syringes the only items required for special purchase will be the  $^{131}\text{I}$ mIBG. The U. of Michigan charges \$660.00 per vial to cover the its cost of manufacture, and this will provide enough material to scan two patients. The radiopharmaceutical will be acquired with departmental funds. The radiopharmaceutical will be stored in a locked refrigerator located in the radiopharmacy and will not be resold to any other party.

VI. Preclinical information and pharmacology: See enclosed manufacturers information.

VII. Clinical Information:

A. Objectives

- 1) To evaluate the use of  $^{131}\text{I}$ mIBG as an aid in the diagnosis, evaluation and localization of pheochromocytomas, paragangliomas, neuroblastomas and/or adrenal medullary hyperplasia.

B. Background:

- 1) In preliminary distribution studies, at the University of Michigan,  $^{125}\text{I}$ -mIBG demonstrated a specific affinity for adrenal medullae of dogs. Subsequently, they successfully imaged the adrenal medullae of dogs and monkeys at 3-5 days following administration of  $^{131}\text{I}$ -mIBG. The University of Michigan Nuclear Medicine and its clinical investigators have completed a large number of human studies in which the clinical value of the radiopharmaceutical has been established.

There are currently no NDA-approved radiopharmaceuticals available for diagnostic imaging of adrenal medullae, pheochromocytomas, paragangliomas or neuroblastomas (tumors histologically related to the adrenal medullae). The use of  $^{131}\text{I}$ -mIBG would be of considerable value in the diagnosis and localization of intra- and extra-adrenal pheochromocytomas and neuroblastomas during their early stages of development prior to metastasis. The importance of such an agent is obvious when one considers that neuroblastomas are the second leading cause of death in children due to cancer. This agent may prove useful in evaluating the status of the adrenal medullae (i.e., medullary hyperplasia) in patients highly suspect for the future development of medullary disease(i.e. MEN II, neurofibromatosis).

2) Protocol Design

- a) Those patients having pheochromocytoma, paraganglioma or medullary hyperplasia will be admitted to the study after referral to Nuclear Medicine by a primary physician.
- b) A total of 100 patients will be studied.
- c) Because of the occurrence of these lesions in both sexes and at any age, all suspected patients will be studied. Those who are pregnant or breast feeding, and those in whom the possibility of pregnancy has not been ruled out will be excluded from this study. When administered to children (under age 18) the dose of 0.5 mCi will be adjusted on the basis of body weight using Clark's Rule.

3) Dosage and Imaging Protocol:

- a) The uptake of free  $^{131}\text{I}$ -iodide by the thyroid will be prevented by the administration of SSKI (1 drop t.i.d.) beginning 1 day before and continuing 6 days after administration of  $^{131}\text{I}$ -mIBG.
- b) patients over 18 will receive 0.5 mCi. In patients under 18 years of age, the dosage will be adjusted on the basis of body weight using Clark's rule.

$$\frac{(\text{patient weight})(\text{adult dose})}{150 \text{ lbs}}$$

- c) Routine images will be obtained 48 hours following the injection of  $^{131}\text{I}$ -mIBG. Additional imaging may be performed at 24 and 72 hours at the discretion of the Nuclear Medicine physician.

4) Radiation Dosimetry for injected  $^{131}\text{I}$ -mIBG:

ESTIMATED INTERNAL RADIATION DOSE per 0.5 mCi  $^{131}\text{I}$ -mIBG

Organ	Rads/0.5 mCi
Thyroid*	17.3
Adrenal Medullae	49.7
Adrenal Cortex	0.46
Ovary(Testes)	0.48
Liver	0.18
Pancreas	0.26
Spleen	0.74
Kidney	0.17
Whole Body	0.06

\* Data from unblocked thyroid. Radiation dose to thyroid resulting from  $^{131}\text{I}$ -Iodide liberated in vivo will be further reduced by administration of SSKI (See B.3.a. Dosing and Imaging Protocol).

VIII. Informed Consent: See enclosed Informed Consent Form.

IX. Qualifications of Investigators: See enclosed curriculum vitae.