SUBJECT VISIT PLAN RECORD

Inclusion Criteria

Patients with suspected PPGLs

Male and female patients (all ages, including children above 5 years) with suspected PPGLs are included on the basis of one or more of the following:

(i) Patients with a previous history of PPGLs.
(ii) New onset of hypertension or hypertensive episodes and/or symptoms suggestive of PPGLs (sweating, headache, pallor, palpitations, or other suspicious spells).
(iii) Therapy-resistant hypertension, defined as an office blood pressure of >140/90 mmHg despite treatment with >3 antihypertensive agents at full dose (including a diuretic).
(iv) Family history of PPGL or genetic mutations known to predispose individuals to develop PPGLs.
(v) Presence of an adrenal or retroperitoneal mass discovered incidentally during abdominal imaging studies carried out for investigations unrelated to clinical suspicion of PPGLs.
(vi) Any other situation involving reasonable clinical suspicion of a PPGL (e.g., patients with a vasopressor response during anesthesia, surgery or angiography).

Patients with suspected GEP tumors

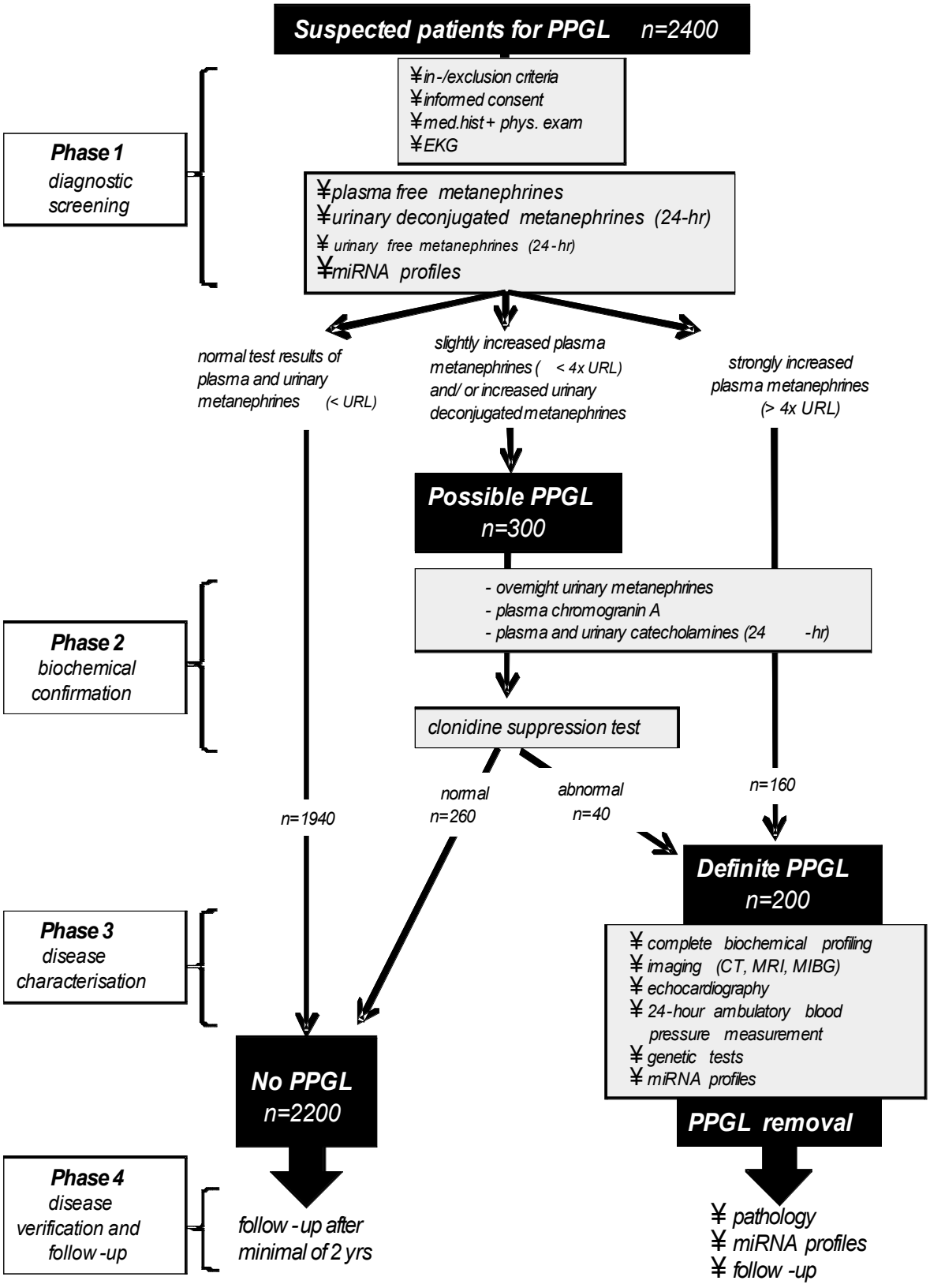
Adult male and female patients (all ages above 18 yr) with proven or suspected GEP tumors are included on the basis of one or more of the following:

(i) Patients referred or recruited because established GEP tumors.
(ii) Patients suspected to have GEP tumors based on clinical signs and presenting features (e.g., flushing, diarrhea, steatorrhea, wheezing, dyspepsia, ulcers, hypoglyceamia, heart disease, deep vein thrombosis, anorexia, nausea, vomiting, constipation, hypotension, fainting, skin disorders, dumping syndrome, pernicious anaemia, autoimmune disorders, diabetes, gall bladder disease).
(iii) Patients suspected to have GEP tumors based on previous biochemical testing and/or imaging studies.

Exclusion Criteria

(i) Subjects with impaired mental capacity that precludes informed consent.
(ii) Subjects who require medications that would interfere with or invalidate primary outcome parameters (e.g., tricyclic antidepressants).
(iii) Pregnant women will not be included as part of either normotensive or hypertensive control groups. Apart from this pregnancy or advanced age does not constitute criteria for exclusion from the protocol. However, pregnant women are excluded from receiving clonidine under the protocol and from all portions of the protocol involving administration of radioactivity. In women of childbearing age (up to age 50) a pregnancy test is performed. In those with a positive result, MRI will be used as an imaging modality but no PET scanning, MIBG scanning or contrast CT will be performed under the protocol.
(iv) Children will not be included as part of either normotensive or hypertensive control groups. Children below 5 years of age are also excluded from all portions of the protocol. Apart from the above, children aged 5 to 18 yrs are not excluded from the protocol. CT scans, MIBG scans and fluororodeoxyglucose PET scans will be offered to children as part of the protocol and as clinically indicated. However, children are excluded from the clonidine test under the protocol.
(v) Patients at risk from injury from the MRI magnet due to implantable metal or who suffer from anxiety in enclosed spaces are excluded from parts of the study involving MRI.

Flow chart for patients with PPGLs illustrating the four phases of the study,
(the summarized procedures for each phase and the numbers of patients expected to participate through each phase)



PHASE 1

1. Last Name: _____ 2. First Name: _____

3. Gender: _____ 4. DOB: _____

4. Address: _____

6. City: _____ 7. Post Code: _____

8. Tel (home): _____ 9. Mobile: _____

10. Email: _____

11. NOK:

A: Last Name: _____ B: First Name: _____

C: Address: _____

D: City: _____ E: Post Code: _____

F: Tel (home): _____ G: Mobile: _____

12. Referring or Personal Physician: _____

13. Study Center: _____

14. Subject type: _____

15. Entry/protocol: _____ If no, reason: _____

Unique patient identifier and Date Consent signed

16. Main inclusion criterion:

- ☐ Suspicion based primarily on signs and symptoms
- ☐ Therapy resistant hypertension
- ☐ Incidental finding on imaging for unrelated condition
- ☐ Routine screening due to known mutation or hereditary syndrome
- ☐ Routine screening due to previous history of pheochromocytoma
- ☐ Other: _____

17. Date: H&P Performed: _____ 18. EKG performed: _____

Affix HEP MET Record Label with date of sample	Affix URIN 24 MET Record Label with date of sample	Affix SER RNA Record Label with date of sample

18. In case of suspected or known genetic mutation:

Affix EDTA DNA Record Label with date of sample

Genetics:

☐ positive ☐ negative

In case of positive genetics see special procedures

Genetic Intitute Referral:

PHASE 1 (additional sampling for patients with suspected GEP-tumor)

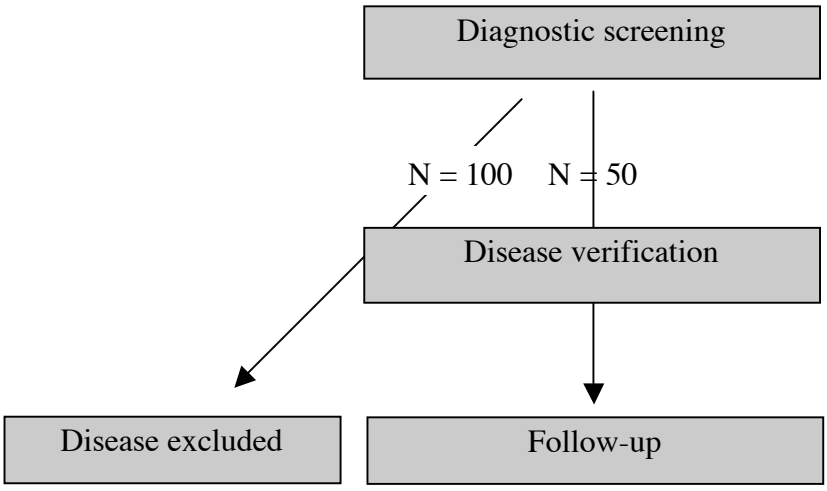
1. measurement of plasma Chromogranin A (EDTA): _____

2. measurement of plasma Serotonin (CTAD): _____

3. measurement of serum Serotonin: _____

4. urine 5HIAA (24 h; acidified): _____

Special Flow Chart for Patients with suspected GEP-Tumor



5. Telephone follow-up: _____

6. persisting signs/symptoms: ☐ YES ☐ NO

History and Physical examination

History:

Medications:

Antihypertensive Medications:

Other prescribed and over the counter medications or dietary:

Specific questions:

A)

History of hypertension

Patient has history of hypertensio ☐ If yes, since whe ☐ Year

If yes, hypertension sustained or episod ☐

B)

Medical History

Patient has history of previous PPGL ☐ If YES, number of tumors ☐

	Date diagnosed Year	Mth	Tumor Resected	Tumor location A or E	Details	Dimensions (cm) x	y	z
1								
2								
3								
4								
5								

Patient has residual disease ☐ Residual disease is metastatic ☐

If YES, locations and no. of lesions

Bones	Lymph nodes	Lungs	Liver

History of cardiovascular or ☐ History of other neoplasms ☐

If YES, detail what disease		**If YES, detail what neoplasms**	
Diabetes mellitus	☐	Skin	☐
Cardiomyopathy	☐	Central nervous system	☐
Heart failure	☐	Gastrointestinal	☐
Coronary artery disease	☐	Pancreas	☐
Myocardial infarction	☐	Urogenital	☐
Cerebrovascular disease	☐	Lung	☐
Renal vascular disease	☐	Bone/Con. Tissue	☐
Renal insufficiency	☐	Breast cancer	☐
Shock	☐	Prostate cancer	☐
Multiple organ failure	☐	Leukemia/Lymphoma	☐
Other	☐	Thyroid	☐
		Other	☐

Specific questions:

C)

Signs & symptoms

Symptom(s) Present	Presence in past 30 days	Symptom associated with others	Frequency of symptom	Duration of symptom occurrence
Headaches				
Sweatiness				
Palpitations				
Tremor				
Pallor				
Flushing				
Panic/Anxiety				
Nausea/Vomitting				
Weakness/Fatigue				
Pain in abdomen				
Pain in chest				
Constipation				

D)

Hereditary PPGL syndromes

Patient has evidence of hereditary syndrome y/n	
Evidence includes family history of PPGL`s y/n	
Indicate number of 1e degree relatives with PPG	
Indicate number of 2e degree relatives with PPGL`s	
Evidence includes clinical stigmata y/n	
Indicate syndrome	
Specific details	
Evidence includes clinical stigmata y/n	
Specific affected gene(s)	

VHL		MEN2		NF1	
Ren cyst/carc		MTC		Cafe au lait	
CNS HBLAST		PTH		Neurofibroma	
Ret. Angiom		Muc.Neur.		Freckling skin	
Pancr cyst/ad		Marfanoid		Opt. glioma	
Endolymph.TU				Lisch noduli	
Epid.cysts				Oss. Lesions	

Other Considerations:

_____

_____

_____

_____

_____

_____

Physical Examination:

Blood Pressure L: _____ Pulse L: _____ Waist: _____

Blood Pressure R: _____ Pulse R:_____ Height: _____

2. Blood Pressure: _____ 2. Pulse: _____ Weight: _____

3. Blood Pressure: _____ 3. Pulse: _____ Allergy: _____

Physical Examination (continued):

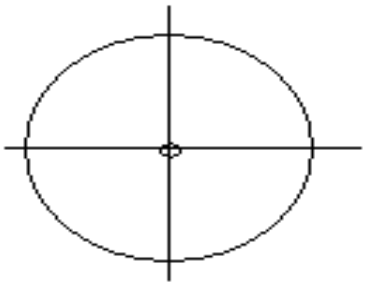
Skin: • necrolytic migratory erythema: Yes ☐ No ☐

Head: Eyes:

Mouth/Pharynx: Thyroid:

Thorax: Heart:

Abdomen: Extremities:



CNS:

PHASE 2 - (ENTRY-DATE: _____)

Has patient changed medications since previous phases: ☐ NO

Changed Medications:

Antihypertensive Medications: _____

_____

_____

_____

Other prescribed and over the counter medications or dietary:

_____

_____

_____

_____

_____

PHASE 2 for pregnant woman and pregnant children/teens (5-18 years)

1. Pregnancy test positive: ☐ 2. Date Pregnancy test performed: _____

Affix HEP CLON BL Record Label with date of sample	Affix EDTA CGA Record Label with date of sample
Affix URIN ON MET Record Label with date of sample	Affix URIN DY CAT Record Label with date of sample

PHASE 2 for children/teens (5-18 years) (Pregnancy test negative)

G. Eisenhofer	Affix HEP CLON BL Record Label with date of sample	21/9/11	Affix EDTA CGA Record Label with date of sample	PMT STUDY

Affix URIN ON MET Record Label with date of sample	Affix URIN DY CAT Record Label with date of sample

PHASE 2 (Pregnancy test negative, no child)

Time: _____ Time: _____

BP BL: _____ (mmHg) BP 3hr: _____ (mmHg)

Pulse BL: _____ Pulse 3hr:_____

Affix HEP CLON BL Record Label with date of sample	Affix HEP CLON 180 Record Label with date of sample

Test cancel: ☐ YES, REASON

COMPLICATIONS:

☐ **Dry mouth**	☐ **Ringing in the ears**	☐ **Confusion**
☐ **Flushing**	☐ **Lightheadedness**	☐ **Drowsiness**
☐ **Headache**	☐ **Fainting**	☐ **Tiredness**
☐ **Nausea**	☐ **Vomiting**	

☐ **Other:** _____

Affix URIN ON MET Record Label with date of sample	Affix URIN DY CAT Record Label with date of sample	Affix EDTA CGA Record Label with date of sample

PHASE 3 - (ENTRY-DATE: _____)

PHASE 3 for pregnant woman and pregnant children/teens (5-18 years)
Pregnancy test positive □ (DATE:)

	Ordered (Date)	Performed (Date)
A. ABPM:	_____	_____
B. Echocardiography:	_____	_____
C. MRI-Scan:	_____	_____

Affix HEP CAT Record Label with date of sample	Affix EDTA CGA Record Label with date of sample	Affix URIN 24 Record Label with date of sample

PHASE 3 for children/teens (5-18 years) (Pregnancy test negative)

	Ordered (Date)	Performed (Date)
A. ABPM:	_____	_____
B. Echocardiography:	_____	_____
C. MRI-Scan:	_____	_____
D. MIBG-Scan:	_____	_____
E. Ga-DOTATOC:	_____	_____

Affix HEP CAT Record Label with date of sample	Affix EDTA CGA Record Label with date of sample	Affix URIN 24 Record Label with date of sample

PHASE 3 (Pregnancy test negative, no child)

	Ordered (Date)	Performed (Date)
A. ABPM:	_____	_____
B. Echocardiography:	_____	_____
C. MRI-Scan:	_____	_____
D. CT-Scan:	_____	_____
E. MIBG-Scan:	_____	_____
F. Ga-DOTATOC:	_____	_____

Affix HEP CAT Record Label with date of sample	Affix EDTA CGA Record Label with date of sample	Affix URIN 24 Record Label with date of sample

PHASE 3 – METABOLIC STUDIES (All patients):

Affix SER INS Record Label with date of sample	Affix FLU HBA GLUC Record Label with date of sample

PHASE 4 – EXCLUSION (ENTRY-DATE: _____)

1. Telephone follow-up: _____

PHASE 4 – OPERATION (ENTRY-DATE: _____)

PHASE 4 – post OP (2-4 weeks after surgery)

1. Operation: ☐ YES, DATE OF SURGERY: _____

☐ NO, go to PHASE 4- INOPERABLE PATIENTS

Affix TUMOR Record Label with date of sample

Reason why patient was not operated:

_____

2. Surgical pathology: _____

Affix HEP MET Record Label with date of sample	Affix URIN 24 MET Record Label with date of sample

PHASE 4 – One Year

1. EKG: _____

	Ordered (Date)	Performed (Date)
2. Echocardiography:	_____	_____
3. ABPM:	_____	_____

PHASE 4 – One Year

Affix HEP MET Record label with date of sample	Affix HEP CAT Record Label with date of sample	Affix EDTA CGA Record Label with date of sample

Affix SER RNA Record Label with date of sample	Affix URIN 24 Record Label with date of sample

PHASE 4 – OPERATION

PHASE 4 – YEAR 2 FOLLOW UP

Affix
HEP MET Record
Label with date of sample

PHASE 4 – YEAR 3 FOLLOW UP

Affix
HEP MET Record
Label with date of sample

PHASE 4 – YEAR 4 FOLLOW UP

Affix
HEP MET Record
Label with date of sample

PHASE 4 – YEAR 5 FOLLLOW UP

Affix
HEP MET Record
Label with date of sample

PHASE 4 – SPECIAL PROCEDURES

1. FDG-PET (Pregnancy excluded, no child) in inoperable patients, patients with SDHB mutation or metastatic disease confirmed on MRI/CT or MIBG:

	Ordered (Date)	Performed (Date)
	_____	_____

2. Positive Genetics (SDHB or SDHD mutations):

	Ordered (Date)	Performed (Date)
MRI-scan: (Neck, Thorax, Abdomen)	_____	_____
CT-scan: (Neck, Thorax, Abdomen)	_____	_____

Schedules: