PPMI MODAG-009-P1-01 PET Imaging Substudy

Inclusion/Exclusion Criteria

All inclusion criteria must be marked "Yes" and all exclusion criteria must be marked "No" before proceeding to enrollment. Otherwise, complete "Screen Fail" CRF for this substudy.

A. Assessment Date: __ __ /__ __/ __ __ __ __ (mm/dd/yyyy)

Inclusion Criteria – All Cohorts:

1. Able and willing to provide informed consent.
   ○ Yes ○ No
2. Ability and willingness to comply with all study procedures and requirements.
   ○ Yes ○ No
3. Male or Female (Females must meet additional criteria specified below, as applicable)
   a. Females must be of non-childbearing potential or using a highly effective method of birth control 14 days prior to until at least 24 hours after injection of [^{18}F]-MODAG-009.
      i. Non-childbearing potential is defined as a female that must be either postmenopausal (no menses for at least 12 months prior to PET scan) or surgically sterile (bilateral tubal ligation, bilateral oophorectomy or hysterectomy).
      ii. Highly effective method of birth control is defined as practicing at least one of the following: A birth control method that results in a less than 1% per year failure rate when used consistently and correctly, such as oral contraceptives for at least 3 months prior to injection, an intrauterine device (IUD) for at least 2 months prior to injection, or barrier methods, e.g., diaphragm or combination condom and spermicide. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) is not acceptable.
   b. Females of childbearing potential must not be pregnant, breastfeeding or lactating, or planning pregnancy during the duration of the study.

   ○ Yes ○ No

Inclusion Criteria – Healthy Control:

4. Enrolled in the PPMI 002 Clinical study as a healthy control participant.
   ○ Yes ○ No
5. Any gender aged 50 to 75 years of age.
   ○ Yes ○ No
6. Negative CSF α-synuclein seed amplification assay (SAA)
   ○ Yes ○ No

7. Previously acquired (since inclusion in PPMI) brain MRI without evidence of significant neurological pathology.

   ○ Yes ○ No

8. Movement Disorders Society Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS III) score of <6 at the last PPMI annual visit which is within the past 18 months.

   ○ Yes ○ No

9. Cognitively intact with Montreal Cognitive Assessment (MoCA) >=26 at the last PPMI annual visit which is within the past 18 months.

   ○ Yes ○ No

Inclusion Criteria – Parkinson's Disease and Prodromal PD:

10. Enrolled in the PPMI 002 Clinical study as a Parkinson's Disease (PD) or Prodromal participant.

    ○ Yes ○ No

11. Any gender aged 50 to 80 years of age.

    ○ Yes ○ No

12. Positive CSF SAA.

    ○ Yes ○ No

13. A current or previously acquired brain MRI (since the onset of motor symptoms for PD or since enrolled in PPMI for the prodromal PD) without evidence of significant neurological pathology other than changes expected for PD.

    ○ Yes ○ No

14. Montreal Cognitive Assessment (MoCA) >=24 at the last PPMI annual visit which was within the past 18 months.

    ○ Yes ○ No

Exclusion Criteria:

1. Clinical evidence of other neurodegenerative diseases, such as Alzheimer's disease.

   ○ No ○ Yes

2. Any other medical or psychiatric condition or lab abnormality, which in the opinion of the investigator might preclude participation.

   ○ No ○ Yes

3. Received any of the following drugs: dopamine receptor blockers (neuroleptics), metoclopramide, lithium and reserpine, within 6 months of Baseline Visit.

   ○ No ○ Yes

4. Any other reason that in the opinion of the investigator, including abnormal labs, that could interfere with the safety with radiotracer injection, would render the participant unsuitable for the study enrollment.

   ○ No ○ Yes

5. Participation in an investigational drug trial targeting α-synuclein within the past 6 months prior to enrollment.

   ○ No ○ Yes

6. Currently being treated with and unable to safely hold antiplatelets (other than low dose aspirin up to 100mg/day) or anticoagulants prior to the procedure that might preclude safe attempt of Lumbar puncture, if applicable.

   ○ No ○ Yes

7. Condition that precludes the safe performance of routine lumbar puncture, if applicable, such as prohibitive lumbar spinal disease, bleeding diathesis, or clinically significant and uncorrected coagulopathy or thrombocytopenia.

   ○ No ○ Yes

8. Conditions or medications that preclude safe performance of imaging procedures (MRI or DaTscan), including but not limited to severe claustrophobia, MRI-incompatible metal implants, or known hypersensitivity to imaging agents.

   ○ No ○ Yes

9. Known hypersensitivity to DaTscan or iodine-containing compounds used as premedication for DaTscan. Participants with iodine sensitivity may still complete the imaging without iodine premedication at the investigator's discretion.

   ○ No ○ Yes

10. Use of medications known to interfere with DaTscan imaging (e.g., bupropion, amphetamines, methylphenidate, modafinil, alpha-methyldopa), unless the participant is willing and medically able to discontinue the medication for at least 5 half-lives prior to imaging.

    ○ No ○ Yes