

CHAPTER 30. Participant Study Visits

30.1 Introduction: This Manual of Operations chapter describes study visits for all three groups of participants who consented to participate in the PVDOMICS Study. These three groups of participants include:

- Pulmonary vascular disease (PVD)
- PVD comparators
- Healthy controls

Note: PVD and PVD comparators will undergo the same study protocol. Healthy controls will NOT undergo right heart catheterization (RHC) and V/Q scan.

The PVDOMICS Study is not a treatment trial, other drugs considered necessary for any participant's welfare may be given at any time. Participation in PVDOMICS will not prohibit access to new or novel therapies, but participants will be asked to refrain from participating in a clinical trial involving biologic medications or other PH therapies during the time of participation in PVDOMICS. Medications will not be withheld except for the conduct of specific procedures where withhold of medications is part of routine care.

30.2 Study Visit(s) Overview: PVDOMICS Study visits need to be completed within 6 weeks and participants will undergo many tests and procedures during this time. Some of these tests and procedures will be for clinical care as well as for the PVDOMICS Study. In some cases, historical test data may be used.

Procedures that participants will undergo at each recommended study visit are shown in the table below. The number of visits held will depend on each clinical center's scheduling procedures. The complexity of procedures requires careful planning and scheduling of participants.

IMPORTANT: There are specific tests that **MUST** be completed before or after other tests:

- CBC, CMP, PT/INR, pregnancy test (if applicable) must be completed and resulted before right heart catheterization
- OMICS blood draw #1 must be completed before RHC , CPET, CT (with contrast), and V/Q scan
- All blood draws need to be done either before the V/Q scan or at least 3 days following V/Q
- Pregnancy testing (either blood or urine) needs to be completed and resulted prior to completion of any other testing at each study visit.

It is anticipated that research coordinators and investigators will have screened and contacted the participant in advance of visit 1 in anticipation of testing. For example: Visit 1 requires blood draw in fasting conditions. Thus participants should be asked to come to Visit 1 fasting for a minimum of 8-10 hours.

Table 30.21. RECOMMENDED VISIT SCHEDULE – Note: times are approximate

Test/Procedure	Historical	Visit 1 5 hours	Visit 2 6-8 hours	Visit 3 3-4 hours	Visit 4 1-2 hours	Notes
Consent		X				
Medical and Medication History		X				
Vital Signs: pulse, BP, temperature, respiratory rate		X	X	X		Rest for 15 minutes prior to vital signs
Bioelectrical Impedance/Waist Hip		X				
HRQOL surveys (SF-36, MLHF, emPHasis-10)		X				Completed on site
6MWT		X				
Overnight oximetry	X	X (give)	(return)			Up to one year prior to enrollment
Research labs - (OMICS) blood and urine		X (venous blood)	X			- Cath blood for PVD and comparators - Venous blood for healthy controls - Must be fasting for at least 8-10 hours for OMICS bloods
*Center-measured clinical labs (CBC, CMP, INR,HIV, hepatitis panel, ANA)	See specific test	X				Hgb for DLCO should must be done within 2 wks of PFTs but up to 30 days is allowed
Center-measured pregnancy test (urine or blood)		X	X	X	X	Must be done in all women by CLIA certified lab or by study personnel with CLIA waiver per local institutional protocol
ECG		X				
Spirometry, DLCO, Lung Volumes	X	X				Historical acceptable if within 1 year of enrollment, or 3 months if lung disease is present
Echocardiogram		X				
Right heart catheterization (RHC)			X			Not done in healthy controls
CPET, non-invasive -OR- CPET, invasive (iCPET)			X	X(non-invasive)		- iCPET is center-specific; only on PVD/comparators - May be done at visit 3 if <i>not</i> doing iCPET
Cardiac MRI/MRA			X			
Lung CT	X			X		Historical acceptable if within 1 year of enrollment
**Ventilation-perfusion scan (V/Q)	X			X-last	X	Historical acceptable if within 1 year of enrollment; not done in healthy controls.

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*Center CBC w Diff Results and CMP Results	Lab draw must be no more than 1 month before the Form 100 date.
Center Antinuclear Antibody (ANA) Results	Lab draw must be no more than 45 days before the Form 100 date.
Center Prothrombin Time (PT) Results	Lab draw <u>must be on or after</u> the Form 100 date.
Center HIV Antigen/Antibody Screen and Hepatitis Screen Results	If HIV and Hepatitis screens were positive then no need to repeat; if either HIV and/or Hepatitis screen was negative but more than one year ago, then repeat; If either screen was completed <u>within the past year</u> , no need to repeat screen.

VQ scan required if the participant has lung parenchymal disease and has had a CT angiogram (CTA) in the past year from which the results (images) are provided to the Lung Imaging Core. If needed, VQ scan can be done after lung CT. VQ Scan Tracer (radioactive) is detectable for 1 week in blood and can affect HRCT and may expose lab to radiation. Suggest VQ scan be done last after all blood samples and urine are obtained to avoid tracer exposure of lab personnel to radiation. If urine or blood products are collected after the VQ scan, these samples should be collected a minimum of 3 days after the scan.

30.3

Visit 1, 2 or 3 procedures and tests may be performed over more than one day. For example, the site may choose to consent and perform some of the study items (QOL and history), and schedule the fasting blood draws and other testing on a separate day. These are all still considered visit 1, but dates of testing will be recorded for each item. Visit 1 and 2 could be combined if local IRB allows for total quantity of blood to be drawn.

30.7 Telephone calls

Frequent phone contact with participants will facilitate adherence with visits. Suggested frequency of phone call contact is listed below:

- Reminder phone calls one day prior to each study visit and to remind participants to fast and/or hold certain medications.
- Check-up phone calls at least once (at the mid-point) between consecutive study visits
- Other phone calls may include calls to retune missed calls from participants and any phone calls in response to labs that necessitate scheduling an unscheduled visit.

Visits and Windows

There is no rigid timing between visit 1 and 2 and 3, but it is required that completion of all visits will occur within 6 weeks. Timely visit adherence should be encouraged. **Right heart catheterization (with invasive CPET at centers performing this), echocardiogram, MRI and omics blood draws should be performed within two weeks of each other..**

30.8 Retention

Because this is a procedure-intensive study, some attrition is possible. Therefore retention efforts will focus on ease of visits and informational rewards. Visits will occur at times convenient to the participants. Sites will make every effort to minimize parking inconveniences and other limitations to visits. A monetary compensation for time will be given for each visit. A study coordinator and physician will be available by phone during off-hours to aid in management of procedure or study-related adverse events.

30.9 Priority of Requirements for Passive or Partially Compliant Participants

Once a participant is enrolled, the center will need to continue to follow the participant through all study visits. If the participant at any time states that they no longer want to participate or does not want a specific study procedure done, the Principal Investigator should speak with the participant. If at the end of the discussion, the participant still does not want to be in the study or does not want a specific study procedure done, then complete all data that the participant is willing to complete. It is important that communication with the participant continue. It may be that the participant will return to full procedure capabilities after a period of rest.

30.10 Longitudinal Follow-up

All patients, or their designated contacts, will be contacted by telephone and/or letter at least annually after enrollment up to the end of the study (maximum of 3.5 years) if not seen at the enrolling center

for follow-up. Vital status and occurrence/date of any lung, heart or heart-lung transplantation will be determined from this contact or by using center medical records. Cause of death will be ascertained by the site investigators.

30.11 Adverse Events

Participants will be followed for adverse events occurring during the PVODMICS Study visits and up to 2 weeks after the last study visit. MOP Chapter 48 provides details on reporting adverse events.

Participants experiencing minor illnesses may continue in the study if the nature, severity, and duration of the illness are recorded. Examples of minor illnesses include gastroenteritis and skin disorders. Medications are allowed for treatment of these conditions.

30.11.1 Risk-benefit ratio

It is the belief of the investigators involved in this research that risks of the tests and procedures associated with this study are justifiable given the knowledge to be gained.