

Online Supplement

Original Research

Rationale and Design of the Alpha-1 Biomarkers Consortium Study

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**Members of the Alpha-1 Biomarker Consortium Study Group are listed in the Acknowledgements section.*

APPENDIX

Table 1. Primary inclusion and exclusion criteria for enrollment into the Alpha-1 Longitudinal Biomarker Study

<i>Inclusion Criteria</i>
1. Males and females, age 18 years or older
2. Understand the study procedures, risks, benefits, purpose
3. Able and willing to comply with the study procedures
4. Have PiZZ alpha-1 antitrypsin deficiency
5. Be an existing member of the Alpha-1 Foundation Clinical Cohort (also known as the Alpha-1 Foundation Research Registry)
6. Agree to have the data collected in this study be shared with the Alpha-1 Foundation Research Registry
<i>Exclusion</i>
1. AATD non-PiZZ status, including heterozygous patients
2. Current lung, hematologic, or solid organ malignancy other than skin or cervical Stage 1 cancers within the past 3 years
3. COPD exacerbation or other pulmonary infection within 6 weeks of baseline visit
4. Pregnancy at the time of the screening visit
5. Inability to lie still in a supine position for 15 minutes during CT acquisition
6. Inability to perform quality-controlled lung function testing
7. Allergy to albuterol
8. Currently receiving intravenous or subcutaneous immunoglobulin for any disease state
9. Past or present major surgery on the lungs including pneumonectomy or lobectomy. Wedge resections, past segmentectomy, and pleurodesis surgeries are allowed
10. Previous lung or liver transplantation or currently on the transplant list
11. Current presence of endobronchial coils or valves in the lung
12. Clinically significant bronchiectasis as defined by the investigator. In general, this would exclude patients with chronic infection of the lungs requiring treatment within the past 6 months including non-tuberculous mycobacterial disease, chronic fungal disease, allergic bronchopulmonary aspergillosis, or known colonization of bronchiectasis with pseudomonas or stenotrophomonas species
13. Participation in the active treatment arm of a therapeutic clinical trial at baseline visit unless using one of the Alpha-1 augmentation therapies in alternative doses
14. Patient with Automatic Implantable Cardioverter-Defibrillator and permanent pacemakers
15. Patient receiving biologic immunomodulators that will affect the assessment of the serum biomarkers (as determined by the site PI)
16. Patient with in-dwelling pleural catheters
17. Any condition that in the opinion of the investigator might adversely influence the study outcome

Table 2: Study schedule of events

Procedures	Screen	Visit #1 Baseline	PRO AlphaNet	Phone call	PRO AlphaNet	Phone call	PRO AlphaNet	Visit #2	PRO AlphaNet	Phone call	PRO AlphaNet	Phone call	PRO AlphaNet	Visit #3
Months from baseline visit	-1	0	1-5	6 +/- 1	7-11	12 +/- 1	13-17	18 +/- 3	19-23	24 +/- 1	25-29	30 +/- 1	31-35	36 +/- 3
Informed Consent	X (oral)	X (sign)												
Assessment of Eligibility	X													
Review Medical History	X	X		X		X		X		X		X		X
Review Medication List	X	X		X		X		X		X		X		X
Vitals		X						X						X
Blood draw		X						X						X
Dried blood spot card ¹		X						X						X
Urine Pregnancy Test ²		X						X						X
PFT Spirometry Pre & post		X						X						X
CT scan		X						X						X
Induced Sputum* (varies by site)		X						X						X
Nasal Swab*		X						X						
PROs		X	X ³	X ³	X ³	X ³	X ³	X ⁴	X ³	X ³	X ³	X ³	X ³	X ⁴
Assessment of Events of Clinical Significance		X						X						X

Abbreviations: PRO=Patient Reported Outcomes

¹Dried Blood Spot Card = In addition to study visits, collect DBS cards on onset, 3-day and 7-days post a COPD Exacerbation Event.

²Urine Pregnancy Test = Complete Radiation Pregnancy Form when applicable.

³X= Monthly AlphaNet COPD Exacerbation questionnaire only.

⁴X= Excludes Exposure Questionnaire (administered at baseline visit only).

*= Optional procedures.

Table 3. A1BC Exposure Questionnaire

Smoking	
Have you ever smoked cigarettes? No means less than 20 packs of cigarettes, or 12 ounces of tobacco, or less than 1 cigarette a day for one year at any time in your life.	Yes No
2. How old were you when you first started regular cigarette smoking?	
3. Do you smoke cigarettes (as of one month ago)?	Yes No
4. About how many cigarettes do you smoke per day now?	<i>Individual cigarettes, not packs</i>
5. How old were you when you completely stopped smoking?	
6. On average of the entire time you smoked, how many cigarettes did you smoke per day?	
7. Have you ever smoked a pipe regularly? YES means more than 12 oz of tobacco in a lifetime	Yes No
8. How old were you when you first started to smoke a pipe regularly?	
9. Do you smoke a pipe (as of one month ago)?	Yes No
10. How many ounces of pipe tobacco do you smoke per day now?	
11. How old were you when you completely stopped smoking a pipe	
12. On average of the entire time you smoked a pipe, how many ounces of tobacco did you smoke per week?	
13. Have you ever smoked cigars regularly? Yes means more than 1 cigar a week for one year at any time in your life	Yes No
14. How old were you when you first started to smoke cigars regularly?	
15. Do you smoke cigars now (as of one month ago)?	Yes No

16. How many cigars do you smoke per day?	
17. How old were you when you completely stopped smoking cigars?	
18. On average of the entire time you smoked cigars, how many cigars did you smoke per week?	
Vaping	
19. Have you ever used an electronic cigarette or vape product?	Yes No
20. Did your electronic cigarette or vape product contain any of the substances below?	Nicotine Cannabis / marijuana / THC Don't know Other
21. Do you still use e-cigarettes or vape products?	Yes No
22. How often do you use e-cigarettes or vape products?	Everyday Most days 4+ days per week 1-3 days per week Less than once per week Less than once per month
23. How many years in total have you used electronic cigarettes or vape products?	
Second Hand Smoke	
24. Do you currently live in the same household with someone who smokes tobacco products?	Yes No
25. Have you ever lived in the same household with someone who smoked tobacco products?	Yes No
26. Growing up until age 18, were there any adults in your household who smoked at home?	Yes No
27. For how many years in total did you live in the same household with someone else who smoked tobacco products?	
28. Have you been regularly exposed to tobacco smoke in the last 12 months? (Regularly means on most days or nights)	Yes No
29. Do people smoke regularly in the room where you work?	Yes No
Occupational	
30. What is your occupation?	

31. Does your current job expose you to vapors, gas, dust, or fumes?	Yes Don't know No Not applicable
32. In your longest held job, what kind of work did you do. What was your occupation?	
33. Did your longest job expose you to vapors, gas, dust, or fumes?	Yes Don't know No Not applicable
34. Is an air cleaner/filter used in your residence (stand-alone or central)?	Yes No
35. What type of air filter?	Stand-alone / portable Central Don't know
36. Within the last 12 months have you had wet or damp spots on surfaces inside your home other than in the basement (for example on walls, wall paper, ceilings or carpets)?	Yes No I don't know
37. Has there ever been any mold or mildew on any surface, other than food, inside the home?	Yes No I don't know
38. Do you keep a cat inside the house?	Yes No
39. Do you keep a dog inside the house?	Yes No
40. Do you keep any birds inside the house?	Yes No
Cleaning Chemicals	
41. Are you responsible for cleaning or washing in your home?	Yes No
42. Have you ever worked as a cleaner?	Yes No
43. How many days per week did you use cleaning products?	Never Less than one day per week 1-3 days per week 4-7 days per week
44. How many days per week did you use cleaning sprays?	Never Less than one day per week 1-3 days per week 4-7 days per week

Table 4. Baseline Exacerbation Questionnaire

1. Over the past year, how many times have you experienced worsening ("exacerbations" or "flares") of your lung problems?	Every month Every 3 months Every 4 months Every 6 months Once Never
2. Over the past 2 years, have you coughed up sputum/mucus from your lungs on a regular basis for at least three months each year?	Yes No
3. Over the past 12 months, how many times have you experienced the following? Please note these are number of events and not days of hospitalization	
3a. Admitted to the hospital?	0, 1, 2, 3, >3
3b. Admitted to the intensive care unit?	
3c. Seen in the emergency room?	
3d. Seen by a healthcare practitioner for an unscheduled office visit?	
4. If you were hospitalized over the past year, was the primary reason lung related?	Yes No

Table 5. Monthly Exacerbation Questionnaire

1. Did you have a new upper respiratory infection, cold, or flu-like illness in the last month? Please note that you should not repeat events reported one month ago.	Yes No
2. How did you manage any lung problems you had this past month? Check all that apply	I spoke with my regular primary care physician, nurse practitioner, or physician's assistant. I spoke with my pulmonary specialist. I visited a health care practitioner in his/her office. I went to an emergency room or urgent care center. I treated the problem myself. Not Applicable
3. Over the past month, how many times have you been seen for lung disease and experienced the following? Please note these are number of events and not days of hospitalization	
3a. Admitted to the hospital?	0, 1, 2, 3, >3
3b. Admitted to the intensive care unit?	
3c. Seen in the emergency room?	
3d. Seen by a healthcare practitioner for an unscheduled office visit?	
4. Have you experienced any worsening of respiratory symptoms (an "exacerbation" or "flare") in the last month? Please note that you should not repeat events reported 1 month ago.	Yes No
5. Have you had any of these symptoms within the past month? Check all that apply	a) More shortness of breath b) More cough c) Increased sputum amount d) New wheezing e) Worsening of wheezing f) Sputum changed color g) Fever Not Applicable
5.1. Do you have any of these symptoms now? Check all that apply	a) More shortness of breath b) More cough c) Increased sputum amount d) New wheezing e) Worsening of wheezing f) Sputum changed color

	g) Fever
	Not Applicable
6. Did you have chest imaging (chest X-ray or chest CT) in the past month?	Yes No
7. Did you start oxygen or change your oxygen over the past month?	Yes No
<p>If you need to edit a report from one month ago, please report the changes here.</p> <p>Examples of an updated report would include that the event from last month had not ended at the time of last report and you would like to add the total duration of the event or that you began new treatments not reported previously.</p>	