**Online Supplement**

# Losartan Effects on Emphysema Progression Randomized Clinical Trial: Rationale, Design, Recruitment, and Retention

American Lung Association Airways Clinical Research Centers*

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**eTable 1. Exclusion Criteria**

- Current therapy with angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB)
- Known intolerance to ACE inhibitor or ARB
- History of angioedema
- Conventional indication for ACE inhibitor or ARB (including history of myocardial infarction, known cardiomyopathy
- Renal insufficiency (GFR <30 mL/min by Cockcroft-Gault calculation)
- Current regular use of non-steroidal anti-inflammatory drugs (NSAIDs) defined as daily use 5 or more days of the week for more than one month
- Current treatment with a potassium sparing diuretic
- Potassium supplementation or serum potassium level of ≥ 5.0 mEq/L at V1
- COPD exacerbation requiring treatment within 6 weeks at V1
- Chronic systemic corticosteroid use > 10mg/day of prednisone
- Resting SpO2 <89% on 2L nasal cannula continuous flow; unless at altitude > 4,000 feet, then resting SpO2 <89% on 4L NC continuous flow
- Untreated arterial hypertension (systolic blood pressure >140 mm Hg, diastolic blood pressure > 90 mm Hg)
- Blood pressure less than 90 mm Hg systolic or 60 mm Hg diastolic while standing or sitting
- Known unilateral or bilateral renal artery stenosis >70%
- Previous lung resection surgery
- Evidence of interstitial, occupational or chronic infectious lung disease
- Changes to chest that preclude adequate HRCT imaging (e.g. Metallic objects in the chest such as shrapnel or pacemaker leads)
- For women of child bearing potential, positive pregnancy test or unwillingness to use two methods of birth control or abstinence for the duration of the study
- Major chronic illnesses which in the judgment of the study physician would interfere with participation in the study e.g. including but not limited to: cardiac, renal, hepatic (LFTs>2.5x normal upper limit), neurological, psychiatric, endocrine or neoplastic diseases, uncontrolled diabetes, uncontrolled HIV infection or other immune system disorder, hyperthyroidism, seizure disorders, non–skin cancer, rheumatic diseases
- Failure to keep screening appointments or other indicators of non-adherence
- Inability to be contacted by telephone
- Intention to leave area within 12 months

**eTable 2: Data Collection Schedule**

| Visit | V1 | V2 | V3 | V4 | V5 | V6 | V7 |
|---|---|---|---|---|---|---|---|
| **Target (weeks)** | -4 | 0 | 2 | 12 | 24 | 36 | 48 |
| **Visit window (weeks)** | -4 to 0 | 0 | 2-4 | 10-14 | 22-26 | 34-38 | 46-50 |
| Informed consent, eligibility evaluation | ● | | | | | | |
| Baseline medical history | ● | | | | | | |
| Adverse events/Interval health history | | ● | ● | ● | ● | ● | ● |
| Pregnancy testing as indicated | ● | ● | ● | ● | ● | ● | ● |
| Spirometry (pre and post BD) | ● | | | | ● | | ● |
| Anthropometrics (height & weight) | ● | ● | ● | ● | ● | ● | ● |
| ATS-DLD | ● | | | | | | |
| SGRQ-C mMRC | ●* | ● | | ● | ● | ● | ● |
| CAT | ● | ● | | ● | ● | ● | ● |
| PROMIS-20a | ● | ● | | ● | ● | ● | ● |
| Vital signs, Orthostatic blood pressure check, SpO2 | ● | ● | ● | ● | ● | ● | ● |
| Physical examination | ● | | | | ● | | ● |
| CBC, CMP | ● | | | ● | | | ● |
| Collect blood & urine for biorespository | | ● | | | ● | | ● |
| HRCT | ● | | | | | | ● |
| Treatment assignment | | ● | | | | | |
| Drug distribution | | ● | | ● | ● | ● | |
| Drug titration | | | ● | | | | |
| Drug return/capsule count | | | | ● | ● | ● | ● |
| Exit interview | | | | | | | ● |

* mMRC included in ATS-DLD at V1

Abbreviations:
(V#) Visit Number
(ATS-DLD) modified American Thoracic Society Division of Lung Disease Questionnaire
(BD) Bronchodilator
(CAT) COPD Assessment Test
(CBC) Complete blood count
(CMP) Comprehensive metabolic panel
(HRCT) High resolution computed tomography
(mMRC) modified Medical Research Council Dyspnea score
(PROMIS-20a) Patient Reported Outcomes Measurement Information System: Physical Function – Short Form 20a
(SGRQ-C) St. George's Respiratory Questionnaire for COPD Patients
($SpO_2$) peripheral capillary oxygen saturation

**eTable 3: Reasons for ineligibility among consented participants**

| **Exclusion Criteria*** | **Total** |
|---|---|
| Ineligible based on at least one criterion | 340 |
| Spirometry | 107 |
| Ineligible % emphysema† based on HRCT | 105 |
| Hypertension | 53 |
| ACE/ARB use, indication or intolerance | 12 |
| COPD exacerbation requiring treatment within 6 weeks of V1 | 6 |
| Hypotension | 6 |
| AST or ALT greater than 2.5x the upper limit of normal or creatinine clearance <30 mL/min or serum potassium ≥5 mEq/dL | 6 |
| Regular use of NSAIDS | 5 |
| Potassium supplementation | 5 |
| Decline | 5 |
| Major chronic illness/ study physician judgement | 4 |
| Unable to have HRCT/metal | 4 |
| Ineligible due to HRCT finding | 3 |
| Taking potassium sparing diuretic | 3 |
| Smoking history < 10 pack years | 2 |
| Previous lung resection surgery | 2 |
| Did not return | 2 |
| Resting Sp02 <89% on 2L nasal cannula | 1 |
| Other | 24 |

† % emphysema is the % voxels of density <-950 HU

Abbreviations: AST =aspartate aminotransferase; ALT =alanine aminotransferase; ACE =angiotensin-converting enzyme inhibitors; ARB = angiotensin-receptor blockers; HRCT= computed tomography; NSAID=nonsteroidal anti-inflammatory drugs