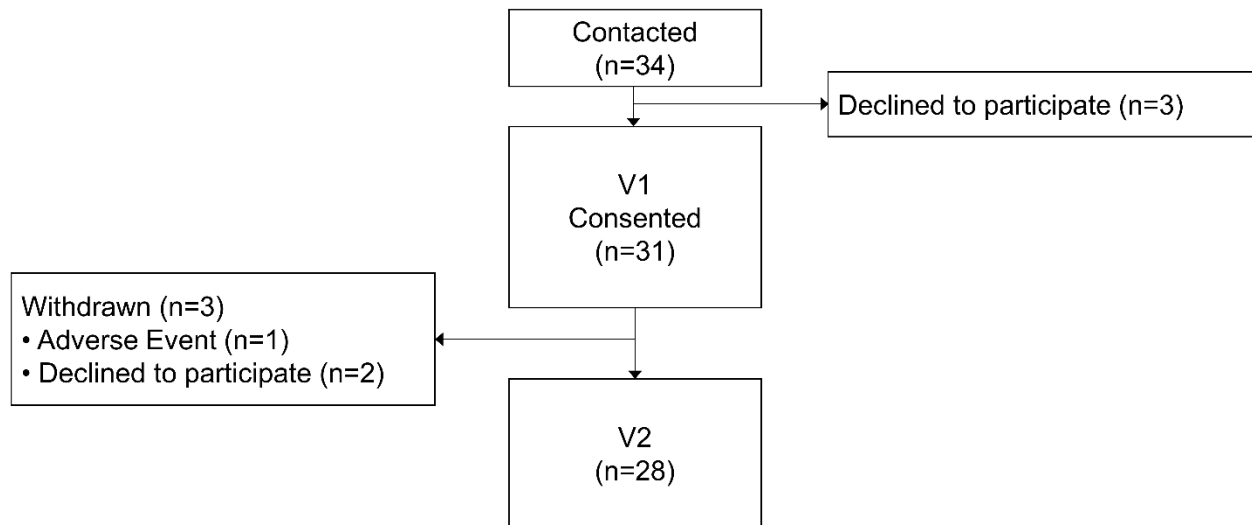


## **Participant Flow**



**Figure 1. CONSORT Diagram**

## **Baseline Characteristics**

**Table 1. Baseline Measurements for participants completing V1 and V1+V2**

| Parameter                       | V1             | V1+V2          |
|---------------------------------|----------------|----------------|
| Mean (SD)                       | (N=31)         | (n=28)         |
| Age years                       | 54 (15)        | 54 (15)        |
| BMI kg/m <sup>2</sup>           | 31 (7)         | 30 (7)         |
| Female n (%)                    | 24 (77)        | 21 (75)        |
| GINA-4 n (%)                    | 29 (94)        | 27 (96)        |
| Pack-years                      | 4 (9)          | 5 (9)          |
| Asthma duration years           | 31 (19)        | 31 (20)        |
| Pre-BD FEV <sub>1</sub> L       | 2.1 (0.7)      | 2.1 (0.7)      |
| Post-BD FEV <sub>1</sub> L      | 2.4 (0.8)      | 2.4 (0.8)      |
| Pre-BD FEV <sub>1</sub> /FVC %  | 65 (12)        | 65 (12)        |
| Post-BD FEV <sub>1</sub> /FVC % | 68 (12)        | 68 (12)        |
| Eos cells/ $\mu$ L*             | 340 (240)      | 350 (240)      |
| FeNO ppb                        | 34 (38)        | 36 (40)        |
| Mucus-Score                     |                |                |
| Mean (SD) median [range]        | 3 (4) 2 [0-12] | 3 (4) 2 [0-12] |
| ACQ-6                           | 2.1 (1.0)      | 2.0 (1.0)      |
| AQLQ                            | 4.5 (1.2)      | 4.5 (1.2)      |
| SGRQ                            | 49 (16)        | 47 (16)        |

\*V1 n=29, V2 n=26

*BMI=body mass index; GINA=Global Initiative for Asthma; BD=bronchodilator; FEV<sub>1</sub>=forced expiratory volume in 1 second; FVC=forced vital capacity; Eos=blood eosinophil count; FeNO=fraction of exhaled nitric oxide; ppb=parts per billion; ACQ-6=Asthma Control Questionnaire; AQLQ=Asthma Quality-of-Life Questionnaire; SGRQ=St. George's Respiratory Questionnaire.*

## Outcome Measures

**Table 2. Pulmonary Function and Imaging Results**

| Parameter<br>Mean (SD)                               | V1<br>(n=28) | V2<br>(n=28) | V1-2<br>P    |
|------------------------------------------------------|--------------|--------------|--------------|
| Pre-BD VDP %                                         | 14 (12)      | 9 (8)        | <b>.0007</b> |
| Post-BD VDP %                                        | 10 (10)      | 7 (6)        | .3           |
| Pre-BD FEV <sub>1</sub> L                            | 2.1 (0.7)    | 2.3 (0.8)    | <b>.01</b>   |
| Post-BD FEV <sub>1</sub> L                           | 2.4 (0.8)    | 2.5 (0.9)    | .5           |
| Pre-BD FVC L                                         | 3.2 (1.0)    | 3.4 (1.2)    | .9           |
| Post-BD FVC L                                        | 3.6 (1.1)    | 3.6 (1.2)    | .5           |
| Pre-BD FEV <sub>1</sub> /FVC %                       | 65 (12)      | 70 (11)      | <b>.0009</b> |
| Post-BD FEV <sub>1</sub> /FVC %                      | 68 (12)      | 71 (11)      | <b>.02</b>   |
| Pre-BD RV L                                          | 2.5 (0.8)    | 2.5 (0.7)    | 1.0          |
| Post-BD RV L                                         | 2.1 (0.6)    | 2.3 (0.8)    | .8           |
| Pre-BD TLC L                                         | 6.8 (1.4)    | 5.9 (1.3)    | 1.0          |
| Post-BD TLC L                                        | 5.7 (1.3)    | 5.9 (1.4)    | 1.0          |
| Pre-BD RV/TLC %                                      | 44 (8)       | 42 (9)       | 1.0          |
| Post-BD RV/TLC %                                     | 37 (7)       | 40 (10)      | .5           |
| Pre-BD LCI n breaths                                 | 12 (3)       | 11 (3)       | .4           |
| Post-BD LCI n breaths                                | 11 (3)       | 10 (3)       | .3           |
| Pre-BD R <sub>5</sub> cmH <sub>2</sub> O/(L/sec)     | 5.6 (1.7)    | 4.5 (1.4)    | <b>.0001</b> |
| Post-BD R <sub>5</sub> cmH <sub>2</sub> O/(L/sec)    | 4.8 (1.4)    | 4.3 (1.3)    | <b>.008</b>  |
| Pre-BD R <sub>19</sub> cmH <sub>2</sub> O/(L/sec)    | 3.7 (1.2)    | 3.3 (1.1)    | <b>.02</b>   |
| Post-BD R <sub>19</sub> cmH <sub>2</sub> O/(L/sec)   | 3.5 (1.0)    | 3.3 (0.9)    | .08          |
| Pre-BD R <sub>5-19</sub> cmH <sub>2</sub> O/(L/sec)  | 1.9 (1.0)    | 1.1 (0.8)    | <b>.0001</b> |
| Post-BD R <sub>5-19</sub> cmH <sub>2</sub> O/(L/sec) | 1.4 (0.9)    | 1.0 (0.8)    | <b>.01</b>   |
| FeNO ppb                                             | 36 (40)      | 29 (17)      | .3           |
| ACQ-6                                                | 2.0 (1.0)    | 1.3 (1.0)    | <b>.006</b>  |
| AQLQ                                                 | 4.5 (1.2)    | 5.5 (1.1)    | <b>.001</b>  |
| SGRQ                                                 | 47 (16)      | 33 (20)      | <b>.001</b>  |

V1 n=27 for post-BD VDP, R<sub>5</sub>, R<sub>19</sub>, R<sub>5-19</sub>; V1 n=26 for pre-BD VDP, RV, TLC, RV/TLC, post-BD RV, TLC, RV/TLC.

V2 n=27 for pre/post-BD FEV<sub>1</sub>, FEV<sub>1</sub> %<sub>pred</sub>, FVC, FVC %<sub>pred</sub>, FEV<sub>1</sub>/FVC, pre-BD LCI, R<sub>5</sub>, pre-BD R<sub>19</sub>, R<sub>5-19</sub>, X<sub>5</sub>, AQLQ; V2 n=26 for pre/post-BD RV, TLC, RV/TLC, ACQ-6, SGRQ; V2 n=24 for pre-BD VDP, post-BD VDP.

P=Holm-Bonferroni corrected paired samples t-test; BD=bronchodilator; VDP=ventilation defect percent; FEV<sub>1</sub>=forced expiratory volume in 1 second; FVC=forced vital capacity; RV=residual volume; TLC=total lung capacity; LCI=lung clearance index; R<sub>5</sub>=total airway resistance; R<sub>19</sub>=central airway resistance; R<sub>5-19</sub>=peripheral airway resistance; FeNO=fraction of exhaled nitric oxide; ppb=parts per billion; ACQ-6=Asthma Control Questionnaire; AQLQ=Asthma Quality-of-Life Questionnaire; SGRQ=St. George's Respiratory Questionnaire.

## **Adverse Events**

**Table 3: Adverse Event Summary**

| Adverse Event                       | Participants<br>Effected (n) | AE or SAE | Related |
|-------------------------------------|------------------------------|-----------|---------|
| Chest infection                     | 5                            | AE        | No      |
| Seasonal allergies                  | 1                            | AE        | No      |
| COVID infection                     | 2                            | AE        | No      |
| Light-headedness during breath-hold | 2                            | AE        | Yes *   |
| Dry Mouth                           | 1                            | AE        | Yes     |
| Gastroenteritis                     | 1                            | AE        | No      |
| Cough                               | 2                            | AE        | No      |
| Cough when Inhaling Study Drug      | 1                            | AE        | Yes     |
| Increased mucous/wheezing           | 1                            | AE        | No      |
| ER Admission                        |                              |           |         |
| 5-6 fractured ribs MVA              | 1                            | AE        | No      |
| Increased appetite                  | 1                            | AE        | No      |
| Chest congestion                    | 1                            | AE        | No      |

\*Related to Xenon Breath-hold

There were no serious adverse events associated with this study.