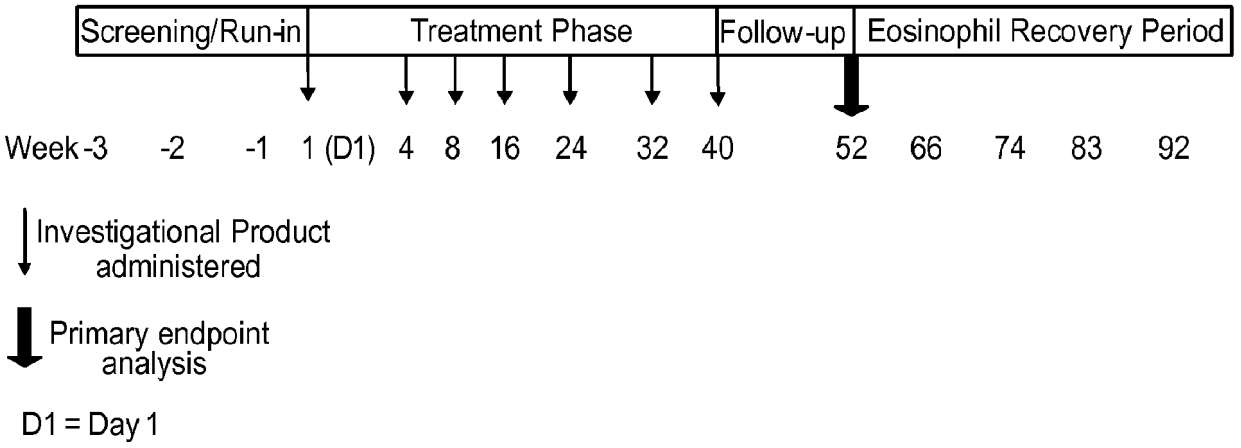
# FIG. 1

Study Flow Diagram



# FIG. 2

Exacerbation Rate by Blood Eosinophil Count

| EOS | | Interim Analysis | | | | Stage I Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Treatment Group | N | Rate | Reduction | *p*-value | N | Rate | Reduction | *p*-value |
| <300 | Placebo | 139 | 0.48 | | | 139 | 0.49 | | |
| | 2mg | 16 | 0.25 | 47% | --- | 16 | 0.21 | 57% | --- |
| | 20mg | 11 | 0.75 | --- | --- | 11 | 0.82 | --- | --- |
| | 100mg | 124 | 0.40 | 18% | 0.481 | 124 | 0.42 | 16% | 0.479 |
| ≥ 300 | Placebo | 83 | 0.65 | | | 83 | 0.68 | | |
| | 2mg | 65 | 0.66 | 1% | 0.987 | 65 | 0.75 | --- | 0.822 |
| | 20mg | 70 | 0.24 | 63% | 0.011 | 70 | 0.30 | 57% | 0.014 |
| | 100mg | 97 | 0.38 | 41% | 0.073 | 97 | 0.38 | 43% | 0.049 |

# FIG. 3

Exacerbation Rate by Baseline ICS Status

| ICS | | Interim Analysis | | | | Stage I Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Treatment Group | N | Rate | Reduction | *p*-value | N | Rate | Reduction | *p*-value |
| Medium | Placebo | 122 | 0.52 | | | 122 | 0.52 | | |
| | 2mg | 41 | 0.39 | 25% | 0.473 | 39* | 0.42 | 19% | 0.578 |
| | 20mg | 39 | 0.24 | 53% | 0.125 | 39 | 0.28 | 46% | 0.169 |
| | 100mg | 117 | 0.30 | 42% | 0.064 | 117 | 0.33 | 37% | 0.100 |
| High | Placebo | 100 | 0.57 | | | 100 | 0.62 | | |
| | 2mg | 40 | 0.80 | --- | 0.378 | 42* | 0.85 | --- | 0.326 |
| | 20mg | 42 | 0.39 | 33% | 0.370 | 42 | 0.46 | 25% | 0.436 |
| | 100mg | 105 | 0.49 | 14% | 0.598 | 105 | 0.48 | 22% | 0.331 |

*: Additional baseline ICS information was added after interim for two subjects.

# FIG. 4

Exacerbation Rate by Blood Eosinophil Count and Baseline ICS Status

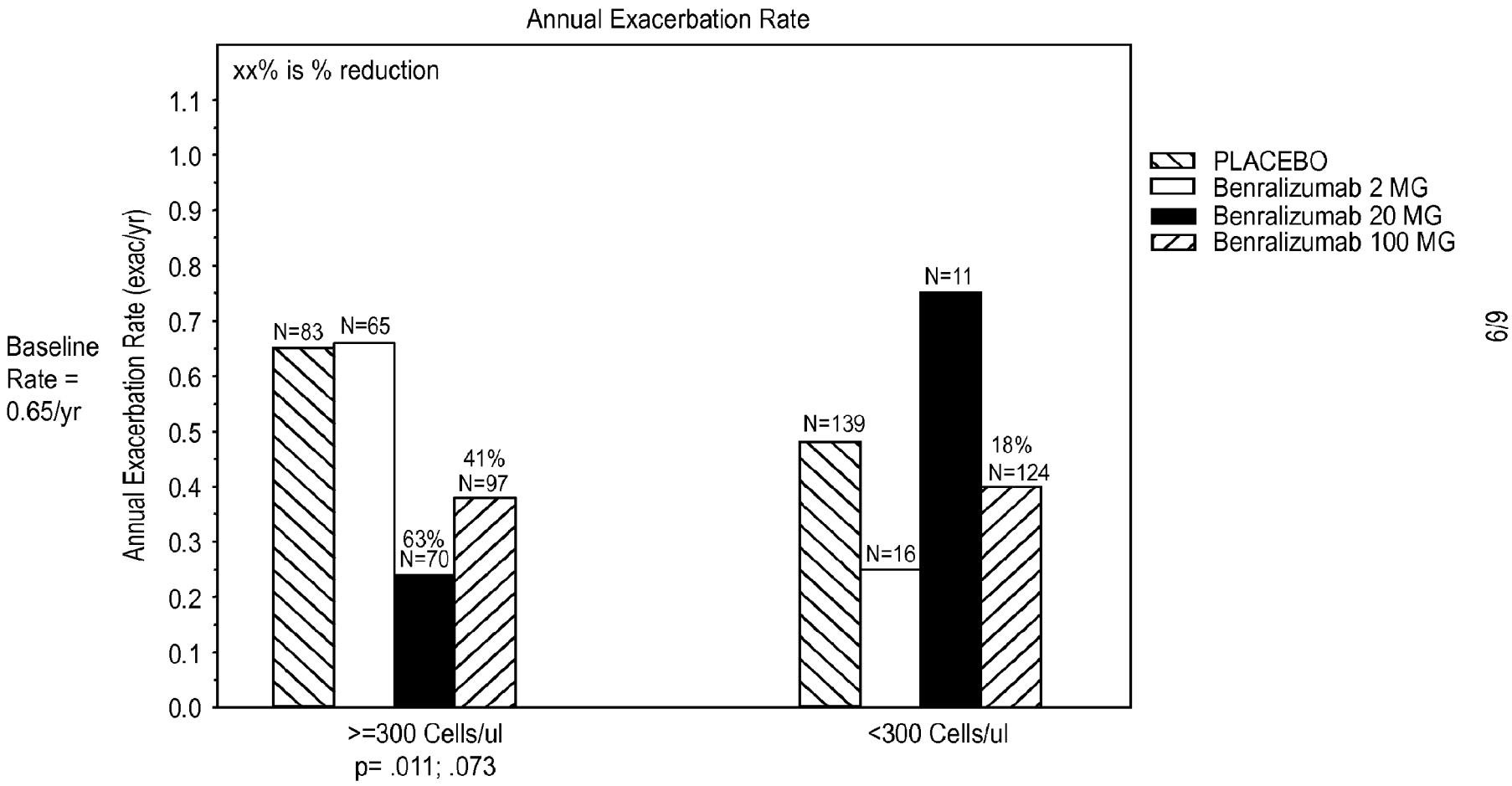
| ICS | | Interim Analysis | | | | Stage I Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Treatment Group | N | Rate | Reduction | *p*-value | N | Rate | Reduction | *p*-value |
| ICS=Medium EOS<300 | Placebo | 79 | 0.51 | | | 79 | 0.51 | | |
| | 2mg | 9 | 0.47 | 9% | --- | 7 | 0.49 | 4% | --- |
| | 20mg | 4 | 0.85 | --- | --- | 4 | 1.00 | --- | --- |
| | 100mg | 63 | 0.29 | 44% | 0.167 | 63 | 0.33 | 37% | 0.233 |
| ICS=High EOS<300 | Placebo | 60 | 0.43 | | | 60 | 0.47 | | |
| | 2mg | 7 | 0.00 | 100% | --- | 9 | 0.00 | 100% | --- |
| | 20mg | 7 | 0.68 | --- | --- | 7 | 0.71 | --- | --- |
| | 100mg | 61 | 0.51 | --- | 0.682 | 61 | 0.51 | --- | 0.795 |

# FIG. 5

Exacerbation Rate by Blood Eosinophil Count and Baseline ICS Status

| ICS | | Interim Analysis | | | | Stage I Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Treatment Group | N | Rate | Reduction | *p*-value | N | Rate | Reduction | *p*-value |
| ICS=Medium EOS ≥ 300 | Placebo | 43 | 0.53 | | | 43 | 0.52 | | |
| | 2mg | 32 | 0.37 | 29% | 0.475 | 32 | 0.41 | 22% | 0.583 |
| | 20mg | 35 | 0.17 | 67% | 0.039 | 35 | 0.19 | 64% | 0.044 |
| | 100mg | 54 | 0.31 | 41% | 0.216 | 54 | 0.32 | 38% | 0.264 |
| ICS=High EOS ≥ 300 | Placebo | 40 | 0.80 | | | 40 | 0.86 | | |
| | 2mg | 33 | 0.97 | --- | 0.668 | 33 | 1.07 | --- | 0.566 |
| | 20mg | 35 | 0.32 | 60% | 0.102 | 35 | 0.41 | 52% | 0.118 |
| | 100mg | 43 | 0.47 | 42% | 0.201 | 43 | 0.46 | 46% | 0.102 |

# FIG. 6


Annual Exacerbation Rate
xx% is % reduction
Annual Exacerbation Rate (exac/yr)
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Baseline Rate = 0.65/yr
N=83
N=65
63% N=70
41% N=97
N=139
N=16
N=11
18% N=124
>=300 Cells/ul
p= .011; .073
<300 Cells/ul
PLACEBO
Benralizumab 2 MG
Benralizumab 20 MG
Benralizumab 100 MG

# FIG. 7A

Exacerbations by Baseline EOS Count

| EOS Counts Cut -off | Treatment Group | N | Exacerbation Rate Ratio (90% CI) | Rate Reduction (%) | *p*-value |
|---|---|---|---|---|---|
| ≥150 | Placebo** | 158 | | | |
| | 2 mg | 76 | 1.23 (0.77, 1.97) | | 0.475 |
| | 20mg | 78 | 0.65 (0.38, 1.14) | 35 | 0.206 |
| | 100mg** | 171 | 0.63 (0.42, 0.94) | 37 | 0.056 |
| <150 | Placebo | 64 | | | |
| | 2 mg | 5 | | | |
| | 20mg | 3 | | | |
| | 100mg | 50 | 0.97 (0.53 1.80) | 3 | 0.941 |
| ≥200 | Placebo | 139 | | | |
| | 2 mg | 75 | 1.24 (0.77, 2.01 | | 0.457 |
| | 20mg | 78 | 0.67 (0.39, 1.15) | 33 | 0.224 |
| | 100mg | 151 | 0.67 (0.44, 1.01) | 33 | 0.110 |
| <200 | Placebo | 83 | | | |
| | 2 mg | 6 | | | |
| | 20mg | 3 | | | |
| | 100mg | 70 | 0.82 (0.46, 1.45) | 18 | 0.565 |

# FIG. 7B

Exacerbations by Baseline EOS Count

| EOS Counts Cut -off | Treatment Group | N | Exacerbation Rate Ratio (90% CI) | Rate Reduction (%) | *p*-value |
|---|---|---|---|---|---|
| ≥300 | Placebo** | 83 | | | |
| | 2 mg | 65 | 0.99 (0.59, 1.68) | 1 | 0.987 |
| | 20mg | 70 | 0.37 (0.19, 0.70) | 63 | 0.011 |
| | 100mg** | 97 | 0.59 (0.36, 0.96) | 41 | 0.073 |
| <300 | Placebo | 139 | | | |
| | 2 mg | **16** | 0.53 (0.14, 1.95) | | 0.423 |
| | 20mg | **11** | 1.62 (0.65, 4.00) | | 0.385 |
| | 100mg | 124 | 0.82 (0.51, 4.31) | 18 | 0.481 |
| ≥400 | Placebo | 52 | | | |
| | 2 mg | 50 | 0.90 (0.51, 1.60) | 10 | 0.765 |
| | 20mg | 53 | 0.36 (0.17, 0.78) | 64 | 0.028 |
| | 100mg | 58 | 0.36 (0.18, 0.72) | 64 | 0.015 |
| <400 | Placebo | 170 | | | |
| | 2 mg | 31 | 1.17 (0,57, 2.39) | | 0.721 |
| | 20mg | 28 | 0.92 (0.44, 1.93) | 8 | 0.852 |
| | 100mg | 163 | 0.87 (0.59, 1.29) | 13 | 0.566 |

FIG. 8

Eosinophil Depletion in Patients with at least 300 eosinophils/μl

