

Astegolimab for chronic obstructive pulmonary disease in patients with a history of frequent exacerbations: the Phase III, randomized, double-blind, placebo-controlled, multicenter ARNASA trial

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Disclosures

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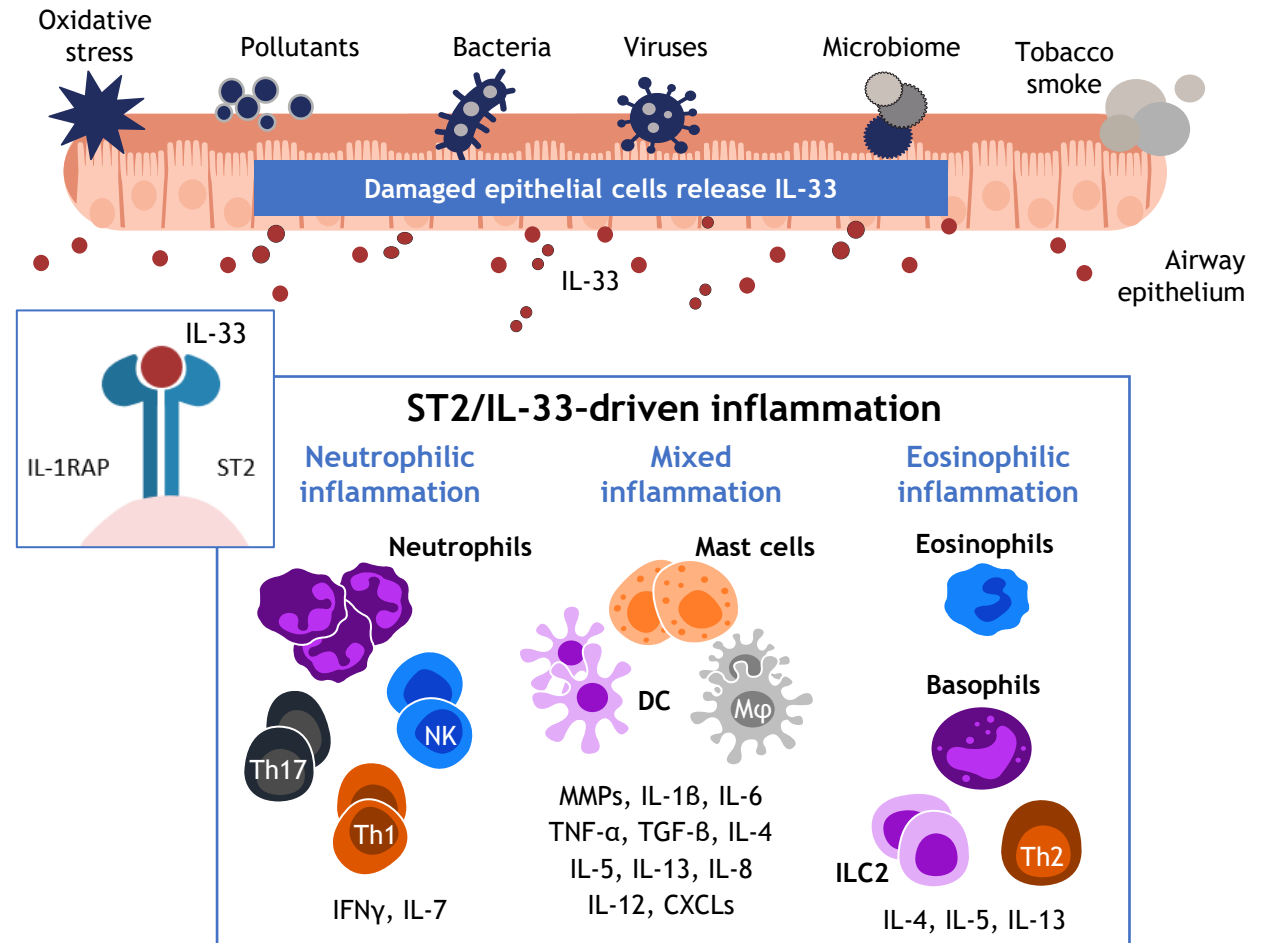
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The ST2/IL-33 pathway drives airway inflammation in COPD^{6,7}

Background

- Exacerbations of COPD increase the risk of future exacerbations, hospitalization, and mortality^{1,2}
- Triggers of these exacerbations can lead to epithelial release of alarmin IL-33 in the respiratory system³
 - IL-33 binds to the receptor ST2 (IL1RL1) on various immune cells, resulting in neutrophilic and eosinophilic inflammation
- Astegolimab is a human IgG2 monoclonal antibody that blocks ST2-mediated IL-33 activity and subsequent inflammation^{4,5}



Background

- The efficacy and safety of astegolimab in patients with COPD with frequent exacerbations were evaluated in two similarly designed pivotal, randomized, double-blind, placebo-controlled trials: ALIENTO and ARNASA^{1,2}
- The results from the Phase IIb ALIENTO trial (NCT05037929) have been reported previously³

Efficacy of astegolimab Q2W vs placebo in ALIENTO³

Primary endpoint:
Annualized rate of moderate or severe COPD exacerbations

15%
reduction

Adjusted rate ratio:
0.85 (95% CI 0.72, 1.00)
 $P = 0.049$

Secondary endpoint:
Annualized rate of severe COPD exacerbations

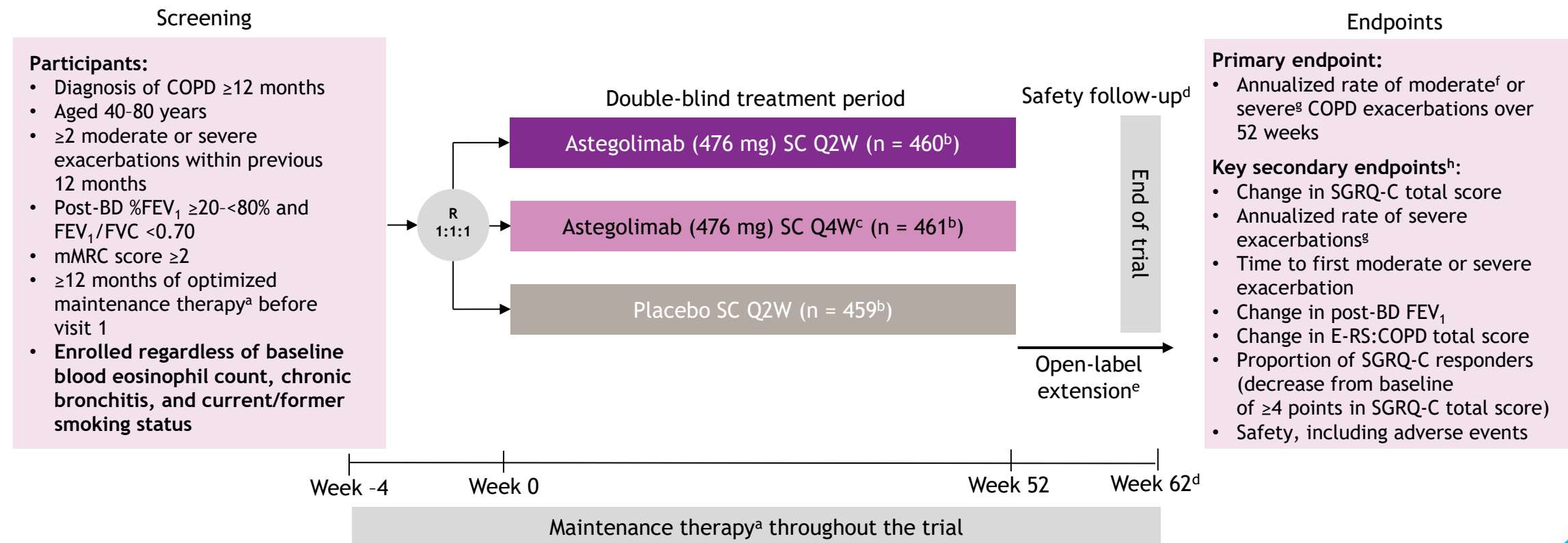
29%
reduction

Adjusted rate ratio:
0.71 (95% CI 0.49, 1.05)

Here, we report the results of ARNASA (NCT05595642), a Phase III trial of astegolimab in patients with COPD and a history of frequent exacerbations, regardless of current/former smoking status or baseline eosinophil count

ARNASA trial design

A Phase III, randomized, double-blind, placebo-controlled trial conducted at 319 sites across 35 countries

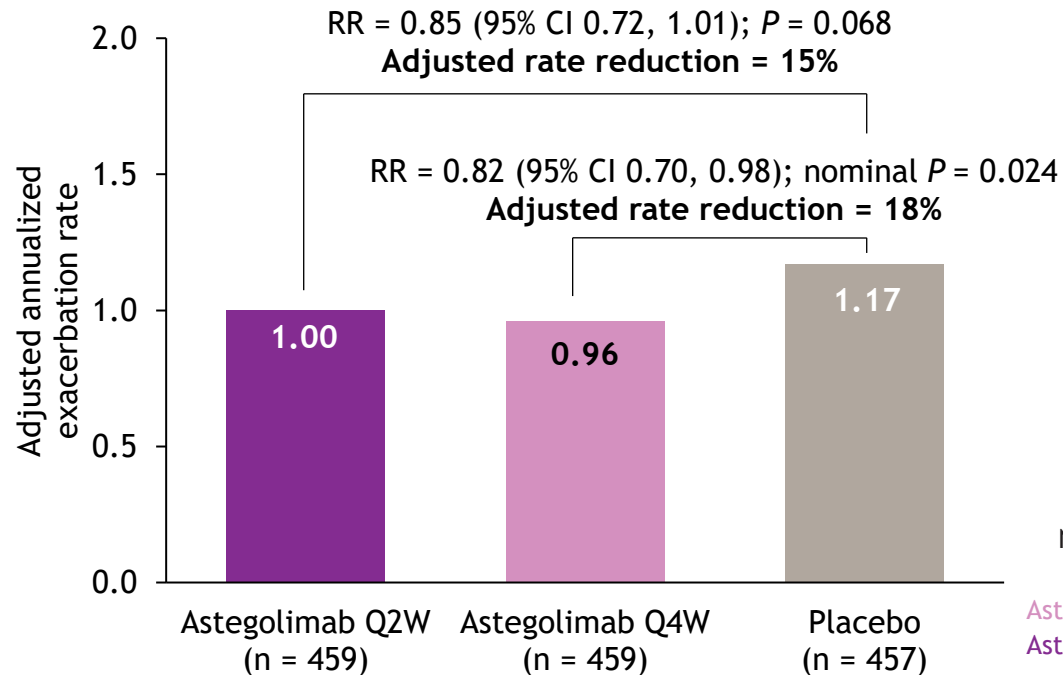


Baseline demographics and characteristics (mITT population)

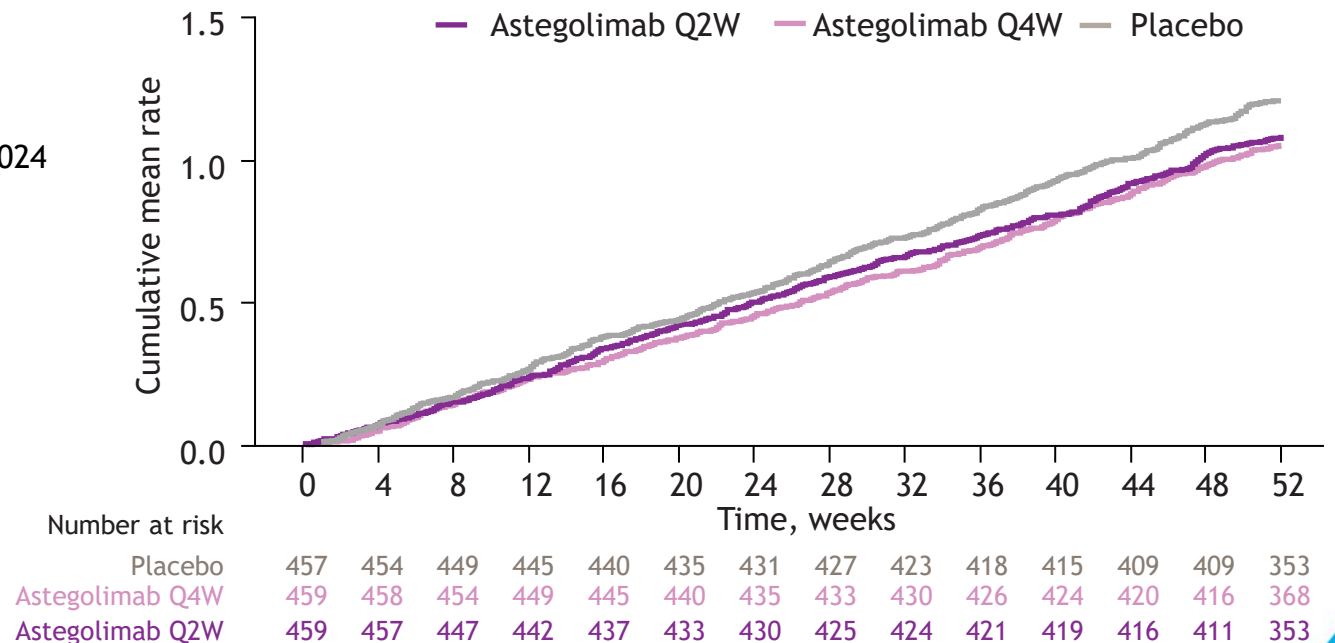
Characteristic	Astegolimab Q2W (n = 459)	Astegolimab Q4W (n = 459)	Placebo (n = 457)
Age, mean (SD), years	66.8 (7.6)	66.6 (7.4)	66.8 (6.9)
Male, n (%)	288 (62.7)	296 (64.5)	302 (66.1)
Current smoker, n (%)	153 (33.3)	153 (33.3)	153 (33.5)
>2 COPD exacerbations within prior 12 months, n (%) ^a	143 (31.2)	139 (30.3)	102 (22.4)
Baseline blood eosinophil count ^b			
Mean (SD), cells/ μ L	177.3 (134.6)	199.2 (255.2)	176.0 (113.1)
<150 cells/ μ L, n (%)	231 (50.8)	222 (48.5)	221 (48.4)
$\geq$ 150 to <300 cells/ μ L, n (%)	163 (35.8)	170 (37.1)	180 (39.4)
$\geq$ 300 cells/ μ L, n (%)	61 (13.4)	66 (14.4)	56 (12.3)
Post-BD predicted %FEV ₁ , mean (SD), ^c	45.2 (15.0)	44.9 (14.9)	46.7 (15.9)
SGRQ-C total score, mean (SD) ^d	59.7 (18.6)	61.7 (17.7)	59.7 (18.8)
ICS+LAMA+LABA, n (%)	357 (77.8)	340 (74.1)	326 (71.3)
Diagnosis of chronic bronchitis, n (%) ^e	188 (41.0)	213 (46.4)	197 (43.1)

Primary endpoint of adjusted annualized rates of moderate or severe exacerbations was not met for either astegolimab arm vs placebo

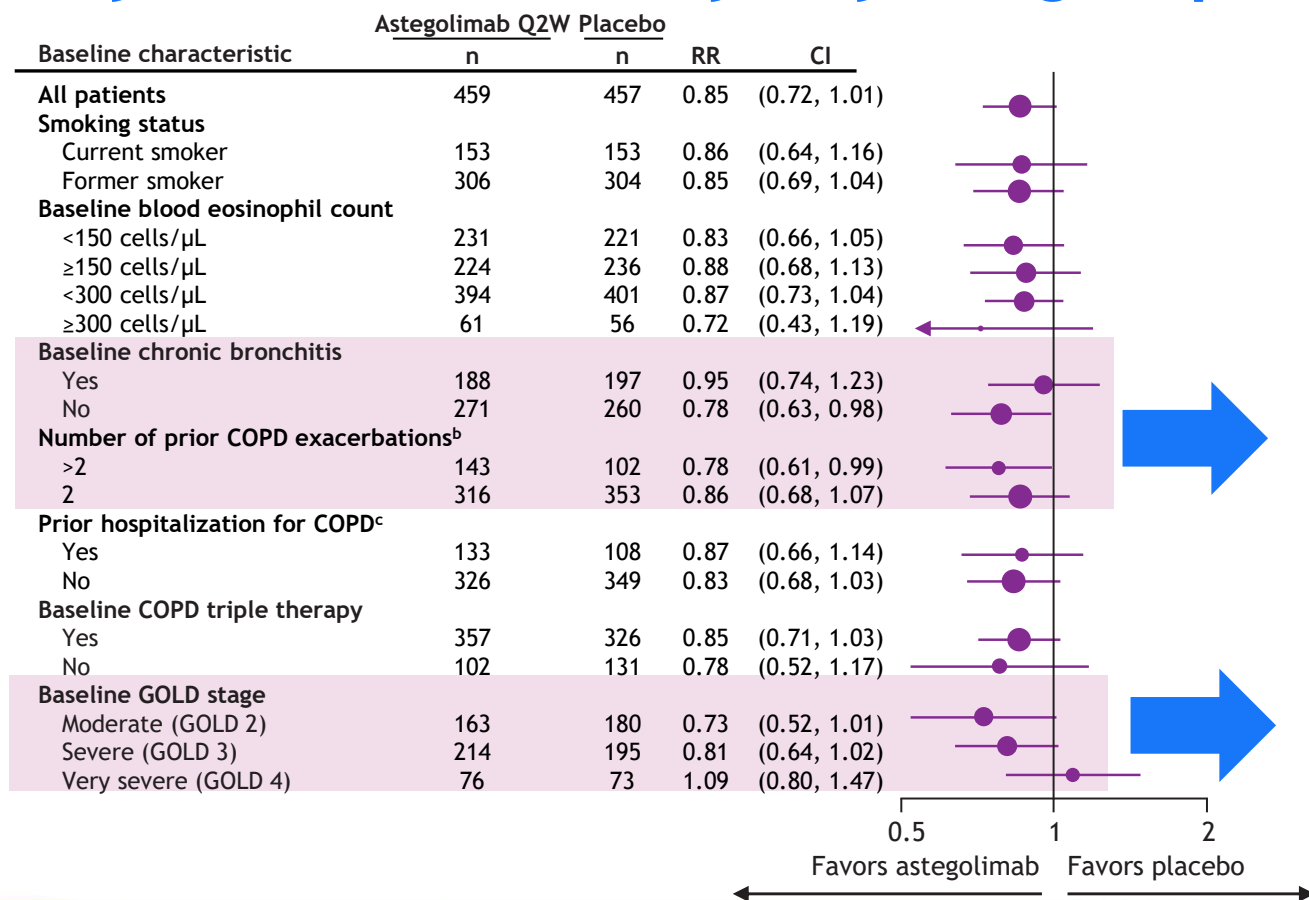
Adjusted annualized rate of moderate or severe COPD exacerbations over 52 weeks^a



Cumulative mean rate of moderate or severe COPD exacerbations



Reductions in moderate/severe exacerbation frequency may not be driven by key subgroups

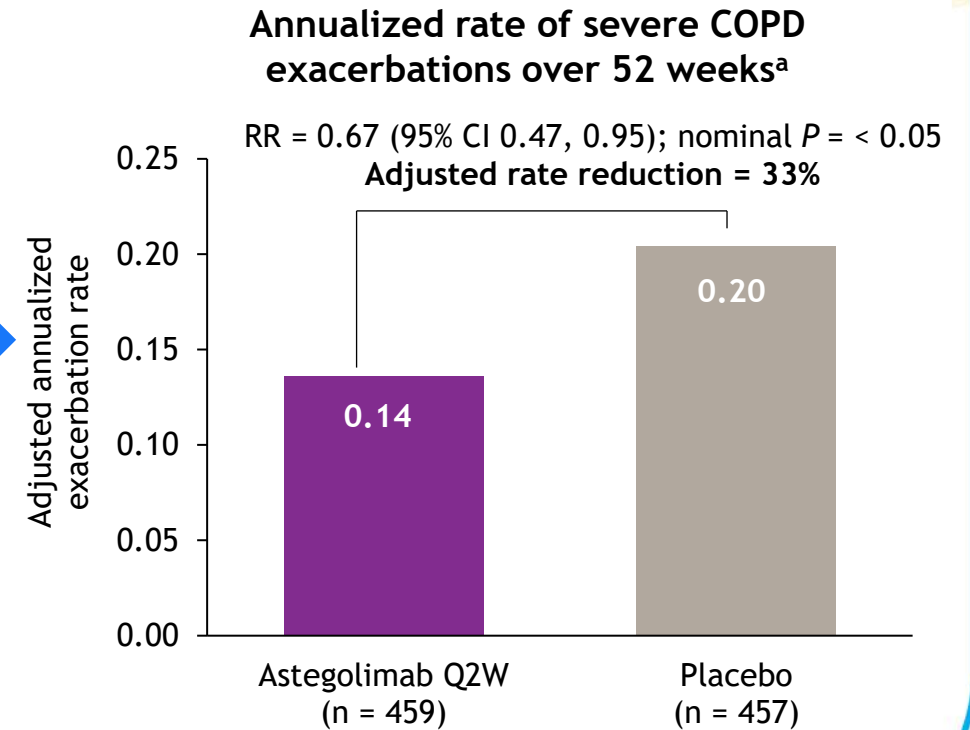


Consistent with ALIENTO,¹ there may be potentially greater treatment benefit of astegolimab Q2W vs placebo in those with:

- History of >2 prior exacerbations^b
- Moderate airflow obstruction
- No chronic bronchitis at baseline

Astegolimab Q2W achieved a 33% reduction in severe exacerbations and an increase in the proportion of SGRQ-C responders versus placebo

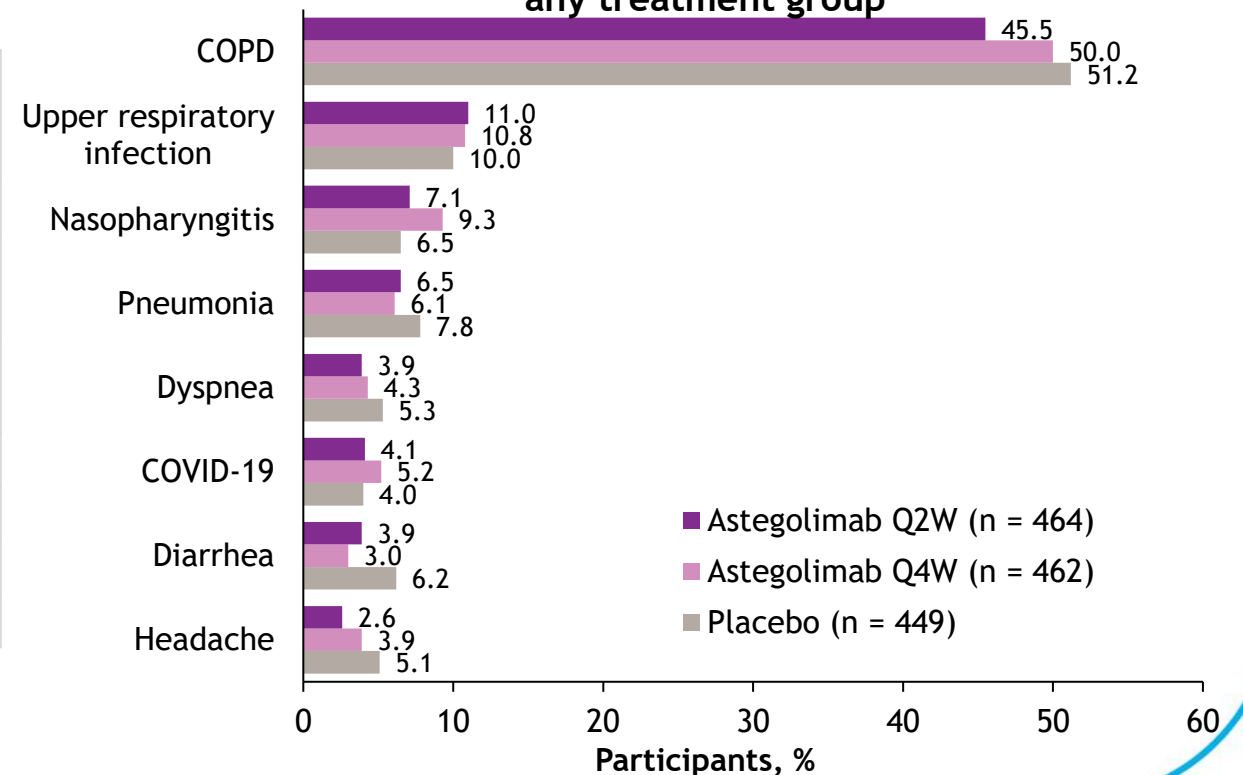
Key secondary endpoints, at/over 52 weeks	Astegolimab Q2W vs placebo (95% CI) ^a
Change from baseline in SGRQ-C total score	Difference in adjusted means ^b : -0.77 (-3.23, 1.68)
Annualized rate of severe COPD exacerbations	Adjusted RR^c: 0.67 (0.47, 0.95); nominal <i>P</i> < 0.05
Time to first moderate or severe exacerbation	HR ^c : 0.90 (0.75, 1.08)
Change from baseline in post-bronchodilator FEV ₁	Difference in adjusted mean, mL ^d : 14 (-17, 46)
Change from baseline in E-RS:COPD total score	Difference in adjusted means ^e : -0.05 (-0.83, 0.73)
Proportion of SGRQ-C responders (decrease of ≥4 points in SGRQ-C total score)	OR^f: 1.49 (1.14, 1.96); nominal <i>P</i> < 0.01



Astegolimab was well tolerated, AEs were balanced between treatment arms, and the safety profile was consistent with prior trials, with no new potential risks identified^{1,2}

Participants with, n (%)	Astegolimab Q2W (n = 464)	Astegolimab Q4W (n = 462)	Placebo (n = 449)
≥1 AE	386 (83.2)	406 (87.9)	384 (85.5)
≥1 serious AE	113 (24.4)	124 (26.8)	107 (23.8)
≥1 AE of Grade ≥3	135 (29.1)	167 (36.1)	122 (27.2)
≥1 AE leading to withdrawal from trial	18 (3.9)	21 (4.5)	20 (4.5)
≥1 AE leading to death	11 (2.4)	18 (3.9)	15 (3.3)
≥1 AE of infection	227 (48.9)	234 (50.6)	216 (48.1)
≥1 MACE ^a	8 (1.7)	13 (2.8)	13 (2.9)
≥1 injection site reaction	17 (3.7)	22 (4.8)	17 (3.8)

Most common AEs occurring in ≥5% of participants in any treatment group



Discussion and conclusions

- In ARNASA, astegolimab 476 mg Q2W was associated with a non-statistically significant 15% reduction in the annualized rate of moderate or severe exacerbations in patients with COPD and a history of frequent exacerbations, regardless of baseline blood eosinophil count
 - The effect size in ARNASA was consistent with the statistically significant 15% reduction for astegolimab Q2W vs placebo in ALIENTO¹
- Nominally significant 33% reduction in the annualized rate of severe exacerbations and nominally significant increase in the proportion of SGRQ-C responders vs placebo
- AEs were balanced between treatment arms and both doses of astegolimab were well tolerated, with a safety profile consistent with prior trials^{1,2}

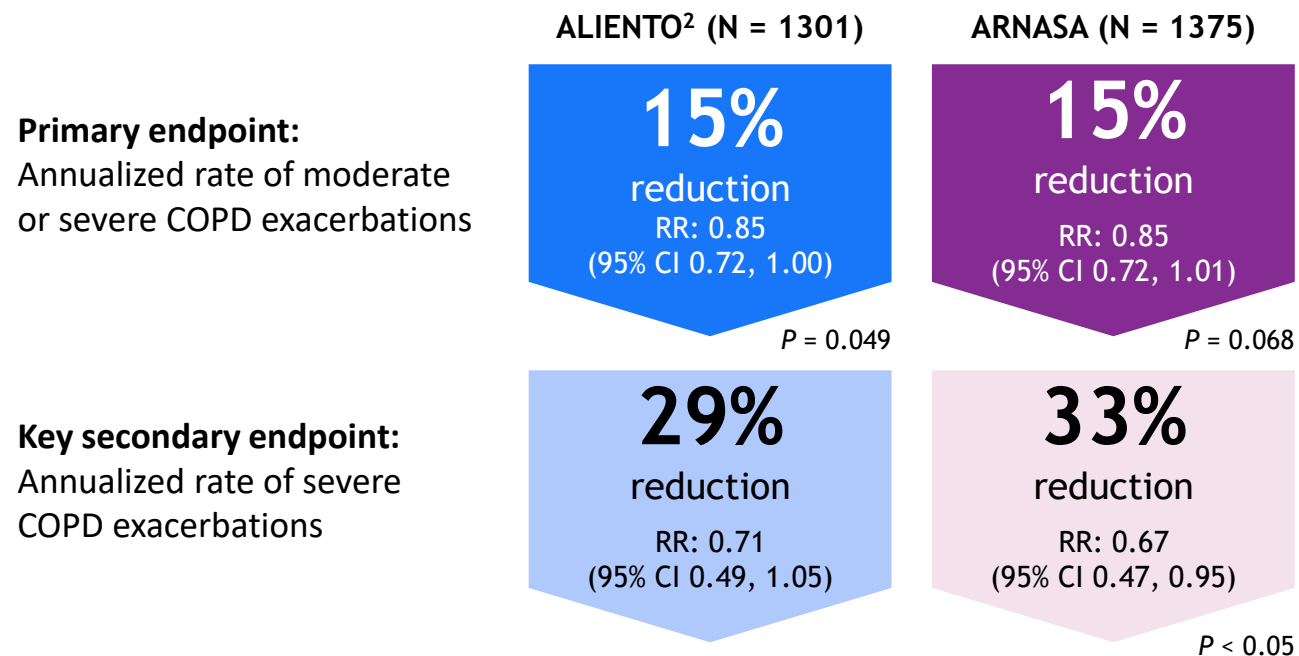
ALIENTO and ARNASA: impact of astegolimab on exacerbation rates



The reduction in exacerbation rates in ARNASA is consistent with results from ALIENTO, despite ARNASA not meeting statistical significance for the primary endpoint

Reducing COPD exacerbations is clinically important as even one moderate exacerbation can negatively affect health status, accelerate disease progression, and increase the risk of hospitalization or death¹

Adjusted rate reductions for astegolimab Q2W vs placebo^a



Simultaneously published in *The Lancet*

THE LANCET

Safety and efficacy of astegolimab for COPD with frequent exacerbations regardless of baseline blood eosinophil counts (ALIENTO and ARNASA): randomised, double-blind, placebo-controlled, phase 2b and 3 trials



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