# Global Medical Affairs Cover Sheet

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| **Asset Name** | **Benralizumab: Life Cycle Management Deck** | | |
| **Intended Use** | Reactive | | |
| **Approved for Distribution** | Yes | **Therapy Area** | Respiratory |

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|---|---|---|---|---|---|
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# Benralizumab: Life Cycle Management

Last Updated: March 2019

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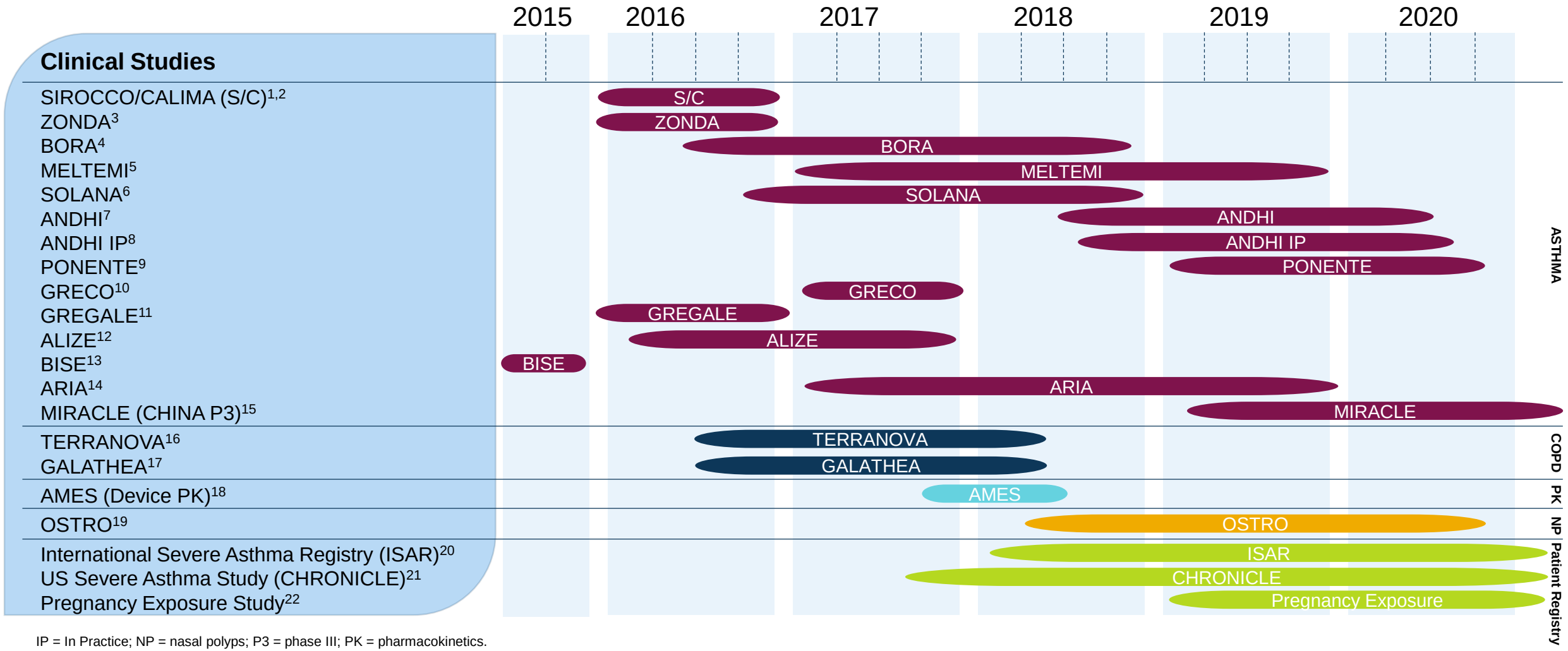
# Benralizumab: AstraZeneca Clinical Trials Timeline




IP = In Practice; NP = nasal polyps; P3 = phase III; PK = pharmacokinetics.

1. FitzGerald JM et al. *Lancet*. 2016;388:2128-2141; 2. Bleecker ER et al. *Lancet*. 2016;388:2115-2127; 3. Nair P et al. *N Engl J Med*. 2017;376:2448-2458; 4. Busse WW et al. *Lancet Respir Med.* 2019; 5. Study NCT02808819. ClinicalTrials.gov website; 6. Study NCT02869438. ClinicalTrials.gov website; 7. Study NCT03170271. ClinicalTrials.gov website; 8. In House Data, AstraZeneca Pharmaceuticals LP. CSP D3250C00045; 9. Study NC03557303. ClinicalTrials.gov website; 10. Study NCT02918071. ClinicalTrials.gov website; 11. Ferguson GT et al. *J Asthma Allergy*. 2018;11:63-72; 12. Zeitlin PL et al. *J Asthma Allergy*. 2018;11:181-192; 13. Ferguson GT et al. *Lancet Respir Med*. 2017;5:568-576; 14. Study NCT02821416. ClinicalTrials.gov website; 15. Study NCT03186209. ClinicalTrials.gov website; 16. Study NCT02155660. ClinicalTrials.gov website; 17. Study NCT02138916. ClinicalTrials.gov website; 18. Study NCT02968914. ClinicalTrials.gov website; 19. Study NCT03401229. ClinicalTrials.gov website; 20. ISAR. http://isaregistries.org/. Accessed February 6, 2019; 21. Study NCT03373045. ClinicalTrials.gov website; 22. Study NCT03794999. ClinicalTrials.gov website.

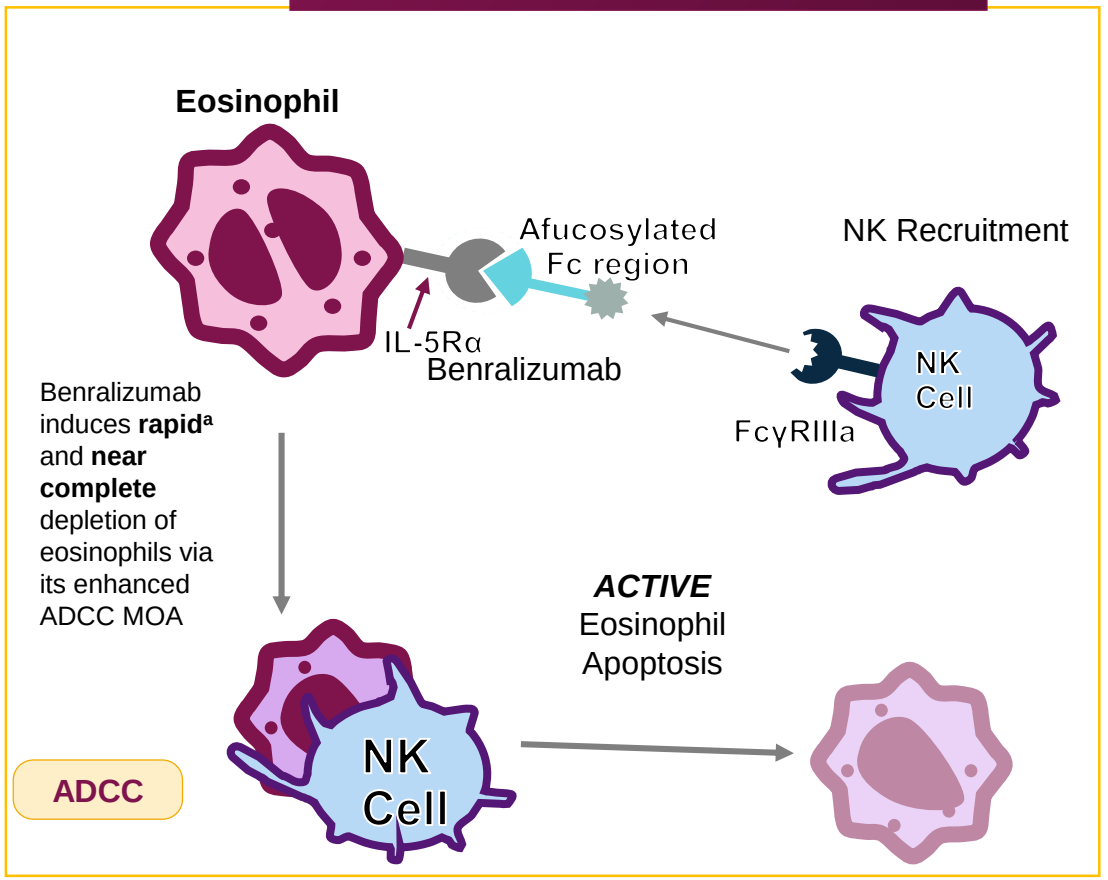
# Benralizumab: Asthma Studies

# Benralizumab: Description

## Benralizumab

- Benralizumab is the only humanized, anti-IL-5Rα monoclonal antibody[1-3]
  - Benralizumab binds to the alpha chain of the IL-5R (IL-5Rα) on the surface of eosinophils and basophils[1,3]
  - Other eosinophil-lowering modalities (mepolizumab and reslizumab) bind IL-5, preventing its interaction with the IL-5 receptor[1,3]
- Benralizumab MOA extends beyond blocking the receptor by actively promoting the 'programmed cell death' (apoptosis) of eosinophils and basophils
  - Afucosylation of the Fc region of benralizumab increases its affinity for the Fc gamma receptor 3A (FcγRIIIa; CD16) on NK cells[2-4]
  - Benralizumab recruits and activates NK cells to the eosinophil, efficiently inducing apoptosis via antibody-dependent cell-mediated cytotoxicity[5]

## Anti-IL-5Rα Mechanism[5,7,8]




ADCC = antibody-dependent cell-mediated cytotoxicity; COPD = chronic obstructive pulmonary disease; Fc = constant region; EMA = European Medicines Agency; FDA = US Food and Drug Administration; IL = interleukin; IL-5Rα = interleukin-5 receptor alpha; MOA = mechanism of action; IL-5Ra = interleukin-5 receptor alpha; NK = natural killer.

[a]Benralizumab induces eosinophil apoptosis within 6 hours in vitro[7]; blood eosinophils were depleted within 24 hours in a clinical study[8]

1. Molfino NA et al. *Clin Exp Allergy*. 2012;42:712-737; 2. Tan LD et al. *J Asthma Allergy.* 2016;9:71-81; 3. Busse W et al. Interleukin-5 receptor-directed strategies 2013:587-591; 4. Ghazi A et al. *Expert Opin Biol Ther*. 2012;12:113-118; 5. Kolbeck R et al. *J Allergy and Clin Immunol*. 2010;125:1344-1353; 6. Patterson MF et al. *J Asthma Allergy.* 2015;8:125-134; 7. Laviolette M et al. *J Allergy Clin Immunol.* 2013;132:1086-1096; 8. Dagher R et al. Poster presented at: International Eosinophil Society 10th Biennial Symposium; July 21, 2017; Gothenburg, Sweden.

# Benralizumab: Phase III Asthma Trials – Completed

| Study | Description / Patient Population | N | Study Design | Primary Outcome Measure | Status | Completion Date[a] |
|---|---|---|---|---|---|---|
| **SIROCCO**[1] | Severe asthma inadequately controlled with high-dose ICS + LABA (ages 12-75 years) | 1204 | 48-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter | Annual asthma exacerbation rate reduction | Completed | April 2016 |
| **CALIMA**[2] | Severe asthma inadequately controlled with medium- to high-dose ICS + LABA (ages 12-75 years) | 1306 | 56-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter | Annual asthma exacerbation rate reduction | Completed | March 2016 |
| **ZONDA**[3] | Severe asthma inadequately controlled with high-dose ICS + LABA and chronic OCS (ages 18-75 years) | 220 | 28-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter | Percent reduction of OCS dose from baseline, while maintaining asthma control at Week 28 | Completed | July 2016 |
| **BORA**[4] (Adult study) | Severe asthma safety extension of CALIMA, SIROCCO, and ZONDA for up to 2 years (ages 12-75 years) | 1576 | 56-Week (adults)/108-week (adolescents), randomized, double-blind, parallel-group, multicenter | Number of patients with AEs/abnormal lab variables, physical examinations (Week 0-56 and through follow-up [16 weeks after last dose])<br>Number of adolescents with AEs/abnormal lab variables, physical examinations (Week 0-108 and through follow-up [16 weeks after last dose]) | Completed | July 2018 |
| **SOLANA**[5,6] | Uncontrolled, severe asthma with eosinophilic inflammation (ages 18-75 years) | 235 | 16-week, randomized, double-blind, parallel-group, multicenter | Change in lung function (pre-BD $FEV_1$ and body plethysmography [residual volume]) at Week 12 | Completed | August 2018 |

[a]Study completion date. AE = adverse events; BD = bronchodilator; $FEV_1$ = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LABA = long-acting $\beta_2$-agonist; OCS = oral corticosteroid.



1. Bleecker ER et al. *Lancet*. 2016;388:2115-2127; 2. FitzGerald JM et al. *Lancet*. 2016;388:2128-2141; 3. Nair P et al. *N Engl J Med*. 2017;376:2448-2458; 4. Busse WW et al. *Lancet Respir Med*. 2019;7:46-59; 5. Study NCT02869438. ClinicalTrials.gov website; 6. AstraZeneca Pharmaceuticals LP. Clinical trials appendix-November 8, 2018.

# Benralizumab: Phase III Asthma Trials – Completed (continued)

| Study | Description / Patient Population | N | Study Design | Primary Outcome Measure | Status | Completion Date[a] |
|---|---|---|---|---|---|---|
| **GRECO**[1] | Autoinjector usability in severe asthma (ages 18-75 years) | 121 | 28-week, open-label, multicenter | Proportion of patients/caregivers who successfully administered benralizumab SC with an AI device at home until Week 16; Proportion of returned AI devices used to administer benralizumab at home that have been evaluated as functional until Week 16; Proportion of AI devices used to administer benralizumab at home or in the clinic and have been reported as malfunctioning until Week 16; | Completed | August 2017 |
| **GREGALE**[2] | Accessorized prefilled syringe usability in severe asthma (ages 18-75 years) | 116 | 28-week, open-label, multicenter | Proportion of patients/caregivers who successfully administered benralizumab SC with an APFS at home; Proportion of returned APFS used at home and evaluated as functional; Proportion of APFS used to administer benralizumab at home or in the clinic and reported as malfunctioning | Completed | March 2016 |
| **ALIZE**[3] | Humoral immune response following seasonal influenza virus vaccination in adolescent and young adult patients with severe asthma (ages 12-21 years) | 103 | 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter | Postdose strain-specific HAI antibody GMFRs at Week 12; Postdose strain-specific serum HAI antibody GMTs at Week 12; Proportion of patients who experienced a strain-specific postdose antibody response ≥4-fold rise in HAI antibody titer at Week 12; Postdose HAI antibody titer ≥40 at Week 12 | Completed | January 2017 |
| **BISE**[4] | Mild to moderate persistent asthma (ages 18-75 years) | 211 | 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter | Change from baseline in predose $FEV_1$ at Week 12 | Completed | October 2015 |

[a]Study completion date. AI = autoinjector; APFS = accessorized pre-filled syringe; $FEV_1$ = forced expiratory volume in 1 second; GMFRs = geometric mean fold rises; GMT = geometric meant titers; HAI = hemagglutination-inhibition; SC = subcutaneous.



1. Study NCT02918071. ClinicalTrials.gov website; 2. Ferguson GT et al. *J Asthma Allergy*. 2018;11:63-72; 3. Zeitlin PL et al. *J Asthma Allergy*. 2018;11:181-192; 4. Ferguson GT et al. *Lancet Respir Med.* 2017;5:568-576.

# SIROCCO: Phase III Severe Asthma Clinical Trial

**ClinicalTrials.gov identifier:** NCT01928771
**Status:** Completed
**Completion Date:** April 2016[1]

| Trial Overview[2] | |
|---|---|
| A 48-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study of benralizumab compared with placebo in patients with severe asthma inadequately controlled with high-dose ICS plus a LABA with or without chronic OCS (ages 12-75 years)[1] | |
| **Endpoints include** | ***Primary:*** Annual asthma exacerbation rate reduction<br>***Key Secondary:*** • Prebronchodilator $FEV_1$<br>• Total asthma symptom score |

**Study Design**

A 48-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study

N=1204

**Randomization**

- Benralizumab 30 mg Q8W SC
- Benralizumab 30 mg Q4W SC
- Placebo SC

$FEV_1$ = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LABA = long-acting β$_2$-agonist; OCS = oral corticosteroid; Q4W = every 4 weeks; Q8W = every 8 weeks; SC = subcutaneous.





1. Study NCT01928771. ClinicalTrials.gov website.; 2. Bleecker ER et al. *Lancet*. 2016;388:2115-2127; 2.

# CALIMA: Phase III Severe Asthma Clinical Trial[1]

**ClinicalTrials.gov identifier:** NCT01914757
**Status:** Completed
**Completion Date:** March 2016[1]

| Trial Overview[2] | |
|---|---|
| A 56-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study to evaluate the efficacy and safety of benralizumab in patients with severe asthma inadequately controlled with medium- to high-dose ICS plus a LABA with or without chronic OCS (ages 12-75 years) | |
| **Endpoints include** | ***Primary:*** Annual asthma exacerbation rate reduction<br>***Key Secondary:*** • Prebronchodilator $FEV_1$<br>• Total asthma symptom score |

**Study Design**

A 56-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study

N=1306

**Randomization**

- Benralizumab 30 mg Q8W SC
- Benralizumab 30 mg Q4W SC
- Placebo SC

$FEV_1$ = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LABA = long-acting $\beta_2$-agonist; OCS = oral corticosteroids; Q4W = every 4 weeks; Q8W = every 8 weeks; SC = subcutaneous.





1. Study NCT01914757. ClinicalTrials.gov website; 2. FitzGerald JM et al. *Lancet*. 2016;388:2128-2141.

# ZONDA: Phase III OCS Reduction Trial

**ClinicalTrials.gov Identifier:** NCT02075255
**Status:** Completed
**Completion Date:** August 2016[1]

| Trial Overview[2] | |
|---|---|
| A 28-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study of benralizumab in patients with severe asthma, inadequately controlled on high-dose ICS plus LABA and chronic OCS therapy (ages 18-75 years) | |
| **Endpoints include** | ***Primary:*** Percent reduction in OCS dose from baseline, while maintaining asthma control<br>***Secondary[a]:***<br>• Proportion of patients with ≥50% reduction in average daily OCS dose<br>• Proportion of patients with average final OCS dose ≤5.0 mg daily<br>• Proportion of patients with ≥1 asthma exacerbation after randomization |

**Study Design**

A 28-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study

N=220

**Randomization**

- Benralizumab 30 mg Q8W SC
- Benralizumab 30 mg Q4W SC
- Placebo SC

[a]Select secondary endpoints listed.

ICS = inhaled corticosteroid; LABA = long-acting $\beta_2$-agonist; OCS = oral corticosteroid; Q4W = every 4 weeks; Q8W = every 8 weeks; SC = subcutaneous.





1. Study NCT02075255. ClinicalTrials.gov website; 2. Nair P et al. *N Engl J Med*. 2017;376:2448-2458.

# BORA: Phase III Safety and Tolerability Extension Trial[1]

**ClinicalTrials.gov Identifier:** NCT02258542
**Status:** Completed
**Estimated Study Completion Date:** July 2018[1]

| Trial Overview[2] | |
|---|---|
| A 56-week (adults)/108-week (adolescents), double-blind, randomized, parallel-group, multicenter safety extension study of benralizumab in patients with severe asthma who completed CALIMA, SIROCCO, and ZONDA (ages 12-75 years); previous benralizumab patients remained on the same blinded regimen as in the controlled study; PBO patients were randomized to benralizumab Q4W or Q8W | |
| **Endpoints include** | ***Primary:*** Safety and tolerability of benralizumab (AEs, labs, physical exam)<br>***Secondary*[a]:** Maintenance of efficacy: asthma exacerbations, AQLQ(S)+12, ACQ-6, ADA, blood EOS |

**Study Design**

A 56-week (adults)/ 108-week (adolescents), double-blind, randomized, parallel-group, multicenter study

N=1576

**Randomization**

- Benralizumab 30 mg Q4W SC
- Benralizumab 30 mg Q8W SC

[a]Select secondary endpoints listed.

ACQ-6 = asthma control questionnaire 6; ADA = anti-dug antibodies; AEs = adverse events; AQLQ(S)+12 = asthma quality of life questionnaire for 12 years and older; EOS = eosinophils; Q4W = every 4 weeks; Q8W = every 8 weeks; SC = subcutaneous.





1. Study NCT02258542. ClinicalTrials.gov website; 2. Busse WW et al. *Lancet Respir Med*. 2019;7:46-59.

# SOLANA: Phase III Onset and Lung Function in Severe Asthma Trial

**ClinicalTrials.gov Identifier:** NCT02869438
**Status:** Completed
**Estimated Completion Date:** August 2018

| Trial Overview[1] | | |
|---|---|---|
| A 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study to evaluate the onset of effect and time course of change in lung function (time frame day with benralizumab in patients with uncontrolled, severe asthma with eosinophilic inflammation (ages 18-75 years) | | |
| **Endpoints include** | ***Primary:*** | • Change in lung function (pre-BD $FEV_1$)<br>• Body plethysmography (RV) |
| | ***Secondary[a]:*** | • Change in and maintenance of lung function<br>• Blood EOS count; and correlate changes in EOS depletion with lung function<br>• Change from baseline in ACQ-6 scores |

**Study Design**

A 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study

N=235

**Randomization**

- Benralizumab 30 mg Q4W SC[2]
- Placebo SC

[a]Select secondary endpoints listed. ACQ-6 = asthma control quesitonnaire-6; BD = bronchodilator; EOS = eosinophil; $FEV_1$ = forced expiratory volume in the 1 second; Q4W = every 4 weeks; RV = residual volume; SC = subcutaneous.





1. Study NCT02869438. ClinicalTrials.gov website; 2. AstraZeneca Pharmaceuticals LP. Clinical trials appendix. March 4, 2019.

# GRECO: Phase III Autoinjector Usability Trial

**ClinicalTrials.gov Identifier:** NCT02918071
**Status:** Completed
**Completion Date:** August 2017

| Trial Overview | |
|---|---|
| A 28-week, open-label, multicenter, functionality, reliability, and performance study of a single-use autoinjector with home-administered benralizumab SC in adult patients with severe asthma (ages 18-75 years) | |
| **Endpoints include** | ***Primary:*** Proportion of: patients/caregivers who successfully administered benralizumab SC with an AI device at home; returned AI devices used to administer benralizumab at home that have been evaluated as functional; AI devices used to administer benralizumab at home or in the clinic and have been reported as malfunctioning<br>***Secondary:*** Change from baseline in ACQ-6 score, serum concentration of benralizumab, peripheral blood EOS counts, ADA |

**Study Design**

A 28-week, open-label, multicenter, functionality, reliability, and performance study

N=121

Benralizumab 30 mg Q4W SC via AI



ACQ-6 = Asthma Control Questionnaire-6; ADA = antidrug antibodies; AI = autoInjector; EOS = eosinophil; Q4W = every 4 weeks; SC = subcutaneous.

Study NCT02918071. ClinicalTrials.gov website.

# GREGALE: Phase III Prefilled Syringe Usability Study

**ClinicalTrials.gov identifier:** NCT02417961
**Status:** Completed
**Completion Date**: March 2016[1]

## Trial Overview[2]

A 28-week, open-label, multicenter (30 centers across approximately 4 countries) study of benralizumab Q4W SC examining the usability of an accessorized prefilled syringe in patients with severe asthma (ages 18-75 years)

**Endpoints include**

***Co-Primary:*** Proportion of: patients/caregivers who successfully administered benralizumab SC with an accessorized prefilled syringe at home; returned APFS used to administer benralizumab at home that have been evaluated as functional; APFS used to administer benralizumab at home or in the clinic and have been reported as malfunctioning at Week 16

***Secondary[a]:***
- Change from baseline in mean ACQ-6 score
- Serum concentration of benralizumab
- Peripheral blood EOS counts
- ADA

**Study Design**

A 28-week, open-label, multicenter study

N=116

Benralizumab 30 mg Q4W SC



ACQ-6 = Asthma Control Questionnaire-6; ADA = antidrug antibodies; APFS = accessorized prefilled syringe; EOS = eosinophils; Q4W = every 4 weeks; SC = subcutaneous.



1. Study NCT02322775. ClinicalTrials.gov website; 2. Ferguson GT et al. *J Asthma Allergy*. 2018;11:63-72.

# ALIZE: Phase III Humoral Immune Response Trial

**ClinicalTrials.gov Identifier:** NCT02814643
**Status:** Completed
**Completion Date:** January 2017[1]

| Trial Overview[2] | |
|---|---|
| A 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study to evaluate humoral immune response following seasonal influenza virus vaccination in adolescent and young adult patients with severe asthma (ages 12-21 years) | |
| **Endpoints include** | ***Primary:*** Postdose strain-specific HAI antibody GMFRs at Week 12; Postdose strain-specific serum HAI antibody GMTs at Week 12; Proportion of patients who experience a strain-specific postdose antibody response ≥4 fold rise in HAI antibody titer at Week 12; Postdose HAI antibody titer ≥40 at Week 12<br>***Secondary*:** Proportion of patients who achieve a strain-specific postdose HAI antibody titer ≥320; postdose strain-specific MN antibody GMFRs, postdose strain-specific serum MN GMTs obtained |

**Study Design**

A 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study

N=103

**Randomization**

- Benralizumab 30 mg Q4W SC
- Placebo SC

[a]Select secondary endpoints listed. GMFRs = geometric mean fold rises; GMTs = geometric mean titers; HAI = hemagglutination-inhibition; MN = microneutralization; Q4W = every 4 weeks; SC = subcutaneous.





1. Study NCT02814643. ClinicalTrials.gov website; 2. Zeitlin PL et al. *J Asthma Allergy*. 2018;11:181-192.

# BISE: Phase III Mild to Moderate Asthma Trial

**ClinicalTrials.gov identifier:** NCT02322775
**Status:** Completed
**Completion Date**: October 2015[1]

| Trial Overview[2] | |
|---|---|
| A 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study of benralizumab in patients with mild to moderate persistent asthma (ages 18-75 years) | |
| **Endpoints include** | ***Primary:*** Change from baseline in predose $FEV_1$<br>***Secondary[a]:*** Change from baseline in:<br>• Morning and evening PEF<br>• Total asthma symptom score<br>• Total asthma rescue medication use (puffs) |

**Study Design**

A 12-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study

N=211

**Randomization**

- Benralizumab 30 mg Q4W SC
- Placebo SC

[a]Select secondary endpoints listed.

$FEV_1$ = forced expiratory volume in 1 second; PEF = peak expiratory flow; Q4W = every 4 weeks; SC = subcutaneous.





1. . Study NCT02322775. ClinicalTrials.gov website; 2. Ferguson GT et al. *Lancet Respir Med.* 2017;5:568-576.

# Benralizumab: Phase III Asthma Trials – Recruiting / Ongoing

| Study | Description / Patient Population | Estimated Enrollment | Study Design | Primary Outcome Measure | Status | Completion Date[a] |
|---|---|---|---|---|---|---|
| **MELTEMI**[1] | Safety / pharmacodynamics extension of BORA for patients on ICS + LABA (ages 18-75 years) | 446 | 130-week, open-label, multicenter | • Number of AEs/SAEs (Week 0-130 and through follow-up [12 weeks after last dose])<br>• Shift from baseline to maximum and minimum in standard chemistry/lab parameters (up to Week 130 in study treatment and through follow-up [12 weeks after last dose]) | Active, not recruiting | December 2019 |
| **ANDHI**[2] | Uncontrolled severe asthma with eosinophilic phenotype (EOS 150 µL to 300/µL, history of exacerbations) on standard of care treatment (ages 18-75 years) | 630 | 24-week, randomized, double-blind, parallel-group, multicenter | Annual asthma exacerbation rate reduction a Week 24 | Recruiting | August 2020 |
| **ANDHI IP**[3] | Uncontrolled severe asthma with eosinophilic phenotype (EOS 150 µL to 300/µL, history of exacerbations) on standard of care treatment (ages 18-75 years) | - | 56-week, open-label substudy of the ANDHI trial | Number of adapted GINA step category changes from Visit 15 to the EOS Visit 27 (Day 560/Week 80) | - | - |

[a]Estimated study completion date.

AEs = adverse events; AI = auto-Injector; EOS = eosinophils; $FEV_1$ = forced expiratory volume in 1 second; GINA = Global Initiative for Asthma; ICS = inhaled corticosteroid; IP = In Practice; LABA = long-acting β2-agonist; SAEs = serious adverse events.





1. Study NCT02808819. ClinicalTrials.gov website; 2. Study NCT03170271. ClinicalTrials.gov website; 3. In House Data, AstraZeneca Pharmaceuticals LP. CSP D3250C00045.

# Benralizumab: Phase III Asthma Trials – Recruiting / Ongoing

| Study | Description / Patient Population | Estimated Enrollment | Study Design | Primary Outcome Measure | Status | Completion Date[a] |
|---|---|---|---|---|---|---|
| **PONENTE**[1] | Patients with severe eosinophilic asthma receiving high-dose ICS + LABA and chronic OCS with or without additional asthma controller(s). (ages ≥18 years) | 600 | 38-week, open-label, multicenter | • Reduction of OCS dose<br>• Reduction or a daily OCS dose of ≤5 mg | Recruiting | October 2020 |
| **ARIA**[2] | Allergen-induced inflammation in mild, atopic asthma (ages 18-65 years) | 45 | 20-week, randomized, double-blind, parallel-group, placebo-controlled | • Change in percent of EOS in sputum 7 hours after allergen challenge (from prechallenge to 7 hours after allergen challenge during Week 9)<br>• Maximal percentage decrease in $FEV_1$ 3-7 hours after allergen challenge (from prechallenge to 3-7 hours after allergen challenge during Week 9) | Recruiting | September 2019 |
| **MIRACLE**[3,4] | Asthma inadequately controlled with medium- to high-dose ICS + LABA (ages 12-75 years) | 666 | 56-week, randomized, double-blind, parallel-group, multicenter | Annual asthma exacerbation rate reduction at Week 48 | Recruiting | February 2021 |

[a]Estimated study completion date.

EOS = eosinophils; $FEV_1$ = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LABA = long-acting β2-agonist; OCS = oral corticosteroids.



1. Study NCT03557307. ClinicalTrials.gov website; 2. Study NCT02821416. ClinicalTrials.gov website; 3. Study NCT03186209. ClinicalTrials.gov website; 4. AstraZeneca Pharmaceuticals LP. Clinical trials appendix. March 4, 2019.

# MELTEMI: Phase III Safety Extension Trial

**ClinicalTrials.gov Identifier:** NCT02808819
**Status:** Active, not recruiting
**Estimated Completion Date:** December 2019

| Trial Overview |
| --- |
| An open-label, multicenter, safety/pharmacodynamics extension of BORA for adults on ICS + LABA with/without chronic OCS treatment (ages ≥18 years) |

| | |
| --- | --- |
| **Endpoints include** | ***Primary:*** AEs, chemistry and hematology lab parameters<br>***Secondary*:** Asthma exacerbations, absolute EOS counts, ADA |

**Study Design**

An open-label, multicenter, safety extension study

N=446

**Continued Treatment Regimens**

- Benralizumab 30 mg Q4W SC
- Benralizumab 30 mg Q8W SC

ADA = antidug antibodies; EOS = eosinophils; ICS = inhaled corticosteroid; LABA = long-acting β2-agonist; OCS = oral corticosteroid; Q4W = every 4 weeks; Q8W = every 8 weeks; SC = subcutaneous.





Study NCT02808819. ClinicalTrials.gov website.

# ANDHI: Phase IIIb Severe Asthma Trial

**ClinicalTrials.gov Identifier:** NCT03170271
**Status:** Recruiting
**Estimated Completion Date:** August 2020

| Trial Overview |
| --- |
| A 24-week, double-blind, randomized, parallel-group, multicenter study of benralizumab in patients with uncontrolled severe asthma with eosinophilic phenotype (EOS 150/µL[a] to 300/µL[a], history of exacerbations) on standard of care treatment (ages 18-75 years) |

| Endpoints include | ***Primary:*** Asthma exacerbation rate<br>***Key Secondary***: SGRQ |
| --- | --- |

**Study Design**

A 24-week, double-blind, randomized, parallel-group, multicenter study

Estimated N=630

**Randomization**

- Benralizumab 30 mg Q8W SC
- Placebo SC

[a]Additional criteria required if EOS are ≥150 µL to 300 µL. ACQ-6 = Asthma Control Questionnaire 6; EOS = eosinophils; Q8W = every 8 weeks; SC = subcutaneous; SGRQ = St George's Respiratory Questionnaire.





Study NCT03170271. ClinicalTrials.gov website.

# ANDHI IP: Severe Asthma Substudy

- Enrollment in the ANDHI IP study will stop after the last ANDHI controlled patient completes their EOT, Visit 11[1]

| Trial Overview[1,2] | |
|---|---|
| A 56-week, open-label substudy of the ANDHI trial to assess the potential for benralizumab treated patients to taper concomitant asthma medications (ICS/LABA combination ± other controllers [eg, LAMA, LTRA, theophylline, or OCS] per a defined protocol while maintaining asthma control (ages 18-75 years) | |
| **Endpoints include** | ***Primary:*** Number of adapted[a] GINA step category changes from Visit 15[b] to the EOS Visit 27 (Day 560/Week 80)<br>***Other***: Change in continuous asthma efficacy measures (ACQ-6 and SGRQ) from Visit 15[b] to the EOS Visit 27 (Day 560/Week 80) |

**Study Design**

A 56-week, open-label, substudy of the ANDHI trial

**Open Label**

Benralizumab 30 mg Q8W SC

[a]Does not consider add-on benralizumab as part of the assessment. [b]End of open label run-in period (Visits 13-15) to introduce benralizumab to previous placebo patients from the ANDHI trial prior to entering the reduction phase. ACQ-6 = Asthma Control Questionnaire-6; EOS = end of study; EOT = end of treatment; GINA = Global Initiative for Asthma; ICS = inhaled corticosteroid; IP = In Practice; LABA = long-acting $\beta_2$-agonist Q8W = every 8 weeks; IP = In Practice; SC = subcutaneous; SGRQ = St George's Respiratory Questionnaire.





1. In House Data, AstraZeneca Pharmaceuticals LP. CSP D3250C00045; 2. Eu Clinical Trials Register. Accessed April 2, 2019.

# PONENTE: Phase IIIb OCS Reduction Trial

**ClinicalTrials.gov Identifier:** NCT03557307
**Status:** Recruiting
**Estimated Completion Date:** October 2020[1]

| Trial Overview[1,2] | |
|---|---|
| An open-label, multicenter study in patients with severe eosinophilic asthma receiving high-dose ICS/LABA and chronic OCS therapy (ages ≥18 years) | |
| **Endpoints include** | ***Primary:*** At the end of the OCS reduction phase (up to 38 weeks):<br>• Patients who achieve 100% reduction in daily OCS dose<br>• Patients who achieve 100% reduction or a daily OCS dose of ≤5 mg<br>***Secondary***: Additional OCS dose reduction outcomes |

**Study Design**

An open-label, multicenter study

Estimated N=600

**Open Label[2]**

Benralizumab 30 mg Q8W SC



ICS = inhaled corticosteroid; LABA = long-acting $\beta_2$-agonist; OCS = oral corticosteroid; Q8W = every 8 weeks; SC = subcutaneous.



1. Study NCT03186209. ClinicalTrials.gov website; 2. AstraZeneca Pharmaceuticals LP. Clinical trials appendix. March 4, 2019.

# ARIA: Phase III Allergen Challenge in Atopic Asthma Trial

**ClinicalTrials.gov Identifier:** NCT02821416
**Status:** Recruiting
**Estimated Completion Date:** September 2019

| Trial Overview | |
|---|---|
| A 16-week, randomized, double-blind, parallel-group, placebo-controlled study to evaluate the effect of benralizumab on allergen-induced inflammation in patients with mild, atopic asthma (ages 18-65 years) who previously demonstrated a dual-phase response to an inhaled allergen challenge during screening | |
| **Endpoints include** | ***Primary:*** Change in percent of eosinophils in sputum 7 hours after allergen challenge; Maximal % decrease in $FEV_1$ 3-7 hours after allergen challenge (ie, $LAR_{3-7}$)<br>***Secondary[a]:*** • Basophils in sputum • Decrease in $FEV_1$ 0-2 hours after allergen challenge, • AUC of time adjusted % decrease in $FEV_1$ curve in early asthmatic response |

**Study Design**

A 16-week, randomized, double-blind, parallel-group, placebo-controlled study

Estimated N=45

**Randomization**

- Benralizumab 30 mg Q4W SC
- Placebo SC

[a]Select secondary endpoints listed.

AUC = area under the curve; $FEV_1$ = forced expiratory volume in 1 second; LAR = late asthmatic response; Q4W = every 4 weeks; SC = subcutaneous

Study NCT02821416. ClinicalTrials.gov website.

# MIRACLE: Phase IIIb Severe Asthma Trial

**ClinicalTrials.gov Identifier:** NCT03186209
**Status:** Recruiting
**Estimated Completion Date:** February 2021

| Trial Overview |
| --- |
| A 48-week, double-blind, randomized, parallel-group, placebo-controlled, multicenter study of benralizumab in patients with uncontrolled severe asthma receiving medium- to high-dose ICS/LABA (ages 12-75 years) |

| Endpoints include | |
| --- | --- |
| | ***Primary:*** Annual asthma exacerbation rate<br>***Select Secondary***: $FEV_1$, Asthma Symptom Score, ACQ-6, SGRQ |

**Study Design**

A 48-week, double-blind, randomized, parallel-group, multicenter study

Estimated N=666

**Randomization**

- Benralizumab 30 mg Q8W SC
- Placebo SC

ACQ-6 = Asthma Control Questionnaire-6; $FEV_1$ = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LABA = long-acting $\beta_2$-agonist; Q8W = every 8 weeks; SC = subcutaneous; SGRQ = St. George's Respiratory Questionnaire.





Study NCT03186209. ClinicalTrials.gov website.

# Benralizumab: Asthma Registries and Observational, Prospective Cohort Studies

| Study | Description / Patient Population | N | Study Design | Key Outcome Measures | Status | Completion Date[a] |
|---|---|---|---|---|---|---|
| **ISAR**[1,2] | Patients with severe asthma from >14 countries | ~10,000 | International patient registry | • Describe and characterize the natural history of the severe asthma patient population overall, where appropriate, and by different subgroups (eg, by age, sex, disease severity, exacerbation frequency, different comorbidities, physician type, and by country to understand regional differences in patient characteristics)<br>• Facilitate the phenotyping and endotyping of patients with severe asthma and describe these patient groups by burden of illness, disease management patterns, and clinical evolution in an international setting | 9 countries enrolled, 5 countries in enrollment process | NA |
| **Pregnancy Exposure Study**[3] | Pregnant women with asthma exposed to benralizumab anytime during pregnancy or within 8 weeks prior to the last menstrual period | ~800 | Prospective, observational, cohort study | • Major structural birth defects, spontaneous abortion/miscarriage, preterm delivery, small for gestational age infants, spontaneous abortion, stillbirth, elective termination, and small for age postnatal growth to 1 year old | Not yet recruiting | November 2025 |
| **CHRONICLE**[4] | Severe asthma inadequately controlled with high-dose ICS therapy plus additional controllers, and/or requiring systemic corticosteroid or monoclonal antibody therapy (age ≥18 years) | ~4000 | Multicenter, non-interventional, prospective cohort study | • Longitudinal change of healthcare utilization, asthma treatment, treatment adherence, ACT, patient-reported exacerbations, WPAI asthma questionnaire scores, SGRQ, GTE, AEs associated with corticosteroid therapy | Recruiting | January 2026 |

[a]Estimated study completion date. ACT = Asthma Control Test; AEs = adverse events; GTE = Global evaluation of Treatment Effectiveness; ICS = inhaled corticosteroids; ISAR = International Severe Asthma Registry; SGRQ = St George's Respiratory Questionnaire; WPAI = Work Productivity and Activity Impairment.





1. ISAR. http://isaregistries.org; 2. ENCePP. ISAR protocol OR00617; 3 Study NCT03794999. ClinicalTrials.gov website; 4.Study NCT03373045. ClinicalTrials.gov website.

# International Severe Asthma Registry (ISAR)

**Status:** 9 countries enrolled (>5000 patients), 5 countries in enrollment process

| Overview[1,2] |
|---|
| Global collaborative initiative to gather anonymous, standardized, longitudinal, real-life data for patients with severe asthma from >14 countries in order to conduct further research. |

| | |
|---|---|
| **Objectives** | ***Primary***:<br>• Describe and characterize the natural history of the severe asthma patient population overall, where appropriate, and by different subgroups (eg, by age, sex, disease severity, exacerbation frequency, different comorbidities, physician type, and country)<br>• Facilitate the phenotyping and endotyping of patients with severe asthma and describe these patient groups by burden of illness, disease management patterns, and clinical evolution in an international setting<br>***Select Secondary***:<br>• Evaluate the real-life effectiveness and safety of treatments for severe asthma overall and in specific patient groups/phenotypes |

| Patients | Prospective Data Collection | Research Topics |
|---|---|---|
| Adult patients:<br>GINA Step 4 uncontrolled / Step 5<br>Estimated N = 10,000 | New registries: Electronic case report forms<br><br>Existing registries will follow data collection standards established by the ISAR steering group to enable combination with datasets from other countries | Priority topics selected each year by the ISAR steering committee |





1. ISAR. http://isaregistries.org/; 2. ENCePP. ISAR protocol OR00617.

# Benralizumab Pregnancy Exposure Study

**ClinicalTrials.gov Identifier:** NCT03794999
**Status:** Not yet recruiting
**Estimated Completion Date:** November 2025

| Trial Overview | |
|---|---|
| Prospective, observational cohort study of pregnancy and infant outcomes in women with asthma exposed to benralizumab any time during pregnancy or within 8 weeks prior to the first day of the last menstrual period | |
| **Endpoints include** | ***Primary***: Major structural birth defects<br>***Secondary***: Preterm delivery, small for gestational age infants, spontaneous abortion, stillbirth, elective termination, and small for age postnatal growth to 1 year |

**Study Design**

Prospective, observational, cohort study with 20-month follow-up target duration

Estimated N=800

**Pregnancy Exposure Cohorts**

- Exposed to benralizumab
- Exposed to asthma medications, except benralizumab
- No asthma diagnosis, not exposed to benralizumab or any known human teratogen




Study NCT037994999. ClinicalTrials.gov website.

# CHRONICLE: Observational, Prospective Cohort, Asthma Study in the US

**ClinicalTrials.gov Identifier:** NCT03373045
**Status:** Recruiting
**Estimated Completion Date:** January 2026

| Trial Overview | |
|---|---|
| Multicenter, non-interventional, prospective cohort study of adult patients with severe asthma who do not achieve control with high-dose ICS therapy with additional controllers and/or require systemic corticosteroids or monoclonal antibody therapy. In addition, the study will describe the use and outcomes associated with monoclonal antibody therapies for severe asthma. | |
| **Primary endpoints include** | Assessed up to 7 years:<br>• Healthcare utilization (hospitalizations, clinic visits, asthma exacerbations)<br>• Asthma treatment<br>• Treatment adherence<br>• Patient reported outcomes: exacerbations, ACT, WPAI-Asthma, SGRQ, GETE<br>• AEs associated with corticosteroid therapy/ AEs of special interest (eg, malignancy)<br>• Comorbidities<br>• Variables for asthma evaluation (eg, FVC, $FEV_1$, IgE, $Fe_{NO}$) |

| Estimated N | Data Collection | | Patient Follow-up |
|---|---|---|---|
| 4000 | **Asthma Specialists**<br>Electronic case report form | **Patients**<br>Web-based surveys | Until study discontinuation/withdrawal<br>Target: ≥3 years |

ACT = Asthma Control Test; AE = adverse events; $Fe_{NO}$ = fractional exhaled nitric oxide; $FEV_1$ = forced expiratory volume in 1 second; FVC = forced vital capacity; GETE = global evaluation of treatment effectiveness; ICS = inhaled corticosteroids; IgE = immunoglobulin E; SGRQ = St George's Respiratory Questionnaire; US = United States; WPAI-Asthma = Work Productivity and Activity Impairment Asthma Questionnaire.





Study NCT03373045. ClinicalTrials.gov website.

# Benralizumab: COPD Studies

# Benralizumab Is in Development for COPD

## Benralizumab

- COPD is a highly heterogenous disease, with up to 40% of patients having an eosinophil phenotype[1]
- Some, but not all, studies have demonstrated that elevated blood eosinophil counts were associated with increased risk of exacerbations[2-6]
- Type 2 cytokines (eg, IL-5) are the main mediators of eosinophil recruitment into the lungs and are thought to contribute to Type 2 inflammation in COPD[7,8]
- Benralizumab depletes eosinophils by specifically binding to the IL-5Rα of the eosinophil and then inducing apoptosis via ADCC[9]
- Benralizumab is currently in Phase III clinical development for COPD[10]

ADCC = antibody-dependent cell-mediated cytotoxicity; COPD = chronic obstructive pulmonary disease; IL-5 = interleukin- 5 receptor; IL-5Rα = interleukin- 5 receptor alpha.

1. Bafadhel M et al. *Lancet Respir Med*. 2017;5:747-759; 2 Yun JH et al. *J Allergy Clin Immunol.* 2018;141:2037-2047; 3. Pascoe S et al. *Lancet Respir Med*. 2015;3:435-442; 4. Kerkhof M et al. *Eur Respir J.* 2017;50; 5. Bafadhel M et al. *Lancet Respir Med.* 2018;6:117-126; 6. Bafadhel M et al. *Am J Respir Crit Care Med*. 2012;186:48-55; 7. Tripple JW et al. *Immunol Allergy Clin N Am*. 2917;37:345-355; 8. Hastie AT et al. *Lancet Respir Med.* 2017;5:956-967; 9. Molfino NA et al. *Clin Exp Allergy.* 2012;42:712-737; 10. AstraZeneca Pharmaceuticals LP. Clinical trials appendix. March 4, 2019.

# Benralizumab: Phase III COPD Trials

| Study | Description / Patient Population | Enrollment | Study Design | Primary Outcome Measure | Status | Completion Date[a] |
|---|---|---|---|---|---|---|
| **TERRANOVA**[1] | Moderate to very severe COPD with previous exacerbations[1] | 2255 | 56-week, randomized, double-blind, double-dummy, parallel-group, placebo-controlled, multicenter | Annual rate of COPD exacerbation | Completed | April 2018 |
| **GALATHEA**[2] | Moderate to very severe COPD with previous exacerbations[2] | 1656 | 56-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter | Annual rate of COPD exacerbation | Completed | April 2018 |

[a]Study completion date.
COPD = chronic obstructive pulmonary disease.





1. Study NCT02155660. ClinicalTrials.gov website; 2. Study NCT02138916. ClinicalTrials.gov website.

# TERRANOVA: Phase III COPD Clinical Trial

**ClinicalTrials.gov identifier:** NCT02155660
**Status:** Completed
**Study Completion Date:** April 2018

## Trial Overview[1]

A 56-week, randomized, double-blind, double-dummy, placebo-controlled, parallel-group, multicenter study in patients with moderate to very severe COPD and history of previous exacerbations (ages 40-85 years)

**Endpoints include**

***Primary:*** Annual COPD exacerbation rate

***Secondary[a]:***
- Effect of benralizumab on health status/health-related quality of life
- Effect of benralizumab on pulmonary function
- Effect of benralizumab on respiratory symptoms

**Study Design**

A randomized, double-blind, double-dummy, placebo-controlled, parallel-group, multicenter study

N=2255

**Randomization[2]**

- Arm 1: Benralizumab SC 10 mg Q8W SC
- Arm 2: Benralizumab SC 30 mg Q8W SC
- Arm 3: Benralizumab SC 100 mg Q8W SC
- Arm 4: Placebo SC

[a]Select secondary endpoints.

COPD = chronic obstructive pulmonary disease; Q8W = every 4 weeks for the first 3 doses followed by every 8 weeks; SC = subcutaneous.





1. Study NCT02155660. ClinicalTrials.gov website; 2. In House Data, AstraZeneca Pharmaceuticals LP. CSP D3251C00004.

# GALATHEA: Phase III COPD Clinical Trial

**ClinicalTrials.gov identifier:** NCT02138916
**Status:** Completed
**Study Completion Date:** April 2018

| Trial Overview[1] | |
|---|---|
| A 56-week, randomized, double-blind, placebo-controlled, parallel-group, multicenter study in patients with moderate to very severe COPD and history of previous exacerbations (ages 40-85 years) | |
| **Endpoints include** | ***Primary:*** Annual COPD exacerbation rate<br>***Secondary[a]:*** • Effect of benralizumab on health status/health-related quality of life<br>• Effect of benralizumab on pulmonary function<br>• Effect of benralizumab on respiratory symptoms |

**Study Design**

A randomized, double-blind, placebo-controlled, parallel-group, multicenter study

N=1656

**Randomization[2]**

- Arm 1: Benralizumab SC 30 mg Q8W SC
- Arm 2: Benralizumab SC 100 mg Q8W SC
- Arm 3: Placebo SC



[a]Select secondary endpoints. COPD = chronic obstructive pulmonary disease; Q8W = every 4 weeks for the first 3 doses followed by every 8 weeks; SC = subcutaneous.



1. Study NCT02138916. ClinicalTrials.gov website; 2. In House Data, AstraZeneca Pharmaceuticals LP. CSP 3251C00003.

# Benralizumab: Nasal Polyposis

# Role of Eosinophils in Chronic Rhinosinusitis With Nasal Polyps

80% of Caucasian patients with CRSwNP have major eosinophilic inflammation[1]

Cytokines, including IL-5 on eosinophils and IL-4/IL-13 on a host of cells, in addition to inflammatory cells, including basophils and eosinophils, have been implicated in the pathogenesis of one type of CRSwNP[2]

CRSwNP refractory to medical and surgical therapy has been associated with eosinophilia, asthma, and allergy[3]

The comorbid association between CRS and asthma suggests a similar immunologic pattern of inflammation occurring at the epithelial cell layers of the upper and lower airways[4]

Compared with placebo, benralizumab treated NP+ patients showed improved efficacy measures, including asthma exacerbation rates, $FEV_1$, asthma control (ACQ-6), and asthma-related quality of life symptoms (AQLQ[S]+12)[5]

ACQ-6 = Asthma Control Questionnaire-6; AQLQ(S)+12 = Asthma Quality of Life Questionnaire for 12 years and older; CRS = chronic rhinosinusitis; CRSwNP = chronic rhinosinusitis with nasal polyps; $FEV_1$ = forced expiratory volume in 1 second; IL = interleukin; NP+ = nasal polyp.



1. Van Zele T et al. *Allergy Clin Immunol.* 2010;125:1069-1076; 2. Schleimer R. *Annu Rev Pathol.* 2017;12:331-357; 3. Hull BP et al. *Otolaryngol Clin N Am*. 2017;50:61-81; 4. Lam K et al. *Int Forum Allergy Rhinol*. 2016;6:935-942; 5. Maspero J et al. *J Allergy Clin Immunol*. 2018. AB12.

# Benralizumab: Phase III Trial

| Study | Description / Patient Population | Enrollment | Study Design | Primary Outcome Measure | Status | Estimated Completion Date |
|---|---|---|---|---|---|---|
| **OSTRO** | Severe bilateral nasal polyposis, symptomatic despite current use of intranasal corticosteroids and prior surgery and/or systemic corticosteroids | ~400 | 56-week, randomized, double-blind, placebo-controlled, parallel-group, multicenter study | Change in endoscopic total nasal polyp score; change in mean nasal blockage score | Recruiting | November 2020 |





Study NCT03401229. ClinicalTrials.gov website.

# OSTRO: Phase III Nasal Polyposis Trial

**ClinicalTrials.gov Identifier:** NCT03401229
**Status:** Recruiting
**Estimated Completion Date:** November 2020

| Trial Overview | |
|---|---|
| A 56-week, randomized, double-blind, parallel-group, placebo-controlled, multicenter study to investigate the use of benralizumab as treatment for severe nasal polyposis | |
| **Endpoints include** | ***Primary:*** Changes in endoscopic total nasal polyp score and mean nasal blockage score<br>***Secondary[a]:*** • Change from baseline in SinoNasal Outcome Test (SNOT-22) score<br>• Sinus opacification by CT scan (subset of patients)<br>• Time to first nasal polyp surgery<br>• Proportion of patients with nasal polyp surgery<br>• Proportion of patients with systemic corticosteroid use for nasal polyps |

**Study Design**

A 56-week, double-blind, parallel-group, multicenter, placebo-controlled study

Estimated N=400

**Randomization**

- Benralizumab 30 mg Q8W SC + Mometasone Furoate Nasal Spray
- Placebo SC + Mometasone Furoate Nasal Spray



[a]Select secondary endpoints. CT = computed tomography; Q8W = every 4 weeks for the first 3 doses followed by every 8 weeks; SC = subcutaneous.

Study NCT03401229. ClinicalTrials.gov website.

# Benralizumab: Other Studies

# Benralizumab: Phase I Pharmacokinetic Study

| Study | Description / Patient Population | Enrollment | Study Design | Primary Outcome Measure | Status | Completion Date[a] |
|---|---|---|---|---|---|---|
| **AMES** | Healthy adult volunteers | 180 | 8-week, randomized, open-label, parallel-group, single-dose, multicenter study | AUC and Cmax following single administration with AI and APFS devices at different time intervals | Completed | July 2017 |

[a]Study completion date.

AI = autoinjector; APFS = accessorized prefilled syringe; AUC = area under the curve; Cmax = maximum plasma concentration.

Study NCT02968914. ClinicalTrials.gov website.

# AMES: Phase I Pharmacokinetic Study Comparing APFS and AI Devices

**ClinicalTrials.gov Identifier:** NCT02968914
**Status:** Completed
**Completion Date:** July 2017

| Trial Overview | |
|---|---|
| An 8-week, randomized, open-label, parallel-group, single-dose, multicenter, study to compare the pharmacokinetics of benralizumab administered with an accessorized prefilled syringe (APFS) and an autoinjector (AI) device in healthy adult volunteers | |
| **Endpoints include** | ***Primary:*** AUC and Cmax following single administration of each device at different time intervals |

**Study Design**

An 8-week, randomized, open-label, parallel-group, single-dose, multicenter study

N=180

**Randomization**

- Single dose of benralizumab 30 mg via APFS
- Single dose of benralizumab 30 mg via AI




Study NCT02968914. ClinicalTrials.gov website.

# Benralizumab: Non-AstraZeneca Studies

# Benralizumab: Studies by Other Sponsors in Eosinophilic Asthma

| Study | Description / Patient Population | Enrollment | Study Design | Primary Outcome Measure | Status | Estimated Completion Date[a] |
|---|---|---|---|---|---|---|
| **NCT03327701**[1] | Moderate-to-severe asthma (ages 18-65 years) | ~40 | 20-week, double-blind, placebo-controlled Phase III study | Maximal fall in forced expiratory volume in 1 second after exercise challenge | Not yet recruiting | April 2020 |
| **NCT03733535**[2] | Severe, poorly-controlled eosinophilic asthma (ages 18-75 years) | ~36 | 16-week, open-label, single-arm study | Change from baseline airway function measured using 129-Xenon MRI ventilation defect percent on Day 28 | Not yet recruiting | April 2020 |
| **NCT03652376**[3] | Severe eosinophilic asthma (ages 18-75 years) | ~20 | 5-month, open-label, single arm Phase IV study | Dendritic cell concentrations and phenotypes | Not yet recruiting | December 2019 |
| **NCT03470311**[4] | Severe prednisone-dependent eosinophilic asthma, uncontrolled on mepolizumab or reslizumab (ages ≥18 years) | ~20 | 38-week, single-blind, placebo-controlled Phase III study | Change in percentage of sputum eosinophils | Recruiting | June 2019 |

[a]Study completion date. MRI = magnetic resonance imaging.



1. Study NCT03327701. ClinicalTrials.gov website; 2. Study NCT03733535. ClinicalTrials.gov website; 3. Study NCT03652376. ClinicalTrials.gov website; 4. Study NCT03470311. ClinicalTrials.gov website.

# Benralizumab: Studies by Other Sponsors in Other Eosinophilic Diseases

| Study | Description / Patient Population | Enrollment | Study Design | Primary Outcome Measure | Status | Estimated Completion Date[b] |
|---|---|---|---|---|---|---|
| **BITE**[1,a] | Eosinophilic Granulomatosis with Polyangiitis (EGPA) (ages ≥18 years) | ~10 | 28-week, open-label, single-group Phase II study | Safety and tolerability | Recruiting | December 2018 |
| **NCT02130882**[2,a] | Hypereosinophilic syndrome (ages 18-75 years) | 22 | ≥104-week, randomized, double-blind, placebo-controlled Phase IIa study | 50% reduction in peripheral blood eosinophilia on stable background therapy at 12 weeks after initiation of study drug | Active, not recruiting | June 2020 |
| **NCT02772419**[3] | Eosinophilic chronic rhinosinusitis (ages 20-75 years) | 63 | 24-week, randomized, double-blind, placebo-controlled Phase II study | Change from baseline in nasal polyp score at Week 12 | Completed | March 2017 |
| **NCT03450083**[4] | Severe chronic rhinosinusitis with eosinophilic nasal polyps (ages 18-75 years) | ~32 | 24-week, randomized, quadruple-blind, placebo-controlled Phase II study | Reduction in endoscopic nasal polyp score after 6 months of treatment | Recruiting | June 2020 |
| **NCT03183024**[5] | Chronic idiopathic urticaria (ages 19-70 years) | 12 | 7-month, non-randomized, single-blind Phase IV study | Change in urticarial activity score over 7 days | Recruiting | December 2018 |

[a]AstraZeneca is a study collaborator and has orphan drug designation; [b]Study completion date.



1. Study NCT03010436. ClinicalTrials.gov website; 2. Study NCT02130882. ClinicalTrials.gov website; 3. Study NCT02772419. ClinicalTrials.gov website;
4. Study NCT03450083. ClinicalTrials.gov website; 5. Study NCT03183024. ClinicalTrials.gov website.

# Benralizumab: Studies by Other Sponsors in Other Eosinophilic Diseases

| Study | Description / Patient Population | Enrollment | Study Design | Primary Outcome Measure | Status | Estimated Completion Date[a] |
|---|---|---|---|---|---|---|
| **NCT03473977**[1] | Eosinophilic gastritis or gastroenteritis (ages 12-60 years) | ~26 | 3-year, double-blind, placebo-controlled, with open-label extension | Percentage of patients that achieve histological remission in the stomach as defined by peak eosinophil counts <30/hpf | Recruiting | March 2021 |
| **NCT03563066**[2] | Moderate to severe atopic dermatitis (ages 18-65 years) | ~20 | 65-day, double-blind, placebo-controlled Phase II study | Effect of benralizumab on the number of allergen-induced eosinophils in the skin | Not yet recruiting | July 2019 |

[a]Study completion date.
hpf = high power field.





1. Study NCT03473977. ClinicalTrials.gov website; 2. Study NCT03563066. ClinicalTrials.gov website.