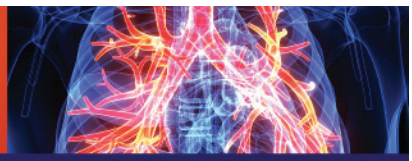

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Abbreviations & References

Abbreviations

ACQ, Asthma Control Questionnaire

AERD, aspirin-exacerbated respiratory disease

AQLQ, Asthma Quality of Life Questionnaire

ATS, American Thoracic Society

CSCR2, chemokine receptor 2

CRTh2, chemoattractant receptor homologue expressed on Th2 cells (alternative name DP2)

DPP4, dipeptidyl peptidase-4

eNO, exhaled nitric oxide

FeNO, fractional exhaled nitric oxide

FEV1, forced expiratory volume in 1 second

GM-CSF, granulocyte-macrophage colony-stimulating factor

HPA, hypothalamic-pituitary-adrenal

ICS, inhaled corticosteroids

IgE, immunoglobulin E

IL-4, interleukin 4

IL-5, interleukin 5

IL-5Ra, interleukin 5 receptor alpha subunit

IL-13, interleukin 13

LABA, long-acting beta-agonists

LAMA, long-acting muscarinic antagonists

LAR, late asthmatic response

LRT, lower respiratory tract

LTRA, leukotriene receptor antagonists

mAbs, monoclonal antibodies

mL, microliter

NO, nitric oxide

OCS, oral corticosteroids

PGD2, prostaglandin D2

PMN, polymorphonuclear;

QoL, quality of life

SQ, subcutaneous TH2, T-helper 2 lymphocytes

TSLP, thymic stromal lymphopoietin

WBC, white blood cells

References

Aghjayan R. *Pulmonology Advisor*. Posted March 3, 2018. Uncontrolled asthma improved with tezepelumab. Available at

https://www.pulmonologyadvisor.com/aaaaiwao-2018/uncontrolled-asthma-treated-with-tezepelumab/article/748045/. Accessed June 18, 2018.

Bagnasco D, Ferrando M, Varricchi G, et al. Anti-interleukin 5 (IL-5) and IL-5Ra biological drugs: efficacy, safety, and future perspectives in severe eosinophilic asthma. *Front Med*. 2017;4:135. doi:10.3389/fmed.2017.00135

Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med*. 2014;371:1189-97.

Bleecker ER, Fitzgerald JM, Chanez P, et al; SIROCCO study investigators. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomized, multicentre, placebo-controlled phase 3 trial. Lancet. 2016;388(10056):2115–2127.

Busse WW, Holgate S, Kerwin E, et al. Randomized, double-blind, placebo-controlled study of brodalumab, a human anti-IL-17 receptor monoclonal antibody, in moderate to severe asthma. *Am J Respir Crit Care Med*. 2013;188(11):1294-302. doi:10.1164/rccm.201212-2318OC

Busse WW, Maspero JF, Rabe KF, et al. Liberty Asthma QUEST: Phase 3 randomized, double-blind, placebo-controlled, parallel-group study to evaluate dupilumab efficacy/safety in patients with uncontrolled, moderate-to-severe asthma. *Adv Ther*. 2018. doi:10.1007/s12325-018-0702-4 [Epub ahead of print]

Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. *N Engl J Med*. 2018;378(26):2486-2496. doi:10.1056/NEJMoa1804092

Cazzola M, Matera MG, Levi-Schaffer F, Rogliani P. Safety of humanized monoclonal antibodies against IL-5 in asthma: focus on reslizumab. *Expert Opin Drug Saf*. 2018;17(4):429-435. doi:10.1080/14740338.2018.1446940

Corren J. Asthma phenotypes and endotypes: an evolving paradigm for classification. *Discov Med*. 2013;15(83):243-9.

Corren J, Parnes JR, Liangwei W, et al. Tezepelumab demonstrates clinically meaningful improvements in asthma control (ACQ-6) in patients with uncontrolled asthma: results from a phase 2b clinical trial. *J Allergy Clin Immunol*. 2018;141(2):AB80. https://doi.org/10.1016/j.jaci.2017.12.259

Corren J, Parnes JR, Wang L, et al. Tezepelumab in adults with uncontrolled asthma. *N Engl J Med*. 2017;377(10):936-946. doi:10.1056/NEJMoa1704064

Corren J, Weinstein S, Janka L, Zangrilli J, Garin M. Phase 3 study of reslizumab in patients with poorly controlled asthma: Effects across a broad range of eosinophil counts. *Chest*. 2016;150(4):799-810. doi:10.1016/j.chest.2016.03.018

Farne HA, Wilson A, Powell C, Bax L, Milan SJ. Anti-IL5 therapies for asthma. *Cochrane Database Syst Rev*. 2017;9:CD010834. doi:10.1002/14651858.CD010834.pub3

Fitzgerald JM, Bleecker ER, Nair P, et al; CALIMA study investigators. Benralizumab, an anti-interleukin-5 receptor α monoclonal antibody, as add-on treatment for patients with severe, uncontrolled eosinophilic asthma (CALIMA): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2016;388(10056):2128–2141.

Fitzpatrick AM, Teague WG, Meyers DA, et al. Heterogeneity of severe asthma in childhood: confirmation by cluster analysis of children in the National Institutes of Health/National Heart, Lung, and Blood Institute Severe Asthma Research Program. *J Allergy Clin Immunol*. 2011;127(2):382-389.e1-13. doi:10.1016/j.jaci.2010.11.015

George L, Brightling CE. Eosinophilic airway inflammation: role in asthma and chronic obstructive pulmonary disease. *Ther Adv Chronic Dis*. 2016;7(1):34-51. doi:10.1177/2040622315609251

Gibson PG, Yang IA, Upham JW, et al. Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2017;390(10095):659-668. doi:10.1016/S0140-6736(17)31281-3

Gonem S, Berair R, Singapuri A, et al. Fevipiprant, a prostaglandin D2 receptor 2 antagonist, in patients with persistent eosinophilic asthma: a single-centre, randomised, double-blind, parallel-group, placebo-controlled trial. *Lancet Respir Med*. 2016;4(9):699-707. doi:10.1016/S2213-2600(16)30179-5

Goorsenberg AWM, d'Hooghe JNS, de Bruin DM, van den Berk IAH, Annema JT, Bonta PI. Bronchial thermoplasty-induced acute airway effects assessed with optical coherence tomography in severe asthma. *Respiration*. 2018:1-7. doi:10.1159/000491676

Hanania NA, Alpan O, Hamilos DL, et al. Omalizumab in severe allergic asthma inadequately controlled with standard therapy: a randomized trial. *Ann Intern Med*. 2011;154:573-82.

Israel E, Reddel HK. Severe and difficult-to-treat asthma in adults. *N Engl J Med*. 2017;377(10):965-976.

Kupczyk M, ten Brinke A, Sterk PJ, et al. Frequent exacerbators—a distinct phenotype of severe asthma. *Clin Exp Allergy*. 2014;44(2):212-21. doi:10.1111/cea.12179

Moore WC, Meyers DA, Wenzel SE, et al. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. *Am J Respir Crit Care Med*. 2010;181(4):315-23. doi:10.1164/rccm.200906-0896OC

Naik SP, Mahesh PA, Jayaraj BS, Madhunapantula SV, Jahromi SR, Yadav MK. Evaluation of inflammatory markers interleukin-6 (IL-6) and matrix metalloproteinase-9 (MMP-9) in asthma. *J Asthma*. 2017;54(6):584-593. doi:10.1080/02770903.2016.1244828

Nair P, Wenzel S, Rabe KF, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. *N Engl J Med*. 2017;376(25):2448-2458. doi:10.1056/NEJMoa1703501

Ortega H, Bradford ES, Albers FC, et al. Long-term safety of mepolizumab in patients with severe eosinophilic asthma: The COLUMBA Study. Presented at the American Thoracic Society 2018 International Conference; San Diego, California; May 18-23, 2018. Abstract A1367.

Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. *Lancet*. 2012; 380:651-9.

Pelaia C, Vatrella A, Bruni A, Terracciano R, Pelaia G. Benralizumab in the treatment of severe asthma: design, development and potential place in therapy. *Drug Des Devel Ther*. 2018;12:619-628. doi:10.2147/DDDT.S155307

Peters SP. Asthma phenotypes: nonallergic (intrinsic) asthma. *J Allergy Clin Immunol Pract*. 2014;2(6):650-2. doi:10.1016/j.jaip.2014.09.006

Price DB, Rigazio A, Campbell JD, et al. Blood eosinophil count and prospective annual asthma disease burden: a UK cohort study. *Lancet Respir Med*. 2015;3(11):849-58. doi:10.1016/S2213-2600(15)00367-7

Rabe KF, Nair P1, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. *N Engl J Med*. 2018;378(26):2475-2485. doi:10.1056/NEJMoa1804093

Santus P, Radovanovic D. Prostaglandin D2 receptor antagonists in early development as potential therapeutic options for asthma. *Expert Opin Investig Drugs*. 2016;25(9):1083-92. doi:10.1080/13543784.2016.1212838

Spector SL, Farr RS. The heterogeneity of asthmatic patients—an individualized approach to diagnosis and treatment. *J Allergy Clin Immunol*. 1976 May;57(5):499-511.

Trejo Bittar HE, Yousem SA, Wenzel SE. Pathobiology of severe asthma. *Annu Rev Pathol*. 2015;10:511-45. doi:10.1146/annurev-pathol-012414-040343

Uddin M, Betts C, Robinson I, et al. The chemokine CxCR2 antagonist (AZD5069) preserves neutrophil-mediated host immunity in non-human primates. *Haematologica*. 2017; 102(2): e65–e68. doi:10.3324/haematol.2016.152371

Wechsler ME. Current and emerging biologic therapies for asthma and COPD. *Respir Care*. 2018;63(6):699-707. doi:10.4187/respcare.06322

Wenzel SE. Asthma phenotypes: the evolution from clinical to molecular approaches. *Nat Med*. 2012;18(5):716-25. doi:10.1038/nm.2678

Wenzel S, Castro M, Corren J, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting β2 agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. *Lancet*. 2016;388:31-44.

Zayed Y, Kheiri B, Banifadel M, et al. Dupilumab safety and efficacy in uncontrolled asthma: a systematic review and meta-analysis of randomized clinical trials. *J Asthma*. 2018 Oct 1:1-10. doi:10.1080/02770903.2018.1520865 [Epub ahead of print]