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THIS TIME NEW FORMAT, LESS ELEGANT FORMAT BUT SIMPLER AND INCLUDES ABSTRACT AND INFO RE OPEN ACCESS ARTICLES.

COPD

J Clin Med

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. 2022 Jun 20;11(12):3539.

doi: 10.3390/jcm11123539.

Use of Inhaled Corticosteroids and Risk of Acquiring *Haemophilus influenzae* in Patients with Chronic Obstructive Pulmonary Disease

Raza Ul Mohsin[1], Christian Kjer Heerfordt[1], Josefin Eklöf[1], Pradeesh Sivapalan[1], Mohamad Isam Saeed[1], Truls Sylvan Ingebrigtsen[1], Susanne Dam Nielsen[2], Zitta Barrella Harboe[3,4], Kasper Karmark Iversen[5], Jette Bangsborg[6], Jens Otto Jarløv[6], Jonas Bredtoft Boel[6], Christian Østergaard Andersen[7], Henrik Pierre Calum[7], Ram B Dessau[8], Jens-Ulrik Stæhr Jensen[1,2,4]

Affiliations expand

- PMID: 35743610

- DOI: 10.3390/jcm11123539

Abstract

Background: Inhaled corticosteroids (ICS) are widely used in chronic obstructive pulmonary disease (COPD), despite the known risk of severe adverse effects including pulmonary infections. **Research Question:** Our study investigates the risk of acquiring a positive *Haemophilus influenzae* airway culture with use of ICS in outpatients with COPD. **Study Design and Methods:** We conducted an epidemiological cohort study using data from 1 January 2010 to 19 February 2018, including 21,218 outpatients with COPD in Denmark. ICS use 365 days prior to cohort entry was categorised into low, moderate, and high, based on cumulated ICS dose extracted from a national registry on reimbursed prescriptions. A Cox proportional hazards regression model was used to assess the future risk of acquiring *H. Influenzae* within 365 days from cohort entry, and sensitivity analyses were performed using propensity score matched models. **Results:** In total, 801 (3.8%) patients acquired *H. Influenzae* during follow-up. Use of ICS was associated with a dose-dependent increased risk of acquiring *H. Influenzae* with hazard ratio (HR) 1.2 (95% confidence interval (CI) 0.9-1.5, *p* value = 0.1) for low-dose ICS; HR 1.7 (95% CI 1.3-2.1, *p* value < 0.0001) for moderate dose; and HR 1.9 (95% CI 1.5-2.4, *p* value < 0.0001) for high-dose ICS compared to no ICS use. Results were confirmed in the propensity-matched model using the same categories. **Conclusions:** ICS use in outpatients with COPD was associated with a dose-dependent increase in risk of isolating *H. Influenzae*. This observation supports that high dose ICS should be used with caution.

Keywords: chronic obstructive pulmonary disease; haemophilus influenzae; inhaled corticosteroids.

SUPPLEMENTARY INFO

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J Inflamm (Lond)

. 2022 Jun 23;19(1):8.

doi: 10.1186/s12950-022-00305-y.

Influenza a virus triggers acute exacerbation of chronic obstructive pulmonary disease by increasing proinflammatory cytokines secretion via NLRP3 inflammasome activation

Shuang Ji[#1,2], Meng-Yuan Dai[#1,2], Yun Huang[#2,3], Xiang-Chun Ren[1,2], Meng-Long Jiang[3], Jin-Ping Qiao[4], Wen-Ying Zhang[1,2], Yuan-Hong Xu[5], Ji-Long Shen[6], Ren-Quan Zhang[7,8], Guang-He Fei[9,10]

Affiliations expand

- PMID: 35739522

- DOI: 10.1186/s12950-022-00305-y

Abstract

Background: Influenza A virus (IAV) triggers acute exacerbation of chronic obstructive pulmonary disease (AECOPD), but the molecular mechanisms remain unclear. In this study, we investigated the role of IAV induced NLRP3 inflammasome activation to increase airway inflammation response in the progression of AECOPD.

Methods: Human bronchial epithelial cells were isolated and cultured from normal and COPD bronchial tissues and co-cultured with IAV. The NLRP3 inflammasome associated genes were identified using RNA sequencing, and the expressions of NLRP3 inflammasome components were measured using qRT-PCR and western blot after cells were transfected with siRNA and treated with MCC950. Moreover, IAV-induced COPD rat models were established to confirm the results; 37 AECOPD patients were included to measure the serum and bronchoalveolar lavage fluid (BALF) of interleukin (IL)-18 and IL-1β.

Results: Increased levels of NLRP3 inflammasome components were not seen until 6 h post-inoculation in normal cells. However, both cell groups reached peak NLRP3 level at 12 h post-inoculation and maintained it for up to 24 h. ASC, Caspase-1, IL-1β and IL-18 were also elevated in a similar time-dependent pattern in both cell groups. The mRNA and protein expression of the NLRP3 inflammasome components were decreased when COPD cells treated with siRNA and MCC950. In COPD rats, the NLRP3 inflammasome components were elevated by IAV. MCC950 alleviated lung damage, improved survival time, and reduced NLRP3 inflammasome components expression in COPD rats. Additionally, the serum and BALF levels of IL-1β and IL-18 were increased in AECOPD patients.

Conclusions: NLRP3 inflammasome is activated in COPD patients as a pre-existing condition that is further exacerbated by IAV infection.

Keywords: Acute exacerbation; Airway inflammation; Chronic obstructive pulmonary disease; Influenza A virus; MCC950; NLRP3 inflammasome pathway.

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- 37 references

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Am J Respir Crit Care Med

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. 2022 Jun 23.

doi: 10.1164/rccm.202201-0209PP. Online ahead of print.

Blood Eosinophils and Chronic Obstructive Pulmonary Disease: A GOLD Science Committee 2022 Review

Dave Singh[1], Alvar Agusti[2], Fernando J Martinez[3], Alberto Papi[4], Ian D Pavord[5], Jadwiga A Wedzicha[6], Claus F Vogelmeier[7], David M G Halpin[8,9]

Affiliations expand

- PMID: 35737975

- DOI: 10.1164/rccm.202201-0209PP

Abstract

COPD is a heterogeneous condition. Some patients benefit from treatment with inhaled corticosteroids (ICS) but this requires a precision medicine approach, based on clinical characteristics (phenotyping) and biological information (endotyping) in order to select patients most likely to benefit. The GOLD 2019 report recommended using exacerbation history combined with blood eosinophil counts (BEC) to identify such patients. Importantly, the relationship between BEC and ICS effects is continuous; no / small effects are observed at lower BEC, with increasing effects at higher BEC. The GOLD 2022 report has added additional evidence and recommendations concerning the use of BEC in COPD in clinical practice. Notably, associations have been demonstrated in COPD patients between higher BEC and increased levels of type-2 inflammation in the lungs. These differences in type-2 inflammation can explain the differential ICS response according to BEC. Additionally, lower BEC are associated with greater presence of proteobacteria, notably haemophilus, and increased bacterial infections and pneumonia risk. These observations support management strategies that use BEC to help identify subgroups with increased ICS response (higher BEC) or increased risk of bacterial infection (lower BEC). Recent studies in younger individuals without COPD have also shown that higher BEC are associated with increased risk of FEV1 decline and the development of COPD. Here we discuss and summarise the GOLD 2022 recommendations concerning the use of BEC as a biomarker that can facilitate a personalised management approach in COPD.

Keywords: BIOMARKER; COPD; MICROBIOME; TYPE 2 INFLAMMATION; eosinophils.

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Clin Respir J

. 2022 Jun 22.

doi: 10.1111/crj.13518. Online ahead of print.

Evaluation of the multimorbidity network and its relationship with

clinical phenotypes in chronic obstructive pulmonary disease: The GALAXIA study

Juan Marco Figueira-Gonçalves[1,2], Rafael Golpe[1,3], Cristóbal Esteban[4,5], Miguel Ángel García-Bello[6], Nagore Blanco-Cid[3], Amaia Aramburu[4], Ignacio García-Talavera[1], María Dolores Martín-Martínez[7], Adrian Baeza-Ruiz[1], Andrea Expósito-Marrero[1]

Affiliations expand

- PMID: 35732615

- DOI: 10.1111/crj.13518

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a complex and heterogeneous condition, in which taking into consideration clinical phenotypes and multimorbidity is relevant to disease management. Network analysis, a procedure designed to study complex systems, allows to represent connections between the distinct features found in COPD.

Methods: Network analysis was applied to a cohort of patients with COPD in order to explore the degree of connectivity between different diseases, taking into account the presence of two phenotypic traits commonly used to categorize patients in clinical practice: chronic bronchitis (CB^+ /CB^-) and the history of previous severe exacerbations (Ex^+ /Ex^-). The strength of association between diseases was quantified using the correlation coefficient Phi (ϕ).

Results: A total of 1726 patients were included, and 91 possible links between 14 diseases were established. Although the four phenotypically defined groups presented a similar underlying comorbidity pattern, with special relevance for cardiovascular diseases and/or risk factors, classifying patients according to the presence or absence of CB implied differences between groups in network density (mean ϕ: 0.098 in the CB^- group and 0.050 in the CB^+ group). In contrast, between-group differences in network density were small and of questionable significance when classifying patients according to prior exacerbation history (mean ϕ: 0.082 among Ex^- subjects and 0.072 in the Ex^+ group). The degree of connectivity of any given disease with the rest of the network also varied depending on the selected phenotypic trait. The classification of patients according to the CB^- /CB^+ groups revealed significant differences between groups in the degree of conectivity between

comorbidities. On the other side, grouping the patients according to the Ex^{-} /Ex^{+} trait did not disclose differences in connectivity between network nodes (diseases).

Conclusions: The multimorbidity network of a patient with COPD differs according to the underlying clinical characteristics, suggesting that the connections linking comorbidities between them vary for different phenotypes and that the clinical heterogeneity of COPD could influence the expression of latent multimorbidity. Network analysis has the potential to delve into the interactions between COPD clinical traits and comorbidities and is a promising tool to investigate possible specific biological pathways that modulate multimorbidity patterns.

Keywords: COPD; chronic bronchitis; comorbidities; exacerbation; network; phenotype.

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- 32 references

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Am J Respir Crit Care Med

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. 2022 Jun 21.

doi: 10.1164/rccm.202203-0458LE. Online ahead of print.

New Guidelines for Bronchodilator Responsiveness in COPD: A Test in Search of a Use

Surya P Bhatt[1], Spyridon Fortis[2], Sandeep Bodduluri[3]

Affiliations expand

- PMID: 35728043

- DOI: 10.1164/rccm.202203-0458LE

No abstract available

Keywords: Bronchodilator Response; Chronic Obstructive Pulmonary Disease; Guidelines.

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Expert Rev Respir Med

. 2022 Jun 20;1-13.

doi: 10.1080/17476348.2022.2090343. Online ahead of print.

A reappraisal of inspiratory capacity in chronic obstructive pulmonary disease: clinical correlates and role of long-acting muscarinic antagonists and long-acting β2 agonists

Fiammetta Danzo[1,2], Dejan Radovanovic[1], Marina Gatti[1,2], Marina Saad[1,2], Luca Perotto[1,2], Elisa Franceschi[1,2], Pierachille Santus[1,2]

Affiliations expand

- PMID: 35722753

- DOI: 10.1080/17476348.2022.2090343

Abstract

Introduction: In patients with chronic obstructive pulmonary disease (COPD), static and dynamic hyperinflation, together with expiratory flow limitation and gas exchange abnormalities, is one of the major causes of dyspnea, decreased exercise performance and ventilatory failure. An increase in functional residual capacity (FRC) is accompanied by a decrease in inspiratory capacity (IC), which is a volume readily available, repeatable, and simple to measure with any spirometer. Changes in IC and FRC after bronchodilation, contrary to changes in FEV_1, have been closely associated with improvements in dyspnea and exercise performance. We systematically searched PubMed and Embase databases for clinical trials that assessed the effects of dual bronchodilation on inspiratory capacity in patients with COPD.

Areas covered: Despite their pivotal role in COPD, IC and static volumes have rarely been considered as primary outcomes in randomized clinical trials assessing the efficacy of bronchodilators. Available studies on dual bronchodilation have shown a significant and persistent positive impact on IC focusing mainly on patients with moderate-to-severe COPD, whereas dynamic hyperinflation is also present at milder disease stages.

Expert opinion: This narrative review discusses the pathophysiological and clinical importance of measuring IC in patients with COPD and how IC can be modified by maximizing bronchodilation combining long-acting muscarinic antagonists and long-acting β2 agonists.

Keywords: Lung volume; bronchodilation; dual bronchodilation; dyspnea; hyperinflation; inspiratory capacity.

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Expert Rev Respir Med

. 2022 Jun 23;1-10.

doi: 10.1080/17476348.2022.2092099. Online ahead of print.

Vaccination and modern management of chronic obstructive pulmonary disease – a narrative review

Oana Joean[1], Tobias Welte[1,2]

Affiliations expand

- PMID: 35713962

- DOI: 10.1080/17476348.2022.2092099

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) carries a tremendous societal and individual burden, posing significant challenges for public health systems worldwide due to its high morbidity and mortality. Due to aging and multimorbidity but also in the wake of important progress in deciphering the heterogeneous disease endotypes, an individualized approach to the prevention and management of COPD is necessary.

Areas covered: This article tackles relevant immunization strategies that are available or still under development with a focus on the latest evidence but also controversies around different regional immunization approaches. Further, we present the crossover between chronic lung inflammation and lung microbiome disturbance as well as its role in delineating COPD endotypes. Moreover, the article attempts to underline endotype-specific treatment approaches. Lastly, we highlight non-pharmacologic prevention and management programs in view of the challenges and opportunities of the COVID-19 era.

Expert opinion: Despite the remaining challenges, personalized medicine has the potential to offer tailored approaches to prevention and therapy and promises to improve the care of patients living with COPD.

Keywords: COPD; COVID-19; endotype; infection; inflammation; influenza; microbiome; personalized medicine; pertussis; pneumococcus; telehealth; vaccination.

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1

J Allergy Clin Immunol Pract

. 2022 Jun 21;S2213-2198(22)00590-6.

doi: 10.1016/j.jaip.2022.05.039. Online ahead of print.

Real-world impact of non-clinical inhaler regimen switches on asthma or COPD: a systematic review

Omar S Usmani[1], Sinthia Bosnic-Anticevich[2], Richard Dekhuijzen[3], Federico Lavorini[4], John Bell[5], Neda Stjepanovic[6], Stephanie Louise Swift[7], Nicolas Roche[8]

Affiliations expand

- PMID: 35750323

- DOI: 10.1016/j.jaip.2022.05.039

Abstract

Background: Switching inhaler regimens can be driven by poor disease control, but also by non-clinical factors, such as cost and environmental impact. The consequences of switching for non-clinical reasons are largely unclear.

Objective: To systematically review the real-world consequences of switching inhaler regimens for non-clinical reasons in asthma and/or COPD patients.

Methods: Embase, MEDLINE, EBM Reviews and EconLit were searched to 21st November 2020. Conference searches and reference checking were also performed. Real-world studies of asthma and/or COPD patients undergoing a switch in inhaler regimen for any reason apart from clinical need were included. Two reviewers screened and extracted data. Key outcomes included symptom control, exacerbations and patient-doctor relationships.

Prospero: CRD42021230427.

Results: 8,958 records were screened and 21 studies included. Higher quality (matched comparative) studies were prioritised. Five matched studies (six datasets) reported on symptom control: five datasets (N=7,530) with unclear patient consent reported improved disease control following switching; and one dataset (N=1,648) with non-consented patients reported significantly worsened disease control. Three matched studies (5 datasets, N=10,084) reported on exacerbation rate ratios; results were heterogeneous depending on the definition used. Two studies (N=137) reported that switching inhaler regimens could have a negative impact on the doctor-patient relationship, especially when the switches were non-consented. Study quality was generally low.

Conclusion: Switching inhaler regimens is a complex issue that can have variable clinical consequences and can harm the patient-doctor relationship. Limited high-quality evidence was identified, and study designs were heterogeneous. A robust framework is needed to guide the personalised switching of inhalers.

Keywords: COPD; asthma; device; inhaler; real-world evidence; switch.

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J Allergy Clin Immunol Pract

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doi: 10.1016/j.jaip.2022.06.006. Online ahead of print.

The Environmental Microbiome, Allergic Disease and Asthma

Michael S Kelly[1], Supinda Bunyavanich[2], Wanda Phipatanakul[3], Peggy S Lai[4]

Affiliations expand

- PMID: 35750322

- DOI: 10.1016/j.jaip.2022.06.006

Abstract

The environmental microbiome represents the entirety of the microbes and their metabolites that we encounter in our environments. A growing body of evidence supports the role of the environmental microbiome in risk for and severity of allergic diseases and asthma. The environmental microbiome represents a ubiquitous, lifelong exposure to non-self antigens. During the critical window between birth and one year of life, interactions between our early immune system and the environmental microbiome have two consequences: our individual microbiome is populated by environmental microbes, and our immune system is trained regarding which antigens to tolerate. During this time, a diversity of exposures appears largely protective, dramatically decreasing the risk of developing allergic diseases and asthma. As we grow older, our interactions with the environmental microbiome change. While it continues to exert influence over the composition of the human microbiome, the environmental microbiome becomes increasingly a source for antigenic stimulation and infection. The same microbial exposure protective against disease development may exacerbate disease severity. While much has been learned about the importance of the environmental microbiome in allergic disease, much more remains to be understood about these complicated interactions between our environment, our microbiome, our immune system and disease.

Keywords: Food allergy (FA); allergic rhinitis (AR); asthma; atopic dermatitis (AD); built environment; environment; exposure; metagenomics; microbiome; microbiota.

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Ann Allergy Asthma Immunol

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. 2022 Jun 21;S1081-1206(22)00535-X.

doi: 10.1016/j.anai.2022.06.017. Online ahead of print.

Viral infection and allergy status impact severity of asthma symptoms in children with asthma exacerbations

Darrell L Dinwiddie [1], Nicholas Kaukis [2], Sarah Pham [3], Olga Hardin [4], Ashley N Stoner [3], John C Kincaid [4], Katherine Caid [3], Catherine Kirkpatrick [5], Kelsi Pomeroy [5], Claire Putt [3], Kurt C Schwalm [6], Tonya M Thompson [7], Elizabeth Storm [7], Tamara T Perry [8], Joshua L Kennedy [9]

Affiliations expand

- PMID: 35750292

- DOI: 10.1016/j.anai.2022.06.017

Abstract

Background: While viral infection is known to be associated with asthma exacerbations, prior research has not identified reliable predictors of acute symptom severity in virus-related asthma exacerbations (VRAE).

Objective: To determine the effect of asthma control and viral infection on the severity of current illness and evaluate biomarkers related to acute symptoms during asthma exacerbations.

Methods: We prospectively enrolled 120 children with physician diagnosed asthma and current wheezing who presented to Arkansas Children's Hospital Emergency Department. The Asthma Control Test (ACT) stratified controlled (ACT>19) and uncontrolled (ACT≤19) asthma, while Pediatric Respiratory Symptoms (PRS) scores assessed symptoms. Nasopharyngeal swabs were obtained for viral analysis, and inflammatory mediators were evaluated by nasal filter paper and Luminex assays.

Results: There were 33 controlled and 87 uncontrolled asthmatics. In uncontrolled asthmatics, 77% were infected with viruses during VRAE compared to 58% of WC. Uncontrolled subjects with VRAE demonstrated more acute symptoms compared to controlled with VRAE or uncontrolled without a virus. Uncontrolled with VRAE and allergy had the highest acute symptom scores (3.363 point PRS; p=0.041). Asthmatics with higher symptom scores had more periostin (p=0.028).

Conclusion: Detection of respiratory viruses is frequent in uncontrolled asthmatics. Uncontrolled subjects with viruses have more acute symptoms during exacerbations, especially in those with allergy. Periostin was highest in subjects with the most acute

symptoms, regardless of control status. Taken together, these data imply synergy between viral infection and allergy in subjects with uncontrolled asthma when considering acute asthma symptoms and nasal inflammation during an exacerbation of asthma.

Keywords: Allergic status; Asthma; Asthma Control; Asthma Exacerbations; Biomarkers; Not-well controlled asthma; Rhinovirus; Viral infections.

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ERJ Open Res

. 2022 Jun 20;8(2):00154-2022.

doi: 10.1183/23120541.00154-2022. eCollection 2022 Apr.

Lung function in young adulthood: differences between males and females with asthma

Ida Mogensen[1], Jenny Hallberg[1,2], Lena Palmberg[3], Sandra Ekström[3,4], Antonios Georgelis[3,4], Erik Melén[1,2], Anna Bergström[3], Inger Kull[1,2]

Affiliations expand

- PMID: 35747229

- PMCID: PMC9209852

- DOI: 10.1183/23120541.00154-2022

Abstract

Background: There are phenotypic differences in asthma in males and females. Differences in lung function between the sexes at the peak lung function level in young adulthood are so far not directly addressed. The aim of the present study was to assess lung function in early adulthood in males and females depending on asthma onset and remission.

Methods: Participants were included from the population-based birth cohort BAMSE and classified as having: never asthma, childhood asthma in remission, adolescent onset asthma or persistent asthma. Pre- and post-bronchodilator lung function (in Z-score) and lung clearance index (LCI) were measured at age 24 years. Lung function was compared stratified for sex between the never asthma and asthma groups univariately and in multiple linear regression analyses adjusted for maternal and paternal asthma, maternal smoking during pregnancy, secondary smoking, daily smoking, early respiratory syncytial virus infection, traffic pollution, childhood allergic sensitisation, and body mass index at age 24 years.

Results: All asthma phenotypes were associated with a lower forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) post-bronchodilation at 24 years. This was most pronounced in males with persistent asthma compared to males with never asthma (regression coefficient: -0.503; 95% CI: -0.708- -0.298). Childhood asthma (in remission or persistent) was associated with a lower FEV_1. After adjustment, the associations remained significant for males. For females, the significant associations with lower FEV_1 and FEV_1/FVC remained only for subjects with asthma in remission. Persistent asthma was associated with higher LCI in females.

Conclusions: In females, in contrast to males, the association between asthma and lower lung function was attenuated after adjustment for known risk factors.

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Conflict of interest statement

Conflicts of interest: I. Mogensen has nothing to disclose. Conflicts of interest: J. Hallberg has nothing to disclose. Conflicts of interest: L. Palmberg has nothing to disclose. Conflicts of interest: S. Ekström has nothing to disclose. Conflicts of interest: A. Georgelis has nothing to disclose. Conflicts of interest: E. Melén has received lecture or advisory board fees from ALK, AstraZeneca, Chiesi, Novartis and Sanofi outside the submitted work. Conflicts of interest: A. Bergström has nothing to disclose. Conflicts of interest: I. Kull has nothing to disclose.

- 40 references
- 3 figures

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Review

Vaccines (Basel)

. 2022 Jun 19;10(6):974.

doi: 10.3390/vaccines10060974.

Biological Therapy of Severe Asthma with Dupilumab, a Dual Receptor Antagonist of Interleukins 4 and 13

Corrado Pelaia[1], Giulia Pelaia[1], Claudia Crimi[2], Angelantonio Maglio[3], Giuseppe Armentaro[4], Cecilia Calabrese[5], Angela Sciacqua[4], Luca Gallelli[1], Alessandro Vatrella[3]

Affiliations expand

- PMID: 35746582

- DOI: 10.3390/vaccines10060974

Abstract

Interleukin-4 (IL-4) and interleukin-13 (IL-13) are key cytokines involved in the pathophysiology of both immune-inflammatory and structural changes underlying type 2 asthma. IL-4 plays a pivotal role in Th2 cell polarization, immunoglobulin E (IgE) synthesis and eosinophil recruitment into the airways. IL-13 synergizes with IL-4 in inducing IgE production and also promotes nitric oxide (NO) synthesis, eosinophil chemotaxis, bronchial hyperresponsiveness and mucus secretion, as well as the proliferation of airway resident cells such as fibroblasts and smooth muscle cells. The biological effects of IL-4 and IL-13

are mediated by complex signaling mechanisms activated by receptor dimerization triggered by cytokine binding to the α-subunit of the IL-4 receptor (IL-4Rα). The fully human IgG4 monoclonal antibody dupilumab binds to IL-4Rα, thereby preventing its interactions with both IL-4 and IL-13. This mechanism of action makes it possible for dupilumab to effectively inhibit type 2 inflammation, thus significantly reducing the exacerbation of severe asthma, the consumption of oral corticosteroids (OCS) and the levels of fractional exhaled NO (FeNO). Dupilumab has been approved not only for the add-on therapy of severe asthma, but also for the biological treatment of atopic dermatitis and nasal polyposis.

Keywords: IL-13; IL-4; dupilumab; severe asthma.

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Review

J Pers Med

. 2022 Jun 18;12(6):999.

doi: 10.3390/jpm12060999.

Biologic Therapies in Pediatric Asthma

Evanthia P Perikleous[1], Paschalis Steiropoulos[2], Evangelia Nena[3], Emmanouil Paraskakis[4]

Affiliations expand

- PMID: 35743783

- DOI: 10.3390/jpm12060999

Abstract

Undeniably, childhood asthma is a multifactorial and heterogeneous chronic condition widespread in children. Its management, especially of the severe form refractory to standard therapy remains challenging. Over the past decades, the development of biologic agents and their subsequent approval has provided an advanced and very promising treatment alternative, eventually directing toward a successful precision medicine approach. The application of currently approved add-on treatments for severe asthma in children, namely omalizumab, mepolizumab, benralizumab, dupilumab, and tezepelumab have been shown to be effective in terms of asthma control and exacerbation rate. However, to date, information is still lacking regarding its long-term use. As a result, data are frequently extrapolated from adult studies. Thus, the selection of the appropriate biologic agent, the potential predictors of good asthma response, and the long-term outcome in the pediatric population are still to be further investigated. The aim of the present study was to provide an overview of the current status of the latest evidence about all licensed monoclonal antibodies (mAbs) that have emerged and been applied to the field of asthma management. The innovative future targets are also briefly discussed.

Keywords: asthma; biologic agents; children; monoclonal antibodies; severe asthma.

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Am J Respir Crit Care Med

. 2022 Jun 23.

doi: 10.1164/rccm.202201-0209PP. Online ahead of print.

Blood Eosinophils and Chronic Obstructive Pulmonary Disease: A GOLD Science Committee 2022 Review

Dave Singh[1], Alvar Agusti[2], Fernando J Martinez[3], Alberto Papi[4], Ian D Pavord[5], Jadwiga A Wedzicha[6], Claus F Vogelmeier[7], David M G Halpin[8,9]

Affiliations expand

- PMID: 35737975

- DOI: 10.1164/rccm.202201-0209PP

Abstract

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Keywords: BIOMARKER; COPD; MICROBIOME; TYPE 2 INFLAMMATION; eosinophils.

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Adv Ther

. 2022 Jun 22.

doi: 10.1007/s12325-022-02214-1. Online ahead of print.

A Response to: Letter to the Editor Regarding "Clinical Remission in Severe Asthma: A Pooled Post Hoc Analysis of the Patient Journey with Benralizumab"

Andrew Menzies-Gow[1], Flavia L Hoyte[2], David B Price[3,4], David Cohen[5], Peter Barker[5], James Kreindler[5], Maria Jison[5], Christopher L Brooks[6], Peggy Papeleu[7], Rohit Katial[5]

Affiliations expand

- PMID: 35731339

- DOI: 10.1007/s12325-022-02214-1

No abstract available

Keywords: Benralizumab; Biologic; Clinical remission; Severe asthma.

- 6 references

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Adv Ther

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. 2022 Jun 22.

doi: 10.1007/s12325-022-02213-2. Online ahead of print.

Letter to the Editor Regarding "Clinical Remission in Severe Asthma: A Pooled Post Hoc Analysis of the Patient Journey with Benralizumab"

Luigino Calzetta[1], Paola Rogliani[2]

Affiliations expand

- PMID: 35731338

- DOI: 10.1007/s12325-022-02213-2

No abstract available

Keywords: Benralizumab; Biologic therapy; CALIMA; Clinical remission; NNT; Oral corticosteroids; Post hoc analysis; SIROCCO; Severe asthma; ZONDA.

- 14 references

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Expert Rev Respir Med

. 2022 Jun 23;1-11.

doi: 10.1080/17476348.2022.2092100. Online ahead of print.

Predictive biomarkers for response to omalizumab in patients with severe allergic asthma: a meta-analysis

Yaqin Li[1], Xiaoyan Li[1], Biyu Zhang[1], Qing Yu[1], Yanming Lu[1]

Affiliations expand

- PMID: 35730466

- DOI: 10.1080/17476348.2022.2092100

Abstract

Background: Predicting omalizumab treatment response has been a challenge and significant aspect for selecting suitable severe allergic asthma patients for omalizumab use.

Objective: To determine which domains of pretreatment baseline characteristics predict omalizumab treatment response among asthmatic patients.

Methods: Electronic bases were searched for eligible studies that reported potential biomarkers that could predict omalizumab responsiveness and efficacy. Patients who accepted omalizumab treatment were stratified into responders and non-responders. WMD, OR, and their 95%CI were used to access the differences between those omalizumab receivers. Sensitivity analysis and subgroup analysis were conducted for potential heterogeneity.

Results: A total of 41 studies evaluating efficacy predictors of omalizumab were included in this meta-analysis. The pooled results showed that omalizumab responders had

significantly younger age in the adult subgroup, higher pretreatment total serum IgE level, percent predicted FEV_1 and FeNO than that non-responder. We further confirmed that higher blood eosinophil counts and total serum IgE levels are useful markers for selecting asthma patients who may benefit more from omalizumab.

Conclusions: Pre-treatment blood eosinophil counts and total serum IgE level can be a useful efficacy predictor in selecting allergic asthma patients for omalizumab treatment.

Keywords: Omalizumab; allergic severe asthma; biomarker; meta-analysis.

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Semin Respir Crit Care Med

. 2022 Jun 21.

doi: 10.1055/s-0042-1745747. Online ahead of print.

Understanding the Updates in the Asthma Guidelines

Deborah L Lee[1], Alan P Baptist[1]

Affiliations expand

- PMID: 35728605

- DOI: 10.1055/s-0042-1745747

Abstract

Asthma is a chronic inflammatory lung disease that affects millions of Americans, with variable symptoms of bronchospasm and obstruction among individuals over time. The National Heart, Lung, and Blood Institute (NHLBI) published the 2020 Focused Updates to the Asthma Management Guidelines based on the latest research since the 2007 Expert Panel Report-3 (EPR-3). The following article reviews the 21 new recommendations on the six core topics in asthma: use of intermittent inhaled corticosteroids, long-acting muscarinic antagonist therapy, use of the fractional exhaled nitric oxide test in asthma diagnosis and monitoring, indoor allergen mitigation, immunotherapy, and bronchial thermoplasty. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to rate recommendations as strong or conditional based on the evidence. The recommendations were based on systematic reviews of the literature and focused on patient-centered critical outcomes of asthma exacerbations, asthma control, and asthma-related quality of life. Understanding the recommendations with consideration of individual values through shared decision-making may improve asthma outcomes.

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Conflict of interest statement

None declared.

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Expert Rev Respir Med

. 2022 Jun 21;1-12.

doi: 10.1080/17476348.2022.2089117. Online ahead of print.

A review of the efficacy and safety of fluticasone propionate/formoterol fixed-dose combination

Satish Chandra Kilaru [1], Avya Gopal Bansal [2], Vaishali Sandeep Naik [3], Meena Lopez [3], Jaideep Ashok Gogtay [4]

Affiliations expand

- PMID: 35727177

- DOI: 10.1080/17476348.2022.2089117

Abstract

Introduction: Fluticasone propionate/formoterol fumarate (FP/FORM) is one of the newer combinations among inhaled corticosteroid (ICS) and long-acting β2-agonist (LABA) combination formulations currently available. To evaluate the efficacy and safety of this FP/FORM combination, it is important to review all the available evidence and take a comprehensive look at the current and relevant data in the patient population suffering from asthma and chronic obstructive pulmonary disease (COPD).

Areas covered: In this focused review, we summarize the available literature published until January 2021 using the PubMed/Medline and Cochrane Controlled Trials Register databases on the efficacy and safety of FP/FORM with its mono-components; concurrent administration of FP+FORM; and with other ICS/LABA combinations in asthma and COPD patients.

Expert opinion: FP/FORM combination therapy is a strong alternative in the treatment of persistent asthma and moderate-severe COPD. Extensive study of several trials has established the superior efficacy of FP/FORM combination therapy over FP or FORM monotherapy, comparable efficacy with FP+FORM and non-inferiority to other ICS/LABA fixed-dose combinations. The safety profile of FP/FORM has also been found to be comparable with respect to its mono-components and their concurrent use, and also other ICS/LABA combinations such as formoterol/budesonide and fluticasone/salmeterol.

Keywords: Asthma; ICS-LABA; chronic obstructive pulmonary disease; fluticasone; formoterol; inhaled corticosteroid; long-acting β2-agonists.

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13

Review

Stem Cell Res Ther

. 2022 Jun 20;13(1):262.

doi: 10.1186/s13287-022-02938-5.

Chronic obstructive pulmonary disease and asthma: mesenchymal stem cells and their extracellular vesicles as potential therapeutic tools

Hossein Abbaszadeh[1], Farzaneh Ghorbani[1], Sanaz Abbaspour-Aghdam[1], Amin Kamrani[1], Hamed Valizadeh[2], Mehdi Nadiri[2], Armin Sadeghi[2], Karim Shamsasenjan[1], Farhad Jadidi-Niaragh[3], Leila Roshangar[4], Majid Ahmadi[5]

Affiliations expand

- PMID: 35725505

- PMCID: PMC9208161

- DOI: 10.1186/s13287-022-02938-5

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Abstract

Chronic lung diseases, such as chronic obstructive pulmonary disease (COPD) and asthma, are one of the most frequent causes of morbidity and mortality in the global. COPD is characterized by progressive loss of lung function through inflammation, apoptosis, and oxidative stress caused by chronic exposure to harmful environmental pollutants. Airway inflammation and epithelial remodeling are also two main characteristics of asthma. In spite of extensive efforts from researchers, there is still a great need for novel therapeutic approaches for treatment of these conditions. Accumulating evidence suggests the potential role of mesenchymal stem cells (MSCs) in treatment of many lung injuries due to their beneficial features including immunomodulation and tissue regeneration. Besides, the therapeutic advantages of MSCs are chiefly related to their paracrine functions such as releasing extracellular vesicles (EVs). EVs comprising exosomes and microvesicles are heterogeneous bilayer membrane structures loaded with various lipids, nucleic acids and proteins. Due to their lower immunogenicity, tumorigenicity, and easier management, EVs have appeared as favorable alternatives to stem cell therapies. Therefore, in this review, we provided an overview on the current understanding of the importance of MSCs and MSC-derived EVs from different sources reported in preclinical and clinical COPD and asthmatic models.

Keywords: Asthma; COPD; Emphysema; Exosomes; Lung diseases; Mesenchymal stromal cells; Microvesicles; Regeneration.

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Conflict of interest statement

The authors indicated no potential conflicts of interest.

- 102 references
- 2 figures

SUPPLEMENTARY INFO

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Published Erratum

Adv Ther

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. 2022 Jun 18.

doi: 10.1007/s12325-022-02209-y. Online ahead of print.

Correction to: New Versus Old: The Impact of Changing Patterns of Inhaled Corticosteroid Prescribing and Dosing Regimens in Asthma Management

Dave Singh[1], Gabriel Garcia[2], Kittipong Maneechotesuwan[3], Peter Daley-Yates[4], Elvis Irusen[5,6], Bhumika Aggarwal[7], Isabelle Boucot[8], Norbert Berend[9]

Affiliations expand

- PMID: 35716320

- DOI: 10.1007/s12325-022-02209-y

No abstract available

Erratum for

- New Versus Old: The Impact of Changing Patterns of Inhaled Corticosteroid Prescribing and Dosing Regimens in Asthma Management.
  Singh D, Garcia G, Maneechotesuwan K, Daley-Yates P, Irusen E, Aggarwal B, Boucot I, Berend N.Adv Ther. 2022 May;39(5):1895-1914. doi: 10.1007/s12325-022-02092-7. Epub 2022 Mar 14.PMID: 35284999 **Free PMC article.** Review.

- 4 references

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Expert Rev Respir Med

. 2022 Jun 23;1-9.

doi: 10.1080/17476348.2022.2090342. Online ahead of print.

Dupilumab-induced hypereosinophilia: review of the literature and algorithm proposal for clinical management

Marco Caminati[1], Bianca Olivieri[1], Annarita Dama[2], Claudio Micheletto[3], Pierluigi Paggiaro[4], Patrick Pinter[5], Gianenrico Senna[1,2], Michele Schiappoli[2]

Affiliations expand

- PMID: 35703018

- DOI: 10.1080/17476348.2022.2090342

Abstract

Introduction: Dupilumab is a human monoclonal antibody that targets both IL-4 and IL-13 signaling. It is currently indicated for the treatment of asthma, moderate-to-severe atopic

dermatitis, and chronic rhinosinusitis with nasal polyps (CRSwNP). Eosinophilia has been reported as a potential adverse event in treated patients.

Areas covered: A selective search on PubMed and Medline up to January 2022 was performed, by focusing on dupilumab-induced hypereosinophilia described in clinical trials, real-life studies, and case reports. The possible mechanisms underlying dupilumab-induced hypereosinophilia and the eosinophil-related morbidity have also been explored.

Expert opinion: Dealing with dupilumab-induced hypereosinophilia represents a clinical challenge for clinicians managing patients on dupilumab therapy. An algorithm for the practical management of dupilumab-induced hypereosinophilia has been proposed, in order to properly investigate potential eosinophil-related morbidity and avoid unnecessary drug discontinuation.

Keywords: Asthma; IL-13; IL-4; algorithm; atopic dermatitis; dupilumab; eosinophils; hypereosinophilia; nasal polyps.

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Expert Rev Clin Immunol

. 2022 Jun 19;1-12.

doi: 10.1080/1744666X.2022.2089654. Online ahead of print.

Comorbid allergic rhinitis and asthma: important clinical considerations

E Nappi[1,2], G Paoletti[1,2], L Malvezzi[1,3], S Ferri[2], F Racca[2], M R Messina[1,2], F Puggioni[1,2], E Heffler[1,2], G W Canonica[1,2]

Affiliations expand

- PMID: 35695326

- DOI: 10.1080/1744666X.2022.2089654

Abstract

Introduction: The numerous links between allergic rhinitis and asthma have been extensively explored in the last two decades, gaining great concern within the scientific community. These two conditions frequently coexist in the same patient and share numerous pathogenetic and pathophysiological mechanisms.

Areas covered: We reviewed major pathophysiological, epidemiological, and clinical links between allergic rhinitis and asthma. We also provided a comprehensive discussion of allergic rhinitis treatment according to current guidelines, with a particular focus on the relevance of allergic rhinitis therapies in patients with comorbid asthma.

Expert opinion: We believe that there are several unmet needs for our patients, however, there are promising advances forecasted for the future. Although allergic rhinitis is a recognized risk factor for asthma, a proper asthma detection and prevention plan in allergic rhinitis patients is not available. Allergen immunotherapy (AIT) represents a promising preventive strategy and may deserve an earlier positioning in allergic rhinitis management. A multidisciplinary approach should characterize the journey of patients with respiratory allergies, with an adequate referral to specialized Allergy/Asthma centers. Molecular Allergy Diagnosis may provide support for optimal AIT use. Finally, a possible evolution of biological treatment can be envisaged, mainly if biosimilars decrease such therapies' costs.

Keywords: United airway disease; allergen immunotherapy; allergic rhinitis; allergic rhinitis treatment; asthma; asthma comorbidities; respiratory allergies.

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17

. 2022 Jun 20;1-14.

doi: 10.1080/02770903.2022.2082305. Online ahead of print.

Over-prescription of short-acting β $_2$-agonists is associated with poor asthma outcomes: results from the Latin American cohort of the SABINA III study

Felicia Montero-Arias[1], Jose Carlos Herrera Garcia[2], Manuel Pacheco Gallego[3], Martti Anton Antila[4], Patricia Schonffeldt[5], Walter Javier Mattarucco[6], Luis Fernando Tejado Gallegos[7], Maarten J H I Beekman[8]

Affiliations expand

- PMID: 35670783

- DOI: 10.1080/02770903.2022.2082305

Abstract

Objective: Short-acting β_2-agonist (SABA) over-reliance is associated with poor asthma outcomes. As part of the SABA Use IN Asthma (SABINA) III study, we assessed SABA prescriptions and clinical outcomes in patients from six Latin American countries.

Methods: In this cross-sectional study, data on disease characteristics/asthma treatments were collected using electronic case report forms. Patients (aged ≥12 years) were classified by investigator-defined asthma severity (guided by the 2017 Global Initiative for Asthma) and practice type (primary/specialist care). Multivariable regression models analyzed the associations between SABA prescriptions and clinical outcomes.

Results: Data from 1096 patients (mean age, 52.0 years) were analyzed. Most patients were female (70%), had moderate-to-severe asthma (79.4%), and were treated by specialists (87.6%). Asthma was partly controlled/uncontrolled in 61.5% of patients; 47.4% experienced ≥1 severe exacerbation in the previous 12 months. Overall, 39.8% of patients were prescribed ≥3 SABA canisters in the preceding 12 months (considered over-

prescription). SABA canisters were purchased over the counter (OTC) by 17.2% of patients, of whom 38.8% purchased ≥3 canisters in the 12 months prior. Of patients who purchased SABA OTC, 73.5% were prescribed ≥3 SABA canisters. Higher SABA prescriptions (vs. 1 - 2 canisters) were associated with an increased incidence rate of severe exacerbations (ranging from 1.31 to 3.08) and lower odds ratios of having at least partly controlled asthma (ranging from 0.63 to 0.15).

Conclusions: SABA over-prescription was common in Latin America, highlighting the need for urgent collaboration between healthcare providers and policymakers to align clinical practices with the latest evidence-based recommendations to address this public health concern.

Keywords: Epidemiology; management/control; treatment.

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Eur Respir J

. 2022 Jun 23;59(6):2102577.

doi: 10.1183/13993003.02577-2021. Print 2022 Jun.

Dupilumab efficacy and safety in patients with asthma and blood eosinophils ≥500 cells·μL $^{-1}$

Klaus F Rabe[1,2], Ian D Pavord[3], Mario Castro[4], Michael E Wechsler[5], Nadia Daizadeh[6], Upender Kapoor[7], Benjamin Ortiz[8], Amr Radwan[8], Robert R Johnson[7], Paul J Rowe[7], Yamo Deniz[8], Juby A Jacob-Nara[7]

Affiliations expand

- PMID: 35487538

- DOI: 10.1183/13993003.02577-2021

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No abstract available

Conflict of interest statement

Conflict of interest: K.F. Rabe is a consultant for and received speaker fees from AstraZeneca, Boehringer Ingelheim, Novartis, Sanofi and Teva. I.D. Pavord received speaker fees from Aerocrine AB, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Teva; received payments for organising education events from AstraZeneca and Teva; received consulting fees from Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Dey Pharma, Genentech, GlaxoSmithKline, Knopp Biosciences, Merck, MSD, Napp Pharmaceuticals, Novartis, Regeneron Pharmaceuticals, Inc., RespiVert, Sanofi, Schering-Plough and Teva; received international scientific meeting sponsorship from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Napp Pharmaceuticals and Teva; and received research grants from Chiesi; and is consultant for Regeneron Pharmaceuticals, Inc. and Sanofi. M. Castro received research support from the American Lung Association, AstraZeneca, GlaxoSmithKline, NIH, Novartis, PCORI, Pulmatrix, Sanofi-Aventis and Shionogi; is a consultant for Genentech, Novartis, Sanofi-Aventis and Teva; received speaker fees from AstraZeneca, Genentech, GlaxoSmithKline, Regeneron Pharmaceuticals, Inc., Sanofi and Teva; and received royalties from Elsevier. M.E. Wechsler reports personal fees from AstraZeneca, Boehringer Ingelheim, Equillium, Gala Therapeutics, Genentech, Genzyme, Mylan, Novartis, Pulmatrix, ResTORbio, Regeneron Pharmaceuticals, Inc., Sentien Biotechnologies and Teva; and grants and personal fees from GlaxoSmithKline and Sanofi. N. Daizadeh, U. Kapoor, R.R. Johnson, P.J. Rowe and J.A. Jacob-Nara are employees and may hold stock and/or stock options in Sanofi. B. Ortiz, A. Radwan and Y. Deniz are employees and shareholders of Regeneron Pharmaceuticals, Inc.

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J Investig Allergol Clin Immunol

. 2022 Jun 20;32(3):220-223.

doi: 10.18176/jiaci.0793. Epub 2022 Feb 15.

Effectiveness of Benralizumab in Severe Eosinophilic Asthma Under Conditions of Routine Clinical Practice

J C Miralles López[1], R Andújar-Espinosa[2], F J Bravo-Gutiérrez[3], M Castilla-Martínez[4], I Flores-Martín[5], M L Alemany-Francés[6], M J Pajarón-Fernández[7], A Mora González[8], J Valverde-Molina[9], V Pérez-Fernández[10], RE-ASGRAMUR GROUP

Affiliations expand

- PMID: 35166673

- DOI: 10.18176/jiaci.0793

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Keywords: Benralizumab; Eosinophils; Nasal polyps; Severe asthma.

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MeSH terms, Substancesexpand

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1

Eur Heart J

. 2022 Jun 25;ehac322.

doi: 10.1093/eurheartj/ehac322. Online ahead of print.

Polygenic risk score for ACE-inhibitor-associated cough based on the discovery of new genetic loci

Jonas Ghouse[1,2], Vinicius Tragante[3], Ayesha Muhammad[4], Gustav Ahlberg[1,2], Morten W Skov[1,2], Dan M Roden[4,5], Ingileif Jonsdottir[3,6,7], Laura Andreasen[1,2], Pia Rengtved Lundegaard[1,2], Linea C Trudsø[1,2], Karina Banasik[8], Søren Brunak[8], Sisse R Ostrowski[9,10], eMERGE consortium; Christian Torp-Pedersen[11,10], Ole V Pedersen[12,10], Erik Sørensen[9,10], Lars Køber[13,10], Kasper Iversen[14,10], Unnur Thorsteinsdottir[3,6], Gudmundur Thorgeirsson[3,15], Henrik Ullum[16], Daniel F Gudbjartsson[3,17], Jonathan D Mosley[5], Hilma Holm[3], Kari Stefansson[3,6], Henning Bundgaard[13,10], Morten Salling Olesen[1,2]

Affiliations expand

- PMID: 35751511

- DOI: 10.1093/eurheartj/ehac322

Abstract

Aims: To search for sequence variants associated with ACEi discontinuation and to test their association with ACEi-associated adverse drug reactions (ADRs).

Methods and results: A genome-wide association study (GWAS) on ACEi discontinuation was conducted, including 33 959 ACEi-discontinuers and 44 041 controls. Cases were defined as persons who switched from an ACEi treatment to an angiotensin receptor blocker. Controls were defined as persons who continued ACEi treatment for at least 1 year. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were computed for ACEi discontinuation risk by mixed model regression analysis. Summary statistics from the individual cohorts were meta-analyzed with a fixed-effects model. To test for association

with specific ACEi-associated ADRs, any genome-wide significant (P < 5 × 10-8) ACEi discontinuation variants was tested for association with ACEi-associated cough and angioedema. A polygenetic risk score (PRS) based on ACEi discontinuation GWAS data was constructed and tested for association with ACEi-associated cough and angioedema in two population-based samples. In total, seven genetic genome-wide loci were identified, of which six were previously unreported. The strongest association with ACEi discontinuation was at 20q13.3 (NTSR1; OR: 1.21; 95% CI: 1.17-1.24; P = 2.1 × 10-34). Five of seven lead variants were associated with ACEi-associated cough, whereas none were associated with ACEi-associated angioedema. The ACEi discontinuation PRS was associated with ACEi-associated cough in a dose-response manner but not with ACEi-associated angioedema. ACEi discontinuation was genetically correlated with important causes for cough, including gastro-esophageal reflux disease, allergic rhinitis, hay fever, and asthma, which indicates partly shared genetic underpinning between these traits.

Conclusion: This study showed the advantage of using prescription patterns to discover genetic links with ADRs. In total, seven genetic loci that associated with ACEi discontinuation were identified. There was evidence of a strong association between our ADR phenotype and ACEi-associated cough. Taken together, these findings increase insight into the pathophysiological processes that underlie ACEi-associated ADRs.

Keywords: ACE inhibitors; ACE-inhibitor associated cough; ADR; Adverse drug reaction; Drug discontinuation; GWAS; Genome-wide association study.

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J Allergy Clin Immunol Pract

. 2022 Jun 21;S2213-2198(22)00591-8.

doi: 10.1016/j.jaip.2022.06.006. Online ahead of print.

The Environmental Microbiome, Allergic Disease and Asthma

Michael S Kelly[1], Supinda Bunyavanich[2], Wanda Phipatanakul[3], Peggy S Lai[4]

Affiliations expand

- PMID: 35750322

- DOI: 10.1016/j.jaip.2022.06.006

Abstract

The environmental microbiome represents the entirety of the microbes and their metabolites that we encounter in our environments. A growing body of evidence supports the role of the environmental microbiome in risk for and severity of allergic diseases and asthma. The environmental microbiome represents a ubiquitous, lifelong exposure to non-self antigens. During the critical window between birth and one year of life, interactions between our early immune system and the environmental microbiome have two consequences: our individual microbiome is populated by environmental microbes, and our immune system is trained regarding which antigens to tolerate. During this time, a diversity of exposures appears largely protective, dramatically decreasing the risk of developing allergic diseases and asthma. As we grow older, our interactions with the environmental microbiome change. While it continues to exert influence over the composition of the human microbiome, the environmental microbiome becomes increasingly a source for antigenic stimulation and infection. The same microbial exposure protective against disease development may exacerbate disease severity. While much has been learned about the importance of the environmental microbiome in allergic disease, much more remains to be understood about these complicated interactions between our environment, our microbiome, our immune system and disease.

Keywords: Food allergy (FA); allergic rhinitis (AR); asthma; atopic dermatitis (AD); built environment; environment; exposure; metagenomics; microbiome; microbiota.

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Allergy Asthma Clin Immunol

. 2022 Jun 20;18(1):56.

doi: 10.1186/s13223-022-00686-y.

Intranasal budesonide for rhinitis during a high airborne pollution period: a randomized controlled trial

Yuan Zhang[1,2,3], Chunguang Shan[4], Weiwei Liu[5], Yaozhong Han[6], Guanggang Shi[7], Yongjian Ma[8], Kerstin Wagner[9], Xiaoyan Tian[10], Lili Zhang[10], Allan Joseph Larona[11], Steven Sacavage[9], Kathleen Franklin[9], Chengshuo Wang[12,13,14], Luo Zhang[15,16,17]

Affiliations expand

- PMID: 35725523

- PMCID: PMC9207822

- DOI: 10.1186/s13223-022-00686-y

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Abstract

Background: Air pollution may induce or reinforce nasal inflammation regardless of allergy status. There is limited direct clinical evidence informing the treatment of airborne pollution-related rhinitis.

Objective: To assess the effectiveness of intranasal budesonide in adults with self-reported rhinitis symptoms triggered/worsened by airborne pollution.

Methods: Adults in northern China with self-reported rhinitis symptoms triggered or worsened by airborne pollution were randomized to budesonide 256 μg/day or placebo for 10 days in pollution season (October 2019 to February 2020). The primary endpoint was

the mean change from baseline in 24-h reflective total nasal symptom score (rTNSS) averaged over 10 days. The secondary endpoints were subject-assessed Global Impression of Change (SGIC), mean change from baseline in individual nasal symptom severity, and mean change from baseline in individual non-nasal symptoms of cough and postnasal drip severity. One-sided P < 0.0125 was considered statistically significant.

Results: After an interruption by COVID-19, an interim analysis showed that the study could be ended for efficacy with n = 206 participants (103/group) since the primary efficacy endpoint demonstrated significant results. The final efficacy results showed that the 10-day-averaged rTNSS change in the budesonide group was greater than with placebo (- 2.20 vs - 1.72, P = 0.0107). Budesonide also significantly improved 10-day-averaged itching/sneezing change (- 0.75 vs - 0.51, P = 0.0009). Results for SGIC and all other individual symptoms did not show significant differences between the two groups.

Conclusions: Intranasal budesonide 256 µg once daily improved the total nasal symptoms and itching/sneezing over 10 days in adults with rhinitis triggered/worsened by airborne pollution.

Keywords: Air quality index; Airborne pollution; Budesonide; Intranasal corticosteroid; Intranasal spray; Non-allergic rhinitis; Perennial allergic rhinitis; Pollution; Rhinitis; Seasonal allergic rhinitis.

© 2022. The Author(s).

Conflict of interest statement

YZ, CS, WL, YH, GS, YM, CW, and LZ are investigators for the clinical trial. KW, XT, LiliZ, AJL, SS, and KF are employees of the Johnson & Johnson Family of Consumer Companies.

- 31 references
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. 2022 Jun 18.

doi: 10.1111/all.15415. Online ahead of print.

Intranasal antihistamine and corticosteroid to treat in allergic rhinitis: A systematic review and meta-analysis

Minji Kim[#1], Gwanghui Ryu[#2], Sung-Yoon Kang[3], Mi-Ae Kim[4], Song-I Yang[5], Il Hwan Lee[6], Gil-Soon Choi[7], Hyun-Jung Kim[8], Sang Min Lee[3], Dong-Kyu Kim[6], Jeong Hee Choi[9], Hyeon-Jong Yang[10], Soo Whan Kim[11], Work Group for Rhinitis, the Korean Academy of Asthma, Allergy and Clinical Immunology

Affiliations expand

- PMID: 35716356

- DOI: 10.1111/all.15415

No abstract available

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. 2022 Jun 19;1-12.

doi: 10.1080/1744666X.2022.2089654. Online ahead of print.

Comorbid allergic rhinitis and asthma: important clinical considerations

E Nappi[1,2], G Paoletti[1,2], L Malvezzi[1,3], S Ferri[2], F Racca[2], M R Messina[1,2], F Puggioni[1,2], E Heffler[1,2], G W Canonica[1,2]

Affiliations expand

- PMID: 35695326

- DOI: 10.1080/1744666X.2022.2089654

Abstract

Introduction: The numerous links between allergic rhinitis and asthma have been extensively explored in the last two decades, gaining great concern within the scientific community. These two conditions frequently coexist in the same patient and share numerous pathogenetic and pathophysiological mechanisms.

Areas covered: We reviewed major pathophysiological, epidemiological, and clinical links between allergic rhinitis and asthma. We also provided a comprehensive discussion of allergic rhinitis treatment according to current guidelines, with a particular focus on the relevance of allergic rhinitis therapies in patients with comorbid asthma.

Expert opinion: We believe that there are several unmet needs for our patients, however, there are promising advances forecasted for the future. Although allergic rhinitis is a recognized risk factor for asthma, a proper asthma detection and prevention plan in allergic rhinitis patients is not available. Allergen immunotherapy (AIT) represents a promising preventive strategy and may deserve an earlier positioning in allergic rhinitis management. A multidisciplinary approach should characterize the journey of patients with respiratory allergies, with an adequate referral to specialized Allergy/Asthma centers. Molecular Allergy Diagnosis may provide support for optimal AIT use. Finally, a possible evolution of biological treatment can be envisaged, mainly if biosimilars decrease such therapies' costs.

Keywords: United airway disease; allergen immunotherapy; allergic rhinitis; allergic rhinitis treatment; asthma; asthma comorbidities; respiratory allergies.

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CHRONIC COUGH

Children (Basel)

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. 2022 Jun 19;9(6):920.

doi: 10.3390/children9060920.

Application of a Cold Dry Air Provocation Test in Pediatric Patients with Asthma

Ji Young Ahn[1], Bong Seok Choi[2]

Affiliations expand

- PMID: 35740856

- DOI: 10.3390/children9060920

Abstract

Asthma is a chronic inflammatory airway disease characterized by reversible airway obstruction and airway hyperreactivity. We proposed a cold dry air (CDA) provocation test and investigated its application in pediatric patients with asthma. We enrolled 72 children and adolescents older than 5 years who presented to our hospital with chronic cough, shortness of breath, and wheezing. We analyzed the results of allergy, pulmonary function,

methacholine provocation, and CDA provocation tests. The FEV1 change 5 min after the provocation was recorded as CDA5 dFEV1; that after 15 min was recorded as CDA15 dFEV1. PT10 was the provocation time causing a 10% decrease in FEV1; a decrease of >10% in dFEV1 was considered a positive CDA test. Among the 72 subjects, 51 were diagnosed with asthma. A positive CDA test in patients with asthma correlated with non-eosinophilic asthma. In patients with asthma, sputum eosinophils and eosinophil cationic protein (ECP) levels of the patients with a positive CDA test were significantly lower than those of patients with a negative test. CDA5 dFEV1 correlated with PC20 and total immunoglobulin E. CDA15 dFEV1 correlated with PC20, sputum eosinophils, and ECP. PT10 became shorter as the peripheral blood eosinophil, FVC, FEV1, FEV1/FVC, and FEF25-75 decreased. The CDA provocation test showed airway hyperreactivity to non-specific stimuli, a high correlation with non-eosinophilic asthma, and the possibility of assessing asthma severity via PT10.

Keywords: asthma; child; chronic inflammatory airway disease; cold dry air provocation.

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Eur Respir J

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Task Force report: European Respiratory Society statement for defining respiratory exacerbations in children and adolescents with bronchiectasis for clinical trials

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Affiliations expand

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Abstract

Bronchiectasis is being diagnosed increasingly in children and adolescents. Recurrent respiratory exacerbations are common in children and adolescents with this chronic pulmonary disorder. Respiratory exacerbations are associated with an impaired quality-of-life, poorer long-term clinical outcomes and substantial costs to the family and health systems. The European Respiratory Society (ERS) clinical practice guideline for the management of children and adolescents with bronchiectasis provided a definition of acute respiratory exacerbations for clinical use but to date there is no comparable universal definition for clinical research. Given the importance of exacerbations in the field, this ERS task force sought to obtain robust definitions of respiratory exacerbations for clinical research. The panel was a multidisciplinary team of specialists in paediatric and adult respiratory medicine, infectious disease, physiotherapy, primary care, nursing, radiology, methodology, patient advocacy and parents of children and adolescents with bronchiectasis. We used a standardised process that included a systematic literature review, parents' survey and a Delphi involving 299 physicians (54 countries) caring for children and adolescents with bronchiectasis. Consensus was obtained for all four statements drafted by the panel as the disagreement rate was very low (range 3.6% to 6.4%). The panel unanimously endorsed the four consensus definitions for: non-severe and severe exacerbations as an outcome measure; non-severe exacerbation for studies initiating treatment and; resolution of a non-severe exacerbation; for clinical trials involving children and adolescents with bronchiectasis. This ERS task force proposes using these internationally derived, consensus-based definitions of respiratory exacerbations for future clinical paediatric bronchiectasis research.

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Review

Purinergic Signal

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ATP, an attractive target for the treatment of refractory chronic cough

Mengru Zhang[1,2], Dominic L Sykes[1], Laura R Sadofsky[1], Alyn H Morice[3]

Affiliations expand

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Free PMC article

Abstract

Chronic cough is the most common complaint in respiratory clinics. Most of them have identifiable causes and some may respond to common disease-modifying therapies. However, there are many patients whose cough lacks effective aetiologically targeted treatments or remains unexplained after thorough assessments, which have been described as refractory chronic cough. Current treatments for refractory chronic cough are

limited and often accompanied by intolerable side effects such as sedation. In recent years, various in-depth researches into the pathogenesis of chronic cough have led to an explosion in the development of drugs for the treatment of refractory chronic cough. There has been considerable progress in the underlying mechanisms of chronic cough targeting ATP, and ongoing or completed clinical studies have confirmed the promising antitussive efficacy of P2X3 antagonists for refractory cough. Herein, we review the foundation on which ATP target was developed as potential antitussive medications and provide an update on current clinical progresses.

Keywords: ATP; Antitussive; Cough hypersensitivity; Gefapixant; P2X3 antagonists; Refractory chronic cough.

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Conflict of interest statement

Mengru Zhang declares that she has no relevant financial or non-financial conflict of interest; Dominic L. Sykes declares that he has no relevant financial or non-financial conflict of interest; Laura R. Sadofsky declares that she has no relevant financial or non-financial conflict of interest; Alyn H. Morice declares that he has received grant funding and advisory board fees from Merck, Shionogi, Bellus, Bayer, and Nerre.

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Pediatr Nephrol

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. 2022 Jun 20.

doi: 10.1007/s00467-022-05647-6. Online ahead of print.

Chronic cough in an adolescent with infantile onset of hypokalemic hypochloremic metabolic alkalosis: Answers

Emre Leventoğlu[1], Bahriye Uzun Kenan[2], Eylül Pınar Çakır[3], Zeynep İlkşen Hocoğlu[3], Tuğba Şişmanlar Eyüboğlu[3], Bahar Büyükkaragöz[2], Ayşe Tana Aslan[3], Oğuz Söylemezoğlu[2]

Affiliations expand

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No abstract available

Keywords: Acute pancreatitis; CFTR gene; Chronic cough; Cystic fibrosis; Infant; Pseudo-Bartter syndrome.

- 25 references

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Pediatr Nephrol

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doi: 10.1007/s00467-022-05641-y. Online ahead of print.

Chronic cough in an adolescent with infantile onset of hypokalemic hypochloremic metabolic alkalosis: Questions

Emre Leventoğlu[1], Bahriye Uzun Kenan[2], Eylül Pınar Çakır[3], Zeynep İlkşen Hocoğlu[3], Tuğba Şişmanlar Eyüboğlu[3], Bahar Büyükkaragöz[2], Ayşe Tana Aslan[3], Oğuz Söylemezoğlu[2]

Affiliations expand

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No abstract available

Keywords: Acute pancreatitis; Antenatal Bartter syndrome; Chronic cough; Infant.

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