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Disproportionality analysis of reslizumab based on the FDA Adverse Event Reporting System

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Abstract

Background: With the increasing prescription of reslizumab for severe asthma with an eosinophilic phenotype, a real-world pharmacovigilance analysis of reslizumab is urgently required to detect potential unreported adverse events (AEs) in clinical practice.

Objectives: We aimed to provide a comprehensive evaluation of reslizumab-related AEs in the real world.

Design: Disproportionality analysis based on the FDA Adverse Event Reporting System (FAERS) database.

Methods: Reslizumab-related AEs between the second quarter of 2016 and the fourth quarter of 2022 from the FAERS database were obtained. A disproportionality analysis was performed to evaluate the safety profile of reslizumab using the reporting odds ratio.

Results: A total of 10,450,353 reports were collected from the FAERS database. Of the 403 reslizumab-related AEs, 42 distinct AEs were identified with positive signals. The most common AEs including dyspnea and oropharyngeal pain were identified, consistent with the instruction and clinical studies. Unexpected AEs of disproportionality such as bronchospasm and chest pain were also observed. Drug ineffective was identified as a noteworthy concern that accounted for 13.90% (56/403) of the overall reslizumab-related reports.

Conclusion: While reslizumab offered a promising treatment option for severe eosinophilic asthma, more attention should be paid to the common AEs and new unexpected AEs. Based on the current findings of signal detection, further prospective studies are needed for the next signal validation and confirmation.

Plain language summary

A pharmacovigilance analysis of reslizumab

Background: Reslizumab is a humanized monoclonal antibody that has been approved by the United States Food and Drug Administration (FDA) since 2016 for the add-on maintenance treatment of eosinophilic severe asthma. A safety profile identifies common and new unexpected adverse events (AEs) based on the data from clinical studies and post-marketing surveillance to guide informed decisions. So far, the safety profile of reslizumab has been unclear.

Methods: In this study, we aimed to provide a comprehensive evaluation of reslizumab-related AEs in the real world based on the FDA Adverse Event Reporting System (FAERS) database. We analyzed the collected data using the reporting odds ratio (ROR).

Results: Our study identified the most common AEs such as dyspnea and oropharyngeal pain, which were consistent with the instruction and clinical studies. We also

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observed unexpected AEs of disproportionality including bronchospasm and chest pain. Moreover, we identified drug ineffective as a noteworthy concern that should be addressed in future research.
Conclusion: We identified new unexpected AEs in addition to the common AEs indicated in the instructions. We also emphasized the importance of correct administration protocols for reslizumab. Based on the current findings of signal detection, further prospective studies are needed for the next signal validation and confirmation.

Keywords: adverse events, disproportionality, pharmacovigilance, reslizumab

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Introduction

Asthma is a chronic heterogeneous disease that affects nearly 400 million people worldwide, and it is estimated that 5%–10% of the total adult asthma population have severe asthma.[1,2] Severe asthma imposes a strong impact on health-related quality of life and public healthcare costs due to uncontrolled asthma and/or recurrent exacerbations. Approximately 50% of severe asthma patients display a persistently eosinophilic phenotype which is characterized by the presence of eosinophils in the airways.[3,4] It has been reported that interleukin-5 (IL-5) was increased in eosinophilic asthma and played a vital role in promoting the maturation, activation, and prolonged survival of eosinophils at the site of inflammation.[5,6] Therefore, inhibition of IL-5 signaling could hamper eosinophil maturation and survival and seems to be a good option for severe eosinophilic asthma treatment.

Reslizumab is a humanized monoclonal antibody (mAb) that specifically targets IL-5 at its IL-5 receptor α subunit (IL-5Rα) binding site.[7] Reslizumab showed promising effects against asthma in clinical trials.[8] Based on the results of clinical trials, an intravenous formulation of reslizumab was approved in the United States and later in Canada and Europe as an add-on maintenance treatment for patients with severe asthma aged 18 years and older and with an eosinophilic phenotype. Although an acceptable safety profile has been observed in clinical studies, common adverse events (AEs) were frequently reported such as anaphylaxis, malignant neoplasm, and myalgia.[9] Of note, with the widespread use of reslizumab, there were likely more administration-related errors. AEs such as therapeutic inefficacy are co-reported with incomplete dose administration or errors in administration procedures in previous studies.[10]

The FDA Adverse Event Reporting System (FAERS) is a publicly accessible database that contains tens of millions of AEs submitted by health professionals, consumers, manufacturers, and others.[11] It was designed to support monitoring for post-marketing drugs and biological products.[12] It has been reported that reslizumab showed positive signals for anaphylaxis and negative signals for parasitic infections and ear and labyrinth disorders based on the large real-world database.[13–15] In addition, no new safety signals with reslizumab in pediatric patients were identified in a pharmacovigilance review of AE reports in the FAERS database from March 2016 to December 2017. Moreover, a recent pharmacovigilance study evaluated the post-marketing safety of anti-IL-5 mAbs (mainly mepolizumab and benralizumab) in the real world.[16] However, the comprehensive safety profile of reslizumab remains unclear. In the present study, we aimed to present a comprehensive and systemic evaluation of the safety profile of reslizumab based on the FAERS database.

Materials and methods

Data sources

The pharmacovigilance study was conducted based on the FAERS database that collected safety reports worldwide from patients, healthcare professionals, and pharmaceutical companies. The FAERS consists of seven datasets that present patient demographic and administrative

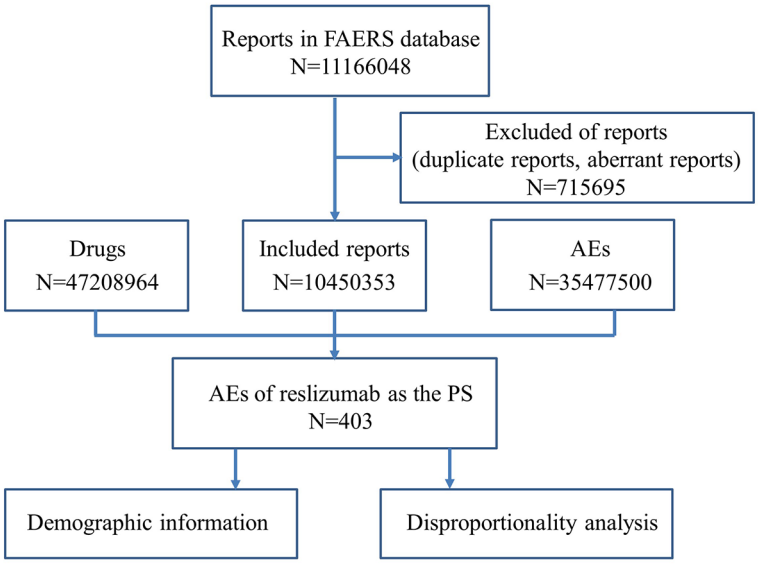

Figure 1. The flow chart of data extraction and analysis from the Food and Drug Administration Adverse Event Report System.
AE, adverse event; FAERS, Food and Drug Administration Adverse Event Reporting System; PS, primary suspect.

Table 1. Calculation of ROR and 95% CI.

Drug category	Event of interest	All other events
Reslizumab	a	b
All other drugs	c	d

ROR = ad/bc; 95%CI = $e^{\ln(ROR)\pm1.96(1/a+1/b+1/c+1/d)^{0.5}}$.
CI, confidence interval; ROR, reporting odds ratio.

information, drug information, indications, outcomes, AEs, report sources, and start and end dates of the reported drugs. Before analysis, a deduplication process was performed according to FDA's guidelines: the latest FDA_DT was chosen when the CASEID was the same, and the higher PRIMARYID was chosen when the CASEID and FDA_DT were the same. In addition, aberrant reports (age older than 100 years, inaccurate date inputs, event date earlier than start date) were removed to minimize false signals. Both the generic name (reslizumab) and brand name (CINQAIR) were applied to extract reslizumab-related AEs from the FAERS database from the second quarter of 2016 to the fourth quarter of 2022. Only drugs with PS (primary suspect) role were included for better signal validity. The Medical Dictionary for Drug Regulatory Authorities (MeDRA) was applied to categorize AEs related to reslizumab at the preferred term (PT) level and system organ class (SOC) level. The clinical characteristics of reslizumab-related AEs, including sex, age, indication, outcome, reporter country, and others were collected to perform the descriptive analysis. The flowchart of data extraction and analysis from the FAERS database is shown in Figure 1.

Statistical analysis

Descriptive analysis was performed to characterize reslizumab-related AEs. Disproportionality analysis was applied to identify signals between reslizumab and AEs in our pharmacovigilance study. The reporting odds ratio (ROR) and 95% confidence interval (CI) were calculated based on the 2×2 contingency table (Table 1) to evaluate the potential association of reslizumab and AEs.

A signal of reslizumab-related AEs was considered when the lower limit 95% CI of the ROR exceeded 1.0 with at least three cases. p less than 0.05 was

considered statistically significant. MySQL 8.0, Navicat Premium 15, Microsoft Excel 2019, and GraphPad Prism 8 were applied for data processing and statistical analysis.

Results

Descriptive analysis

A total of 403 reports out of 10,450,353 reports were collected from the FAERS database from April 2016 to December 2022. The clinical characteristics of these reports are described in Table 2. Patients aged older than 18 years accounted for most reports with only six individuals aged younger than 18 years based on the available 253 reports. AEs were reported more commonly in females than males. America and Canada accounted for over 80% of the submitted reports. Asthma was the most reported indication. However, unapproved indications were also observed in several reports such as eosinophilic granulomatosis with polyangiitis (EGPA; $n=4$) and eosinophilic esophagitis (EoE; $n=3$). The most reported serious outcome was other important medical events, followed by hospitalization, death, life-threatening, and disability.

Signal detection

In the present study, reslizumab-related AEs occurred across 13 SOCs (Table 3). In total, 42 PTs of interest were identified based on the results of the disproportionality analysis. "Dyspnea (PT: 10013968)," "myalgia (PT: 10028411)," "oropharyngeal pain (PT: 10068319)," "urticaria (PT: 10046735)," and "wheezing (PT: 10047924)" were identified which was consistent with the drug instruction. Unexpected AEs which were not included in the label were also observed such as "bronchospasm (PT: 10006482)," "cough (PT: 10011224)," and "swollen tongue (PT: 10042727)." However, "muscle spasms (PT: 10028334)," "musculoskeletal pain (PT: 10028391)," and "neck pain (PT: 10028836)" indicated in the label did not meet the criteria for AE signals of disproportionality in our study.

AE of special interest

In the present study, drug ineffective was frequently reported and accounted for 13.90% (56/403) of the total reslizumab-related reports. We additionally examined the co-reported AEs for reslizumab-related drug ineffective. Seventy percent of the drug ineffective reports had other accompanied AEs. Among the concomitant AEs, dyspnea ($n=10$), asthma ($n=7$), cough ($n=5$), fatigue ($n=5$), and product use in an unapproved indication ($n=3$) were the top five most frequently co-reported AEs. Moreover, the three cases of product use in unapproved indication consisted of one wheezing, one interstitial lung disease, and one sneezing. Interestingly, incorrect dose administered ($n=15$, ROR = 3.67), inappropriate schedule of product administration ($n=7$, ROR = 1.52), off-label use ($n=4$, ROR = 0.18), and product use in an unapproved indication ($n=4$, ROR = 0.58) also accounted for small proportions of the total AEs.

Discussion

Overall, the present study indicated that reslizumab showed a tolerable safety profile in real-world settings. Well-known AEs related to reslizumab such as myalgia and new unexpected AEs including swollen tongue were identified. Moreover, the disproportionality analysis suggested the presence of drug ineffective and errors in administration procedures which required further assessment and investigation.

In the present study, reslizumab-related AEs occurred more commonly in females than in males, which might be due to the increased prevalence and severity of asthma in women as adults.[17] Consistent with the label, reslizumab was prescribed for asthma in the majority of AE reports. However, a minor proportion of reslizumab was used for other eosinophilic conditions such as EGPA and EoE, which was not approved in the drug instruction. Interestingly, previous studies have demonstrated that reslizumab exhibited promising efficacy in various eosinophilic conditions including EoE and EGPA.[18,19]

Based on the disproportionality analysis, AEs such as dyspnea and chest pain were present with positive signals, which were in line with drug instructions and previous studies.[20] In addition, new unexpected AEs not included in the drug label were also identified as positive signals, such as throat tightness and eye pruritus. Interestingly, asthma which is the indication of reslizumab was identified as a positive signal of disproportionality in the current study. In the previous disproportionality analysis of mepolizumab, asthma as the

Table 2. Demographic information of reslizumab-related reports from the FAERS database (April 2016 to December 2022).

Characteristics	Case number, *n*	Proportion, %
Number of events	403	
Sex		
Female	242	60.05
Male	110	27.30
Unknown	51	12.65
Age (years)		
<18	6	1.49
⩾18 and <60	137	34.00
⩾60	110	27.30
Unknown	150	37.21
Indications (top five)		
Asthma	193	47.89
Eosinophilic granulomatosis with polyangiitis	4	0.99
Eosinophilic esophagitis	3	0.74
Aspirin-exacerbated respiratory disease	1	0.25
Asthma prophylaxis	1	0.25
Serious outcome		
Death (DE)	9	2.23
Life-threatening (LT)	5	1.24
Hospitalization (HO)	88	21.84
Disabled (DS)	1	0.25
Other important medical events (OT)	156	38.71
Reported countries (top five)		
America (US)	291	72.21
Canada (CA)	38	9.43
Spain (ES)	11	2.73
Great Britain (GB)	10	2.48
Netherlands (NL)	10	2.48

(Continued)

Table 2. (Contined)

Characteristics	Case number, *n*	Proportion, %
Reporter		
Health professional	7	1.74
Consumer	1	0.25
Unknown	395	98.01
Reporting year		
2022	82	20.35
2021	62	15.38
2020	43	10.67
2019	61	15.14
2018	58	14.39
2017	85	21.09
2016	12	2.98

FAERS, Food and Drug Administration Adverse Event Reporting System.

Table 3. Pharmacovigilance metrics for signals of disproportionality associated with reslizumab in the FAERS database.

SOC	PT	Number (*n*)	ROR (95% two-sided CI)
Blood and lymphatic system disorders			
	Eosinopenia	3	1284.82 (401.47–4111.78)
Eye disorders			
	Eye pruritus	3	4.47 (1.43–13.91)
Gastrointestinal disorders			
	Nausea	26	1.62 (1.09–2.41)
	Swollen tongue	7	13.03 (6.17–27.52)
General disorders and administration site conditions			
	Drug ineffective	56	2.02 (1.52–2.68)
	Chest discomfort	12	5.73 (3.23–10.18)
	Feeling abnormal	12	2.27 (1.28–4.03)
	Peripheral swelling	10	2.19 (1.17–4.10)
	Chest pain	8	2.34 (1.16–4.72)
	Adverse event	6	3.20 (1.43–7.18)

(Continued)

Table 3. (Contined)

SOC	PT	Number (*n*)	ROR (95% two-sided CI)
	Chills	6	2.49 (1.11–5.57)
	Infusion site extravasation	5	26.64 (11.02–64.38)
	Feeling hot	4	3.34 (1.25–8.93)
	Adverse reaction	3	9.48 (3.04–29.52)
	Feeling cold	3	5.07 (1.63–15.79)
Immune system disorders			
	Hypersensitivity	12	2.93 (1.65–5.20)
	Anaphylactic reaction	8	7.78 (3.86–15.66)
	Eosinophilic granulomatosis with polyangiitis	3	61.51 (19.73–191.79)
Infections and infestations			
	Viral infection	3	4.12 (1.32–12.82)
Injury, poisoning, and procedural complications			
	Incorrect dose administered	15	3.67 (2.19–6.15)
	Maternal exposure during pregnancy	7	3.16 (1.50–6.68)
Investigations			
	Weight decreased	12	1.80 (1.01–3.20)
	Oxygen saturation decreased	6	4.46 (1.99–10.00)
Musculoskeletal and connective tissue disorders			
	Myalgia	13	3.86 (2.22–6.72)
	Osteonecrosis	4	4.21 (1.57–11.28)
Renal and urinary disorders			
	Nephrolithiasis	4	3.66 (1.37–9.81)
Respiratory, thoracic, and mediastinal disorders			
	Dyspnea	62	5.80 (4.42–7.60)
	Asthma	38	15.47 (11.07–21.61)
	Wheezing	23	16.23 (10.65–24.73)
	Cough	18	2.74 (1.71–4.40)
	Oropharyngeal pain	15	6.78 (4.05–11.36)

(Continued)

Table 3. (Contined)

SOC	PT	Number (*n*)	ROR (95% two-sided CI)
	Dysphonia	11	8.51 (4.67–15.49)
	Throat tightness	11	22.52 (12.37–41.01)
	Throat irritation	6	6.61 (2.95–14.80)
	Productive cough	5	3.74 (1.55–9.03)
	Bronchospasm	3	11.17 (3.59–34.80)
	Respiratory disorder	3	4.67 (1.50–14.54)
	Respiratory distress	3	5.81 (1.86–18.08)
Skin and subcutaneous tissue disorders			
	Pruritus	18	2.48 (1.54–3.97)
	Erythema	12	2.57 (1.45–4.57)
	Urticaria	11	3.41 (1.87–6.20)
Vascular disorders			
	Flushing	7	4.22 (2.00–8.91)

CI, confidence interval; FAERS, Food and Drug Administration Adverse Event Reporting System; PT, preferred terms; ROR, reporting odds ratio; SOC, system organ class.

mepolizumab indication was removed.[16,21] However, these studies identified asthmatic crisis and bronchospasm and cough which were related to disease progression as positive AE signals. On the other hand, asthma (typically recorded using "asthma exacerbation" or occasionally "worsening of asthma") was observed as the commonly reported AE related to reslizumab in previous clinical trials.[20,22] Our results suggest that new unexpected AEs might occur along with the wide clinical application of reslizumab. Meanwhile, it should be noted that the observed difference in AEs might be due to the inherent selection and reporting bias involved in the spontaneous reporting system. Therefore, more caution and studies are needed to evaluate and validate the observations.

Anaphylaxis was an identified AE of reslizumab which was present as a black box warning in the instruction. In our study, anaphylactic reaction and hypersensitivity as well as manifestations including dyspnea, wheezing, pruritus, and urticaria were identified as positive signals of disproportionality, which was consistent with previous studies.[20] Currently, the mechanisms of the anaphylaxis related to reslizumab remain unclear. It has been proposed that product-related factors in reslizumab such as glycosylation, residual nucleic acids, and host cell proteins might impact the immunogenicity and affect the risk of anaphylaxis.[9] In addition, reslizumab was a humanized mAb with 90% human components and therefore had a higher risk of anaphylaxis compared to dupilumab which was the only fully human mAb with 99% human component among the five mAbs for severe asthma.[14] It has been reported that reslizumab-related anaphylaxis might occur during or shortly after reslizumab infusion in previous trials.[8,23] Also, a case of reslizumab-related anaphylaxis was reported to occur on day 302 after the reslizumab initiation.[20] Therefore, although anaphylaxis could be resolved by standard medications, close monitoring is required when reslizumab is administered.

In the present analysis, drug ineffective was frequently reported and identified as a positive AE signal. It has been reported that in about 25% of patients, reslizumab treatment was interrupted because of a lack of efficacy over 2 years.[3,24] There

might be several reasons: wrong identification of underlying inflammatory profile, the coexistence of conditions such as emphysema, insufficient dose, or subsequent infections.[3] On the other hand, it should be noted that more administration-related errors likely occur with the widespread use of reslizumab in real-world settings. Indeed, incorrect dose administered and infusion site extravasation were identified as potential AE signals of disproportionality in our study. Interestingly, product use in unapproved indications was co-reported in three cases of the reslizumab-related drug ineffective. Potentially inappropriate medications are important enhancers of serious adverse drug reactions, increasing the likelihood of hospitalizations.[25] In addition, though reslizumab is approved for intravenous medication in the instruction, studies evaluating the subcutaneous formulation of reslizumab in patients with asthma and elevated eosinophil levels were ongoing while without desired effects, probably due to differences in drug exposure between the two administration methods.[22] Therefore, further study is required to explore the underlying reasons for drug ineffectively. More attention should be paid to the correct administration of reslizumab in clinical practice.

There were several limitations in the present study. Considering that the vital information including the prior disease history such as malignancy and medication protocols for reslizumab is unavailable, the real percentage of reslizumab-related AEs could not be calculated. In addition, there inevitably existed underreporting or overreporting of AEs as well as reporting bias in spontaneous reporting systems such as FAERS. Therefore, the associations between reslizumab and AEs should be interpreted with more caution. However, the real-world analysis systematically explored the potential risks for reslizumab-related AEs in an unselected population globally and provided earlier detection of suspected AEs for reslizumab. Further clinical and real-world studies are required to confirm the findings in this study to promote rational use of reslizumab.

Conclusion

In conclusion, our study confirmed the well-known AEs related to reslizumab such as myalgia. New unexpected AEs such as throat tightness were also identified. In addition, several potential safety concerns including drug ineffective and errors in administration procedures have been observed by disproportionality analysis. Based on the current findings of signal detection, further prospective studies are needed for the next signal validation and confirmation.

Declaration

Ethics approval and consent to participate

This study was exempt from Institutional Review Board approval or informed patient consent as data were anonymized and collected from a publicly available database.

Consent for publication

Not applicable.

Author contributions

Huqun Li: Conceptualization; Formal analysis; Writing – review & editing.

Cuilian Guo: Formal analysis; Investigation; Methodology; Writing – original draft.

Chongshu Wang: Formal analysis; Investigation; Writing – original draft.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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References

1. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and

national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; 390(10100): 1211–1259.

2. Bousquet J, Mantzouranis E, Cruz AA, et al. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol* 2010; 126(5): 926–938.
3. Pérez de Llano LA, Cosío BG, Lobato Astiárraga I, et al. Asthma control in patients with severe eosinophilic asthma treated with reslizumab: Spanish real-life data. *J Asthma Allergy* 2022; 15: 79–88.
4. Pavord ID. Non-eosinophilic asthma and the innate immune response. *Thorax* 2007; 62(3): 193–194.
5. Hammad H and Lambrecht BN. The basic immunology of asthma. *Cell* 2021; 184(6): 1469–1485.
6. Kandikattu HK, Upparahalli Venkateshaiah S and Mishra A. Synergy of Interleukin (IL)-5 and IL-18 in eosinophil mediated pathogenesis of allergic diseases. *Cytokine Growth Factor Rev* 2019; 47: 83–98.
7. Guilleminault L, Conde E and Reber LL. Pharmacological approaches to target type 2 cytokines in asthma. *Pharmacol Ther* 2022; 237: 108167.
8. Castro M, Zangrilli J, Wechsler ME, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet Respir Med* 2015; 3(5): 355–366.
9. Cazzola M, Matera MG, Levi-Schaffer F, et al. Safety of humanized monoclonal antibodies against IL-5 in asthma: focus on reslizumab. *Expert Opin Drug Saf* 2018; 17(4): 429–435.
10. Sessa M and Andersen M. New insight on the safety of erenumab: an analysis of spontaneous reports of adverse events recorded in the US Food and Drug Administration Adverse Event Reporting System Database. *BioDrugs* 2021; 35(2): 215–227.
11. Cirmi S, El Abd A, Letinier L, et al. Cardiovascular toxicity of tyrosine kinase inhibitors used in chronic myeloid leukemia: an analysis of the FDA Adverse Event Reporting System Database (FAERS). *Cancers (Basel)* 2020; 12(4): 826.
12. Shu Y, Zhang Q, He X, et al. Fluoroquinolone-associated suspected tendonitis and tendon rupture: a pharmacovigilance analysis from 2016 to 2021 based on the FAERS database. *Front Pharmacol* 2022; 13: 990241.
13. Park HT, Park S, Jung YW, et al. Is omalizumab related to ear and labyrinth disorders? A disproportionality analysis based on a global pharmacovigilance database. *Diagnostics (Basel)* 2022; 12(10): 2434.
14. Li L, Wang Z, Cui L, Xu Y, et al. Anaphylactic risk related to omalizumab, benralizumab, reslizumab, mepolizumab, and dupilumab. *Clin Transl Allergy* 2021; 11(4): e12038.
15. Pera V, Brusselle GG, Riemann S, et al. Parasitic infections related to anti-type 2 immunity monoclonal antibodies: a disproportionality analysis in the Food and Drug Administration's Adverse Event Reporting System (FAERS). *Front Pharmacol* 2023; 14: 1276340.
16. Zou SP, Yang HY, Ouyang M, et al. Post-marketing safety of anti-IL-5 monoclonal antibodies (mAbs): an analysis of the FDA Adverse Event Reporting System (FAERS). *Expert Opin Drug Saf* 2024; 23: 353–362.
17. Chowdhury NU, Guntur VP, Newcomb DC, et al. Sex and gender in asthma. *Eur Respir Rev* 2021; 30(162): 210067.
18. Markowitz JE, Jobe L, Miller M, et al. Safety and efficacy of reslizumab for children and adolescents with eosinophilic esophagitis treated for 9 years. *J Pediatr Gastroenterol Nutr* 2018; 66(6): 893–897.
19. Manka LA, Guntur VP, Denson JL, et al. Efficacy and safety of reslizumab in the treatment of eosinophilic granulomatosis with polyangiitis. *Ann Allergy Asthma Immunol* 2021; 126(6): 696–701.e691.
20. Virchow JC, Katial R, Brusselle GG, et al. Safety of reslizumab in uncontrolled asthma with eosinophilia: a pooled analysis from 6 trials. *J Allergy Clin Immunol Pract* 2020; 8(2): 540–548. e541.
21. Zou F, Zhu C, Lou S, et al. A real-world pharmacovigilance study of mepolizumab in the FDA Adverse Event Reporting System (FAERS) database. *Front Pharmacol* 2023; 14: 1320458.
22. Bernstein JA, Virchow JC, Murphy K, et al. Effect of fixed-dose subcutaneous reslizumab on asthma exacerbations in patients with severe uncontrolled asthma and corticosteroid sparing in patients with oral corticosteroid-dependent asthma: results from two phase 3, randomised,

double-blind, placebo-controlled trials. *Lancet Respir Med* 2020; 8(5): 461–474.

23. Corren J, Weinstein S, Janka L, et al. 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.

24. Eger K, Kroes JA, Ten Brinke A, et al. Long-term therapy response to anti-IL-5 biologics in severe asthma: a real-life evaluation. *J Allergy Clin Immunol Pract* 2021; 9(3): 1194–1200.

25. Gomes D, Herdeiro MT, Ribeiro-Vaz I, et al. Adverse drug reactions and potentially inappropriate medication in older patients: analysis of the Portuguese pharmacovigilance database. *J Clin Med* 2022; 11(8): 2229.