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Safety of Adalimumab: An Analysis of the FDA Adverse Event Reporting System (FAERS) Database

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ABSTRACT

Objective: This study aims to assess the safety profile of adalimumab and its biosimilars for each approved indication by analyzing adverse events (AEs) reported in the FDA Adverse Event Reporting System (FAERS) database.

Method: We conducted a retrospective pharmacovigilance analysis of AE reports documented from 2002 to 2022 in the FAERS database. This analysis included descriptive statistics and binary logistic regression analyses. We calculated reporting odds ratios (RORs) with 95% confidence intervals (CI) to investigate safety signals related to the disproportionate reporting of serious AEs for adalimumab and its biosimilars compared to currently available biological products for the same proposed indications.

Results: A total of 543,873 AEs related to adalimumab treatment were reported, with 49.8% classified as serious. Hospitalization was the most frequently reported AE. Risk factors associated with serious AEs included age (≥60 years), male sex, and the concurrent use of adalimumab (ROR >1, P<0.05). Adalimumab exhibited a lower risk of serious AEs compared to abatacept, certolizumab, infliximab, or rituximab. Conversely, etanercept and ixekizumab showed lower odds of serious AEs than adalimumab (ROR <1, P<0.05).

Conclusion: In summary, these findings suggest that adalimumab has a well-tolerated safety profile for approved indications when compared to currently available biological alternatives.

Keywords: Adalimumab, Serious adverse events, FAERS database, Rheumatology, Humira.

INTRODUCTION

Adalimumab is a tumor necrosis factor (TNF) blocker indicated for treating several conditions, including rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC), plaque psoriasis (Ps), hidradenitis suppurativa (HS), and uveitis (UV) [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. Adalimumab is a biological reference product available under the brand name Humira®. Currently, seven other biosimilar products have been authorized by the U.S Food and Drug Administration (FDA) under the following names: adalimumab-atto (Amjevita®), adalimumab-adbm (Cyltezo®), adalimumab-adaz (Hyrimoz®), adalimumab-bwwd (Hadlima®), adalimumab-afzb (Abrilada®), adalimumab-fkjp (Hulio®), and adalimumab-aqvh (Yusimry®). All biosimilars were found to exhibit similar efficacy, safety, and immunogenicity to adalimumab [11].

It is well-established that anti-TNFs are associated with serious adverse events (AEs) [12]. In addition, the rate of adalimumab-related AEs was found to vary among distinct disease populations [13]. A randomized, double-blind, parallel-group phase III clinical trial assessing adalimumab for treating RA revealed that 6.5% of

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patients experienced serious AEs (mainly infections, 27.7%), resulting in 7.1% of patients discontinuing treatment [14]. However, AEs are uncommon when adalimumab is used to treat pediatric patients with JIA. Indeed, 67% did not experience any AE, and 31% had local injection-site reactions/pain [15]. In patients with PsA, adalimumab was associated with 8.5% of severe AEs, predominantly infection-related AEs (30.7%), which led to treatment discontinuation in 4.6% of patients [16]. A multicenter, randomized, double-blind, placebo-controlled study was undertaken to evaluate the safety and efficacy of adalimumab for treating AS. Only 2.9% of patients had serious AEs. Infection (31.7%), nasopharyngitis (12.5%), injection-site reaction (10.1%), and headache (9.6%) were the most reported AEs [5]. A systemic review of adalimumab tolerability in CD revealed that infection, arthralgia, nasopharyngitis, headache, nausea, fatigue, abdominal pain, pyrexia, injection-site reaction, and influenza occurred in ≥5% of the population [17]. Among patients with UC, the incidence of serious AEs was 4.9%, with infection and gastrointestinal disorders reported most frequently [18]. Overall, 3.1% of patients with serious AEs had received adalimumab to treat Ps. All patients discontinued adalimumab owing to AE severity. Upper respiratory tract infections (34.6%) and hypertension (8.2%) were the most common AEs in patients with Ps [19]. In patients with HS, the risk ratio for adalimumab-related serious AEs was 1.23 (when used weekly) and 1.19 (when used every other week). Patients with HS were found to be 1.09 and 2.84 more likely to develop headaches when used weekly and every other week, respectively. Infection-related AEs were 1.57 more likely to occur when adalimumab was administered every other week. However, the risk of infection-related AEs was low when adalimumab was administered weekly, with a risk ratio <1 [20]. In patients with UV, treatment with adalimumab resulted in the highest incidence of serious AEs (24%), with 18% discontinuing treatment owing to AEs [21]. Accordingly, the US FDA has added a black box warning to the adalimumab leaflet regarding infections and serious malignant AEs.

The FDA Adverse Event Reporting System (FAERS) is a publicly available database that records spontaneous AEs reported to the FDA by pharmaceutical industries, healthcare providers, and consumers [22]. In the present study, we evaluated the safety of adalimumab for all approved indications by analyzing AE reports extracted from the FAERS database as of June 2022.

METHODS

Data source

Study data were derived from the FAERS database for Q4, 2002 through Q2, 2022, which covers the time since adalimumab was first authorized. Adalimumab and its biosimilars were derived from the FDA Purple Book Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations [23].

Procedure

We conducted a retrospective analysis of an adalimumab reference biological product and its biosimilars using AE reports for approved indications during the study period. AE reports for each reference and its biosimilar biological products were identified using both proprietary (Humira®, Amjevita®, Cyltezo®, Hyrimoz®, Hadlima®, Abrilada®, Hulio®, and Yusimry®) and nonproprietary names (adalimumab, adalimumab-atto, adalimumab-adbm, adalimumab-adaz, adalimumab-bwwd, adalimumab-afzb, adalimumab-fkjp, and adalimumab-aqvh). Duplicate reports were excluded from the analysis. Furthermore, AE reports were filtered according to their proposed indications and were excluded from the analysis if they were not used for an approved indication (RA, JIA, PsA, AS, CD, UC, Ps, HS, and UV). AE reports were analyzed for each indication, whether employed as monotherapy or in combination

with other drugs.

In addition, AE reports were subdivided into direct reports (submitted directly to the FDA), expedited reports (for serious and unexpected AEs not included in the product package insert submitted by the manufacturer), and non-expedited reports (periodic reports included in the package insert submitted by the manufacturer). AE reports were further categorized into serious and non-serious AEs. Serious AEs were defined as death, life-threatening events, disability, congenital anomaly, hospitalization, necessitating intervention, or other serious AE.

Intervention

The interventions were biological products with the same indication(s). Information on the available biological alternatives relevant to the same proposed indications was obtained from the FDA-approved label. The present study included all reports in the FAERS public database, starting from the date the drug was approved until Q2 2022. The FAERS reports were searched using proprietary (Orencia®, Cimzia®, Enbrel®, Erelzi®, Eticovo®, Remicade®, Avsola®, Inflectra®, Ixifi®, Renflexis®, Rituxan®, Riabni®, Ruxience®, Truxima®, and Taltz®) and nonproprietary names (abatacept, certolizumab pegol, etanercept, etanercept-szzs, etanercept-ykro, infliximab, infliximab-axxq, infliximab-dyyb, infliximab-qbtx, infliximab-abda, rituximab, rituximab-arrx, rituximab-pvvr, rituximab-abbs, and ixekizumab).

Statistical analysis

Descriptive statistics were used to assess the characteristics of all reports. A multivariate logistic regression model, adjusted for age (<60 *vs*. ≥60 years), sex (male *vs*. female), and the number of therapies used (monotherapy *vs*. combination therapy), was used to define the variable(s) that could be associated with serious AEs. Disproportionality analysis using reporting odds ratios (RORs) with 95% confidence intervals (CI) was performed to assess the possible association between drug exposure and the odds of serious AEs related to the adalimumab reference and its biosimilars when compared with available biological alternatives for each indication. The significance level was set at $P<0.05$. Statistical analyses were performed using Microsoft Excel and the R Project for Statistical Computing version R x64 4.0.5.

RESULTS

In total, 543,872 adalimumab-related AEs were documented on the FAERS platform between December 31, 2002, and June 15, 2022. RA, CD, and Ps had the highest number of reports, with 187,966 (34.6%), 123,274 (22.7%), and 71,891 (13.2%) reports, respectively. Overall, 51,792 (9.5%) reports were associated with PsA, 31,576 (5.8%) with UC, and 25,829 (4.7%) with AS. During this period, there were only 8,913 (1.6%) reports related to HS, 4,667 (0.9%) to JIA, and 3,286 (0.6%) to UV in the FAERS database (Table 1).

Table 1. Characteristics of AEs reports associated with adalimumab and its biosimilars from December 2002 to June 2022.

	Indications								
	RA	**JIA**	**PsA**	**AS**	**CD**	**UC**	**Ps**	**HS**	**UV**
AEs Reports_no. (%)	187,966 (34.6%)	4,667 (0.9%)	51,792 (9.5%)	25,829 (4.7%)	123,274 (22.7%)	31,576 (5.8%)	71,891 (13.2%)	8,913 (1.6%)	3,286 (0.6%)
Gender									
Male	34,919 (18.6%)	1,194 (25.6%)	18,752 (36.2%)	12,068 (46.7%)	44,984 (36.5%)	13,222 (41.9%)	31,455 (43.8%)	2,052 (23.0%)	877 (26.7%)
Female	146,502 (77.9%)	3,107 (66.6%)	31,808 (61.4%)	13,217 (51.2%)	75,497 (61.2%)	17,638 (55.9%)	38,505 (53.6%)	6,087 (68.3%)	2,278 (69.3%)
Not Specified	6,545 (3.5%)	366 (7.8%)	1,232 (2.4%)	544 (2.1%)	2,793 (2.3%)	716 (2.3%)	1,931 (2.7%)	774 (8.7%)	131 (4.0%)
Age (years)									
<60	63,108 (33.6%)	3155 (67.6%)	22,994 (44.4%)	13,976 (54.1%)	68,120 (55.3%)	16,059 (50.9%)	33,383 (46.4%)	3,542 (39.7%)	1,366 (41.6%)
≥60	67,092 (35.7%)	56 (1.2%)	11,008 (21.3%)	3,317 (12.8%)	16,912 (13.7%)	5,668 (18.0%)	15,696 (21.8%)	472 (5.3%)	527 (16.0%)
Not Specified	57,766 (30.7%)	1,456 (31.2%)	17,789 (34.3%)	8,536 (33.0%)	38,242 (31.0%)	9,849 (31.2%)	22,811 (31.7%)	4,899 (55.0%)	1,393 (42.4%)
Combination Therapy	95,249 (50.7%)	2,403 (51.5%)	30,052 (58.0%)	12,316 (47.7%)	54,033 (43.8%)	14,944 (47.3%)	35,889 (49.9%)	2,508 (28.1%)	1,928 (58.7%)
Reporter Type									
Consumer	120,839 (64.3%)	2,723 (58.3%)	39,409 (76.1%)	19,256 (74.6%)	91,688 (74.4%)	25,012 (79.2%)	51,365 (71.4%)	6,377 (71.5%)	2,487 (75.7%)
Healthcare Professional	55,889 (29.7%)	1,817 (38.9%)	10,877 (21.0%)	5,895 (22.8%)	27,493 (22.3%)	6,253 (19.8%)	18,477 (25.7%)	2,504 (28.1%)	777 (23.6%)
Not Specified	11,238 (6.0%)	127 (2.7%)	1,506 (2.9%)	678 (2.6%)	4,093 (3.3%)	311 (1.0%)	2,049 (2.9%)	32 (0.4%)	22 (0.7%)
Case Priority									
Direct	8,053 (4.3%)	201 (4.3%)	2,152 (4.2%)	1,051 (4.1%)	3,977 (3.2%)	1,065 (3.4%)	3,281 (4.6%)	911 (10.2%)	100 (3.0%)
Expedited	90,084 (47.9%)	2,391 (51.2%)	21,461 (41.4%)	14,297 (55.4%)	55,847 (45.3%)	13,694 (43.4%)	26,152 (36.4%)	4,435 (49.8%)	2,318 (70.5%)
Non-Expedited	89,829 (47.8%)	2,075 (44.5%)	28,179 (46.1%)	10,481 (40.6%)	63,450 (51.5%)	16,817 (53.3%)	42,458 (59.1%)	3,567 (40.0%)	868 (26.4%)
Serious AEs	98,489 (52.4%)	2,545 (54.5%)	23,862 (46.1%)	15,088 (58.4%)	61,586 (50.0%)	15,052 (47.7%)	29,559 (41.1%)	4,847 (54.4%)	2,349 (71.5%)
Hospitalized	39,559 (21.0%)	1,198 (25.7%)	9,828 (19.0%)	6,040 (23.4%)	34,181 (27.7%)	7,863 (24.9%)	12,941 (18.0%)	1,796 (20.2%)	721 (21.9%)
Life-Threatening	2,205 (1.2%)	108 (2.3%)	535 (1.0%)	273 (1.1%)	830 (0.7%)	278 (0.9%)	686 (1.0%)	52 (0.6%)	32 (1.0%)
Disabled	4,775 (2.5%)	181 (3.9%)	958 (1.8%)	662 (2.6%)	915 (0.7%)	278 (0.1%)	953 (1.3%)	91 (1.0%)	70 (2.1%)
Congenital Anomaly	109 (0.1%)	3 (0.1%)	28 (0.1%)	16 (0.1%)	89 (0.1%)	30 (0.1%)	43 (0.1%)	12 (0.1%)	2 (0.1%)
Required Intervention	592 (0.3%)	2 (0.0%)	37 (0.1%)	11 (0.0%)	46 (0.0%)	5 (0.0%)	32 (0.0%)	3 (0.0%)	3 (0.1%)
Death	8,614 (4.6%)	55 (1.2%)	1,241 (2.4%)	788 (3.1%)	2,701 (2.2%)	824 (2.6%)	2,323 (3.2%)	201 (2.3%)	83 (2.5%)
Other Outcomes	67,501 (35.9%)	1,664 (35.7%)	17,053 (32.9%)	10,527 (40.8%)	37,754 (30.6%)	9,366 (29.7%)	19,749 (27.5%)	3,535 (39.7%)	1,891 (57.5%)
Non-Serious	89,478 (47.6%)	2122 (45.5%)	27,930 (53.9%)	10,741 (41.6%)	61,688 (50.0%)	16,524 (52.3%)	42,332 (58.9%)	4,066 (45.6%)	937 (28.5%)

AEs, adverse events; RA, rheumatoid arthritis; JIA, juvenile idiopathic arthritis; PsA, psoriatic arthritis; AS, ankylosing spondylitis; CD, Crohn's disease; UC, ulcerative colitis; Ps, plaque psoriasis; HS, hidradenitis suppurativa; UV, uveitis.

The majority of reports were associated with female patients for all approved indications. Reports associated with RA were almost equal between patients aged < 60 and ≥ 60 years. In addition, adalimumab and its biosimilars were used more frequently in patients aged < 60 years. However, age was not specified in at least 30% of reports. The drug was used in combination with other drugs in approximately 50% of RA, JIA, PsA, Ps, and UV cases. The combination treatment percentages for AS, UC, and CD were 47.7, 47.3, and 43.8%, respectively. The drug was used mainly as monotherapy to treat HS (28.1% of combination). Considering all indications, consumer reports exceeded those by healthcare professionals. For RA, expedited reports were comparable with non-expedited reports (47.8%). The number of expedited reports was higher than that of non-expedited reports for JIA, AS, HS, and UV. Considering patients with PsA, CD, UC, and Ps, expedited reports were fewer than non-expedited reports. Serious AEs were observed in >50% of patients with RA, JIA, AS, CD, HS, and UV; the remaining patients still experienced a high percentage of serious AEs, with approximately 47.7, 46.1, and 41.1% for UC, PsA, and Ps, respectively. For all the approved indications, hospitalization was the most common AE.

The trend of AE reports over time showed a similar pattern for all indications (Figure 1), with a slight initial increase between 2003 and 2010. Subsequently, there was a significant increase in the number of reports, which peaked in 2016. From 2017 onward, the number of reports decreased drastically, except for RA. In addition, the graph illustrates whether adalimumab and its biosimilars were used as monotherapy or combination therapy.

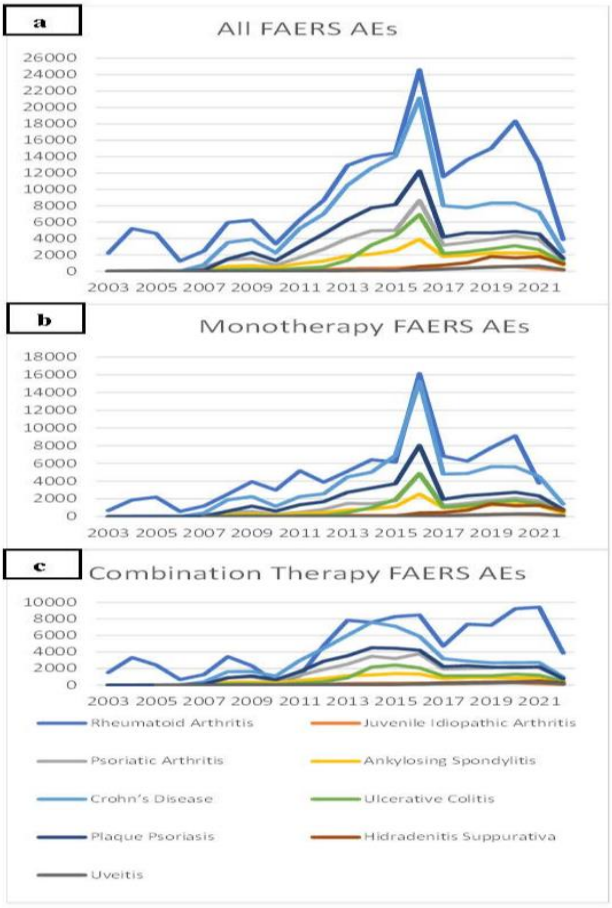

Fig. 1 The number of adalimumab and its biosimilars AE reports for each indication from 2002 to 2022 whenever it was reported (a), reported as monotherapy (b), or in combination (c).

The results of the binary logistic regression showed that patients aged ≥60 years were 1.73 times more likely to experience serious AEs (P < 0.001) (Table 2). In addition, males were 1.30 times more likely to experience serious AEs (P < 0.001). Compared with monotherapy with adalimumab and its biosimilars, patients who received combination therapy were 1.34 more likely to experience serious AEs (P < 0.001).

Table 2. Binary logistic regression for odds of serious outcomes of adalimumab and its biosimilars.

	Serious		
	ROR	**95% CI**	**p-value**
Age			
<60	Ref		
≥60	1.73	1.705–1.756	<0.0001
Gender			
Male	1.30	1.282–1.319	<0.0001
Female	Ref		
Number of therapies			
Monotherapy	Ref		
Combination therapy	1.34	1.318–1.355	<0.0001

ROR: reporting odds ratio; CI: confidence interval; Ref: reference.

Abatacept, certolizumab, etanercept, infliximab, ixekizumab, and rituximab are biological products available for the same proposed indications as adalimumab. Compared with available biological alternatives, the ROR for adalimumab and its biosimilars showed different results depending on the indication and whether the drug was used alone or in combination (Table 3). The ROR for abatacept revealed that adalimumab (whether it was used as monotherapy, combination, or both) was associated with less serious AEs, except when abatacept was used as monotherapy for PsA. Adalimumab was persistently associated with fewer serious AEs than certolizumab, except when employed to treat CD. Etanercept was associated with few serious AEs when used as a monotherapy or in all reports, but the ROR was <1 when used in combination therapy. Infliximab and rituximab RORs were persistently and significantly higher than those of adalimumab for the same indications. Comparing adalimumab with ixekizumab, we noted a ROR >1 in all scenarios, except when adalimumab was used to treat PsA in combination therapy.

Table 3. Disproportionality analysis of adalimumab and its biosimilars compared with the available biological products for the same approved indications.

	All		Monotherapy		Combination Therapy	
Product Name	**ROR (95% CI)**	**p-value**	**ROR (95% CI)**	**p-value**	**ROR (95% CI)**	**p-value**
Adalimumab	Ref		Ref		Ref	
RA						
Abatacept	0.43 (0.419–0.436)	<0.0001	0.61 (0.596–0.624)	<0.0001	0.38 (0.358–0.392)	<0.0001
Certolizumab	0.26 (0.255–0.270)	<0.0001	0.30 (0.293–0.313)	<0.0001	0.25 (0.231–0.266)	<0.0001
Etanercept	1.56 (1.544–1.580)	<0.0001	1.60 (1.576–1.618)	<0.0001	0.84 (0.810–0.863)	<0.0001
Infliximab	0.09 (0.092–0.098)	<0.0001	0.08 (0.077–0.084)	<0.0001	0.24 (0.229–0.257)	<0.0001
Rituximab	0.07 (0.063–0.069)	<0.0001	0.113 (0.107–0.120)	<0.0001	0.10 (0.089–0.105)	<0.0001
JIA						
Abatacept	0.35 (0.298–0.409)	<0.0001	0.80 (0.646–0.981)	0.03	0.29 (0.191–0.438)	<0.0001
Etanercept	2.02 (1.884–2.169)	<0.0001	1.97 (1.816–2.140)	<0.0001	0.84 (0.675–1.055)	**0.14**
PsA						
Abatacept	0.48 (0.428–0.526)	<0.0001	1.41 (1.216–1.642)	<0.0001	0.18 (0.142–0.234)	<0.0001
Certolizumab	0.38 (0.361–0.406)	<0.0001	0.41 (0.386–0.438)	<0.0001	0.37 (0.319–0.438)	<0.0001
Etanercept	1.97 (1.921–2.017)	<0.0001	2.10 (2.041–2.152)	<0.0001	0.84 (0.774–0.901)	<0.0001
Infliximab	0.12 (0.116–0.133)	<0.0001	0.13 (0.119–0.139)	<0.0001	0.20 (0.175–0.231)	<0.0001
Ixekizumab	2.78 (2.548–3.024)	<0.0001	3.84 (3.455–4.626)	<0.0001	0.73 (0.582–0.921)	0.007
AS						
Certolizumab	0.49 (0.454–0.531)	<0.0001	0.50 (0.459–0.540)	<0.0001	0.45 (0.323–0.623)	<0.0001
Etanercept	2.50 (2.409–2.589)	<0.0001	2.74 (2.634–2.842)	<0.0001	0.69 (0.592–0.813)	<0.0001
Infliximab	0.08 (0.069–0.084)	<0.0001	0.07 (0.066–0.082)	<0.0001	0.16 (0.125–0.214)	<0.0001
Ixekizumab	4.68 (3.432–6.383)	<0.0001	5.88 (4.101–8.435)	<0.0001	1.77 (0.723–4.320)	**0.197**
CD						
Certolizumab	1.11 (1.066–1.145)	<0.0001	1.10 (1.062–1.143)	<0.0001	1.13 (0.966–1.330)	**0.131**
Infliximab	0.08 (0.076–0.081)	<0.0001	0.08 (0.074–0.079)	<0.0001	0.19 (0.170–0.215)	<0.0001
UC						
Infliximab	0.08 (0.076–0.085)	<0.0001	0.08 (0.075–0.084)	<0.0001	0.15 (0.128–0.180)	<0.0001
Ps						
Certolizumab	0.24 (0.224–0.265)	<0.0001	0.35 (0.317–0.384)	<0.0001	0.17 (0.128–0.214)	<0.0001
Etanercept	2.14 (2.085–2.187)	<0.0001	2.33 (2.267–2.386)	<0.0001	0.79 (0.721–0.869)	<0.0001
Infliximab	0.06 (0.053–0.064)	<0.0001	0.07 (0.062–0.076)	<0.0001	0.10 (0.085–0.128)	<0.0001
Ixekizumab	2.65 (2.516–2.791)	<0.0001	2.89 (2.730–3.057)	<0.0001	0.93 (0.766–1.135)	**0.518**

ROR, reporting odds ratios; CI, confidence interval; Ref, reference; RA, rheumatoid arthritis; JIA, juvenile idiopathic arthritis; PsA, psoriatic arthritis; AS, ankylosing spondylitis; CD, Crohn's disease; UC, ulcerative colitis; Ps, plaque psoriasis.

Discussion

The anti-TNF agent, adalimumab, was generally well-tolerated. In most cases, adalimumab-related AEs do not necessitate treatment discontinuation. However, serious AEs have also been reported. The most common AEs include infections, injection-site reactions, and malignancy [24, 25]. The present study highlights the safety profile of adalimumab and its biosimilars in patients with RA, JIA, PsA, AS, CD, UC, Ps, HS, and UV. Adalimumab-related AEs were more frequently reported in females (65.7%) than in males (31.3%), consistent with previous findings that females show a higher incidence of several systemic rheumatologic autoimmune diseases than males [26]. Except for RA, adalimumab was mainly used in the < 60-year-old population (44.3%); this could be attributed to five of its indications being approved for the pediatric population (JIA, CD, UC, HS, and UV). Adalimumab-related AEs were mainly reported by consumers (70.5%) rather than healthcare professionals (25.5%), which indicates how incorporating patient assistance can improve the patient safety profile and ensure that measured AEs reflect what matters most to patients. Of the AEs, 50.6% were listed on the package insert (non-expedited). Conversely, 45.3% were serious and unexpected AEs unlisted on the product package insert, primarily for UV (in 70.5% of the AE reports), which could be attributed to the fact that UV was the last indication approved by the FDA in 2016, and the safety profile of adalimumab for this indication is under investigation. Approximately 50% of AE reports were serious (49.8%), and 22.4% required hospitalization.

The number of AE reports was the lowest from 2002 to 2006, given that adalimumab was only approved to treat RA, PsA, and AS during this period. In February 2007, adalimumab was approved for CD. From 2008 to 2016, adalimumab was approved to treat Ps, JIA, UC, HS, and UV [23], which may explain the increased number of reports from 2010 to 2016. Since 2017, the number of AE reports has decreased gradually, as several biological alternatives (reference and biosimilars) have been approved for the same indications as adalimumab, thereby impacting the market share of adalimumab and its biosimilars.

The safety analysis of adalimumab and its biosimilars revealed that age (≥60 years), male sex, and its use in combination are risk factors for serious AEs, corroborating the finding of a previous report [13].

In the present analysis, we found that the ROR of serious adalimumab-related AEs varied depending on the alternative used and the disease treated. This finding is consistent with a study conducted by Cross et al., who found that the same drug could exhibit different safety profiles for different diseases [27]. Considering the treatment of RA, JIA, and PsA, the frequency of serious AEs was significantly lower for adalimumab than that for abatacept, except when adalimumab was used as monotherapy for PsA. Based on certolizumab ROR analysis, adalimumab has a high risk of serious AEs when employed for CD, with less serious AEs observed when used to treat RA, PsA, AS, and Ps. More serious AEs were found to occur when etanercept was used as monotherapy; however, the odds of serious AEs were low when used in combination therapy. Adalimumab was significantly associated with fewer serious AEs than infliximab and rituximab. Ixekizumab was associated with a low number of serious AEs (ROR > 1, where adalimumab is the reference). One exception is ixekizumab, which was used in combination therapy for PsA. A previous study has examined the safety signals of disproportionate reporting of serious AEs associated with adalimumab when compared with currently available biological products. The authors found that adalimumab was associated with a lower incidence of serious AEs than infliximab and certolizumab but with a higher incidence than etanercept [28].

In the present study, we examined safety signals of disproportionate reporting of serious AEs for adalimumab and its biosimilars when compared with those of currently

available biological products for the same proposed indications using a pharmacovigilance analysis approach to evaluate the post-marketing safety of adalimumab.

Limitations

In this analysis, most of the AE reported to the FAERS came from consumers who were not necessarily familiar with medication safety across the continuum of care. Therefore, the outcomes may not be accurate.

We could not identify comorbidities (diseases other than those of interest). These comorbidities may improve the safety profile of adalimumab.

The ROR is a quantitative signal detection method that indicates a potential link to safety problems through a statistical correlation between the drug and AE. However, using ROR can be biased and misleading [29].

Finally, spontaneous AE reports may be biased and do not represent every case reported. Inaccurate estimations and missing information are common, which can affect the outcome [30, 31, 32, 33].

CONCLUSIONS

A significant difference in the signals of disproportionate reporting of serious AE between adalimumab and its biosimilars with the currently available alternatives for the same proposed indications was detected after analyzing the spontaneous AE reports from the FAERS database. However, given the limitations of this study, further research using a head-to-head study design to test the serious AE signals observed in this study is required.

Conflict of Interest

The author declares no conflict of interest.

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سلامة دواء أداليموماب: تحليل قاعدة بيانات نظام الإبلاغ عن الآثار الجانبية

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ملخص

الهدف: تحديد مدى سلامة دواء أداليموماب و بدائله الحيوية لكل إستخدام معتمد من خلال تحليل الأثار الجانبية التي تم الإبلاغ عنها إلى قاعدة بيانات نظام الإبلاغ عن الآثار الجانبية التابعة لإدارة الغذاء و الدواء الأمريكية

الطريقة: قمنا بإجراء تحليل إحصائي رجعي لتقارير الآثار الجانبية الموثقة من عام 2002 الى عام 2022. كما قمنا بمقارنة تقارير الآثار الجانبية لدواء الأدابيموماب و بدائله الحيوية مع البدائل الأخرى المتاحة حاليا لكل إستخدام.

النتائج: بالمجمل، تم الإبلاغ عن 543.873 تقرير لدواء الأداليموماب. من بين هؤلاء كان هناك 49.8٪ من الحالات شديدة الخطورة. الحاجة للذهاب إلى المستشفى كان أكثر الأثار الجانبية شيوعا. الذكور، وكبار السن (<60)، وإستخدام أكثر من دواء في نفس الوقت كانوا أكثر العوامل إرتباطا بالآثار الجانبية شديدة الخطورة .

الخلاصة: تشير نتائج هذه الدراسة إلى أن دواء أداليموماب يعتبر أكثر أمانا مقارنة بالبدائل البيولوجية المتاحة حاليا.

الكلمات الدالة: أداليموماب، الآثار الجانبية شديدة الخطورة، قاعدة ببانات، أمراض الروماتيزم، هوميرا.

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