SIGNAL DETECTION USING DATA FROM FDA ADVERSE EVENT REPORTING SYSTEM (FEARS): Infections IN BIOLOGICS VS. BIOSIMILARS.

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INTRODUCTION

Infections has been reported as a serious adverse effect in patients treated with tumor necrosis factor (TNF) – α targeting drugs. . Biosimilars are relatively new to the market and their pharmacosurveillance has, to date, been limited, but there may be differences in the safety profiles, and hence there is a gap in post marketing pharmaco-surveillance in the United States. Due to manufacturing difference, there may be difference in the safety profile of the drugs and their biosimilars. However, there is no formal pharmacovigilance or epidemiological study which further investigates the specific differences in the adverse effects of these drugs and their biosimilars.

OBJECTIVES

The objective of this study is to compare the safety profile of biologics (adalimumab, etanercept and infliximab) and their biosimilars (adalimumab-adaz, etanercept-szzs and infliximab-dyyb) using spontaneously reported infections from FDA Adverse Event Reporting System (FAERS).

METHODS

FAERS files from 1998 to 2022 were used to obtain case reports for all drugs. After standardizing and mapping of all infections and filtering duplicate reports, disproportionality analysis was used to detect signals by calculating proportional reporting ratio (PRR) and reporting odds ratio (ROR), Empirical Bayesian Geometric Mean (EBGM) and Information Component (IC) comparing each biosimilar to the biologics. A statistically significant signal was defined an ROR >1 or a PRR > 2.

Table 1: Contingency Table

	Adverse event of interest (Y)	All other adverse event of interest	Total
Drug of interest (X)	a	b	a+b
All other drugs of interest	c	d	c+d
Total	a+c	b+d	a+b+c+d

PRR = [a ÷ (a +b)] / [c ÷ (c + d)]
ROR = [a ÷ b] / [c ÷ d]
Observed/Expected = [a ÷ (a +b)] / [(a + c) ÷ (a + b+ c + d)]

RESULTS

Fig 1: Reporting pattern of Adalimumab originator biologics vs biosimilars

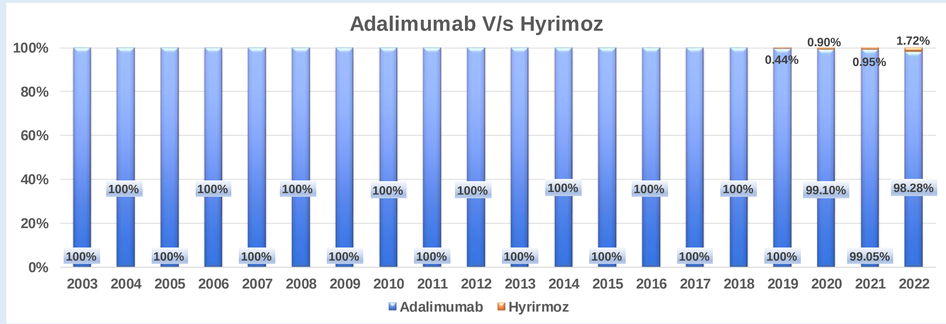


Fig 2: Reporting pattern of Etanercept originator biologics vs biosimilars

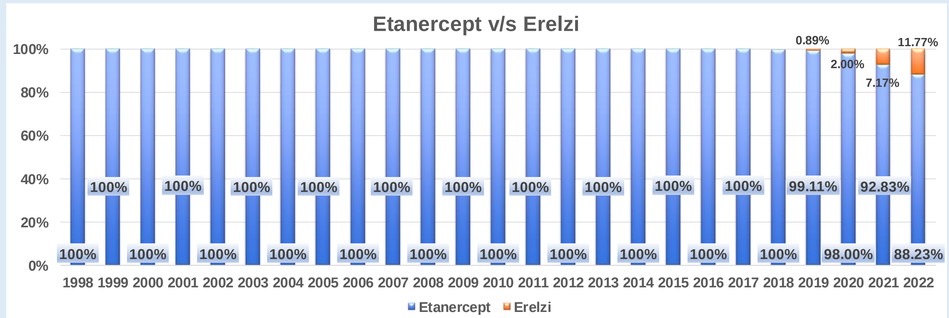
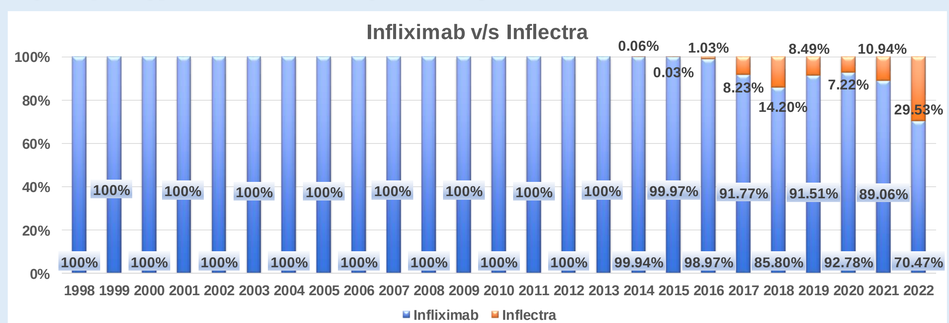


Fig 3: Reporting pattern of Infliximab originator biologics vs biosimilars



RESULTS

Table 2: Association of biosimilars/biologics with infection using signal detection

Medications	ROR	PRR	IC	EBGM
Erelzi	1.65(1.57-1.73)	1.41(1.34-1.48)	0.49	1.4
Hyrimoz	0.84(0.78-0.94)	0.87(0.81-0.94)	-0.19	0.87
Inflectra	1.21(1.18-1.24)	1.15(1.12-1.18)	0.19	1.14
Etanercept	0.74(0.73-0.74)	0.80(0.79-0.80)	-0.2	0.87
Adalimumab	1.66(1.65-1.67)	1.45(1.44-1.46)	0.28	1.21
Infliximab	0.63(0.63-0.64)	0.71(0.66-0.76)	-0.44	0.73

Overall, a total of 1,284,733 AE reports were identified for these medications, from which the biologics comprised of 19,579 reports and 1,265,154 cases were reported for biologics. No disproportionality analyses reached the predefined statistically significant value. However, potential signal was shown for Erelzi, Inflectra and Adalimumab. Other test results for Hyrimoz, Infliximab and Etanercept did not show any evidence of increased infection from these medications.

CONCLUSION

This study shows association (signal) of Erelzi, Inflectra and Adalimumab with infection. However, a signal is not a causal association between a drug and adverse event. Therefore, a formal epidemiological study is warranted as this study sets the stage for further pharmacovigilance investigation of this matter, and further pharmacoepidemiological studies are needed to test the hypotheses generated by this study.

REFERENCES

FDA Adverse Event Reporting System (FAERS) Public Dashboard. 10/22/2021. Accessed 9/15/2022. https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard

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