Identifying Major Adverse Drug Reactions Among Rheumatoid Arthritis Patients Administered Specific Classes of Disease-Modified Anti-Rheumatic Drugs (DMARDs)

EPH126

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Introduction

- There are currently few studies comparing relative risks of different classes of clinically important Disease-Modified Anti-Rheumatic Drugs (DMARDs).[1]
  - Janus Kinase (JAK) inhibitors
  - Tumor Necrosis Factor (TNF)-alpha blockers
  - Conventional DMARDs (CDMARDs)
- Knowing comparative risks associated with different drug classes used in the same indication can help to optimize clinical therapeutic decision making for patients suffering from Rheumatoid Arthritis (RA).

Objectives

- To comparatively examine adverse drug reactions (ADRs) of specific JAK inhibitors, TNF-alpha blockers, and CDMARDs among RA patients
- Highlight clinically significant ADR results reported from the FDA Adverse Event Reporting System (FAERS)

Methodology

- Retrospective data analysis was conducted with FAERS data from the year 2023. Analysis of frequency and types of ADRs was conducted between JAK inhibitors (Baricitinib, Tofacitinib, and Upadacitinib), TNF-alpha blockers (Adalimumab, Certolizumab, Etanercept, Golimumab, and Infliximab), and CDMARDs (Hydroxychloroquine, Leflunomide, Methotrexate, and Sulfasalazine).
- Patients diagnosed with RA and prescribed the medications above were included in the study. Patients not diagnosed with RA or not concurrently taking the medications described above were excluded.
- Descriptive analyses included age, gender, and weight (kg) categories among the reported events.

Total Data Demographics	
Average Age	61 Years Old
Average Gender	71% Female
Average Weight	79 Kg

Results

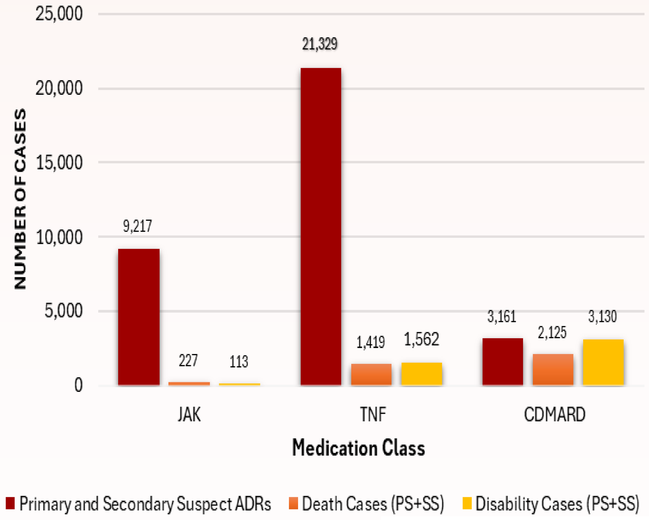

Figure 1. Total ADRs reported for all three analyzed classes were 213,542 cases with JAK inhibitors being the Primary or Secondary Suspect (PS or SS) in 62.8% of their ADR cases, TNF-alpha Blockers being the PS or SS in 22.0% of their ADR cases, and CDMARDs being the PS or SS in 3.1% of their ADR cases. Total Death Cases reported were 3,771 cases with JAK inhibitors being the PS or SS in 6.0% of their death cases, TNF-alpha Blockers being the PS or SS in 37.6% of their death cases, and CDMARDs being the PS or SS in 56.4% of their death cases. Total Disability Cases reported were 4,805 cases with JAK inhibitors being the PS or SS in 2.4% of their disability cases, TNF-alpha Blockers being the PS or SS in 32.5% of their disability cases, and CDMARDs being the PS or SS in 65.1% of their disability cases.

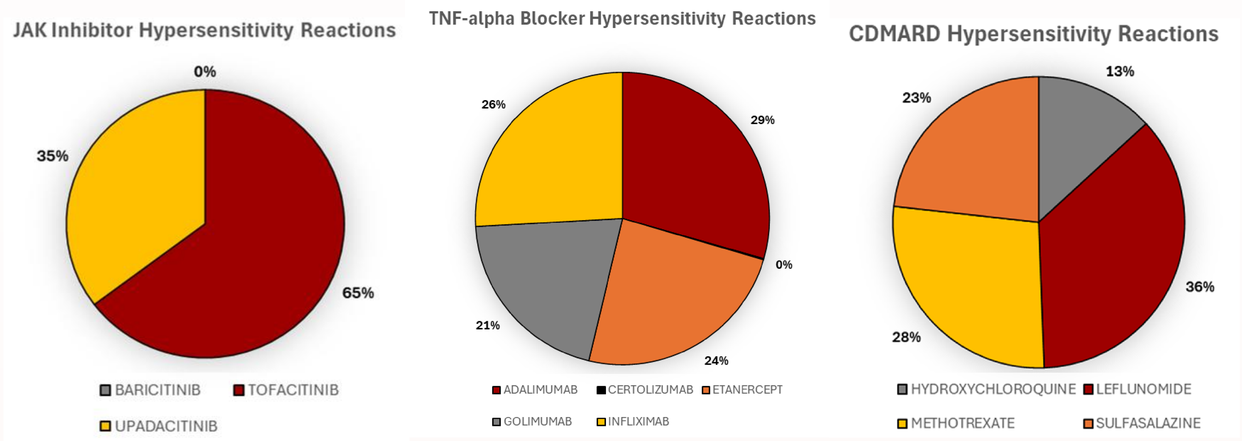

Figure 2. Total hypersensitivity cases reported for JAK inhibitors were 119 cases with reported hypersensitivity cases out of total ADRs reported for each medication were 0% for Baricitinib, 1.62% for Tofacitinib, and 0.23% for Upadacitinib. Total hypersensitivity cases reported for TNF-alpha blockers were 3,115 cases with reported hypersensitivity cases out of total ADRs reported for each medication were 1.54% for Adalimumab, 3.10% for Certolizumab, 1.95% for Etanercept, 1.79% for Golimumab, and 1.90% for Infliximab. Total hypersensitivity cases reported for CDMARDs were 2,999 cases with reported hypersensitivity cases out of total ADRs reported for each medication were 2.08% for Hydroxychloroquine, 2.15% for Leflunomide, 2.01% for Methotrexate, and 2.02% for Sulfasalazine.

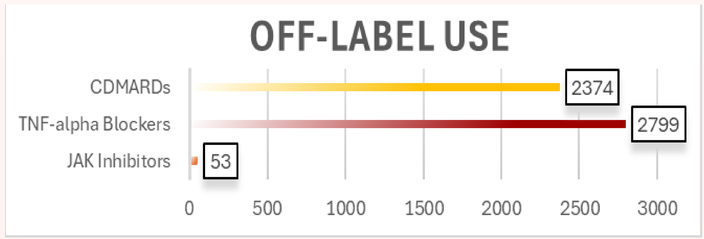

Figure 3. When conducting our analysis, we also observed high frequencies of off-label use reported with certain TNF-alpha blockers, and CDMARDS but close to none observed with JAK inhibitors. Multiple TNF-alpha blockers off-label use within their top 5 most frequent reactions and multiple CDMARDS reported instances of off-label use within their top 3 most frequent reactions.

Limitations

- Not all medications are used in the same frequency as each other and could possibly affect frequencies of ADRs for specific medications
- Cannot determine actual causes of adverse events with FAERs reports
- Information in reports are not verified
- Reports can contain incomplete information
- Cannot determine incidence rates of occurrence due to reporting being voluntary

Conclusion

- JAK inhibitors were the most likely to be the primary suspect if they were associated with an adverse drug event
  - Tofacitinib had an increased frequency of hypersensitivity reactions compared to the other JAK inhibitors analyzed
- TNF-alpha blockers had the most reports of general ADRs as well as total hypersensitivity reaction reports
- CDMARDs had the most reports of PS and SS death cases and disability cases compared to JAK inhibitors and TNF-alpha blockers
- Off label use is a potential confounder for affecting the frequencies of different reactions reported
  - The JAK inhibitors analyzed had far fewer off-label reports compared to both TNF-alpha blockers and CDMARDs

Next Steps

Further evaluation needs to be conducted to analyze off-label use confounding effects that could have possible over-expression or under-expression of certain ADRs .

References

1. Frontiers | Potential Adverse Events Reported With the Janus Kinase Inhibitors Approved for the Treatment of Rheumatoid Arthritis Using Spontaneous Reports and Online Patient Reviews. Accessed Oct 7, 2024. https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2021.792877/full
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Acknowledgements

We would like to give special thanks to the Ferris State University College of Pharmacy Alumni Advisory Board (AAB) for graciously providing the co-curricular funding to make this poster presentation possible as well as Dr. Dane Shiltz for his guidance and clinical perspective with data interpretation.