Long-Term Safety of Emerging Biologic Therapies in Autoimmune Disease: A Systematic Review and Osteopathic Perspective

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Introduction

- Biologics (IL-17, IL-23 inhibitors) and JAK inhibitors revolutionize autoimmune disease management
  a. RA, PsA, AS, psoriasis, IBD
- Long-term safety remains incompletely defined, especially >3 years.
- Rare but serious adverse effects often underreported
- Osteopathic Manipulative Medicine emphasizes systemic connections aligning with safety-focused patient care.
  a. Immune, musculoskeletal, and autonomic regulation

Methods

- Databases: PubMed (2015–2025).
- Keywords: (“IL-17 inhibitor” OR “IL-23 inhibitor” OR “JAK inhibitor”) AND (“autoimmune disease*”) AND (“long-term safety” OR “adverse effects”).
- Inclusion: Adults ≥18, ≥1 year follow-up, reporting safety/adverse events.
- Exclusion: Pediatrics, <1 year follow-up, efficacy-only, case reports, non-English.
- Study Types: RCT extensions, cohort studies, registries, systematic reviews

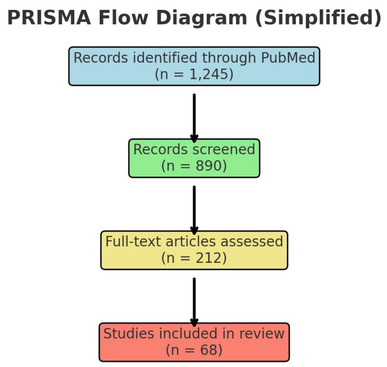

Figure 1. PRISMA Flow Diagram
Flow of studies through the systematic review process, including identification, screening, eligibility, and final inclusion of articles.

Results

- 68 studies included (RCT extensions, registries, systematic reviews).
- IL-17 inhibitors (e.g., secukinumab, ixekizumab): ↑ mild respiratory/skin infections, low malignancy risk.
- IL-23 inhibitors (guselkumab, risankizumab, ustekinumab): Favorable safety, low discontinuation rates, infections most common AE.
- JAK inhibitors (tofacitinib, baricitinib, upadacitinib): Higher risk of VTE, MACE, and herpes zoster reactivation; FDA black box warnings noted.
- Long-term malignancy signal remains inconclusive, but ongoing monitoring required.

Table 1. Summary of Long-Term Adverse Effects Reported with Emerging Biologic Therapies
Comparison of major adverse events associated with IL-17, IL-23, and JAK inhibitors, based on published long-term safety studies (≥1 year follow-up).

Therapy	Most Common AEs	Serious AEs	Long-Term Signal (>3 yrs)
IL-17 inhibitors	URIs, skin infections	Rare TB, fungal infection	Stable safety; low malignancy
IL-23 inhibitors	Mild infection, injection reactions	Rare serious infection	Favorable long-term safety
JAK inhibitors	Herpes zoster, cytopenia	↑ VTE, ↑ MACE, malignancy signal	FDA warnings, higher vigilance

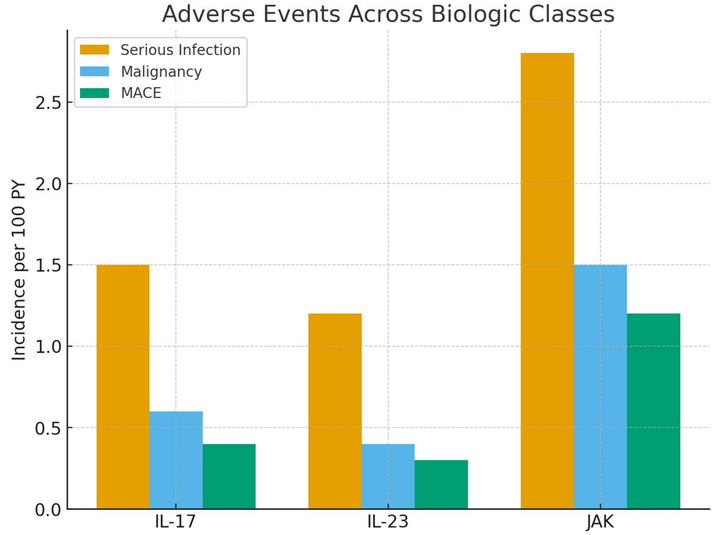

Figure 2. Adverse Events by Drug Class
Distribution of reported long-term adverse effects associated with IL-17 inhibitors, IL-23 inhibitors, and JAK inhibitors, highlighting infection, malignancy, cardiovascular, and thromboembolic outcomes.

References

Author Info

Discussion

- IL-17/23 inhibitors: generally favorable long-term safety.
- JAK inhibitors: higher risk profile, requiring individualized risk–benefit analysis.
- Limitations
  - Heterogeneous reporting
  - Underrepresentation of rare AEs.
- Osteopathic integration:
  - Help reduce systemic inflammation
  - Modulate autonomic tone, and
  - Complement biologic therapy.

Conclusion

- IL-17 and IL-23 inhibitors show sustained long-term safety.
- JAK inhibitors need closer monitoring
  - Thromboembolic and CV risk.
- Osteopathic approaches offer a holistic adjunct
  - Enhance outcomes and reduce systemic inflammation.
- Ongoing multidisciplinary care are critical.

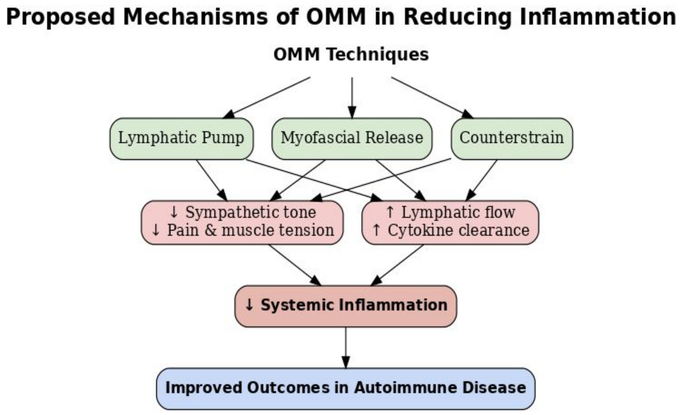

Figure 3. Proposed Mechanisms of OMM in Reducing Inflammation
Schematic representation of osteopathic manipulative medicine (OMM) techniques that may reduce systemic inflammation and improve outcomes in autoimmune disease.