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REVIEW ARTICLE

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Recent advances in biologic therapies for ankylosing spondylitis: A 2024 update

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Abstract
Background: Ankylosing spondylitis (AS), a long-term autoimmune disorder characterized by systemic inflammation, manifests as gradually worsening arthritis predominantly affecting the spinal column and sacroiliac joints. While emerging biologic agents have broadened treatment possibilities, their clinical application raises notable safety considerations.
Objective: To comprehensively summarize recent advancements in bDMARD applications (including tumor necrosis factor-alpha inhibitors (TNFi), interleukin 17 inhibitors (IL17i), and Janus kinase inhibitors (JAKi)) for AS management.
Material and Methods: A thorough bibliographic search was conducted to identify studies meeting the inclusion criteria in the Pubmed (MEDLINE) and EMBASE databases in July 2025 for nearly a year. Our search strategy included both medical subject headings (MeSH) and free text terms relevant to the biologics.
Results: A total of 147 studies were screened and 37 clinical studies were ultimately selected in this review, drawing on peer-reviewed studies released within the previous calendar year. Adalimumab, infliximab, etanercept, golimumab, certolizumab pegol, secukinumab, bimekizumab, ixekizumab, tofacitinib, upadacitinib, and baricitinib had greater remittance in AS, with some side effects.
Conclusion: This comprehensive analysis assesses therapeutic outcomes and adverse effects of TNFi, IL17i, and JAKi in AS care.

Introduction

Ankylosing spondylitis (AS), classified under axial spondyloarthritis (axSpA), represents a persistent inflammatory disorder characterized by chronic inflammation and aberrant bone proliferation within the spinal column. This pathological process results in disrupted skeletal remodeling, diminished physical flexibility, and potential long-term

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functional impairments.[1,2] This condition encompasses various immune-mediated inflammatory disorders, including reactive arthritis, psoriatic arthritis, and inflammatory bowel disease (IBD)-related arthritis.[2] The disease's cardinal manifestation involves enthesitis—inflammatory processes occurring at musculoskeletal attachment points where connective tissues interface with bone structures. Clinically, this presents as progressive spinal rigidity and discomfort, frequently evolving into permanent joint dysfunction. Pathologically, AS demonstrates concurrent osteogenesis and osteolytic activity, driving structural deterioration and eventual joint fusion.[3] While the exact pathogenic mechanisms of AS are not fully elucidated, substantial research indicates significant genetic contributions. AS pathogenesis stems from intricate interplays among hereditary susceptibility factors, notably the *HLA-B27* gene variant, and disrupted immune mechanisms centered on the interleukin-23 (IL-23)–IL-17A cytokine pathway, which collectively drive disease initiation and advancement.[4-8] Global prevalence estimates for AS demonstrate significant variation (0.1–1.4%), influenced by hereditary susceptibility patterns and regional HLA-B27 allele distribution.[9] The disease burden extends beyond physical limitations, substantially compromising quality of life and predisposing patients to psychological comorbidities. Epidemiological investigations reveal a heightened cardiovascular disease burden among AS populations compared to matched controls, accounting for 20–40% of mortality cases and emerging as the predominant fatal outcome.[10,11] These clinical realities underscore the urgent requirement for innovative therapeutic strategies targeting AS pathophysiology.

The pharmacological management of AS endorsed by three major rheumatology organizations—the Assessment of Spondylo Arthritis International Society (ASAS), the European League Against Rheumatism (EULAR), and the Chinese Society of Rheumatology (CSR)—includes five therapeutic categories: non-steroidal anti-inflammatory drugs (NSAIDs), biologic disease-modifying antirheumatic drugs (bDMARDs), sulfasalazine, methotrexate, and corticosteroids.[12] As primary therapeutic agents, NSAIDs, such as indomethacin, diclofenac, ibuprofen, and naproxen, effectively alleviate axial symptoms, including spinal discomfort, morning rigidity, and articular inflammation. Their clinical utility faces restrictions due to multiple adverse effects spanning insufficient therapeutic response, renal impairment, cardiovascular risks, hepatic toxicity, and medication tolerance.[13] Conventional synthetic DMARDs, such as sulfasalazine and methotrexate, serve as alternative options for patients demonstrating peripheral joint manifestations or having biological therapy contraindications. These agents present challenges, including slow onset of therapeutic effects and gastrointestinal disturbances, with methotrexate showing particular limitations in clinical practice. Clinical considerations for these medications include potential adverse effects, such as liver toxicity and susceptibility to infections.[13] bDMARDs, encompassing tumor necrosis factor-alpha inhibitors (TNF-αi), interleukin inhibitors, and Janus kinase pathway modulators (JAKi), represent a precision-targeted pharmacological approach for AS intervention. By specifically blocking key inflammatory signaling cascades, these advanced therapies demonstrate remarkable capacity to alleviate clinical manifestations, stabilize physiological parameters, and enhance patient-reported outcomes in AS patients, particularly serving as second-line options for NSAID-resistant patients.[13,14] However, safety profiles remain a critical consideration in therapeutic decision-making.

This comprehensive review synthesizes recent advancements in bDMARD applications (including TNFi, IL17i, and JAKi) for AS management, focusing on peer-reviewed studies published within the preceding 1 year. A thorough bibliographic search was conducted to identify studies meeting the inclusion criteria in the Pubmed (MEDLINE) and EMBASE databases in July 2025 for nearly a year. Our search strategy included both medical subject headings (MeSH) and free text terms relevant to the biologics. The specific index terms included "ankylosing spondylitis" AND "adalimumab," "ankylosing spondylitis" AND "infliximab," "ankylosing spondylitis" AND "etanercept," "ankylosing spondylitis" AND "golimumab," "ankylosing spondylitis" AND "certolizumab pegol," "ankylosing spondylitis" AND "secukinumab," "ankylosing spondylitis" AND "bimekizumab," "ankylosing spondylitis" AND "ixekizumab," "ankylosing spondylitis" AND "tofacitinib," "ankylosing spondylitis" AND "upadacitinib," "ankylosing spondylitis" AND "baricitinib." A total of 147 studies were screened and 37 clinical studies were ultimately selected in this review.

Tumor Necrosis Factor-alpha Inhibitors

Tumor necrosis factor-alpha serves as a key mediator in both spondylitis pathogenesis and sacroiliitis development, while contributing to systemic complications such as uveitis.[15,16] Among therapeutic interventions for AS, TNF represents the most extensively researched and clinically utilized biological agents.[15,16] The therapeutic landscape for AS underwent substantial transformation following TNFi introduction during the initial decade of the 2000s. The current clinical practice incorporates five approved TNFi agents: certolizumab pegol, golimumab, infliximab, etanercept, and adalimumab.[17,18] A South Korean tertiary hospital's rheumatology unit conducted a 19-year longitudinal analysis of 313 AS patients initiating TNFi therapy, revealing adalimumab as the most frequently administered agent (69.3%), with etanercept and infliximab accounting for 21.4% and 9.3%, respectively.[19] Chilean cost-effectiveness evaluations of biological therapies for AS incorporated multiple TNF inhibitors, including adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab, in their comparative analysis. The results showed that all treatments had a positive impact on equity relative to treatment as usual.[20]

Adalimumab

Adalimumab, a fully human monoclonal immunoglobulin (Ig)G1 antibody, prevents TNF-α from interacting with cellular receptors through subcutaneous administration.[21] This biological agent ranks among the world's most widely utilized targeted therapies.[22] Both controlled trials and observational studies confirm that adalimumab monotherapy or combined with conventional DMARDs (e.g., methotrexate)

effectively reduces clinical disease manifestations and enhances therapeutic outcomes.[23,24]

Clinical outcomes demonstrated rapid reduction in the ankylosing spondylitis disease activity score and the bath ankylosing spondylitis functional index following adalimumab treatment for a female patient in her 20s, with sustained low-disease activity (LDA) or remission achieved post-intervention.[25] A Taiwanese longitudinal observational study evaluated therapeutic responses to adalimumab in AS patients, revealing significant clinical improvements. Post-treatment analysis showed 50% enhancement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores alongside increased achievement proportions of inactive disease (ID) <1.3 and LDA <2.1) per ankylosing spondylitis disease activity score-C-reactive protein (ASDAS-CRP) and ASDAS-erythrocyte sedimentation rate (ASDAS-ESR). Therapeutic benefits extended to reduced incidence of entheseal inflammation, peripheral joint involvement, digit inflammation, and ocular complications. Safety monitoring documented treatment-emergent adverse events (TEAEs) and serious adverse events (AEs) without mortality cases. Predominant TEAEs included nasopharyngeal infections (5.7%) and bronchial irritation (3.4%).[26]

A nationwide retrospective cohort analysis of 34,621 AS patients with no prior documented patients of acute anterior uveitis (AAU) was performed utilizing a national healthcare claims repository. The investigation revealed that patients receiving adalimumab exhibited a significantly reduced likelihood of developing AAU, compared to those treated with alternative bDMARDs, including etanercept, infliximab, and secukinumab. These findings highlight adalimumab's potential as a first-line therapeutic option for preventing both initial and recurrent AAU episodes in the AS population.[27]

A clinical study documented the management approach for a juvenile female diagnosed with cat scratch disease (CSD) undergoing immunosuppressive therapy (adalimumab and baricitinib) for AS, who subsequently contracted COVID-19 during CSD treatment.[28] Another case involving a 32-year-old AS patient manifested progressive demyelinating disorders following adalimumab administration, as detailed in medical records.[29] Analysis of Korean claims data (2010–2021) revealed that AS patients receiving adalimumab therapy demonstrated markedly elevated incidence of tuberculosis (TB), while IBD risks showed no statistical significance, compared to bDMARD-naïve counterparts. The investigation further established adalimumab exposure as an independent risk factor for TB development.[30]

A documented case involved a 36-year-old male undergoing combination therapy (adalimumab, sulfasalazine, and etoricoxib) for AS, who subsequently developed psoriatic eruptions alongside dysgeusia and strawberry tongue manifestations.[31] In another instance, adalimumab administration in a patient concurrently diagnosed with Crohn's disease (CD) and AS resulted in the emergence of proteinase 3-anti-neutrophil cytoplasmic antibodies (PR3-ANCA)-associated vasculitis complicated by tubulointerstitial nephritis.[32] Clinical documentation demonstrated development of Candida meningitis in an AS and psoriasis patient following adalimumab treatment.[33] A Mexican migrant worker (aged 53 years) undergoing adalimumab therapy for concurrent psoriasis and AS exhibited newly developed extremity rashes as a treatment complication.[34]

ABP 501 (marketed as AMGEVITA® in the European Union and AMJEVITA™ in the United States) represents a biosimilar medication authorized by European Medicines Agency (EMA) regulatory bodies, designed to match the reference biologic adalimumab (HUMIRA®), entering clinical application within European markets during October 2018.[15] This therapeutic agent was subsequently accessible in the US market from January 2023 onward, joining eight other approved biosimilar counterparts currently available.[16] European clinical observations from the Adelphi disease-specific program documented ABP 501's therapeutic performance in AS management. Post-treatment evaluations revealed moderate disease progression in AS patients receiving ABP 501, accompanied by favorable health outcomes. Therapeutic satisfaction proportion exceeded 89% among clinicians and surpassed 86% in patient cohorts regarding symptom management efficacy.[35] Humira®, developed by Abbott Laboratories, initially received the US Food and Drug Administration (FDA) authorization for AS treatment in 2006, with subsequent approval extending to the Chinese patient population after a 7-year interval.[36,37] The medication's limited adoption within Chinese healthcare systems primarily stems from substantial cost barriers. In 2020, adalimumab by Innovent (IBI303) received regulatory clearance from China's National Medical Products Administration for treating AS. An observational cohort analysis compared treatment persistence and tolerability profiles in clinical practice between the biosimilar IBI303 and reference product Humira among AS patients. The investigation revealed that both cohorts documented two cases of treatment-emergent AEs, all categorized as mild infusion-related responses. Notably, no participant withdrew from the treatment because of these transient reactions, with detailed findings documented by Cheng et al.[38]

Infliximab

Infliximab, a chimeric monoclonal antibody composed of 75% human and 25% murine components, inhibits TNF-α-mediated activation of cellular receptor complexes through intravenous administration.[39] Clinical documentation highlights a 38-year-old male with coexisting psoriatic arthritis and AS who underwent infliximab treatment for 1 year. Post-treatment evaluation revealed substantial enhancements in disease progression metrics, functional capacity, and the overall life quality indicators.[40] Another case study details a juvenile-onset AS patient who developed new-onset IBD during golimumab treatment for spinal inflammation. Cessation of golimumab therapy led to significant alleviation of gastrointestinal manifestations, although subsequent AS reactivation prompted the switch to infliximab. This therapeutic adjustment successfully controlled both spinal inflammation and intestinal pathology.[41]

A 70-year-old male patient developed right pleural effusion and lymphadenopathy following infliximab therapy for sarcoidosis and AS, with subsequent biopsy confirming concurrent diffused large B-cell lymphoma and peripheral T-cell lymphoma not otherwise specified.[42] Clinical documentation describes a 47-year-old female

physician with pre-existing AS who experienced abdominal discomfort progressing to acute abdominal crisis secondary to Mycobacterium tuberculosis infection after initiating infliximab treatment.[43] Epidemiological analysis of Korean healthcare claims data (2010–2021) revealed tuberculosis incidence elevation among AS patients receiving infliximab, with biologic exposure demonstrating elevated tuberculosis risk while showing no statistically significant variation in IBD occurrence, compared to non-bDMARD cohorts.[30]

CT-P13, an authorized biosimilar of infliximab, demonstrated clinical efficacy in managing AS and related inflammatory disorders, providing cost-effective therapeutic alternatives with comparable outcomes.[44,45] A longitudinal monitoring investigation in South Korea tracked 34 AS patients receiving intravenous CT-P13, revealing substantial improvements in disease severity and functional capacity from baseline measurements after 6 months of treatment. Post-intervention analysis indicated rising serum drug concentrations alongside detectable anti-drug antibody levels, with pharmacokinetic data demonstrating an inverse relationship between CT-P13 serum levels and immunogenicity markers.[46] The nationwide ReFLECT cohort study evaluated real-world CT-P13 performance in AS management, reporting 62.7% treatment continuation proportion at 2-year follow-up. Comparative analysis revealed higher persistence proportion among patients transitioning from originator infliximab, compared to biological-naïve individuals with AS. Among AS patients, 57.9% experienced at least one AE, with serious AEs documented in 11.4% of cases. The predominant AEs involved infectious complications, including severe infections, tuberculosis, opportunistic infections, and hepatitis B.[47]

Etanercept

Etanercept functions as a dimeric fusion protein that merges the extracellular ligand-binding portion of human TNF receptor-2 with the constant fragment of humanized IgG1.[48] This molecular configuration prevents TNF from interacting with cellular receptors, thereby suppressing inflammatory signaling pathways. Delivered through subcutaneous injection, etanercept holds distinction as the inaugural TNF inhibitor approved by the FDA for managing rheumatic conditions.[49]

A propensity score-matched investigation conducted through the Czech ATTRA registry revealed that patients receiving etanercept exhibited notably extended median survival durations, compared to those administered monoclonal TNFi.[50] In a clinical case involving a 16-year-old male presenting concurrent juvenile spondyloarthritis and ocular toxocariasis, combined subtenon triamcinolone administration and subcutaneous etanercept therapy achieved stabilization of visual function.[51] Analysis of South Korean insurance claims data spanning 2010–2021 indicated that AS patients undergoing etanercept treatment demonstrated comparable proportions of tuberculosis and IBD incidence relative to biological DMARD-naïve counterparts, with no statistically significant risk elevation observed[30] A nationwide retrospective cohort analysis revealed that etanercept-exposed patients had elevated likelihood of recurrent AAU compared to adalimumab-treated individuals, positioning etanercept as the least favorable biological DMARD option (among adalimumab, golimumab, infliximab, and other agents) for both primary prevention and recurrence mitigation of AAU episodes.[27]

Golimumab

Golimumab, a completely human-derived monoclonal antibody, selectively targets soluble and membrane-bound TNF molecules. This mechanism effectively prevents their binding to TNF receptors, as demonstrated in prior research.[52] Exhibiting strong binding affinity toward TNF-α, golimumab demonstrates therapeutic efficacy when administered through either intravenous infusion or subcutaneous injection, as supported by clinical studies.[53,54]

Analysis of South Korean healthcare claims records spanning 2010–2021 revealed that AS patients receiving golimumab therapy demonstrated occurrence of tuberculosis and IBD. The study showed substantially elevated tuberculosis risk with golimumab exposure, compared to non-bDMARD users, while IBD incidence showed no statistically significant variation.[30] A clinical case report documented the emergence of new-onset IBD in a juvenile-onset AS patient undergoing golimumab treatment for active spinal inflammation.[41] Pharmacovigilance research utilizing the FDA Adverse Event Reporting System (FAERS) data from Q1 2010 to Q4 2023 identified golimumab as having the most pronounced association with infection-related AEs among AS patients during stratified analysis.[55] A nationwide retrospective cohort analysis involving 34,621 AS patients without prior AAU history, conducted through insurance claims data, indicated that golimumab treatment can lead to incident AAU.[27]

Certolizumab pegol

Certolizumab pegol represents a polyethylene glycol (PEG)-attached (PEGylated) antigen-binding component derived from a humanized monoclonal antibody. This biological agent specifically targets soluble and membrane-associated TNF-α molecules for neutralization, requiring subcutaneous administration.[56]

In a clinical scenario involving a 30-year-old male presenting with concurrent ulcerative colitis, Crohn's disease, and AS, extensive therapeutic regimens, including TNF inhibitors, vedolizumab, ustekinumab, and upadacitinib, failed to achieve disease control. Notably, concurrent administration of certolizumab pegol with ustekinumab and vedolizumab demonstrated efficacy in alleviating AS symptoms.[57]

Interleukin-17 inhibitors (IL-17i)

Interleukin-17 serves as a pivotal inflammatory mediator within mammalian immune responses, with extensive research documenting its critical role in immunological processes.[58] Clinical studies detected markedly increased IL-17 concentration in the circulatory systems of AS patients relative to control groups.[59] Experimental evidence demonstrated that IL-17A and IL-17F exhibit synergistic interactions with TNF, collectively exacerbating inflammatory

cascades during *in vitro* investigations.[60] These findings propelled IL-17i into clinical prominence as second-line biological therapies for AS management, demonstrating notable efficacy in alleviating axial discomfort and enhancing patients' quality of life parameters.[61,62]

Secukinumab

Secukinumab, a human-derived monoclonal antibody targeting IL-17A, holds authorization for managing axSpA spectrum disorders, including AS.[63,64] Clinical practice guidelines endorse both 150-mg and 300-mg therapy for AS treatment.[63,65-67] A multicenter randomized controlled trial (phase 4, double-blind design) compared treatment outcomes between dose-adjusted groups in AS patients showing insufficient response to initial 150-mg therapy by week 16. At 52-week follow-up, ASDAS scores below 1.3 were achieved in 8.8% of subjects receiving escalated 300-mg dosage versus 6.7% maintaining 150-mg regimen. Safety monitoring revealed comparable treatment-emergent AE proportions across both cohorts during the observation period. These findings suggest that comparable therapeutic outcomes and safety profiles persist through 1-year treatment regardless of dosage intensification in suboptimal responders.[68] Interim data from the prospective SERENA, *an ongoing European noninterventional longitudinal,* cohort study tracking Greek patients over 36 months further supports secukinumab's effect on AS patients. Among AS patients, medication persistence proportions reached 89.9% after the first year, decreasing to 80.5% by year 2 and stabilizing at 77.3% in the third year of treatment. Treatment-emergent AEs linked to secukinumab occurred in 13.6% of AS cases, with no reported instances of candidiasis, significant cardiovascular complications, IBD, or ocular inflammation.[69]

A Polish observational study involving 139 psoriatic arthritis patients, 112 AS subjects, and 28 non-radiographic spondyloarthritis patients demonstrated secukinumab's therapeutic performance. Clinical response proportion reached 88.2% within 3 months and maintained at 88.9% through 6 months, accompanied by measurable enhancements across all clinical indicators. Treatment continuation proportion stood at 87% after 12 months but diminished to 59% over 58-month follow-up.[70] In a clinical case, a 32-year-old female initially diagnosed with AS subsequently developed treatment-resistant relapsing polychondritis. After unsuccessful combination therapy with TNFi and methotrexate, complete disease remission was attained through secukinumab administration.[71]

An exploratory analysis was conducted to investigate associations between systemic and ocular inflammatory biomarkers in AS patients receiving secukinumab therapy. Findings from this observational cohort analysis revealed reduced levels of *interleukin-1 receptor antagonist (*IL-1Ra) in both tear fluid and blood serum post-treatment.[72] Comprehensive cost-utility evaluations demonstrated that biological therapies, including secukinumab, etanercept, certolizumab pegol, infliximab, adalimumab, and golimumab, exhibited beneficial equity outcomes, compared to standard care, with secukinumab particularly showing enhanced societal well-being through improved health resource allocation.[20]

Utilizing South Korean health insurance records from 2010–2021, researchers evaluated tuberculosis and IBD occurrence among biological-treated AS patients. Analysis revealed IL-17i therapy maintained TB and IBD frequencies within expected low thresholds, demonstrating marginally reduced mycobacterial infection proportions but slightly elevated intestinal inflammation incidence relative to TNFi. Among secukinumab recipients, documented TB/IBD cases showed comparable risk profiles to biological-naïve populations in referenced studies.[30] A separate analysis of 34,621 AAU-free AS patients through national databases identified secukinumab exposure correlating with anterior uveitis development, displaying heightened risk compared to adalimumab-treated counterparts.[27] A clinical report details a 31-year-old female AS patient presenting with chronic lower back. Therapeutic intervention with Yisaipu (etanercept biosimilar) combined with secukinumab triggered unforeseen adverse effects, including anterior chest discomfort and palmoplantar pustular eruptions, indicating a paradoxical manifestation of Synovitis–Acne–Pustulosis–Hyperostosis–Osteitis (SAPHO) syndrome.[73] Another clinical report documented an unusual presentation of localized oral histoplasmosis in a 42-year-old Brazilian patient receiving secukinumab therapy for AS.[74]

Bimekizumab

Bimekizumab, a humanized IgG1 monoclonal antibody, uniquely targets both IL-17A and IL-17F, distinguishing itself as the first biological therapy that received dual approval from both EMA and FDA for treating axSpA. Clinical trial data demonstrate that simultaneous blockade of these two cytokines induces prompt symptom relief and sustained therapeutic outcomes across various axSpD subtypes.[62,75] A 5-year extension study evaluating bimekizumab's long-term profile in AS revealed that clinical responses observed at 48 weeks remained consistent through 260 weeks, with persistent enhancements in multiple patient-reported outcomes, including pain severity, energy levels, mobility, and the overall wellbeing. Treatment-emergent AEs affected 95.4% of participants, with nasopharyngitis (21.8%) and upper respiratory tract infections (14.5%) emerging as the most frequent safety concerns during extended follow-up periods.[76]

Ixekizumab

Ixekizumab, a potent IL-17A antagonist with high binding affinity, demonstrated therapeutic effectiveness in managing clinical manifestations of radiographic axSpA (r-axSpA) across multiple studies.[61,77,78] This biological agent's clinical value was further validated in Chinese populations through a rigorous phase 3 clinical trial.[79] Analysis of South Korean insurance records from 2010 to 2021 revealed TB and IBD occurrences among AS patients receiving ixekizumab therapy.[30] A clinical case involving a 64-year-old female with 3-year AS history demonstrated unexpected adverse effects, as the patient developed patchy hair loss after starting ixekizumab treatment following inadequate responses to standard treatments.[80]

Janus Kinase Inhibitors

The Janus kinase–signal transducer and activator of transcription (JAK-STAT) signaling pathway is disrupted by JAK inhibitors through suppression of JAK enzymes (JAK1, JAK2, JAK3, and TYK2), modulating the production of multiple pro-inflammatory cytokines implicated in autoimmune disorders and inflammatory conditions.[81] Following the 2012 authorization of tofacitinib for rheumatoid arthritis (RA), subsequent JAK inhibitors, such as baricitinib, upadacitinib, filgotinib, and peficitinib, have entered clinical use.[82] These therapeutics exhibited significant effectiveness in managing disease progression, frequently surpassing conventional TNFi agents in clinical outcomes.[83] However, the extensive influence of JAK inhibitors on the JAK-STAT cascade—a critical component of various cellular signaling networks—prompted scrutiny regarding unintended biological interactions and corresponding safety implications.

Tofacitinib

As the inaugural JAKi receiving regulatory approval (primarily targeting JAK1/JAK3 with secondary activity against JAK2), tofacitinib revolutionized autoimmune disease management through oral administration. This small-molecule therapeutic agent alters activity within the JAK-STAT cellular signaling cascade, a pivotal biochemical pathway governing cytokine-mediated immune responses and inflammatory processes. Originally authorized to manage rheumatoid arthritis, this medication's therapeutic scope expanded to include psoriatic joint inflammation and colonic ulcerative conditions, while demonstrating therapeutic promise across diverse autoimmune disorder.[84] The scientific basis for investigating JAK pathway modulation in AS lies in the compound's capacity to simultaneously disrupt multiple pro-inflammatory mechanisms, potentially offering a superior efficacy profile, compared to monoclonal antibodies targeting single cytokine pathways.

Subsequent retrospective evaluations of Phase II/III clinical studies revealed enhanced therapeutic responses to tofacitinib, compared to placebo in AS patients, with prevalent AEs comprising nasopharyngeal inflammation, upper airway infections, and joint discomfort.[85] Examination of fatigue progression patterns in a phase III randomized controlled trial demonstrated that tofacitinib recipients experienced accelerated alleviation of fatigue manifestations relative to placebo-treated individuals.[86] A clinical report documented a 31-year-old female AS patient presenting with persistent lumbar discomfort. Therapeutic interventions using Yisaipu (etanercept biosimilar) and seckinumab unexpectedly induced manifestations of sternal pain and palmoplantar pustulosis, indicative of paradoxical SAPHO syndrome. Subsequent tofacitinib administration successfully resolved these clinical manifestations.[73]

Upadacitinib

Upadacitinib, a next-generation JAKi, demonstrates 74-fold greater selectivity for JAK1 over JAK2, thereby offering enhanced specificity for JAK1-mediated pathways. Clinical observations in AS revealed that patients receiving upadacitinib demonstrated a lower incidence of uveitis development compared to the placebo cohort.[87] In a notable case involving a 30-year-old male with concurrent ulcerative colitis, Crohn's disease, and AS, combination therapy utilizing upadacitinib alongside biological agents, including anti-TNF therapies, vedolizumab, and ustekinumab, enabled sustained clinical activity across all conditions.[57]

Baricitinib

Baricitinib, a low molecular weight compound administered orally, functions as a selective inhibitor targeting JAK1 and JAK2 enzymes. The EMA initially authorized this therapeutic agent in 2017 for managing rheumatoid arthritis,[88] with subsequent approval by the FDA in mid-2018 for treating moderate-to-severe rheumatoid arthritis patients.[89] A clinical case study documented an adolescent female patient receiving immunosuppressive therapy (baricitinib combined with adalimumab) for AS, who contracted COVID-19 while undergoing therapy for CSD.[28]

Conclusion

While conventional primary therapies such as NSAIDs form the therapeutic foundation for AS management, their effectiveness remains inadequate for addressing the condition's diverse clinical manifestations. The therapeutic landscape has evolved with advanced biological agents and precision-engineered synthetic DMARDs, encompassing TNF blockers, IL-17A antagonists, and JAK pathway modulators. Current clinical practice faces ongoing hurdles in optimization of AS treatment. Although biological therapies and kinase inhibitors demonstrate notable clinical efficacy, they carry potential safety risks requiring careful consideration in patients with pre-existing cardiovascular conditions or susceptibility to infections. The substantial financial burdens associated with advanced biologicals further limit treatment accessibility across different socioeconomic groups. These persistent challenges underscore the critical need for innovative therapeutic strategies. Emerging investigations should prioritize protocol refinement, development of molecular-specific interventions, and synergistic treatment combinations to maximize clinical outcomes while minimizing adverse effects. Moreover, the existing treatment strategies for AS frequently demonstrate suboptimal effectiveness while prompting apprehensions regarding notable adverse effects. Furthermore, advancing our comprehension of AS pathogenesis remains essential to devise innovative therapeutic interventions with enhanced precision and efficacy.

Availability of Data

All data generated or analyzed during this study are included in this published article.

Author's Contribution

All authors contributed to the study's conception and design. Material preparation and the experiments were performed by Guimei Yu. Data collection and analysis were performed by Na Yuan, Di Liu, and Daqing Nie. The first draft of the manuscript was written by Huiping Li, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

The authors stated that there was no conflict of interest to disclose.

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