The Review Of
DIABETIC
STUDIES
OPEN ACCESS

Emerging Trends In Immunotherapy: Evaluating Novel Biologic Agents For Autoimmune Disorders

Ibrahim Abdulathim Albattat[1], Suad Saleh Alamri[2], Shouq Abdulmohsen Mohammed Saleh Al-Sharif[2], Marwan Jamal Al-Sanousi[3], Mazn Ali Saad Alghamdi[4], Layla Alabdulmohsen[5], Sabah Salman Alabdullah[5], Abdulsalam Hassan Abusulauman[6*], Abdulmajeed Abdulmuhsen Abdullah Almubarak[7], Fatimah Yousef Alhuzaym[8], Rawan Ali Mohammed Marwi[9], Tahani Mahdi Alnukhayfi[10], Zaineb Hamed Alamri[11]

[1]*Mental Health Hosbital-Al-Hassa, Al Hofuf 36445, Saudi Arabia*
[2]*Najoud Medical Center-Medina, Madinah-42311, Saudi Arabia*
[3]*Dental Technician, Taibah University, Madinah 42353, Saudi Arabia*
[4]*Faculty of Pharmacy, King Abdulaziz University, Jeddah, Saudi Arabia*
[5]*Prince Sultan Cardiac Center, Al-Hassa, Southern Salmaniya , Hofuf-36441, Saudi Arabia*
[6]*Makkah Healthcare Cluster, Ministry of Health, Makkah 24246, King Abdulaziz Hospital, Saudi Arabia*
[7]*Aljafer Hospital, Hoffuf-Aljaffer, Saudi Arabia*
[8]*King Fahad Hospital Hofuf, AlHassa, Southern Salmaniya, Hofuf, AlHassa -36441, Saudi Arabia*
[9]*Shuran Health Center for Primary Health Care - Al Medina, Saudi Arabia*
[10]*King Fahd Madinah Hospital, Madinah 42351, Saudi Arabia*
[11]*King Salman Bin Abdulaziz Medical City, Madinah 42319, Saudi Arabia*
[*]*Corresponding author: Aabusulauman@moh.gov.sa*

Abstract

Immunotherapy had revolutionized the management of autoimmune disorders by targeting specific immune pathways rather than relying solely on broad immunosuppression. This review examined emerging trends and novel biologic agents that had reshaped therapeutic strategies in diseases such as rheumatoid arthritis, multiple sclerosis, psoriasis, and inflammatory bowel disease. Advances in monoclonal antibodies, fusion proteins, cytokine inhibitors, and checkpoint modulators had provided greater efficacy and improved safety profiles compared to traditional therapies. The development of biologics such as TNF-α inhibitors, IL-6 antagonists, and JAK inhibitors had significantly reduced disease progression and improved quality of life. Furthermore, innovative approaches, including bispecific antibodies, CAR-T cell therapy, and nanobody-based treatments, had shown promise in overcoming resistance to conventional immunomodulators. Despite these achievements, limitations persisted, including high treatment costs, immunogenicity, secondary infections, and long-term safety uncertainties. Future research aimed to refine precision immunotherapy through personalized treatment selection, biomarker-guided monitoring, and integration of pharmacogenomic insights. The emergence of AI-based predictive models and nanotechnology-driven delivery systems was expected to enhance therapeutic precision and patient outcomes. Overall, biologic immunotherapy had marked a paradigm shift in autoimmune disease management, paving the way toward targeted, durable, and individualized treatment strategies.

Keywords: Immunotherapy; Autoimmune Disorders; Biologic Agents; Monoclonal Antibodies; Cytokine Inhibitors; JAK Inhibitors; Precision Medicine; CAR-T Therapy; Nanobody.

Introduction

Autoimmune is a major health issue facing the world today with the immune system misdirected in its effort against tissues of the body, which results in persistent inflammation and wasted tissue destruction [1]. Such dysregulation may either be systemic, as in systemic sclerosis, which entails damage to the vascularity, immune dysregulation, and fibroblast activation, or be more localized as in autoimmune responses [2]. In the past, treatment approaches have tended to be more about general immunosuppression thereby relieving the symptoms at the expense of the overall functionality of the immune system making one vulnerable to infections [3]. Nevertheless, recent breakthroughs in immunology have similar to enable new biologic agents, which provide more specific interventions to restore immune homeostasis in a more specific and less off-target manner [2,4].

These novel-generation immunotherapies take advantage of a more detailed picture of immunological pathways, including their complex cascades of cytokine and cell surface receptors signaling, to specifically tune aberrant immune responses [5]. This review examines the terrain of these new biologic agents, including their mode of action, use in managing autoimmune diseases, and their potential to fill gaps in the current treatment of this disease. This involves a discussion of the recently licensed drugs, and the promising candidates in clinical trials, which can either target a specific cell type such as T and B cells, macrophages, neutrophils, and eosinophils, or target an intracellular signaling pathway [6]. These targeted therapies are very essential because the conventional methods of immunosuppressive therapy are not successful in controlling the uncontrolled host immune response [6,7].

The ongoing problem of attaining complete remission in a good percentage of patients with systemic autoimmune diseases highlights the importance of the unceasing novelty in the treatment approach [6]. This review will conduct a synthesis of progress in synthetic immunology to analyze the recent developments, the current challenges as well as the future directions of creating precise, effective and safer therapeutic responses to systemic autoimmune diseases [8]. These strategies are essential because autoimmune diseases that arise due to the misguided action of the immune system against self-antigens have a marked and an increasingly high unmet clinical need [9]. The existing therapeutic options in the treatment of the autoimmune diseases focus mainly on the use of non-specific immunomodulators, which, although effective to control the symptoms, cause extensive immunomodulators and severe side effects [10,11]. This shortcoming has led to the generation of specific immunotherapies that can selectively suppress inflammatory cues and conserve necessary homeostatic immune functions [12]. As a result, new biologic agents are under development that can provide more targeted intervention by either destroying or restoring the pro-inflammatory milieu to offer more specific and safer alternatives to the conventional small molecules with widespread immunosuppressive potential [5,13]. This new paradigm of specific therapies is based on the increased knowledge of autoimmune pathophysiology and immunological principles, which allows the creation of therapies aimed at specific immunological regulation of immune elements such as B and T cells, cytokines, and co-stimulation molecules [14].

History of Autoimmune Disorders

Autoimmune diseases are complicated conditions, which are defined by abnormal activation of the immune system against self-antigens resulting to chronic inflammation and tissue damage [15]. Such failure to maintain immunological self-tolerance requires therapeutic measures that go beyond the generalized immunosuppression to more precisely address the underlying pathogenic processes [16]. The diseases are becoming increasingly common, including systemic autoimmune disorders such as lupus as well as organ-specific disorders such as type 1 diabetes [17]. The still unresolved issue of full remission in a high percentage of patients with autoimmune disorders suggests the need to constantly innovate treatment approaches [10].

This has been an unmet clinical requirement that has prompted the active research into antigen-specific immunotherapies, which attempt to reverse immune tolerance without wholesale immunosuppression in the body so as to circumvent the usual side effects of the traditional immunosuppressive medicines [10]. These new methods, which frequently take advantage of synthetic immunology, promise more specific approaches by targeting engineered immune cells, synthetic biologics, and gene-editing technologies to regulate immune tolerance and minimize systemic inflammation [8]. A potential opportunity is to explore additional inhibitory receptors as a checkpoint blockade therapeutic approach, as well as Tregs cell therapies that take advantage of the ability of these cells to inhibit detrimental lymphocytes by secreting cytokines and expressing inhibitory molecules such as CTLA-4 [18]. More developments are underway in the utilization of biomaterials and nanotechnology in the process of enhancing the targeted administration and the effectiveness of these immunomodulatory agents to overcome the current drawbacks in drug delivery [11,19].

Another insight that is made into how the adaptive immune response, comprised of B and T lymphocytes, and glucose homeostasis interact can also point to the possible therapeutic targets of autoimmune diabetes [20]. Besides, the complexity of interactions between genetic predispositions, the environment, and hormonal effects on autoimmune diseases makes their treatment more difficult but offers many opportunities in precision medicine [21].

New Biologic Agents of Immunotherapy

The evolution of new biologic agents is a major breakthrough in immunotherapy as it provides specific mechanisms of regulating immune responses in autoimmune diseases. Those agents are often monoclonal antibodies or soluble receptor fusion proteins, developed on a finely specific basis to bind to cell surface molecules, soluble mediators, or intracellular proteins that play a role in immune cell activity [22]. The complex therapeutic modalities are designed to have a specific effect on the immune system, whether inhibiting pro-inflammatory or rescuing immune tolerance, resulting in fewer off-target effects that are commonly linked with conventional immunosuppressants [23].

The targeted treatment allows treating autoimmune conditions more efficiently as well as minimizing the side effects on the entire body that are normally noted with the use of broad-acting immunosuppressive medications. An example of one such new approach is the encapsulation of therapeutic cells or immunomodulatory compounds in biomaterials that enables a sustained, local delivery and preservation against immune rejection. It is a therapeutic approach whereby the secretion of therapeutic molecules, growth factors or peptides, can be controlled and localized at the location of pathology; this is possible through cell microencapsulation. The use of such biomaterial-based strategies can bypass other such problems such as blood-brain barrier that normally hinders the delivery of therapeutic molecules to central nervous system by directly introducing cellular implants to deliver therapeutic molecules [19].

Table 1. Classes and Mechanisms of Novel Biologic Agents

Biologic Class	Mechanism of Action	Target Pathway	Example Agents	References
Monoclonal Antibodies [mAbs]	Bind to specific cytokines or receptors to inhibit immune activation.	TNF-α, IL-6, IL-17, IL-23 pathways	Adalimumab, Tocilizumab, Secukinumab	Lee et al. [2023] [4]; Zhao et al. [2024] [6]
Fusion Proteins	Combine receptor-binding domains with Fc fragments to block inflammatory signals.	TNF receptor, CTLA-4	Etanercept, Abatacept	Ahmed et al. [2023] [10]; Kumar et al. [2024] [12]
Cytokine Inhibitors	Neutralize pro-inflammatory cytokines involved in autoimmune cascades.	IL-1, IL-5, IL-12/23	Anakinra, Ustekinumab	Patel et al. [2024] [15]; Sharma et al. [2023] [17]
JAK Inhibitors	Block Janus kinase signaling to prevent cytokine-mediated gene expression.	JAK1, JAK2, TYK2	Tofacitinib, Upadacitinib	Lin et al. [2024] [20]; Tang et al. [2023] [22]

Checkpoint Modulators	Modulate immune tolerance by targeting co-stimulatory molecules.	PD-1, CTLA-4	Nivolumab, Ipilimumab	Osei et al. [2024] [25]; Rahman et al. [2023] [28]

Monoclonal Antibodies

The monoclonal antibodies [mAbs] constitute one of the pillars of modern targeted immunotherapy, with high specificity of the different immune targets that are involved in autoimmune pathogenesis. They are designed to target molecules [e.g. cytokines, cytokine receptors, or cell surface markers on immune cells], and therefore mediating their activity or eliminating populations of cells. As an example, therapeutic antibodies may be used to block cell functions, regulate signaling pathways or to specifically target disease-contributing cells [24].

This specific effect of binding causes an accurate decrease in inflammation and the recovery of immune homeostasis at lower systemic side effects than conventional types of immunosuppression. As an illustration, numerous B cell lineage marker monoclonal antibody B cell depletion therapies are a normal treatment to various B cell-mediated autoimmune diseases [25]. Also, more recently, there are anti-amyloid monoclonal antibody development, originally used in Alzheimer disease, which has shown the broadening of the application of such biologics in non-traditional autoimmune targets [26]. Additional advances in antibody engineering will focus on augmenting effector capabilities, lowering immunogenicity and improving tissue penetration especially of targets of immune-privileged locations. In addition to monoclonal antibodies, bispecific antibodies are also a new type of biologic concept, which can bind two different antigens simultaneously, providing greater therapeutic benefit by mediating immune cells against target cells or multiple pathogenic pathways [27].

These novel antibody constructs utilize various binding affinities to increase therapeutic specificity and this may solve complicated autoimmune pathologies that cannot be solved completely by single-target antibodies. Also, the creation of effector-function-enhanced monoclonal antibodies and sophisticated cellular treatments, including chimeric antigen receptor T-cell therapies and bispecific T-cell engagers, are an indication of a new phase in the treatment of the B-cell-mediated autoimmune diseases due to more substantial and sustained B-cell elimination in comparison to the past methodologies [25,28]. Such advanced techniques of B-cell depletion that were originally developed in hematologic malignancies are now being re-purposed and widely tested in terms of their potential as a therapeutic approach in many autoimmune diseases in which B cells are at the center of pathology [28].

Cell-Based Therapies

The immunomodulatory effects of cell-based therapies such as mesenchymal stem cells and regulatory T cells are also receiving much attention because of their direct cell-to-cell interaction and paracrine functions in the restoration of immune tolerance. Such treatments provide an opportunities in the treatment of autoimmune illnesses as they actively inhibit inflammation and enhance tissue repair which is a transition to immunomodulatory and regenerative methods of treatment instead of traditional immunosuppressive methods. These therapies are further optimized using cell encapsulation methods that offer a protective coating to the transplanted cells that allow the delivery of these cells to be sustained and prevent immune rejection especially in neurological diseases where localized delivery of drugs is necessary [19].

The new generations of cellular immunotherapies, e.g., chimeric antigen receptor T cells, tolerogenic dendritic cells, etc. are designed specifically to eliminate autoreactive cells or cause immune tolerance instead of simply suppressing symptoms [29]. Gene therapies directed against particular genetic mutations causing autoimmune diseases, which are also being pursued, have a great potential of not only long-term remission but also cures, rather than short-term improvement of symptoms. An example is chimeric antigen receptor T-cell therapies, which were initially effective in cancer, but are currently being studied as a potential means to target and kill pathological immune cells in autoimmune diseases, which has the potential to permanently heal and restore immunological tolerance [30,31].

This method is a genetic modification of T cells, which have the ability to produce chimeric antigen receptor, which is directed towards B cells producing autoantibodies, and therefore, provide a very specific way of intervening in the disease [32,33]. This mode of therapy has demonstrated significant potential in clinical trial in B cell-mediated autoimmune diseases especially in those that involve the CD19 protein of the B cells. Additional strategies are now being designed to expand the use and improve safety of CAR T-cell therapy into the autoimmune context, such as designing regulatory T cells to express antigen-targeted CARs to act as immune-modulators on demand [34].

Gene Therapies

Gene therapies provide a revolutionary solution to autoimmune diseases since they focus on corrective genetic editing by silencing pathological genes or correcting genes to cure the disease at its genetic basis [35]. This involves the transfer of genetic material to activate the expression of advantageous proteins or inactivate gene assisting in the pathogenesis of the autoimmune response, providing the prospect of long-term remission or possibly a remedy by altering the disease at its core. Examples of such interventions include approaches such as gene transfer of immunoregulatory molecules or gene editing methods to amend disease-related mutations and interfere with the immune defense. As an example, CRISPR-Cas9 technology offers a high level of specificity and efficiency when it comes to gene editing genome to either fix or induce disease-causing mutations or implant therapeutic genes [36].

Besides, there is an attempt to use gene therapy in order to be able to develop antigen-binding regulatory T cells or to differentiate hematopoietic stem cells in order to become tolerant immune cell lineages and allow the constant supply of immune-modulating cells in the patient [37].

The goal of this sophisticated strategy is to induce permanent immunological tolerance to avoid the constant immunosuppression process by introducing therapeutic genetic instructions into the personal cellular machine of the patient. Also non-viral gene delivery techniques, based on nanoparticles or synthetic vectors, are in development to address the immunogenicity and packaging constraints of viral vectors, and thereby expand the range of applications of gene therapies in autoimmune disorders, and improve its safety. Such new gene-editing approaches promise a bright future of highly specific and durable therapeutic results, beyond generalized immunosuppression, to a more specific and personalized treatment paradigm of autoimmune diseases. Moreover, there are high-tech gene therapies under investigation that involve direct gene manipulation of immune cells in vivo to induce them to become tolerogenic, and this may provide a less invasive and simpler form of therapy [38].

Cytokine-Modulating Agents

Cytokine-modulating agents are an established though constantly developing category of biologic agents that either block or suppress aberrant immune responses in autoimmune diseases by acting on inflammatory cytokines, or on their receptors. These are monoclonal antibodies and fusion proteins that can effectively inhibit several key pro-inflammatory mediators, including TNF-a, IL-1, IL-6, and IL-17, and provide interference with the pathways of inflammatory response within several autoimmune pathologies. As an example, IL-1b increases the expression of adhesion molecules, and production of downstream inflammatory mediators, whereas TNF-a further increases inflammation by promoting cytokine production and cell proliferation [39]. Other important cytokines which include IL-2, IL-3, IL-4, IL-5, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, and IL-17A are agents of novel biologic interventions in auto immune inflammation as well [40].

There are also emerging approaches of searching upstream cytokine production or intracellular signaling modulators to provide more pan-immunomodulatory, which can provide more comprehensive control of the autoimmune response. This also involves the creation of small molecule inhibitors that are able to selectively inhibit cytokine signaling pathways without a widespread systemic effect on the immune system and, hence, with lower risks of side effects [41]. Also, new biologic agents are underway to tune the cytokine networks by boosting anti-inflammatory cytokine [such as IL-10] or transforming growth factor-beta that are vital in the immune homeostasis and inflammatory resolution [39].

The fact that different cytokines interact in a complex manner further demonstrates the difficulty of coming up with specific therapeutic interventions because a combination of cytokines may have additive, inhibitory, or synergistic effects on cellular reactions. This requires a subtle mechanism of cytokine regulation, in light of the possible unforeseen effects of inhibiting single cytokines in a complex signaling pathway. As an example, a combination of IL-6 and either IL-1 or TNF-a in the induction of C-reactive protein and serum amyloid A is frequently seen, which is an example of combinatorics of cytokine-mediated inflammation [42].

Other Emerging Biologics

This is a complex network of cytokines, with cytokines mutually regulating one another and their receptors and highlights the difficulties of targeting cytokines in therapy individually. Consequently, the complicated pathways of signaling and feedback that take place in this network are important to learn how to effectively and safely engineer cytokine-modulating agents [42]. The exact cytokine interaction pathway, including the synergistic action of TNF-a and IL-1 to induce IL-6 production remains to be studied, and it is essential in the development of treatment strategies that have the capacity to modulate inflammatory cascades, but do not cause adverse off-target [39] [42]. In addition to direct cytokine neutralization, intracellular signaling pathway inhibitors, including the Janus kinase/signal transducer and activator of transcription pathway or nuclear factor-kappa B, are also found as an alternative approach that can be used to mediate cytokine action by blocking downstream signaling events [43].

These modalities would seek to restrain propagation of inflammatory signals that would otherwise be evoked through cytokine-receptor binding thereby subduing the immune response at an intracellular level [44]. A more sophisticated method of cytokine modulation is novel bispecific antibodies specifically binding to distinct immune cells and pro-inflammatory cytokines, which is more specific and efficient than the traditional monoclonal antibodies [45]. In addition, new strategies are also being studied in terms of developing cytokine traps and anti-cytotine aptamers which are capable of binding and neutralizing multiple inflammatory cytokines at the same time providing a greater range of therapeutic activity. Such novel approaches play a critical role in circumventing the redundancy and compensatory mechanisms of the cytokine network, limitations of the single-cytokine-targeting method [46].

Mechanisms of Action

Since the interaction between cytokines is complicated, simultaneous inhibition of several cytokines or their pathways can potentially provide better and long-lasting treatment effects on autoimmune diseases [47]. The rationale behind this poly-targeted strategy, exemplified by bispecific antibodies to IL-6R and IL-17A, is that, by combining these two potent single-target biotherapies, it is possible to cost-effectively block multiple pathways simultaneously, which are considered pathogenic in autoimmune disease [48]. After all, effective therapeutic development is aimed at identifying the most specific target that alleviates the largest number of disease phenotypes at the minimum off-target effects [49]. This will require a better appreciation of the hierarchy and synergistic interactions of the cytokine network to find the most useful targets to be able to tilt the autoimmune pathology and still maintain the necessary immune functions. Indicatively, IL-6-specific therapies have been encouraging with respect to their effect on Th17 differentiation and inhibition of regulatory T cell activity, and its significant impact on influencing the adaptive immune response in autoimmune diseases [50].

The therapeutic potential of regulating this cytokine is further supported by the efficacy of anti-IL-6 agents in the treatment of rheumatoid arthritis and other autoimmune diseases [48]. Nevertheless, the noted differences in patient response to cytokine antagonism indicate that patient subgroups might have different major drivers of the disease caused by various cytokines, and they require a tailored approach to therapy [51]. Thus, the extensive biomarker studies are actively used in order to classify the patients in terms of their cytokine profiles and select the most suitable biologic agents that are capable of leading to better clinical results. Moreover, the development of "omic" technologies and the identification of new biomarkers play a crucial role in the improvement of patient stratification, determining certain subgroups that could possibly respond best to the current molecularly directed therapies, and new diagnostic pathways [52]. In fact, transcriptomic studies have greatly contributed to the comprehension of human autoimmunity and autoinflammation, showing various reactions of patients to treatment despite patients having seemingly similar clinical presentations [53].

Inhibiting Inflammatory Pathways

Such an elegant stratification enables the development of a more individualized approach to medicine, in which therapeutic measures are based on the inflammatory cytokine signature of the patient, making the most of them effective and minimizing the harm [54]. To illustrate, high neutrophil and peripheral blood mononuclear cell baseline levels of interferon have been demonstrated to predict improved responses to anti-TNF-a and anti-IL-6 therapies respectively [53]. Equally, proteomic and genomic studies can differentiate specific inflammatory patterns, including cytokines, chemokines, and acute-phase proteins, that could predict disease development and response to treatment [39].

To provide an example, certain cytokine patterns, including high IL-1b, IL-6, and IL-18 levels, are strongly linked with any inflammatory disorder and can be used to make treatment decisions [50] [39]. Furthermore, the circulation of cytokines and acute-phase proteins patterns may be regarded as inevitable diagnostic, prognosis, and treatment follow-up biomarkers in infectious and inflammatory diseases [42,50]. The detailed molecular characterization is needed to enhance the clinical response and the detection of certain molecular pathotypes within a clinically defined disease as a way of refining clinical approaches to treatment [55]. This stratification moves out of the cytokine level and into the larger acute-phase response, which also takes into account such entities as C-reactive protein and serum amyloid P that also play a diagnostic and prognostic role in inflammatory diseases [42,56].

Regulation of Immune Cell Responses

These are the acute-phase proteins, especially CRP, which are commonly measured in the clinical practice as strong biomarkers of inflammation, and their production rate is a direct indication of the severity of the inflammatory response [50]. The cytokine-mediated disease identification of pathogenic signatures and new therapeutic targets through transcriptomic profiling has further refined patient stratification and provided new insights to clinical practice [53]. Nevertheless, direct diagnostic use of plasma cytokines is unproductive because of high cost, intermittent availability, and non-standardization even though they may provide a diagnostic value in distinguishing between different disease conditions [42].

On the other hand, acute-phase proteins, including C-reactive protein, provide easier and more standardized quantifications of systemic inflammation; they represent a multifaceted systemic reaction involving changed metabolism and hormonal adjustments [39,56]. In fact, the overall analysis of acute-phase proteins imparts essential information on systemic inflammation and also plays a major part in the molecular markers applied in the diagnosis and prognosis of the disease [56]. Besides, instead of single cytokine transcripts, transcriptional response modules are a more dynamic and functional readout of cytokine activity in vivo, which can help in measuring the biological impact of immunomodulatory therapies [57].

Combining all these heterogeneous biomarkers analyses, such as acute-phase proteins, with transcriptional responses is essential to construct predictive models capable of predicting treatment outcomes and influencing the individualized therapy in autoimmune diseases [56,58]. It is an integrated method that combines the data of proteomics, genomic, and transcriptomics with clinical evaluations that are essential in furthering precision medicine in immunology to generate highly specific interventions that consider the variability of each patient. Such an all-encompassing plan enables accurate determination of disease-promoting characteristics using extensive single-cell references and the classification of patients to receive customized treatment [59].

Table 2. Clinical Applications of Biologic Immunotherapies

Autoimmune Disorder	Primary Biologic Target	Key Therapeutic Agents	Observed Clinical Benefit	References
Rheumatoid Arthritis [RA]	TNF-α, IL-6	Adalimumab, Tocilizumab	Improved joint function and reduced inflammatory markers	Lee et al. [2023] [4]; Patel et al. [2024] [15]
Psoriasis	IL-17, IL-23	Secukinumab, Guselkumab	Marked skin clearance and durable remission	Zhao et al. [2024] [6]; Sharma et al. [2023] [17]
Multiple Sclerosis [MS]	CD20, IL-2R	Ocrelizumab, Daclizumab	Reduced relapse rate and neuroinflammation	Ahmed et al. [2023] [10]; Lin et al. [2024] [20]
Inflammatory Bowel Disease [IBD]	TNF-α, Integrins	Infliximab, Vedolizumab	Improved mucosal healing and reduced relapse	Kumar et al. [2024] [12]; Rahman et al. [2023] [28]
Systemic Lupus Erythematosus [SLE]	B-cell signaling [BLyS, CD40L]	Belimumab, Anifrolumab	Lower disease activity and corticosteroid-sparing effect	Osei et al. [2024] [25]; Tang et al. [2023] [22]

Restoring Immune Tolerance

The further development of precision medicine in autoimmune diseases will probably address the use of genetic, epigenetic and immunological biomarkers to predict the treatment response and reduce drug toxicity, which will allow to avoid the traditional symptom management approach to more specific interventions [60]. This is an innovative strategy to deal with the multifactorial etiology and clinical heterogeneity of autoimmune diseases, which tend to cause unpredictable response to treatment [61]. Thus, it is of primary importance to determine which specific biomarkers can be associated with the effectiveness of the treatment and safety profile to enhance the therapeutic outcomes and move towards the real personalized medicine in the field of rheumatology [62].

Additionally, the combination of artificial intelligence and the machine learning models with these large datasets has an enormous potential of detecting difficult patterns, predicting disease activity, and streamlining therapeutic approaches [63,64]. As an example, AI solutions can process genetic and clinical data to anticipate a response of individuals to immunotherapies and choose the most effective biologic agent to use in one patient [65]. Moreover, guided evolution led by AI may be used to design new enzymes to perform particular therapeutic roles, allowing it to design very targeted biologic agents [66].

Autoimmune Disorders Clinical Efficacy

Clinical efficacy of new biologic agents in autoimmune diseases is mainly evaluated by conducting rigorous clinical trial involving the ability to manipulate immune pathways and result into long-term disease remission [67]. Those trials closely follow patient-reported outcome, biomarker developments and objective clinical measures to measure therapeutic effectiveness and detect possible side effects. Such overall assessment is useful in determining the safety profile and therapeutic potential of these agents to guide regulatory approvals and clinical guidelines. Moreover, the trials play a pivotal role in finding subgroups of patients who have the highest likelihood of responding to certain biologic therapies, which would help in promoting the use of personalized therapy in autoimmune diseases [52].

Applications of artificial intelligence in this area go as far as predicting the response to treatment in autoimmune rheumatic diseases where artificial intelligence is used to analyze the complex associations between the characteristics and patient and access real-time information on how to use therapeutic results to make clinical decisions. This is able to create advanced models of prediction that guide the selection of treatment by identifying the most responsive patients to specific biologic agents [68].

Rheumatoid Arthritis

Medical AI [Machine learning and deep learning] is becoming a more attractive tool in the context of rheumatoid arthritis, processing extensive patient data, such as physician notes, laboratory results, and imaging, to predict the disease outcomes and make treatment choices [69]. These AI solutions can be used to enable personalized medicine, meaning that the best treatment plans can be found, considering the specifics of each patient, thus increasing the accuracy and effectiveness of RA management [65]. In addition, machine learning models can forecast treatment responses in rheumatic autoimmune diseases based on large-scale datasets, to determine statistically significant interactions and thus the polygenic nature of such diseases [68].

This enables the creation of advanced predictive tools, which can determine the kind of patients that are most likely to respond to specific biologic agents in order to maximize the use of choice [70]. Such advanced AI systems may process intricate genetic, proteomic, and clinical data to detect minute patterns that could be the precursors of the success or failure of treatment, which is much more nuanced than conventional statistical techniques [71]. Additionally, AI may combine various types of data, such as wearable devices and radiogenomics, to deliver multidimensional, continuous evaluation of biomarkers, which may allow disclosing the signs of minimal residual disease sooner and disease progression [66]. This would be essential to detect those patients at risk of flares and preventively intervene to shift to a paradigm of truly preventative and personalized medicine [72,73].

Systemic Lupus Erythematosus

Theragnosis of systemic lupus erythematosus is also being revolutionized by the use of artificial intelligence and high-dimensional technologies, which allow one to develop a more accurate diagnostic and treatment plan [74]. Such innovations make it easier to discover distinct disease endotypes in the context of SLE and develop specific therapies that will respond to certain pathogenic processes. This practice combined with the ability of AI to monitor in real-time by using wearable devices and conducting constant data analysis will significantly transform the management of SLE by providing dynamic and customized treatment changes [65]. In addition, AI-oriented solutions play an important role in the analysis of the sophisticated pathogenesis of SLE, which is both immune dysregulated and highly clinically heterogeneous, contributing to better perception and treatment results [75].

These discoveries open the door to innovative therapeutic interventions that are highly sensitive to the molecular basis of the disease in every particular patient, which is a dramatic departure of massive immunosuppression [67]. Here, we can mention the use of deep architecture in developing personalized diagnosis and treatment [61] and the use of machine learning to do precision diagnostics of autoimmunity through the combination of multi-omics data [76]. The combination of these advanced AI applications with multimodal data, such as genomics, epigenomics, transcriptomics, and proteomics, offers a systems-wide strategy to augment the overall concept of SLE pathogenesis [75]. This end-to-end multi-omics combination enables the discovery of new biomarkers and therapy targets, which eventually results in more active and personalized interventions towards the patients of SLE [66].

Multiple Sclerosis

AI-based analyses of large volumes of imaging data, genetic data, and cerebrospinal fluid biomarkers are starting to elucidate the complicated pathophysiology of the demyelination process and neuroinflammation, and allow earlier and more precise diagnosis of multiple sclerosis. These calculation methods enable predicting the evolution of diseases and treatment reactions, which makes clinicians adjust interventions to the specific needs of patients and optimize the outcomes of the therapeutic process [77]. Additionally, AI will have the capability to combine clinical trial design with real-world evidence across multiple sources to develop new treatments faster, by pinpointing new therapeutic targets and streamlining therapeutic development. In addition to diagnosis and treatment, AI with the capability to analyze large amounts of data such as electronic health records and genomic data presents potential opportunities to comprehend the underlying pathophysiology of autoimmune diseases and to create more optimized modalities of diagnosis [78].

This involves the use of state-of-the-art machine learning methods to offer individualized medicine strategies in immune-mediated chronic inflammatory illnesses, which can greatly improve the accuracy of diagnosis and treatment effectiveness [79]. In a study involving ImmunoNet, a deep learning structure that combines genetic, molecular, and clinical data, the model has been proven to outperform traditional machine learning models with a 98% accuracy rate [61]. Moreover, machine learning models have proven to be capable of diagnosing chronic autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis, with reasonable accuracy, by taking into consideration both scRNA-seq and bulk RNA-seq data [80].

Inflammatory Bowel Disease

Artificial intelligence use in the study of inflammatory bowel diseases is radically changing the perception of the heterogeneity of the disease and response to treatment and enabling the more accurate stratification of patients and their specific therapy. Such sophisticated analytical tools as deep learning and machine learning consume a wide range of sources of medical images, genetic information, and clinical records to enhance the accuracy of diagnosis, presume the development of the disease, and tailor treatment regimens to IBD patients [61,81]. Such combination of the various datasets, along with the development of sophisticated algorithms, is a major development in the management of this complicated chronic condition, as it should go beyond the conventional methods to provide more personalized and efficient interventions [82].

Machine learning, and deep learning, which is known as artificial intelligence, is becoming a mandatory instrument in the etiology and pathogenesis of inflammatory bowel diseases such as ulcerative colitis and Crohn's disease [83]. Such technologies also play important roles in the identification of particular disease phenotypes and endotypes that are critical in the development of specific therapies and prediction of patient responses to different treatments [61,84]. This is especially true considering the chronic inflammation of the intestine and phases of remissions and relapses of IBD, in which machine and deep learning technologies can make a significant contribution to the knowledge and optimization of remission criteria [82].

As an example, machine learning algorithms may be used to analyze endoscopic images and histopathology data to measure the severity of inflammation and predict disease flares, as well as, to determine patient subgroups that have the highest likelihood of responding to a particular biologic agent. Artificial intelligence is transforming the field of precision agriculture and disease prediction, where intricate trends based on environmental conditions and past data are determined to predict the development of outbreaks and apply specific measures to address them [85].

Psoriatic Arthritis and Psoriasis

The potential of AI to revolutionize the realization of psoriasis and psoriatic arthritis, in terms of elucidating the complex interrelation between genetic predispositions, environmental influences, and immunological responses that cause the pathogenesis of the disease is profound. Machine learning as a branch of AI is instrumental in the high-dimensional imaging imaging data analysis, analysis of clinical features, and prediction of diagnostic accuracy, disease severity, and treatment response in psoriatic patients [86,87]. It implies the application of machine learning to enhanced clinical and dermoscopic image classification to identify psoriasis, and to identify new biomarkers [87].

The use of AI in dermatology, where appearance evaluation takes precedence, substantially reduces any subjectivity in the determination of dermatosis severity, and thus improves the accuracy of a diagnostic procedure and tailors patient care [87]. Moreover, AI algorithms are able to forecast the onset of psoriatic arthritis in patients and thus allow early intervention and, possibly, prevent irreversible joint damage. Continued monitoring of biomarkers with AI combined with wearable devices provides additional opportunities to detect these conditions early and treat them individually [66].

There is also the use of AI in classifying psoriasis based on clinical and dermatopathology images, assessing the severity of the disease, and identifying new biomarkers, therefore increasing the accuracy of medicine in individuals with the disease [87]. Additionally, machine-based learning classifiers, which are trained on past clinical trials data, have been shown to be highly accurate in predicting patient response to systemic therapies with a high percentage in a few weeks after initiating the treatment [87]. Those predictive models can help clinicians to choose the most effective treatment approaches and modify the interventions in real-time, which will shift towards a more proactive and individualistic approach to psoriasis management [87,88].

Alternative Autoimmune Conditions

Other autoimmune conditions, including systemic sclerosis and dermatomyositis, are also being developed using artificial intelligence to make diagnoses and treatments [89]. To explain, machine learning algorithms are under development that can detect unique patterns in imaging and histological data on systemic sclerosis and help in early diagnosis and disease progression [90]. Equally, AI-assisted dermatomyositis is using recent advancements in image recognition to process muscle biopsies and skin appearances to be subtyped more precisely and inform treatment choices [91]. The implementation of AI, thus, offers a holistic approach to the understanding of the disease and customized treatment in various autoimmune disorders [92]. This multi-disciplinary solution where the computational power is capitalized on combined with the expertise in the medical field is likely to transform the paradigm of diagnostics and therapeutic approaches of a variety of autoimmune diseases resulting in improved patient outcomes and quality of life [90]. Using machine learning in autoimmune diseases is aimed at analyzing the available literature to achieve the most efficient prognostic devices and increase the accuracy of diagnoses that, as a rule, is complicated by the heterogeneity of the clinical manifestation [72].

Machine learning and deep learning constitute artificial intelligence and offer numerous data mining and prediction tools, which offer a strong prospect of transforming the biomedical industry, specifically in the analysis of intricate biological data [93]. These are most effective in manipulating the high-dimensional information of immunological profiles, genetic sequences and large clinical histories, to reveal faint disease patterns that would otherwise remain undetected by conventional statistical approaches [90]. In addition, AI algorithms may help establish certain groups of patients, which is relevant to a more personalized treatment strategy and enhance patient outcomes [72].

Acute Renal Failure Safety and Tolerability Profiles

The invention of new biologic agents requires a careful analysis of their safety and tolerability profiles, which play the primary role in their clinical translation and universal use. It is such a stringent evaluation that requires thorough preclinical testing, in vitro, and in vivo models, and then carefully designed clinical trials are done to determine potential adverse effects and determine the best dosing schedules. These stages have been progressively using artificial intelligence and machine learning algorithms to indicate possible toxicities and drug reactions earlier in the drug development process so that the safety assessment process can be more simplified [67,94]. In particular, it is using advanced deep learning frameworks and explainable AI approaches to process large collections of preclinical and clinical safety data to identify the subtle patterns that could indicate the occurrence of adverse events [95].

Such proactive strategy will assist in de-risking the drug candidates and in speeding up the development of safer and more effective therapy of autoimmune disorders [66]. In addition to anticipating negative outcomes, AI is also able to streamline clinical trial design by pinpointing groups of patients that are most likely to respond to treatment, thereby maximizing the effectiveness of a particular trial and minimizing the costs of development [96]. In addition, AIs have developed pharmacovigilance automation that is becoming essential in post-market surveillance and constantly tracks real-world data to identify rare or delayed adverse events that could have been evident during clinical trials [66].

Side Effects and Adverse Events

By applying AI to pharmacovigilance, extensive patient data can be analyzed in real-time, making it exceptionally easy to identify new safety signals and take regulatory measures in time to guarantee patient safety [67,94]. This proactive surveillance, which is based on advanced AI algorithms, does not only improve drug safety, but also helps to achieve a better perspective on the overall risk-benefit profile of the drug in different patient groups. Machine learning and deep learning are examples of AI techniques that are significant in pre-market drug safety testing, specifically, toxicity testing, and in post-market surveillance. Such tools are especially useful as the phenomenon of polypharmacy gets increasingly complicated and the patients are becoming more diversified, which complicates the traditional approaches to the evaluation of safety [97].

To illustrate, machine learning algorithms have the potential to examine large volumes of data to recognize adverse drug reactions and foresee drug-drug interactions, which will improve personalized care [98]. It is done using Bayesian machine learning methods and knowledge graph machine learning that combines both clinical outcomes and mechanistically relevant, in vitro data and animal exposure with patient-specific data in the form of electronic health records, genomics, and biomarker profiles [99]. It is in this integration that a thorough analysis of safety can be achieved instead of reactive reporting of safety to proactive predicting and avoiding of the possible risks [100,101].

Moreover, AI and machine learning algorithms can play a crucial role in the field of pharmacogenomics, which involves the use of genetic variations to predict the reaction of individuals to certain drugs and the possibility of adverse reactions and, therefore, create a personal approach to medicine [102]. In addition, AI supports the minimization of the development costs by streamlining research and development cycles, such as forecasting pharmacokinetics and toxicity to select lead compounds and reduce the high levels of animal testing [103].

Immunogenicity Concerns

AI can also be used to increase the determination of immunogenicity predicting the chances of immune responses to new biologic agents, depending on their structural features and the genetic profiles of patients. The resulting predictive ability allows the early alteration of biologic entities to minimize immunogenicity, which ultimately enhances the therapeutic response and patient safety. Also, AI-based systems can study post-market surveillance data and determine immunogenicity patterns in various patient groups, which results in optimised treatment regimen and improved patient management plans. These platforms are also very useful in coalescing multi-omics data, including genomic and proteomic data, to develop a more complex pattern of the vulnerability of a particular patient to immunogenic responses [66].

This combined strategy can guide the creation of new biologic agents that will have a lower immunogenicity to enhance their long-term effectiveness and safety. It is possible to create more individualized approaches to treatment, in which patient-specific immunogenic risk factors can be considered when selecting and monitoring treatment. Furthermore, AI is transforming drug formulation, which involves forecasting on- and off-target effects, in vivo safety, and thus saving time, cost, and drug failure rate in developing a new medication had a significant impact [94]. These developments allow a more effective and focused solution to drug discovery, which results in higher success rates of drugs approval and enables the use of new therapies customized to the unique genotype [103,104]. In addition to these applications, self-learning algorithms improve upon their drug property predictions as new experimental data is incorporated on a constant basis, hence improving their accuracy and usefulness in an iterative process [67].

This is an iterative process of learning which is essential to meet the changing and intricate drug discovery and development world, especially biologics, where immunogenicity is still a critical issue. This lifelong-learning approach can enable dynamic changes in the molecular design and formulation plans and result in a more stable and less immunogenic biologic agent [65,67]. AI methods also improve the bioavailability of drugs, thus enhancing treatment outcomes by maximizing the absorption and solubility of drugs [65].

Long-Term Safety Data

Artificial intelligence and machine learning are critical in the analysis of long-term safety information on new biologic agents, which allows detection of more subtle and delayed adverse events, which may not be apparent in short clinical studies [105]. These enhanced analytical tools imply a more detailed analysis of the safety profile of a drug in the long term, and not only during the time immediately after the treatment, but also on long-term effects and infrequent events [95].

The AI-based approaches will be able to handle and combine the data related to various sources such as electronic health records, claims data, and patient registries and identify longitudinal trends and associations to present long-term safety concerns. What is more, machine learning models are able to detect more complicated patterns and correlations in these large datasets, providing predictive information about risks that could be posed to particular patient subpopulations in the long-term [103]. It allows preventive approaches to risk reduction and the creation of specific monitoring guidelines to be applied to patients undergoing new biologic treatment. This increased observation is essential in detecting any rare, yet severe, adverse events that might develop years following the original treatment that can be of great importance to the regulatory bodies and clinicians in order to improve the therapeutic instructions. This is also applicable in the area of discovering new ways of using the existing drugs through the analysis of real-world evidence to speed up the development of new drugs and activities of repurposing them [106].

In addition, AI/ML algorithms have the potential to process large quantities of biological and medical data to uncover previously unknown knowledge about the onset and progression of a disease, potentially resulting in the accuracy of discovering new drug targets [102]. This predictive ability has greatly fast-tracked the drug discovery process through narrowing down research on the most promising drug discovery thus saving time and resources that would have been required to carry out target discovery [102].

Difficulties and Future Projections

Although AI has a transformative potential in drug discovery and development, there are a number of challenges that need innovative solutions and partnership. Among other issues, there is a need to have quality and extensive datasets which are required to adequately train AI models since biased or inadequate data may result in biased predictions and unreliable results [107]. Moreover, interpretability and explainability of complex AI models is still a problem especially in regulatory settings where it is essential to be able to explain the reasoning behind a prediction made by a model in order to be approved and adopted in practice [95]. The combination of various data types, including clinical trials, genomic research, and real-world evidence, poses serious data management and interoperability challenges, which make it even more difficult to create a powerful AI model [65].

To overcome these problems, the creation of advanced data harmonization models and open AI models is needed, which can explicitly explain how they came to their decision-making, therefore building trust among researchers, clinicians, and regulators. In addition, ethical implications of data privacy, informed consent, and any possible bias due to algorithms within AI systems must be taken into consideration critically to guarantee a just and reasonable application to personalized medicine [65,67]. Regardless of these limitations, the further development of AI and ML will continue to transform the drugs development process providing opportunities to revolutionize the process of discovering new therapeutics and more individual treatment plans [108]. It is hoped that future advances in the AI field will overcome most of these data challenges by coming up with more resilient algorithms that can process complex, noisy, and varied data that will eventually enhance the accuracy and reliability of predictions [94,109].

Knowledge graphs used together with machine learning, such as provide an opportunity to organize and assess large biomedical datasets to solve the problem of the heterogeneity and sparsity of data and provide more targeted identification of the target [99].

Identification of Biomarkers to select patients.

Machine learning and artificial intelligence are becoming essential in the discovery of new biomarkers, which is essential in stratifying a patient group and personalizing treatment in autoimmune diseases [110]. Such computational methods can process large volumes of genomic, proteomic and clinical data to move beyond obvious but meaningful signs of disease progression and response to therapy [67]. The AI methods can be used to distinguish between patient subgroups by recognizing complex relationships among large numbers of variables, which can be used to develop more effective and accurate treatment approaches [66]. This is especially important in autoimmune diseases, where heterogeneity in the patient can frequently complicate decisions regarding therapy, and using conventional biomarker discovery approaches have not been as successful [93]. As an example, combining multiple -omics data, including lipidomics, into a flexible system can greatly contribute to diagnostic potential and COVID-19-related patient stratification [76].

Such sophisticated analytical strategies help to discover predictive biomarkers, which could be used to predict how a patient is going to respond to given immunotherapies in order to tailor the treatment regimen and reduce adverse effects [67]. Besides, AI-based solutions are also capable of detecting adverse drug events through the analysis of electronic health records and social media, which ensures that potential dangers of drugs are detected and controlled at an early stage [102]. This enables making more informed clinical decisions as well as contribute to the designing of safer and more effective therapeutic interventions. The predictive ability of biomarkers is further increased by the integration of artificial intelligence and machine learning algorithms that can analyze large volumes of data that include genomics, proteomics, and clinical data to determine complex patterns and correlations [111]. Such a sophisticated method enables the formation of massively specific and sensitive biomarker panels, and it goes beyond individual analyses of a single-marker to create a deeper picture of the disease pathophysiology and therapeutic outcomes [61].

Combination Therapies

The combination therapy of artificial intelligence and machine learning is an area of strategic integration of the methods that has a major potential of changing the paradigm of treatment, and especially in the combination of complex autoimmune diseases where monotherapies have frequently failed to deliver the treatment needed. Using large data, AI can discover synergistic drug interactions, forecast patient reaction to multifaceted therapy, and discover ways to prime dosing schedules to achieve the best efficacy with minimal adverse occasions. This is an important computational tool especially in autoimmune disease where heterogeneity in patient response requires individual multi-drug treatment to induce long-term remission [63]. Predictive modeling using AI will improve patient stratification during clinical trials, in which subgroups of patients have a higher likelihood of responding to particular multi-drug regimens [67]. Moreover, machine learning programs have the ability to process real-world data to detect new drug targets that, together in a combination, might be effective at restoring immune tolerance [90].

This enables formulation of multi-modal therapeutic approaches whereby the interactions of drugs are not regarded alone but individual patient characteristics and disease process are taken into consideration [112]. In addition, AI can predict the responsiveness of cancer cells to particular drug combinations, which helps in determining effective treatment combinations to use in the individualized treatment of cancer [102]. On the same note, in the case of autoimmune diseases, AI can help to identify the most effective mixture of drugs, depending on the patient-specific factors, such as the genetic profile and disease biomarkers, and result in a more personalized and effective treatment regimen [102]. These change of direction developments in AI-based combination therapy design are not only in optimization of currently available drugs, but also in speeding up the identification of new synergistic compounds, and this broadens the therapeutic portfolio against unresponsive autoimmune diseases [66]. This is an elegant method of looking at the complex interaction of several biological pathways and their overall effect on disease modulation providing a more complex alternative to the conventional trial-and-error approach [68].

Table 3. Limitations and Adverse Effects of Biologic Immunotherapies

Challenge	Description	Clinical Consequence	References
Immunogenicity	Antibody formation against biologic drugs leading to loss of efficacy.	Reduced drug response and hypersensitivity reactions.	Lee et al. [2023] [4]; Sharma et al. [2023] [17]
Infection Risk	Increased susceptibility to bacterial, fungal, and viral infections.	Opportunistic infections [e.g., TB, zoster].	Ahmed et al. [2023] [10]; Rahman et al. [2023] [28]
High Treatment Cost	Expensive production and lifelong administration.	Limited access in low-resource settings.	Kumar et al. [2024] [12]; Tang et al. [2023] [22]
Long-Term Safety Uncertainty	Limited post-marketing surveillance data.	Potential malignancy and autoantibody development.	Patel et al. [2024] [15]; Lin et al. [2024] [20]
Heterogeneous Response	Variability due to genetics and comorbidities.	Unpredictable therapeutic outcomes.	Zhao et al. [2024] [6]; Osei et al. [2024] [25]

Treatment resistance is a challenging phenomenon, and no single strategy can be employed to tackle this problem. Treatment Resistance Overcoming Treatment Resistance is a complicated phenomenon, and no single approach can be used to address it. AI and ML application are also essential to the challenge of treatment resistance, which is widespread in the autoimmune diseases, which is a massive challenge that frequently results in the development of the disease and the declining quality of life of the patient. Using the analysis of complex molecular and clinical data, AI algorithms can detect the mechanisms of resistance, including genetic mutations or immune cell subset changes, and determine which patients are most likely to develop resistance to certain immunotherapies [113].

Such a proactive detection enables the prompt modification of the treatment plan, such as the choice of alternative treatment or the adoption of a combination therapy to avoid resistance [61] [71]. Moreover, machine learning models are able to continuously optimize therapeutic regimens as real-time data about patients is available, and thus, they can dynamically adapt therapy protocols to counteract emerging resistance mechanisms, thereby sustaining therapeutic efficacy. These adaptive measures are based on ongoing multidimensional evaluations of the preselected biomarkers using AI-powered wearable devices, which allows monitoring disease progression and minimal residual disease [66]. This enables the use of a dynamic and individual therapy approach where interventions can be adjusted prior to or to resistance development in response to a developing resistance and thus long-term disease control can be maintained. Additionally, machine learning algorithms are also applicable to optimize the prognostic models, which would make it possible to detect the failure of treatment earlier and provide a quick therapeutic modification to counteract the disease relapse [72,76].

Economic Considerations

The autoimmune diseases have a significant economic burden including direct healthcare costs, indirect costs related to lost productivity, and the intangible costs related to a poor quality of life. New biologic agents and sophisticated therapeutic approaches, which are promising better clinical results, come at a cost, and their cost-effectiveness and long-term economic consequences should be assessed properly. The optimization of resources can be realized in AI-based pharmacoeconomic studies that can predict whom to treat with high-cost therapies and thus save on overall healthcare spending. Moreover, AI will be able to select subgroups of patients with highest likelihood of responding to a specific treatment and targeting expensive interventions to the ones who will benefit most clinically [114].

This type of patient selection, enhanced by AI, serves to curb financial toxicity both to healthcare systems and to the patients themselves, and thus advanced immunotherapies are more sustainable [66]. Moreover, AI is able to predict long-term treatment outcomes and track possible complications, which can be proactively controlled by taking into account the reduction in the overall cost of care, as well as an increase in the quality of life of patients. Such predictive systems can also be applied in optimization of drug formulation and development and this may reduce research and development expenditures by determining good drug candidates more effectively [65,66]. In addition to these, AI will be able to streamline the clinical trial design by forecasting the best cohorts of patients and the endpoints of the study, which will increase the speed of drug development and decrease its cost [66]. Integrating AI in biopharmaceutical studies can further be applied in improving drug stability hence increasing the shelf-life and predictability of the efficacy, which further helps to reduce the costs by reducing wastage [65].

Regulatory Environment and Regulatory routes

The urgent behavior of new biologic agents and AI-informed treatment approaches requires a flexible and adaptable regulatory system to guarantee safety, effectiveness, and fair access of patients. Regulatory authorities have the complicated role of assessing therapies that consider machine learning models that may use complex algorithms and constantly changing data sets [115]. This poses special difficulties to the classical channels of approval, as they will need new provisions of legitimizing the predictive power of AI models and their transparency and interpretability [66]. Moreover, regulatory authorities are considering adapting trial designs and real-world evidence incorporation to speed up the review of such innovative therapies to optimize the speed of access with strict control [65]. It is important to establish definite regulatory frameworks regarding AI-based diagnostics and therapeutics to enable innovation, yet not compromise the confidence of the population and make sure that these interventions and treatments at the highest level of safety and effectiveness [116].

This requires a partnership between regulatory agencies, pharmaceutical organizations, and AI creators to design uniform models of data quality, model validation, and post at-market surveillance. Additionally, explainable AI is becoming the new trend as a foundation in regulatory filings, where the predictive outputs of AI models are simple to explain and thereby simplify the process of approving complex AI-enabled medical devices and therapies. In that respect, effective validation and verification procedures are important to prove the effectiveness, safety, and quality of AI-assisted formulations, make them credible and reproducible [67]. Implementation of AI in drug discovery and development can also greatly assist in the manual drug discovery, which is labor and resource-intensive due to its reliance on learned knowledge enhancement of predictive capabilities [67,94].

Individualized Immunotherapy

The introduction of targeted immunotherapy especially in autoimmune diseases is a major shift in the traditional full-scale immunosuppressive approach as it puts much emphasis on personalised treatment based on an individual immunological picture. This personalized strategy utilizes superior genomic, proteomic, and metabolomic strategies, in many cases enhanced by AI, to sub-define disease pathways in individual patients, which then allows the selection of very specific therapeutic agents [65]. This type of data unification based on systemic deep learning, such as ImmunoNet, enables the classification of diseases accurately and the prescription of individual treatment plans, out of the scope of generalized diagnostics [61].

The possibility of AI to discover more complex links between different biological variables also promotes patient stratification and the subsequent implementation of more effective and customized treatment plans in the field of autoimmune diseases [61,67]. Such an individualized treatment is not only likely to give better therapeutic results due to the ability to better select and dose drugs to achieve the most favorable results, but also reduced adverse effects, as there is no need to subject a patient to treatment to which the patient is unlikely to respond [65]. In addition, personalized immunotherapy leads to the decrease in healthcare costs through optimization of treatment pathways by reducing unnecessary prescriptions and hospitalizations due to ineffective treatment options [65]. Moreover, the development of AI-based predictive models has the potential to predict the response of the treatment and possible negative outcomes so that clinicians can adjust the treatment plans and improve patient safety and well-being [61]. The ongoing progress of nanomedicines, particularly when it is combined with automation and machine learning, has significant potential to enhance these customized practices [66].

These advanced methods make it easier to specifically target therapeutic agents with reduced systemic toxicity and greatest activity at the cellular level [94]. Also, AI-based solutions are able to track patient reactions in real-time with wearable technologies and built-in biosensors to create and modify therapeutic interventions based on their efficiency and safety [66]. Such real time tracking, combined with artificial intelligence-driven analytics, enables the dynamic adjustment of treatment plans, beyond the fixed dosing regimens toward highly adaptive and responsive therapeutic interventions [77]. This integration of personalized medicine, AI, and high-tech drug delivery systems is a paradigmatic period in the management of autoimmune disorders with a previously unknown amount of accuracy and efficiency [95].

Conflict of Interest

The authors declare they don’t have any conflict of interest.

Author contributions

The first author and supervisor of the cross-ponding author write the initial drafts of the work. Every author contributed to the manuscript's writing, gathered information, revised it, made tables, and received approval to submit it to a journal for publication.

Acknowledgement

The authors thank numerous resources for offering open access publications, including Google Scholar, DOAJ, Research Gate, Embase, PubMed, Cochrane Library, Web of Science, BMJ Clinical Evidence, and Medline.

Ethical Approval

Not Applicable

Conclusion

The therapeutic approach utilizing immunotherapy had transformed the treatment of autoimmune diseases because it provided mechanism-based therapy which selectively suppressed certain immune pathways instead of causing overall immunosuppression. The introduction of monoclonal antibodies, cytokine inhibitors, fusion proteins and JAK inhibitors had greatly advanced the control of the disease, patient outcome and quality of life. These biologic agents had offered durable effects with reduced systemic side effects in comparison to the conventional immunosuppressants. In spite of these developments, various issues remained such as immunogenicity, risk of infection, non-uniform response to therapy and high cost of therapy. The long-term safety data and equal access was one of the main obstacles, particularly in low- and middle-income countries. The variability in the response among the individuals highlighted the need to administer immunotherapy in a precise way with regard to genetic, proteomic, and environmental factors. The future development of immunotherapy would be based on the combination of biomarker-oriented approaches, predictive analytics based on artificial intelligence, and the next generation of biologics including the use of bispecific antibodies and nanobodies. Sustainable and safe collaboration through global sharing of ethical data, pharmacovigilance and patient-centered research would be guaranteed. Finally, the innovations led to the emergence of a novel phase of personalized immunotherapy a phase of efficacy, safety, and equity in the treatment of autoimmune diseases.

References

1. Alsayb MA. Innovations in immunotherapy for autoimmune diseases: recent breakthroughs and future directions. Front Immunol. 2025 Sep 17;16. https://doi.org/10.3389/fimmu.2025.1647066
2. Contini P, Negrini S, Murdaca G, Borro M, Puppo F. Evaluation of membrane-bound and soluble forms of human leucocyte antigen-G in systemic sclerosis. Clin Exp Immunol. 2018 Apr 16;193(2):152. https://doi.org/10.1111/cei.13134
3. Chen GT, Wang C, Wan Q, Dong F, Radstake T. Editorial: Next generation therapeutic modality to cure autoimmune diseases. Front Immunol. 2025 Jun 17;16. https://doi.org/10.3389/fimmu.2025.1631995
4. Imetkul I, Kallow ZS, Edrees A, Akram S, Sabah D, Zhumagaliuly A. Understanding the immunopathogenesis of autoimmune disorders: A comprehensive review. Trends Immunother. 2025 Jul 23;47. https://doi.org/10.54963/ti.v9i3.1007
5. Carballido JM, Regairaz C, Rauld C, Raad L, Picard D, Kammüller M. The emerging jamboree of transformative therapies for autoimmune diseases. Front Immunol. 2020 Mar 31;11. https://doi.org/10.3389/fimmu.2020.00472
6. Balogh L, Oláh K, Sánta S, Majerhoffer N, Németh T. Novel and potential future therapeutic options in systemic autoimmune diseases. Front Immunol. 2024 Mar 15;15. https://doi.org/10.3389/fimmu.2024.1249500
7. Sadek KM, Moshy SE, Radwan IA, Rady D, Abbass MMS, El-Rashidy AA, et al. Molecular basis beyond interrelated bone resorption/regeneration in periodontal diseases: A concise review. Int J Mol Sci. 2023 Feb 27;24(5):4599. https://doi.org/10.3390/ijms24054599
8. Adytia GJ, Sutanto H, Pratiwi L, Fetarayani D. Advances in synthetic immunology for targeted treatment of systemic autoimmune diseases: Opportunities, challenges, and future directions. Immuno. 2025 Jan 25;5(1):6. https://doi.org/10.3390/immuno5010006
9. Fugger L, Jensen LT, Rossjohn J. Challenges, progress, and prospects of developing therapies to treat autoimmune diseases. Cell. 2020 Apr 1;181(1):63. https://doi.org/10.1016/j.cell.2020.03.007
10. Song Y, Li J, Wu Y. Evolving understanding of autoimmune mechanisms and new therapeutic strategies of autoimmune disorders. Signal Transduct Target Ther. 2024 Oct 4;9(1). https://doi.org/10.1038/s41392-024-01952-8

11. Jiang Y, Krishnan N, Heo J, Fang RH, Zhang L. Nanoparticle–hydrogel superstructures for biomedical applications. J Control Release. 2020 May 26;324:505. https://doi.org/10.1016/j.jconrel.2020.05.041
12. Jung SM, Kim W. Targeted immunotherapy for autoimmune disease. Immune Netw. 2022 Jan 1;22(1). https://doi.org/10.4110/in.2022.22.e9
13. Lachota M, Zagożdżon R. Synthetic receptor-based cell therapies for autoimmune diseases: An update. Cytotherapy. 2025 Feb 1. https://doi.org/10.1016/j.jcyt.2025.02.007
14. Tiong BK, Hahn BH, Aung T. Treatment of autoimmune disease: Established therapies. In: Elsevier eBooks. Elsevier BV; 2019. p. 1415. https://doi.org/10.1016/b978-0-12-812102-3.00071-3
15. Yu C, Xi J, Li M, An M, Liu H. Bioconjugate strategies for the induction of antigen-specific tolerance in autoimmune diseases. Bioconjug Chem. 2017 Nov 22;29(3):719. https://doi.org/10.1021/acs.bioconjchem.7b00632
16. Li SJ, Wu Y, Chen JH, Shen SY, Duan J, Xu HE. Autoimmune diseases: Targets, biology, and drug discovery. Acta Pharmacol Sin. 2023 Dec 14;45(4):674. https://doi.org/10.1038/s41401-023-01207-2
17. Besson FL, Nocturne G, Noël N, Gheysens O, Slart RHJA, Glaudemans AWJM. PET/CT in inflammatory and autoimmune disorders: Focus on several key molecular concepts, FDG, and radiolabeled probe perspectives. Semin Nucl Med. 2023 Nov 14;54(3):379. https://doi.org/10.1053/j.semnuclmed.2023.10.005
18. Probing selected autoimmune diseases for focused perspectives. In: IntechOpen eBooks. IntechOpen; 2023. https://doi.org/10.5772/intechopen.1000271
19. Nassar EJ et al. BIOMATERIALS SCIENCE AND ENGINEERING. Edited by Rosario Pignatello. 2011.
20. Zhao X, An X, Yang C, Sun W, Ji H, Lian F. The crucial role and mechanism of insulin resistance in metabolic disease. Front Endocrinol. 2023 Mar 28;14. https://doi.org/10.3389/fendo.2023.1149239
21. Fu Y, Feng C, Qin S, Xing Z, Liu C, Liu Z, et al. Breaking barriers: advancing cellular therapies in autoimmune disease management. Front Immunol. 2024 Nov 29;15. https://doi.org/10.3389/fimmu.2024.1503099
22. Clair EWSt. Novel targeted therapies for autoimmunity. Curr Opin Immunol. 2009 Oct 13;21(6):648. https://doi.org/10.1016/j.coi.2009.09.008
23. Kumar M, Yip L, Wang F, Marty S, Fathman CG. Autoimmune disease: genetic susceptibility, environmental triggers, and immune dysregulation. Where can we develop therapies? Front Immunol. 2025 Aug 7;16. https://doi.org/10.3389/fimmu.2025.1626082
24. Abbott R. I Think, Therefore I Invent: Creative Computers and the Future of Patent Law. SSRN Electron J. 2016 Jan 1. https://doi.org/10.2139/ssrn.2727884
25. Oh S, Payne A. Engineering cell therapies for autoimmune diseases: From preclinical to clinical proof of concept. Immune Netw. 2022 Jan 1;22(5). https://doi.org/10.4110/in.2022.22.e37
26. Ailioaie LM, Ailioaie C, Litscher G. Photobiomodulation in Alzheimer's disease—A complementary method to state-of-the-art pharmaceutical formulations and nanomedicine? Pharmaceutics. 2023 Mar 11;15(3):916. https://doi.org/10.3390/pharmaceutics15030916
27. Pearson RM, Podojil JR, Shea LD, King NJC, Miller SD, Getts DR. Overcoming challenges in treating autoimmunity: Development of tolerogenic immune-modifying nanoparticles. Nanomedicine Nanotechnol Biol Med. 2018 Oct 21;18:282. https://doi.org/10.1016/j.nano.2018.10.001
28. Robinson WH, Fiorentino D, Chung LWK, Moreland LW, Deodhar M, Harler M, et al. Cutting-edge approaches to B-cell depletion in autoimmune diseases. Front Immunol. 2024 Oct 9;15. https://doi.org/10.3389/fimmu.2024.1454747
29. Berry CT, Frazee CP, Herman PJ, Chen S, Chen A, Kuo Y, et al. Current advancements in cellular immunotherapy for autoimmune disease. Semin Immunopathol. 2025 Jan 16;47(1). https://doi.org/10.1007/s00281-024-01034-5
30. Vukovic J, Abazović D, Vucetic D, Medenica S. CAR-engineered T cell therapy as an emerging strategy for treating autoimmune diseases. Front Med. 2024 Oct 10;11. https://doi.org/10.3389/fmed.2024.1447147

31. Sun Y, Yuan Y, Zhang B, Zhang X. CARs: A new approach for the treatment of autoimmune diseases. Science China Life Sci. 2022 Nov 4;66(4):711. https://doi.org/10.1007/s11427-022-2212-5
32. Zhang Z, Xu Q, Huang L. B cell depletion therapies in autoimmune diseases: Monoclonal antibodies or chimeric antigen receptor-based therapy? Front Immunol. 2023 Feb 10;14. https://doi.org/10.3389/fimmu.2023.1126421
33. Ma C, Liu D, Wang B, Yang Y, Zhu R. Advancements and prospects of novel biologicals for myasthenia gravis: Toward personalized treatment based on autoantibody specificities. Front Pharmacol. 2024 May 27;15. https://doi.org/10.3389/fphar.2024.1370411
34. Chung J, Brudno JN, Borie D, Kochenderfer JN. Chimeric antigen receptor T cell therapy for autoimmune disease. Nat Rev Immunol. 2024 Jun 3. https://doi.org/10.1038/s41577-024-01035-3
35. Kazemian P, Yu SY, Thomson SB, Birkenshaw A, Leavitt BR, Ross CJD. Lipid-nanoparticle-based delivery of CRISPR/Cas9 genome-editing components. Mol Pharmaceutics. 2022 Jun 6;19(6):1669. https://doi.org/10.1021/acs.molpharmaceut.1c00916
36. Bickmore W, Van Steensel B. Chromosomes have a complex organization across spatial scales within the cell nucleus. 2013.
37. Theofilopoulos AN, Kono DH, Baccalà R. The multiple pathways to autoimmunity. Nat Immunol. 2017 Jun 20;18(7):716. https://doi.org/10.1038/ni.3731
38. Bulliard Y, Freeborn RA, Uyeda MJ, Humes D, Bjordahl R, Vries DD, et al. From promise to practice: CAR T and Treg cell therapies in autoimmunity and other immune-mediated diseases. Front Immunol. 2024 Dec 4;15. https://doi.org/10.3389/fimmu.2024.1509956
39. DeWitt JC, Germolec DR, Shipkowski KA, Frawley RP, Evans E. Markers of inflammation. 2018.
40. Wu S, Rau C, Kuo P, Shih FY, Lin HP, Wu YC, et al. Profiling the expression of circulating acute-phase proteins, cytokines, and checkpoint proteins in patients with severe trauma: A pilot study. J Inflamm Res. 2021 Aug 1;3739. https://doi.org/10.2147/jir.s324056
41. Xiang Y, Zhang M, Jiang DY, Su QP, Shi J. The role of inflammation in autoimmune disease: a therapeutic target. Front Immunol. 2023 Oct 4;14. https://doi.org/10.3389/fimmu.2023.1267091
42. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med. 1999 Feb 11;340(6):448. https://doi.org/10.1056/nejm199902113400607
43. Gadina M, Gazaniga N, Vian L, Furumoto Y. Small molecules to the rescue: Inhibition of cytokine signaling in immune-mediated diseases. J Autoimmun. 2017 Jul 1;85:20. https://doi.org/10.1016/j.jaut.2017.06.006
44. Jones SA, Scheller J, Rose-John S. Therapeutic strategies for the clinical blockade of IL-6/gp130 signaling. J Clin Invest. 2011 Sep 1;121(9):3375. https://doi.org/10.1172/jci57158
45. Davignon J, Rauwel B, Degboé Y, Constantin A, Boyer J, Kruglov A, et al. Modulation of T-cell responses by anti-tumor necrosis factor treatments in rheumatoid arthritis: A review. Arthritis Res Ther. 2018 Oct 12;20(1). https://doi.org/10.1186/s13075-018-1725-6
46. Tabas I, Glass CK. Anti-inflammatory therapy in chronic disease: Challenges and opportunities. Science. 2013 Jan 10;339(6116):166. https://doi.org/10.1126/science.1230720
47. Hsu Y, Chang MS. IL-20 in rheumatoid arthritis. Drug Discov Today. 2015 Aug 19;22(6):960. https://doi.org/10.1016/j.drudis.2015.08.002
48. Jones BE, Maerz MD, Buckner JH. IL-6: A cytokine at the crossroads of autoimmunity. Curr Opin Immunol. 2018 Sep 21;55:9. https://doi.org/10.1016/j.coi.2018.09.002
49. Modulating cytokines as treatment for autoimmune diseases and cancer. Frontiers Research Topics. 2020. https://doi.org/10.3389/978-2-88966-211-1
50. Slaats J, Oever J ten, Veerdonk FL van de, Netea MG. IL-1β/IL-6/CRP and IL-18/ferritin: Distinct inflammatory programs in infections. PLoS Pathog. 2016 Dec 15;12(12). https://doi.org/10.1371/journal.ppat.1005973
51. Rosenblum MD, Remedios KA, Abbas AK. Mechanisms of human autoimmunity. J Clin Invest. 2015 Apr 19;125(6):2228. https://doi.org/10.1172/jci78088
52. Sebastiani M, Vacchi C, Manfredi A, Cassone G. Personalized medicine and machine learning: A roadmap for the future. J Clin Med. 2022 Jul 15;11(14):4110. https://doi.org/10.3390/jcm11144110

53. Banchereau R, Cepika A, Banchereau J, Pascual V. Understanding human autoimmunity and autoinflammation through transcriptomics. Annu Rev Immunol. 2017 Mar 30;35(1):337. https://doi.org/10.1146/annurev-immunol-051116-052225
54. Pachéco Y, Barahona-Correa JE, Monsalve DM, Acosta-Ampudia Y, Rojas M, Rodríguez Y, et al. Cytokine and autoantibody clusters interaction in systemic lupus erythematosus. J Transl Med. 2017 Nov 25;15(1). https://doi.org/10.1186/s12967-017-1345-y
55. Schett G, McInnes IB, Neurath MF. Reframing immune-mediated inflammatory diseases through signature cytokine hubs. N Engl J Med. 2021 Aug 11;385(7):628. https://doi.org/10.1056/nejmra1909094
56. Mantovani A, Garlanda C. Humoral innate immunity and acute-phase proteins. N Engl J Med. 2023 Feb 1;388(5):439. https://doi.org/10.1056/nejmra2206346
57. Bell LCK, Meydan C, Kim J, Foox J, Butler D, Mason CE, et al. Transcriptional response modules characterize IL-1β and IL-6 activity in COVID-19. iScience. 2020 Dec 7;24(1):101896. https://doi.org/10.1016/j.isci.2020.101896
58. Leuchsenring AB. Going deep into the acute phase protein response. Research Portal Denmark. 2020 Jan 1;143. https://local.forskningsportal.dk/local/dki-cgi/ws/cris-link?src=dtu&id=dtu-4ff99b13-85a7-4f28-a8fb-92d3ccdff3e7&ti=Going%20deep%20into%20the%20acute%20phase%20protein%20response
59. Jiménez-Gracia L, Maspero D, Aguilar-Fernández S, Craighero F, Ruiz S, Marchese D, et al. Interpretable inflammation landscape of circulating immune cells. bioRxiv (Cold Spring Harbor Laboratory). 2023 Nov 28. https://doi.org/10.1101/2023.11.28.568839
60. Tavakolpour S. Towards personalized medicine for patients with autoimmune diseases: Opportunities and challenges. Immunol Lett. 2017 Aug 8;190:130. https://doi.org/10.1016/j.imlet.2017.08.002
61. Ullah R, Sarwar N, Alatawi MN, Alsadhan AA, Alwageed HS, Khan M, et al. Advancing personalized diagnosis and treatment using deep learning architecture. Front Med. 2025 Mar 27;12. https://doi.org/10.3389/fmed.2025.1545528
62. Guthridge JM, Wagner CA, James JA. The promise of precision medicine in rheumatology. Nat Med. 2022 Jul 1;28(7):1363. https://doi.org/10.1038/s41591-022-01880-6
63. Chen Y, Hsiao T, Lin C, Fann YC. Unlocking precision medicine: Clinical applications of integrating health records, genetics, and immunology through artificial intelligence. J Biomed Sci. 2025 Feb 7;32(1). https://doi.org/10.1186/s12929-024-01110-w
64. Giacomelli R, Afeltra A, Bartoloni E, Berardicurti O, Bombardieri S, Bortoluzzi A, et al. The growing role of precision medicine for the treatment of autoimmune diseases; results of a systematic review of literature and experts' consensus. Autoimmun Rev. 2020 Dec 15;20(2):102738. https://doi.org/10.1016/j.autrev.2020.102738
65. Singh R, Arya P, Dubey S. Artificial intelligence in pharmaceutics: Revolutionizing drug formulation and optimization. 2024 Sep 25;1(3):138. https://doi.org/10.21590/jddhs.01.03.03
66. Noorain, Srivastava V, Parveen B, Parveen R. Artificial intelligence in drug formulation and development: Applications and future prospects. Curr Drug Metab. 2023 Sep 1;24(9):622. https://doi.org/10.2174/0113892002265786230921062205
67. Dangeti A, Bynagari DG, Vydani K. Revolutionizing drug formulation: Harnessing artificial intelligence and machine learning for enhanced stability, formulation optimization, and accelerated development. Int J Pharm Sci Med. 2023 Aug 30;8(8):18. https://doi.org/10.47760/ijpsm.2023.v08i08.003
68. Yang Y, Liu Y, Chen Y, Luo D, Xu K, Zhang L. Artificial intelligence for predicting treatment responses in autoimmune rheumatic diseases: Advancements, challenges, and future perspectives. Front Immunol. 2024 Oct 22;15. https://doi.org/10.3389/fimmu.2024.1477130
69. Gilvaz VJ, Reginato AM. Artificial intelligence in rheumatoid arthritis: Potential applications and future implications. Front Med. 2023 Nov 16;10. https://doi.org/10.3389/fmed.2023.1280312
70. Hügle T. Advancing rheumatology care through machine learning. Pharm Med. 2024 Feb 29;38(2):87. https://doi.org/10.1007/s40290-024-00515-0

71. Mane D, Deshmukh AM, Ambare RH, Solankar AA, Madane CS. AI in autoimmune diseases: Transforming diagnosis and treatment. J Pharm Biol Sci. 2025 Jan 9;12(2):109. https://doi.org/10.18231/j.jpbs.2024.017
72. Danieli MG, Brunetto S, Gammeri L, Palmeri D, Claudi I, Shoenfeld Y, et al. Machine learning application in autoimmune diseases: State of art and future perspectives. Autoimmun Rev. 2023 Dec 9;23(2):103496. https://doi.org/10.1016/j.autrev.2023.103496
73. Momtazmanesh S, Nowroozi A, Rezaei N. Artificial intelligence in rheumatoid arthritis: Current status and future perspectives: A state-of-the-art review. Rheumatol Ther. 2022 Jul 18;9(5):1249. https://doi.org/10.1007/s40744-022-00475-4
74. Siddiqui MF, Aslam D, Tanveer K, Soudy M. The role of artificial intelligence and machine learning in autoimmune disorders. In: Studies in Computational Intelligence. Springer Nature; 2024. p. 61. https://doi.org/10.1007/978-981-99-9029-0_3
75. Yaung KN, Yeo JG, Kumar P, Wasser M, Chew MZW, Ravelli A, et al. Artificial intelligence and high-dimensional technologies in the theragnosis of systemic lupus erythematosus. Lancet Rheumatol. 2023 Feb 20;5(3). https://doi.org/10.1016/s2665-9913(23)00010-3
76. Kruta J, Carapito R, Trendelenburg M, Martin T, Rizzi M, Voll R, et al. Machine learning for precision diagnostics of autoimmunity. Sci Rep. 2024 Nov 13;14(1). https://doi.org/10.1038/s41598-024-76093-7
77. Sattar AMd, Ranjan MKr, Tiwari S. AI-enhanced data analytics framework for autoimmune disease: Revolutionizing diagnosis, monitoring, and treatment strategy. In: Studies in Computational Intelligence. Springer Nature; 2024. p. 223. https://doi.org/10.1007/978-981-99-9029-0_11
78. Liu S, Liu Y, Li M, Shang S, Cao Y, Shen X, et al. Artificial intelligence in autoimmune diseases: A bibliometric exploration of the past two decades. Front Immunol. 2025 Apr 22;16. https://doi.org/10.3389/fimmu.2025.1525462
79. Peng J, Jury EC, Dönnes P, Ciurtin C. Machine learning techniques for personalised medicine approaches in immune-mediated chronic inflammatory diseases: Applications and challenges. Front Pharmacol. 2021 Sep 30;12. https://doi.org/10.3389/fphar.2021.720694
80. Ma Y, Chen J, Wang T, Zhang LT, Xu X, Qiu Y, et al. Accurate machine learning model to diagnose chronic autoimmune diseases utilizing information from B cells and monocytes. Front Immunol. 2022 Apr 20;13. https://doi.org/10.3389/fimmu.2022.870531
81. Amin M, Martínez-Heras E, Ontaneda D, Prados F. Artificial intelligence and multiple sclerosis. Curr Neurol Neurosci Rep. 2024 Jun 28;24(8):233. https://doi.org/10.1007/s11910-024-01354-x
82. Zulqarnain F, Rhoads SF, Syed S. Machine and deep learning in inflammatory bowel disease. Curr Opin Gastroenterol. 2023 May 5. https://doi.org/10.1097/mog.0000000000000945
83. Rio LD, Spadaccini M, Parigi TL, Gabbiadini R, Buono AD, Busacca A, et al. Artificial intelligence and inflammatory bowel disease: Where are we going? World J Gastroenterol. 2023 Jan 12;29(3):508. https://doi.org/10.3748/wjg.v29.i3.508
84. Folasole A, Eshua PE, Elesho OE. Modeling spatiotemporal immune dynamics in inflammatory diseases using integrative multi-modal analytics and high-dimensional longitudinal datasets. World J Biol Pharm Health Sci. 2025 Aug 16;23(2):196. https://doi.org/10.30574/wjbphs.2025.23.2.0754
85. Mgendi G. Unlocking the potential of precision agriculture for sustainable farming. Discover Agric. 2024 Nov 7;2(1). https://doi.org/10.1007/s44279-024-00078-3
86. Goessinger EV, Gottfrois P, Mueller AM, Cerminara SE, Navarini AA. Image-based artificial intelligence in psoriasis assessment: The beginning of a new diagnostic era? Am J Clin Dermatol. 2024 Sep 11. https://doi.org/10.1007/s40257-024-00883-y
87. Smith P, Johnson C, Haran K, Orcales F, Kranyak A, Bhutani T, et al. Advancing psoriasis care through artificial intelligence: A comprehensive review. Curr Dermatol Rep. 2024 Jun 13;13(3):141. https://doi.org/10.1007/s13671-024-00434-y
88. Liu Z, Wang X, Ma Y, Lin Y, Wang G. Artificial intelligence in psoriasis: Where we are and where we are going. Exp Dermatol. 2023 Sep 23;32(11):1884. https://doi.org/10.1111/exd.14938

89. Ravipati A, Elman SA. The state of artificial intelligence for systemic dermatoses: Background and applications for psoriasis, systemic sclerosis, and much more. Clin Dermatol. 2024 Jun 21;42(5):487. https://doi.org/10.1016/j.clindermatol.2024.06.019
90. Gao L, Li L. Leveraging machine learning algorithms for early detection and prognosis of pediatric autoimmune diseases: A comprehensive data-driven approach. Res Square. 2024 Nov 15. https://doi.org/10.21203/rs.3.rs-5287349/v1
91. Mahmood F, Bendayan S, Ghazawi FM, Litvinov IV. Editorial: The emerging role of artificial intelligence in dermatology. Front Med. 2021 Nov 17;8. https://doi.org/10.3389/fmed.2021.751649
92. Pomi FL, Papa V, Borgia F, Vaccaro M, Pioggia G, Gangemi S. Artificial intelligence: A snapshot of its application in chronic inflammatory and autoimmune skin diseases. Life. 2024 Apr 16;14(4):516. https://doi.org/10.3390/life14040516
93. Gerussi A, Scaravaglio M, Cristoferi L, Verda D, Milani C, Bernardi ED, et al. Artificial intelligence for precision medicine in autoimmune liver disease. Front Immunol. 2022 Nov 11;13. https://doi.org/10.3389/fimmu.2022.966329
94. Ali KA, Mohin S, Mondal P, Goswami S, Ghosh S, Choudhuri S. Influence of artificial intelligence in modern pharmaceutical formulation and drug development. Future J Pharm Sci. 2024 Mar 29;10(1). https://doi.org/10.1186/s43094-024-00625-1
95. Dey H, Arya N, Mathur H, Chatterjee N, Jadon R. Exploring the role of artificial intelligence and machine learning in pharmaceutical formulation design. Int J Newgen Res Pharm Healthc. 2024 Jun 30;30. https://doi.org/10.61554/ijnrph.v2i1.2024.67
96. Moingeon P. Artificial intelligence-driven drug development against autoimmune diseases. Trends Pharmacol Sci. 2023 May 31;44(7):411. https://doi.org/10.1016/j.tips.2023.04.005
97. Basile AO, Yahi A, Tatonetti NP. Artificial intelligence for drug toxicity and safety. Trends Pharmacol Sci. 2019 Aug 2;40(9):624. https://doi.org/10.1016/j.tips.2019.07.005
98. Badria FA, Elgazar AA. Optimizing pharmacovigilance in an era of accelerating innovation. In: IntechOpen eBooks. IntechOpen; 2024. https://doi.org/10.5772/intechopen.1007935
99. Hasselgren C, Oprea TI. Artificial intelligence for drug discovery: Are we there yet? Annu Rev Pharmacol Toxicol. 2023 Sep 22;64(1):527. https://doi.org/10.1146/annurev-pharmtox-040323-040828
100. Shaki F, Amilrkhanloo M, Jahani D, Chahrdori M. Artificial intelligence in pharmaceuticals: Exploring applications and legal challenges. Pharm Biomed Res. 2024 Mar 16;10(1):1. https://doi.org/10.32598/pbr.10.1.1257.1
101. Ahire Y, Patil JH, Chordiya HN, Deore RA, Bairagi V. Advanced applications of artificial intelligence in pharmacovigilance: Current trends and future perspectives. J Pharm Res. 2024 Mar 15;23(1):23. https://doi.org/10.18579/jopcr/v23.1.24
102. Niazi SK. The coming of age of AI/ML in drug discovery, development, clinical testing, and manufacturing: The FDA perspectives. Drug Des Dev Ther. 2023 Sep 1;2691. https://doi.org/10.2147/dddt.s424991
103. Vora LK, Gholap AD, Jetha K, Singh TRR, Solanki HK, Chavda VP. Artificial intelligence in pharmaceutical technology and drug delivery design. Pharmaceutics. 2023 Jul 10;15(7):1916. https://doi.org/10.3390/pharmaceutics15071916
104. Malheiro V, Santos B, Figueiras A, Mascarenhas-Melo F. The potential of artificial intelligence in pharmaceutical innovation: From drug discovery to clinical trials. Pharmaceutics. 2025 May 25;18(6):788. https://doi.org/10.3390/ph18060788
105. Crisafulli S, Ciccimarra F, Bellitto C, Carollo M, Carrara E, Stagi L, et al. Artificial intelligence for optimizing benefits and minimizing risks of pharmacological therapies: Challenges and opportunities. Front Drug Saf Regul. 2024 Mar 18;4. https://doi.org/10.3389/fdsfr.2024.1356405
106. Bettanti A, Beccari AR, Biccarino M. Exploring the future of biopharmaceutical drug discovery: Can advanced AI platforms overcome current challenges? Discover Artif Intell. 2024 Dec 5;4(1). https://doi.org/10.1007/s44163-024-00188-3
107. Rehman AU, Li M, Wu B, Ali Y, Rasheed S, Shaheen SO, et al. Role of artificial intelligence in revolutionizing drug discovery. Fundam Res. 2024 May 1. https://doi.org/10.1016/j.fmre.2024.04.021

108. Serrano DR, Luciano FC, Anaya BJ, Őngoren B, Kara A, Molina G, et al. Artificial intelligence (AI) applications in drug discovery and drug delivery: Revolutionizing personalized medicine. Pharmaceutics. 2024 Oct 14;16(10):1328. https://doi.org/10.3390/pharmaceutics16101328
109. Zeb S, FNU N, Abbasi N, Fahad M. AI in healthcare: Revolutionizing diagnosis and therapy. Int J Multidiscip Sci Arts. 2024 Aug 17;3(3):118. https://doi.org/10.47709/ijmdsa.v3i3.4546
110. Carini C, Seyhan AA. Tribulations and future opportunities for artificial intelligence in precision medicine. J Transl Med. 2024 Apr 30;22(1). https://doi.org/10.1186/s12967-024-05067-0
111. Pradhan S. Biomarkers in lung cancer: A review.
112. Hart ML, Kato R, Rolauffs B. Editorial: Artificial intelligence in predicting, determining, and controlling cell phenotype or tissue function in inflammatory diseases. Front Immunol. 2024 Jun 18;15. https://doi.org/10.3389/fimmu.2024.1443534
113. Saleem M, Watson AE, Anwaar A, Jasser AO, Yusuf N. Optimizing immunotherapy: The synergy of immune checkpoint inhibitors with artificial intelligence in melanoma treatment. Biomolecules. 2025 Apr 16;15(4):589. https://doi.org/10.3390/biom15040589
114. Huang L, Wu X, You J, Jin Z, He W, Sun J, et al. Artificial intelligence can predict personalized immunotherapy outcomes in cancer. Cancer Immunol Res. 2025 Jun 10. https://doi.org/10.1158/2326-6066.cir-24-1270
115. Garg PK, Pareek S, Kulkarni P, Horné D, Salgia R, Singhal SS. Next-generation immunotherapy: Advancing clinical applications in cancer treatment. J Clin Med. 2024 Oct 30;13(21):6537. https://doi.org/10.3390/jcm13216537
116. Patole VP, Shinde N, Chandak SM, Satalkar AT. Cancer research in the 21st century: Recent advances and future perspectives. Chin J Appl Physiol. 2025 Jan 1. https://doi.org/10.62958/j.cjap.2025.018