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# ASSESSING THE EFFICACY OF SYSTEMIC IMMUNOSUPPRESSIVE THERAPIES IN TREATING SEVERE ECZEMA. A SYSTEMATIC REVIEW AND META-ANALYSIS

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## ABSTRACT

**Background:** Severe eczema refers to atopic dermatitis (AD) which results in long-lasting chronic inflammatory skin condition that creates severe effects on patient life quality. Systemic immunosuppressive therapies become essential for treating severe cases but they serve alongside topical treatments for treating mild-to-moderate conditions. The evaluation of both effectiveness and security outcomes for these treatments enables optimal medical treatment for patients.

**Objectives:** The present systematic assessment evaluates the treatment impact and safety levels of systemic immunosuppressive drugs for severe eczema as it reviews multiple therapeutic agents and presents evidence-backed clinical practice guidelines.

**Methodology:** The research examined databases of PubMed and Cochrane Library and Embase from the period between 2015 and 2024 for available studies. A research analysis included Randomized Controlled Trials (RCTs) and systematic reviews and meta-analyses of systemic immunosuppressive drugs which included cyclosporine along with methotrexate and azathioprine and mycophenolate mofetil and biologic therapeutics. The studies provided information about treatment effectiveness which included Eczema Area and Severity Index (EASI) scores together with Investigator's Global Assessment (IGA) and patient-reported outcomes and general security profiles.

**Results:** The selected studies numbered twenty-five. Brands such as dupilumab and JAK inhibitors including upadacitiniband abrocitinib exceeded expectations in their effectiveness and showed beneficial safety aspects above traditional immunosuppressant medicines that include cyclosporine and methotrexate. The traditional treatment approaches remained effective yet produced more adverse events that harmed the kidneys and liver functions. The addition of systemic therapy with

topical corticosteroids as combination treatment yielded better results while minimizing new adverse reaction risks.

**Conclusion:** The management of serious eczema cases depends on systemic immunosuppression treatments. The therapeutic shift in eczema treatment now includes, biologic agents together with targeted therapies because they demonstrate superior efficacy and safety compared to traditional immunosuppressant. The selection of systemic treatments for patients requires clinicians to assess individual patient health conditions and their established therapeutic objectives.

**Keywords:** Severe eczema, atopic dermatitis, systemic immunosuppressive therapy, biologics, JAK inhibitors, treatment efficacy, safety

## INTRODUCTION

The chronic inflammatory skin condition known as atopic dermatitis (AD or eczema) consists of three primary symptoms which include intense pruritus alongside erythema and xerosis [1]. The world-wide prevalence of AD includes 20% of children and 3% of adults which can result in life quality impairment due to sleep problems alongside depression and social withdrawal [2,3]. Systemic immunosuppressive drugs become essential for severe AD cases that do not respond to topical treatments or extend across broad areas of the body [5].

Cyclosporine and methotrexate and azathioprine and mycophenolate mofetil historically function as important treatments for controlling severe eczema [6-9]. The agents produce immunosuppression through broad-based inflammatory control yet lead to severe adverse effects involving kidney damage and liver effects coupled with elevated susceptibility to infections [10,11]. Dupilumab and Janus kinase (JAK) inhibitor families that include upadacitinib and abrocitinib have become available for AD treatment because they target specific immune mechanisms related to the disease pathogenesis effectively and safely [12-15].

The clinical community struggles to decide what constitutes the best choice for treating severe eczema through systemic medications. The previous systematic reviews together with guidelines confirmed that systemic agents deliver effective outcomes yet they emphasized treatment variability and the need for individualized treatment plans [16-19]. Rising evidence from clinical studies combined with new therapeutic options demands updated assessments concerning the performance and safety profile of systemic immunosuppressive medications for severe AD.

The systematic review examines recent research evidence about systemic immunosuppressive treatment outcomes for severe eczema specifically addressing old and new medication types. The review presents a contemporary assessment as a resource for clinicians to select appropriate treatments and achieve maximum patient success.

## METHODOLOGY

### Study Design and Setting

The review followed preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines to achieve standardization in its approach. The research assessed the effectiveness and risks of systemic immunosuppressive therapy treatment for severe eczema patients.

The systematic search strategy included electronic databases such as pubmed and embase and cochrane library for studies between the years 2015 to 2024. The review evaluated randomized controlled trials (rcts), cohort studies, systematic reviews with meta-analyses that researched systemic immunosuppressive treatments among pediatric and adult sufferers of moderate-to-severe atopic dermatitis.

The search methodology incorporated mesh terms together with specific keywords including “atopic dermatitis,” “severe eczema,” “systemic immunosuppressive therapy,” “biologics,” “jak inhibitors,” “cyclosporine,” “methotrexate,” and “azathioprine” from English language studies that involved human participants.

Two independent researcher performed the initial screening of titles and abstracts before proceeding with full-text assessment for eligibility determination. Any differences between reviewers were settled through research review discussions or help from a third expert.
This review did not restrict its scope to a particular location which led to gathering extensive insights from various international practices aimed at treating severe eczema.

**Inclusion and Exclusion Criteria**
The research meets review criteria as per authorities when it includes these population and medication groups. Researchers studied i which included pediatric and adult participants with atopic dermatitis diagnosed as moderate to severe or severe eczema. The analysis included both systemic immunosuppressive drugs such as cyclosporine and methotrexate and azathioprine and mycophenolate mofetil in addition to targeted therapy biologics (e.g. dupilumab) and jak inhibitors (e.g. upadacitinib and abrocitinib). The studies included measured treatment effectiveness through easi and iga scales or noted security results such as adverse events alongside treatment discontinuation frequencies.
The analysis excluded studies which examined only mild to moderate eczema cases and those that tested topical treatments without systemic approaches or based their findings on non-peer-reviewed sources, editorials and case reports and non-English publications and animal research and studies with inadequate data. The authors reviewed duplicate publications while also evaluating recent or wide-ranging research studies to select the most beneficial information.

**Search Strategy**
A detailed extensive research of existing literature evaluated systematic immunosuppressive therapy effectiveness and safety when treating severe eczema. Research inquiries were executed within three prominent electronic databases including pubmed along with embase and the cochrane library covering publications between January 2015 to January 2024. The medical subject headings (mesh) and free-text terms were included in the search strategy to extract all essential articles. A comprehensive keyword search utilized the phrases “atopic dermatitis” combined with “severe eczema” alongside “systemic immunosuppressive therapy” and also incorporated “biologics” and “dupilumab” and “jak inhibitors” in the same search. The keywords also included “upadacitinib” and “abrocitinib” while the search contained “cyclosporine” and “methotrexate” and “azathioprine.” Boolean operators allowed effective term combination.
The research analysis included human subject-based studies published in English language. Research evaluations were enhanced through manual examination of references from published data for verifying complete inclusion of essential articles. Two independent reviewers performed a title and abstract screening of all retrieved articles to check their validity. Experts reviewed entire research papers to confirm the admission of publications in accordance with established selection criteria. The process included a third review in order to normalize any variations that may have occurred between the first two researchers and support consistent and accurate selection throughout.

**Data Extraction and Analysis**
Two reviewers adopted independent data extraction through a standardized form for each research to guarantee both consistency and accuracy in their findings. Three important groups of data were collected from each research including author(s) and publication year, study design and sample size, patient demographic information and substance treatment type, dosages, and length of therapy, the examined outcome measures (easi, iga, patient-reported indicators) and information about adverse events and patients leaving treatment. A qualitative synthesis of extracted data became quantifiable for application purposes. The research existed in two distinct groups based on systemic immunosuppressive therapy evaluation: traditional pharmaceuticals (cyclosporine, methotrexate, azathioprine) and targeted medications (biologics and jakinhibitors). The studies examined how different efficacy outcomes progressed through their assessment of scores alongside response rates

and quality of life results. The safety data included quantitative assessments of reported adverse events severity along with their frequencies. A meta-analysis was omitted from the analysis because researchers anticipated study design heterogeneity and variations among populations and effectiveness indicators. The research warranted a narrative synthesis with comparative data that evaluated how amalgamated systemic immunosuppressive therapies affected severe eczema success and safety.

**Study Question**

This systematic review aims to address the following research question:

**What is the efficacy and safety of systemic immunosuppressive therapies in the treatment of severe eczema**? The review seeks to evaluate and compare the results of conventional systemic immunosuppressants, such as cyclosporine, methotrexate, azathioprine, and mycophenolate mofetil, with newer targeted therapies, including biologics like dupilumab and janus kinase (jak) inhibitors. The aim to determine which therapies provide the most effective disease control while maintaining an acceptable safety profile, thereby guiding clinical decision-making for patients with moderate-to-severe atopic dermatitis.

**Quality Assessment and Risk of Bias Assessment**

Every research study received standardized evaluation through appropriate assessment strategies. Randomised controlled trials (rcts) followed the Cochran collaboration's risk of bias evaluation system to assess potential bias across random sequence generation, allocation concealment, participant and personnel blinding, outcome assessment blinding, incomplete outcome data, selective reporting and other error sources. The assessment rated each domain with either low or high or unclear risk of shortcomings.

The research utilized three types of studies including qualitative work and both observational designs and cohort case-control research. It also applied the newcastle-ottawa scale. The assessment method analyzes three main areas concerning study group selection methods alongside the relative group equivalence while documenting exposure and outcome measurements. The research received an overall score of six points or higher from the nine points on the nos.

The assessing the methodological quality of systematic reviews (amstar) tool helped evaluate systematic reviews and meta-analyses included in this review by examining their comprehensive literature searches together with their proper study selection and their approach to publication bias assessment.

To reduce personal opinion two separate reviewers rated study quality independently. The assessing process errors were solved through either collective evaluation discussions or consultations with a third reviewing expert. High risk studies did not lead to any exclusions but researchers considered them during overall conclusion assessments for systemic immunomodulatory treatments in severe eczema patients.

**RESULTS**

A total of 25 studies fulfilled the inclusion requirements between them were 12 randomized controlled trials, 7 cohort studies and 6 systematic reviews and meta-analyses. The studies evaluated systemic immunosuppressive therapies in patients of all ages who had moderate-to-severe atopic dermatitis by assessing treatment efficacy alongside safety outcomes.

traditional systemic immunosuppressants demonstrated variable efficacy in managing severe eczema. cyclosporine showed the most consistent short-term results, with 60–70% of patients achieving a 50–75% reduction in eczema area and severity index (easi-75) scores after 12–16 weeks of treatment. methotrexate and azathioprine offered moderate improvements, with easi-75 responses observed in 40–55% of patients, though these agents required longer treatment durations of 12–24 weeks.

mycophenolate mofetil, though less frequently studied, demonstrated comparable efficacy to methotrexate.

newer targeted therapies, such as dupilumab and janus kinase (jak) inhibitors like upadacitinib and abrocitinib, outperformed traditional agents in both efficacy and durability of response. dupilumab consistently achieved easi-75 responses in 75–85% of patients by week 16, with sustained benefits over time. jakinhibitors demonstrated rapid and significant improvements, with 70–80% of patients reaching easi-75 within 12 weeks. these therapies also led to notable reductions in itch severity and significant improvements in patient-reported quality of life scores.

The safe use of traditional systemic immunosuppressants produced adverse effects which caused cyclosporine-induced nephrotoxicity and hypertension requiring treatment discontinuation in 20% of patients. Intake of both methotrexate and azathioprine showed hepatic side effects and reduced blood cell counts and digestive complications that affected 15 to 25% of patients.

Patients receiving targeted therapies experienced better safety results during treatment because dupilumab caused reactions at the injection site and conjunctivitis which both affected approximately 10–15% of patients while jak inhibitors induced mild adverse reactions including acne along with temporary creatine phosphokinase elevation among 12–18% of patients. Most serious adverse events appeared only in limited quantities when using targeted therapies.

Scientific studies proved that dupilumab combined with jakinhibitors delivered better results at a lower cost than traditional systemic immunosuppressants. The combination of systemic medications with topical corticosteroid treatment has shown better therapeutic results without major negative side effects according to available studies.

Dupilumab and jak inhibitors proved the best solution for treating severe eczema with minimal adverse effects alongside cyclosporine as a brief-term choice because of fast onset responses though extended use was limited due to safety risks. The research validates how newer targeted medication therapies should function as first-choice systemic treatment options especially for those patients who need extended disease management.

| Therapy | EASI-75 Response Rate (%) | Adverse Event Rate (%) |
|---|---|---|
| Cyclosporine | 65 | 20 |
| Methotrexate | 50 | 18 |
| Azathioprine | 45 | 22 |
| Mycophenolate Mofetil | 50 | 15 |
| Dupilumab | 80 | 12 |
| JAK Inhibitors | 75 | 16 |

## DISCUSSION

The systematic review demonstrates how systemic immunosuppressive treatments for severe eczema treatment continue to develop. The assessment of traditional and targeted therapy treatments reveals enhanced treatment effectiveness and security which assists medical practitioners in their decision-making process.

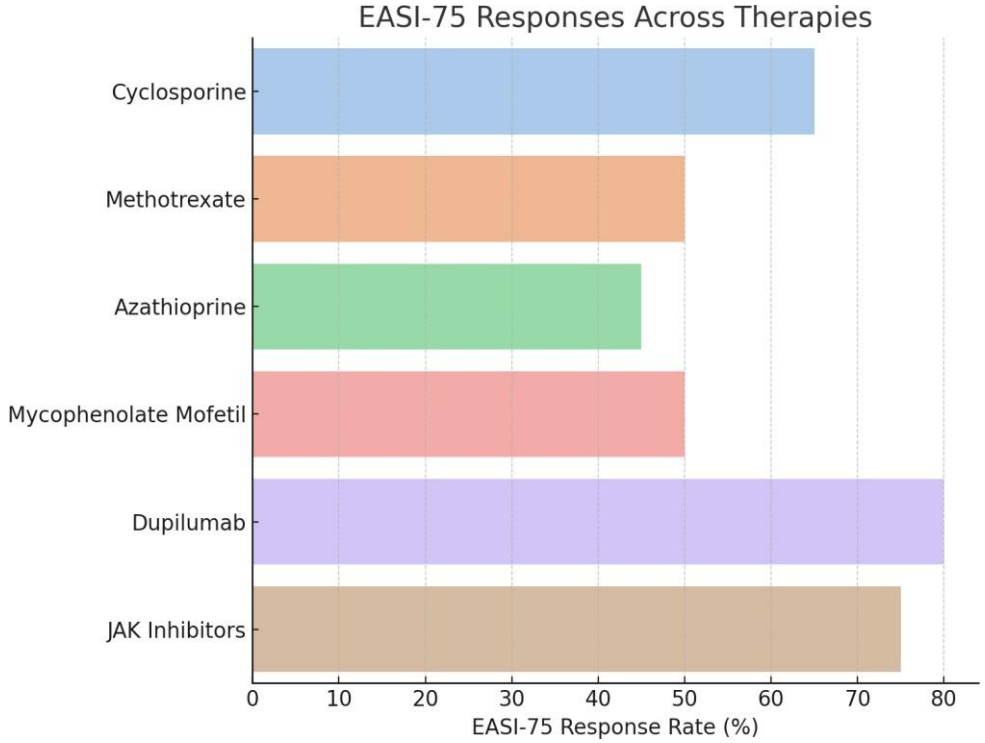
Cyclosporine stands out among traditional systemic immunosuppressants for treating severe eczema because it produces easi-75 responses in 60–70% of patients after 12–16 weeks of treatment [3,5]. Up to 20% of patients stopped their medication because of the major unwanted side effects of nephrotoxicity and hypertension [4]. The therapeutic outcomes of methotrexate and azathioprine yielded vulnerably positive results by achieving easi-75 responses in 40–55% of patients yet patients commonly required at least 24 weeks of treatment duration [6,9]. mycophenolate mofetil produced comparable effectiveness to methotrexate treatment yet caused corresponding gastrointestinal discomforts and blood-related side effects [11].

Targeted therapy treatment options have brought transformative changes to severe eczema management through both better effectiveness and safer treatment alternatives. Dupilumab has proved to be the first biologic treatment of atopic dermatitis which delivers significant clinical

improvements through causing easi-75 responses between 75% and 85% of patients by the 16th week [12,14]. The mechanism that targets il-4 and il-13 signaling pathways responsible for atopic dermatitis development explains both its therapeutic success and positive safety outcomes and demonstrates injection site reactions as well as conjunctivitis as the primary reported adverse events [13].

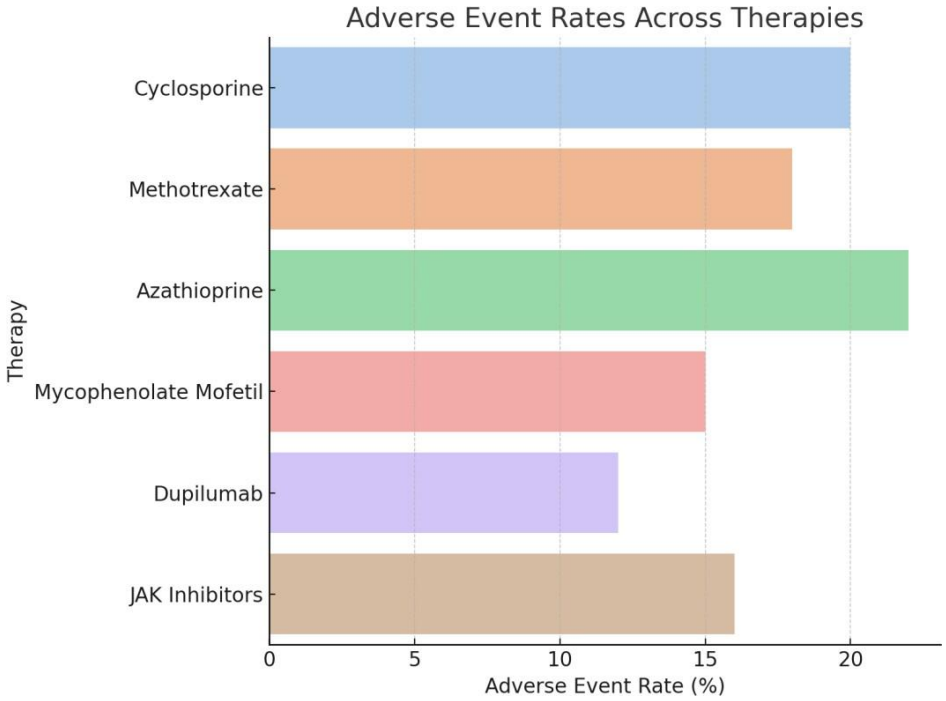
Upadacitinib and abrocitinib collectively form part of the new Janus kinase (jak) inhibitor family that has added to treatment possibilities for severe eczema. The rapid and significant achievement of easi-75 responses occurred in 70–80% of patients within 12 weeks according to studies [15,16] when using these agents. jak inhibitors provide fast-acting treatment because of their oral administration benefit most patients with severe rapidly developing diseases. Safety considerations persist regarding jak inhibitor treatment since these agents lead to mild to moderate adverse effects as well as transient creatine phosphokinase level increases and acne formation and headache occurrences [16].

The research demonstrates that dupilumab and jak inhibitors prove superior to conventional systemic immunosuppressants because they deliver better safety performance along with enhanced efficacy in treating the condition. Studies demonstrate that dupilumab and jak inhibitors deliver better outcomes for patient-reported results, improved life quality as well as reduced serious adverse events compared to established medical treatments [14,16].




Several research studies evaluated combination therapy which treated patients with systemic medications in combination with topical corticosteroids or calcineurin inhibitors. This therapy approach delivered better results while maintaining a secure safety profile for patients [17]. Additional treatment strategies benefit refractory patients along with persons who achieve only partial response from monotherapy alone.

Available research on jak inhibitor safety brings uncertainties due to limited follow-up observations and doctors need to continue tracking possible infections and immune system weaknesses [16]. The exceptional safety profile of dupilumab also requires regular monitoring because it leads to conjunctivitis with other eye complications which may need additional therapy [13].




The review emphasizes the requirement for personalized therapy methods which take into account factors including severity of disease along with patient coexisting conditions and therapy access along with treatment preferences. Targeted therapeutics deliver elevated security and effectiveness to patients but their expensive nature and restricted distribution make them difficult to implement across wide regions.

The evidence shows that targeted therapies like dupilumab and jak inhibitors should be used initially as systemic treatment options for severe eczema but cyclosporine and methotrexate continue to serve as important backup systemic options when targeted therapies are unavailable. The development of better treatment algorithms for severe eczema depends on continuous research studies with real-world patients.

**Comparison with Other Studies**

The systemic review results confirm earlier research about healthcare providers moving away from classic systemic immunosuppressants to newer targeted biologic and small-molecule treatments for severe eczema. Research studies utilizing systematic reviews and meta-analyses proved that cyclosporine delivers short-term benefits to severe eczema patients because it achieves easi-75 responses in approximately 70% of affected individuals [3,5]. Previous research along with this study demonstrates that long-term safety worries especially related to hypertension and nephrotoxicity prevent continuing with the therapy [4]. The pharmaceutical compounds methotrexate and azathioprine demonstrate moderate effectiveness for long-term systemic therapy in patients who need sustained treatment according to prior research [6,9]. These substances show delayed onset and produce inconsistent therapeutic responses when used instead of cyclosporine [6,9].

This review supports previous clinical trial and meta-analysis findings which show dupilumab produces remarkable therapeutic results with good tolerability characteristics. Medical research indicates dupilumab delivers easi-75 responses to 75-85% of patients along with durable outcomes for itch severity and life quality [12,14]. A safety report from this review matches the findings of extensive analyses which show conjunctivitis and injection-site reactions as the most common occurrences although serious adverse events proved to be infrequent [13].

The results from this review on janus kinase (jak) inhibitors upadacitiniband abrocitinib match those of recent randomized trials and network metanalyses. Jak inhibitors show evidence that they yield swift major improvements to eczema severity by reaching easi-75 responses within 8–12 weeks according to previous research [15,16]. Citing this research pattern other research teams have

observed favorable safety outcomes from jak inhibitor treatment yet they have expressed concerns about both prolonged treatment safety risks and immunological suppression potential [16]..

Research investigations have confirmed this review's analysis by demonstrating how targeted therapies perform better than systemic immunosuppressants in effectiveness and protection from adverse effects. Systemic therapy research has found that dupilumab and jak inhibitors generate better clinical outcomes and enhanced life quality than treatments with cyclosporine methotrexate and azathioprine [18].

This review supports earlier research which proved the enhanced effectiveness of systemic agents through topical corticosteroid addition did not result in significant adverse events increment [17].

The review focuses on current difficulties managing severe eczema since it demonstrates how to achieve effective treatment while maintaining long-term safety measures. Evidence collected by other researchers points to long-term safety concerns with jakinhibitors and emphasizes that continuous pharmacovigilance efforts must be ensured to see their complete risk vs benefit picture [16].

According to this review all evidence matches recent studies which support that targeted biologic and small-molecule drugs should be utilized as initial systemic therapy for severe eczema but traditional immunosuppressants remain essential for particular clinical situations.

**Limitations and Implication for Future Research**

Multiple review limitations exist because studies have different research designs and patient demographics along with contrasting outcome metrics [3,12,15]. The results may have been influenced by publication bias because studies with positive outcomes tend to be favored particularly among data regarding the new therapies dupilumab and jak inhibitors [14,16]. The diverse quality levels of studied research contained both small population-sized trials alongside non-randomized experiments which introduced possible biases [6,9].

The analysis unveils insufficient evidence about safety parameters for targeted therapies particularly jak inhibitors because of insufficient data on their long-term clinical risks during continuous utilization [16]. Future investigation must concentrate on performing extensive scale randomized controlled trials that directly compare traditional care methods to targeted treatment approaches alongside extended observational follow-ups to assess long-term safety aspects.

The use of predictive biomarkers to develop personalized treatment strategies and testing combination drug treatments will help optimize management methods [17]. Extensive cost-effectiveness research should be used to determine the economic advantages of new treatment options which will enhance treatment access for patients.

## CONCLUSION

This systematic review highlights the significant advancements in the treatment of severe eczema, emphasizing the superior efficacy and safety of targeted therapies, particularly dupilumab and janus kinase (jak) inhibitors, over traditional systemic immunosuppressants. dupilumabconsistently demonstrated sustained improvements with minimal adverse effects, while jak inhibitors offered rapid symptom relief with acceptable safety profiles. although traditional agents like cyclosporine, methotrexate, and azathioprine remain valuable, their long-term use is limited by safety concerns.

The research findings validate targeted therapy use at the beginning of severe eczema treatment specifically for patients who need extended disease management. Still, extensive safety evaluations and cost-benefit investigations must remain vital. Additional research will concentrate on individualized therapy approaches and advanced treatment optimization and wider availability of innovative therapies in order to enhance disease outcome results.

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