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FEATURES OF THE SELECTION OF CONDITIONING REGIMENS FOR AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH AUTOIMMUNE DISEASES

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Abstract. Autologous hematopoietic stem cell transplantation (AHSCT) has emerged as a promising therapeutic strategy for patients with severe and treatment-refractory autoimmune diseases (ADs), offering the potential for sustained remission through profound immune resetting. The objective of this narrative review is to analyze the key principles and clinical considerations guiding the selection of conditioning regimens for AHSCT across various autoimmune indications. A comprehensive literature search was conducted using PubMed, Scopus, and European Society for Blood and Marrow Transplantation (EBMT) registry data, encompassing studies published between 1998 and 2025. The review identifies three intensity tiers of conditioning regimens—low-intensity (non-myeloablative), intermediate-intensity (immunoablative), and high-intensity (myeloablative)—with intermediate-intensity protocols, specifically cyclophosphamide plus anti-thymocyte globulin (Cy-ATG) and BEAM plus ATG (BEAM-ATG), constituting the current standard. Comparative analyses from EBMT registry data reveal comparable efficacy between Cy-ATG and BEAM-ATG in relapsing-remitting multiple sclerosis, while Cy-ATG demonstrates a superior safety profile. Anti-thymocyte globulin is universally employed across conditioning protocols, though significant variability in dosing and administration persists among transplant centers. Disease-specific factors, including disease type, organ function, comorbidities, and center expertise, critically influence regimen individualization. Metabolic and

electrolyte disturbances during high-dose cyclophosphamide conditioning necessitate close monitoring. Individualized selection of conditioning regimens, guided by disease biology and patient-specific risk factors, remains essential for optimizing transplant outcomes.

Keywords: autologous hematopoietic stem cell transplantation, conditioning regimen, autoimmune diseases, cyclophosphamide, anti-thymocyte globulin, BEAM, immune reconstitution.

Introduction. Autoimmune diseases (ADs) encompass a heterogeneous group of disorders characterized by aberrant immune responses directed against self-antigens, resulting in chronic inflammation and progressive tissue damage across multiple organ systems (Farge et al., 2010). These conditions, including multiple sclerosis (MS), systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA), collectively affect approximately 5–8% of the global population and represent a leading cause of morbidity among young and middle-aged adults. While conventional immunosuppressive therapies and biological agents have substantially improved outcomes for many patients, a significant subset remains refractory to standard treatment approaches, experiencing progressive organ damage, diminished quality of life, and elevated mortality risk (Yang et al., 2024). This unmet therapeutic need has driven the search for more definitive interventions capable of inducing sustained, drug-free remission.

Autologous hematopoietic stem cell transplantation (AHSCT) has emerged as a transformative therapeutic strategy for patients with severe, treatment-refractory ADs. First proposed in the late 1990s, the conceptual basis of AHSCT rests on the principle of immune ablation followed by immune reconstitution, whereby intensive conditioning chemotherapy eliminates the pathogenic immune repertoire, and subsequent infusion of autologous hematopoietic stem cells facilitates the regeneration of a new, self-tolerant immune system (Burt et al., 1998). This approach extends beyond conventional immunosuppression by targeting the fundamental immunological dysregulation underlying autoimmune pathology, rather than merely suppressing its downstream effector mechanisms.

The biological rationale supporting AHSCT in ADs is multifaceted and increasingly well characterized. The conditioning regimen achieves elimination of

autoreactive T and B lymphocytes, including long-lived memory cells that perpetuate disease activity despite conventional immunosuppression. Following transplantation, immune reconstitution proceeds through several complementary mechanisms: thymic reactivation enables de novo generation of naive T cells with a diversified T-cell receptor (TCR) repertoire, effectively replacing the oligoclonal, autoreactive repertoire that characterized the pre-transplant immune system (van Rhijn-Brouwer et al., 2018). Concurrently, expansion of regulatory T cells expressing the transcription factor FoxP3 (Tregs) contributes to the restoration of peripheral immunological tolerance. These processes collectively result in a fundamental resetting of the adaptive immune system, providing the mechanistic basis for the sustained disease remissions observed following AHSCT (Oliveira et al., 2018).

Over the past two decades, accumulating evidence from prospective clinical trials, registry analyses, and observational studies has progressively validated the efficacy and safety of AHSCT in selected autoimmune indications. Current guidelines from the European Society for Blood and Marrow Transplantation (EBMT) now recognize AHSCT as a standard of care for highly active relapsing-remitting multiple sclerosis (RRMS) that has failed conventional disease-modifying therapies, as well as for early severe diffuse-cutaneous systemic sclerosis (dcSSc), where randomized controlled trials have demonstrated significant survival and event-free survival advantages over conventional treatment (Farge et al., 2010; Yang et al., 2024). The application of AHSCT continues to expand to additional autoimmune indications, including SLE, Crohn's disease, and refractory cytopenias, driven by growing clinical experience and improved transplant outcomes.

Central to the success and safety of AHSCT is the selection of an appropriate conditioning regimen—the chemotherapeutic protocol administered prior to stem cell infusion that determines the depth of immune ablation and, consequently, both the therapeutic efficacy and the toxicity profile of the procedure. The choice of conditioning regimen represents a critical clinical decision that must balance sufficient immunoablative intensity to eradicate autoreactive clones against acceptable treatment-related morbidity and mortality. The objective of this review is to analyze the key features and principles guiding the selection of conditioning regimens for AHSCT in patients with various autoimmune diseases, synthesizing current evidence on regimen

composition, intensity classification, disease-specific considerations, and emerging challenges in the field.

Methods. This study was designed as a narrative review of the current clinical literature pertaining to conditioning regimens for autologous hematopoietic stem cell transplantation in patients with autoimmune diseases. A narrative review methodology was selected as the most appropriate approach given the heterogeneity of study designs, disease indications, and regimen protocols in this field, which precludes formal systematic review or meta-analytic synthesis.

A comprehensive literature search was conducted across multiple electronic databases, including PubMed/MEDLINE and Scopus, supplemented by data from the European Society for Blood and Marrow Transplantation (EBMT) Autoimmune Diseases Working Party (ADWP) registry and published clinical practice guidelines. The search was performed for articles published between 1998 and 2025, reflecting the period from the earliest clinical applications of AHSCT in autoimmune diseases through the most recent available evidence. The search was restricted to publications in the English language.

Key search terms employed, individually and in combination, included: “autologous HSCT,” “condditioning regimen,” “autoimmune diseases,” “BEAM,” “cyclophosphamide,” “anti-thymocyte globulin,” “ATG,” and “immune reconstitution.” Boolean operators (AND, OR) were used to combine search terms, and reference lists of identified articles were manually screened for additional relevant publications.

Inclusion criteria encompassed original research articles, registry analyses, clinical trial reports, and clinical practice guidelines that addressed conditioning regimen selection, composition, or outcomes for AHSCT in adult patients with autoimmune diseases. Review articles and expert consensus statements were included when they provided substantive discussion of regimen design principles. Studies focusing exclusively on allogeneic transplantation or pediatric populations were excluded.

Data extracted from identified studies included: conditioning regimen components and dosing schedules, disease indications, efficacy outcomes (including no evidence of disease activity [NEDA], progression-free survival [PFS], and overall survival [OS]), safety and toxicity profiles, and treatment-related mortality (TRM).

Findings were synthesized narratively and organized thematically according to regimen classification, comparative efficacy, and disease-specific considerations.

Results and Discussion. Classification of Conditioning Regimen Intensity

Conditioning regimens employed for AHSCT in autoimmune diseases are classified into three intensity tiers based on their degree of myeloablative and immunoablative activity, a framework that has evolved substantially as clinical experience has accrued over the past two decades (Greco et al., 2025). This classification system directly influences both the therapeutic potential and the toxicity risk of the transplant procedure, making it a foundational consideration in regimen selection.

Low-intensity or non-myeloablative regimens are characterized by the use of high-dose cyclophosphamide alone (HD-Cy), typically administered at a total dose of 200 mg/kg divided over four days. These regimens preserve bone marrow function and hematopoietic recovery proceeds primarily from endogenous residual stem cells rather than the reinfused graft. Low-intensity conditioning has been employed in selected neurological autoimmune diseases and offers the advantage of reduced treatment-related morbidity and mortality. However, this benefit is potentially offset by a lower depth of immunoablation, which may be insufficient to eradicate deeply embedded autoreactive clones in certain disease settings (Bonnin et al., 2023).

Intermediate-intensity or immunoablative regimens represent the most widely employed conditioning approach in contemporary AHSCT practice for autoimmune diseases. The two dominant protocols in this category are BEAM-ATG (carmustine, etoposide, cytarabine, melphalan, and anti-thymocyte globulin) and Cy-ATG (cyclophosphamide and anti-thymocyte globulin). These regimens achieve profound lymphodepletion and effective immune ablation while avoiding the full myeloablative toxicity associated with higher-intensity protocols. The intermediate-intensity approach targets the lymphoid compartment with sufficient intensity to enable meaningful immune resetting while maintaining an acceptable safety profile (Ismail et al., 2024).

High-intensity or myeloablative regimens historically included protocols containing total body irradiation (TBI) or busulfan-based combinations. While these regimens achieved the deepest immune ablation, they were associated with unacceptably high rates of treatment-related mortality, prolonged aplasia, and severe

long-term complications including secondary malignancies and infertility. Accumulating evidence of their unfavorable risk-benefit ratio has led to their progressive abandonment, and current EBMT guidelines no longer recommend myeloablative conditioning for autoimmune disease indications (Greco et al., 2025). The field has thus converged on intermediate-intensity regimens as the standard of care, with ongoing refinement focused on optimizing the balance between immunoablative efficacy and treatment-related toxicity.

The Two Dominant Intermediate-Intensity Regimens: BEAM-ATG versus Cy-ATG

The two intermediate-intensity conditioning regimens that dominate current clinical practice—BEAM-ATG and Cy-ATG—differ substantially in their pharmacological composition, mechanisms of immune ablation, and toxicity profiles. Understanding these differences is essential for evidence-based regimen selection across autoimmune indications.

The BEAM-ATG regimen is a multi-agent chemotherapy protocol originally developed for lymphoma conditioning and subsequently adapted for autoimmune disease applications. The standard protocol comprises carmustine (BCNU) at 300 mg/m^2 administered on day −7, etoposide at 100 mg/m^2 twice daily on days −6 through −3 (total dose 800 mg/m^2), cytarabine (Ara-C) at 800 mg/m^2 as a continuous infusion on days −6 through −3, and melphalan at 140 mg/m^2 on day −2. Rabbit anti-thymocyte globulin (thymoglobulin) is added at a total dose of 5 mg/kg, administered on days +1 and +2 following stem cell infusion. This combination achieves potent lymphoablation through complementary cytotoxic mechanisms targeting rapidly dividing lymphocytes (Greco et al., 2025).

The Cy-ATG regimen employs a simpler two-agent approach consisting of cyclophosphamide at a total dose of 200 mg/kg (typically divided over four consecutive days at 50 mg/kg/day) combined with rabbit ATG at a total dose of 6 mg/kg. Cyclophosphamide, an alkylating agent, exerts its immunoablative effect through DNA cross-linking in rapidly proliferating lymphocytes, while sparing quiescent hematopoietic stem cells due to their high expression of aldehyde dehydrogenase, which detoxifies the active cyclophosphamide metabolite. The addition of ATG provides complement-mediated and antibody-dependent cellular cytotoxicity against mature T

lymphocytes, augmenting the immunoablative depth of the conditioning protocol (Greco et al., 2025).

Comparative efficacy data between these two regimens have been generated primarily from retrospective registry analyses, the most comprehensive of which is the EBMT Autoimmune Diseases Working Party study encompassing 1,114 patients with relapsing-remitting multiple sclerosis (RRMS). In this analysis, NEDA failure rates at five years were 42.3% in the BEAM-ATG group compared with 44.1% in the Cy-ATG group, a difference that did not reach statistical significance ($p = 0.081$). After multivariable adjustment for baseline demographic and clinical covariates, the hazard ratio for NEDA failure with BEAM-ATG versus Cy-ATG was 0.90 (95% CI: 0.61–1.34, $p = 0.60$), confirming the absence of a significant efficacy differential between regimens in this indication (Greco et al., 2025).

Despite comparable efficacy, the safety profiles of these two regimens diverge markedly. The BEAM-ATG protocol is associated with significantly higher rates of severe adverse events, including grade 3–4 mucositis, febrile neutropenia, septicemia, Epstein-Barr virus (EBV) reactivation, bacterial infections, and hepatotoxicity. Average hospitalization duration is approximately three days longer in patients receiving BEAM-ATG compared with Cy-ATG ($p < 0.001$), reflecting the greater mucosal and hematological toxicity of the multi-agent regimen (Burman et al., 2024). A trend toward superior magnetic resonance imaging (MRI) outcomes has been observed with BEAM-ATG, suggesting potentially deeper immunoablation at the central nervous system level, but this finding requires validation in prospective randomized trials.

On the basis of currently available evidence, Cy-ATG may be preferred as the conditioning regimen for RRMS due to its favorable safety profile in the context of equivalent clinical efficacy. However, the retrospective nature of existing comparative data and potential unmeasured confounders necessitate confirmation through adequately powered, prospective randomized controlled trials before definitive recommendations can be established (Greco et al., 2025; Burman et al., 2024).

The Role of Anti-Thymocyte Globulin in Conditioning

Anti-thymocyte globulin (ATG) constitutes a central and indispensable component of virtually all conditioning regimens currently employed for AHSCT in

autoimmune diseases. A comprehensive survey of EBMT-affiliated transplant centers conducting AHSCT for autoimmune indications revealed that 100% of responding centers incorporate ATG into their conditioning protocols, underscoring its perceived importance in achieving adequate immune ablation and facilitating immune reconstitution (Ismail et al., 2024).

The immunological mechanisms through which ATG contributes to the conditioning process are multifaceted. ATG is a polyclonal immunoglobulin preparation derived from the immunization of rabbits or horses with human thymocytes, generating antibodies directed against a broad array of T-cell surface antigens. In the conditioning setting, ATG achieves profound in vivo T-cell depletion through complement-mediated lysis and antibody-dependent cellular cytotoxicity. Critically, ATG also targets autoreactive lymphocytes residing in tissue compartments including lymph nodes and bone marrow, as well as long-lived plasma cells that may serve as reservoirs of autoantibody production. Furthermore, ATG depletes T lymphocytes present in the reinfused autologous graft, thereby reducing the risk of reintroducing autoreactive T-cell clones during immune reconstitution. This multifaceted mechanism of action makes ATG a key contributor to the immune resetting process that underlies the therapeutic benefit of AHSCT (Ismail et al., 2024).

Among ATG preparations, rabbit-derived formulations predominate in clinical practice. Thymoglobulin® (Sanofi-Genzyme) is the most widely used preparation, employed by 89.1% of surveyed EBMT centers, with Grafalon® (Neovii) used in the remaining centers. Horse-derived ATG preparations are used less frequently. The choice of ATG preparation is clinically relevant, as different products vary in their antigenic specificity, pharmacokinetic properties, and immunomodulatory effects (Ismail et al., 2024).

Significant variability in ATG dosing practices exists across transplant centers. The EBMT survey documented that 32.6% of centers employ a total dose of 7.5 mg/kg, while 53.6% use total doses below 7.5 mg/kg. Doses are typically fractionated over three to five consecutive days to improve tolerability and reduce the incidence of infusion-related reactions. The pharmacokinetics of ATG are complex and influenced by the patient's absolute lymphocyte count at the time of administration, as circulating lymphocytes serve as an antigen sink that binds and consumes ATG antibodies. This

pharmacokinetic variability has clinical implications: studies in systemic sclerosis have demonstrated that higher ATG exposure correlates with superior treatment response, even at identical weight-based dosing, suggesting that lymphocyte-count-adjusted or pharmacokinetics-guided dosing may optimize outcomes (Ismail et al., 2024).

Emerging data indicate that some centers are incorporating rituximab as an adjunctive serotherapeutic agent. The EBMT survey identified 12 centers (26.1%) that use rituximab in addition to ATG in their conditioning protocols, targeting CD20-positive B lymphocytes to enhance depletion of the autoreactive B-cell compartment. Notably, no center currently employs alemtuzumab, an anti-CD52 monoclonal antibody, in the conditioning setting. Premedication prior to ATG administration is universally applied, consisting of antihistamines (100% of centers), corticosteroids (98%), and paracetamol (91.1%), reflecting the well-established risk of infusion-related cytokine release reactions (Ismail et al., 2024).

Disease-Specific Considerations in Regimen Selection

The selection of an optimal conditioning regimen for AHSCT is fundamentally influenced by the specific autoimmune disease being treated, as each condition presents distinct pathobiological features, organ involvement patterns, and treatment-related risk profiles that necessitate individualized approaches to regimen design.

Multiple sclerosis represents the most frequent autoimmune indication for AHSCT globally, and the evidence base for conditioning regimen selection is most developed in this disease. Current evidence supports the use of intermediate-intensity conditioning with either Cy-ATG or BEAM-ATG for patients with highly active RRMS who have failed conventional disease-modifying therapies. The type and phase of MS represent the major determinants of neurological outcome following AHSCT: patients with active inflammatory relapsing-remitting disease derive the greatest benefit, while those with progressive forms of MS, in which neurodegeneration proceeds independently of ongoing autoimmune inflammation, respond poorly regardless of conditioning intensity (Greco et al., 2025). This observation underscores the critical importance of early patient selection, ideally during the inflammatory phase of disease when immune-mediated mechanisms remain the dominant driver of disability progression. A landmark phase III randomized controlled trial demonstrated that conditioning with cyclophosphamide 200 mg/kg plus ATG 6 mg/kg followed by AHSCT

was superior to approved disease-modifying therapies in preventing disease progression in RRMS, providing the highest level of evidence supporting this regimen in this indication (Farge et al., 2010).

Systemic sclerosis, specifically early severe diffuse-cutaneous systemic sclerosis (dcSSc), represents the second major indication for which AHSCT has achieved standard-of-care status. Two large randomized controlled trials—the ASSIST and SCOT trials—demonstrated significant overall survival and event-free survival advantages of AHSCT over monthly intravenous cyclophosphamide pulse therapy. Contemporary protocols employing nonmyeloablative conditioning with cyclophosphamide 200 mg/kg and ATG, combined with unmanipulated peripheral blood stem cells and mycophenolate mofetil (MMF) maintenance therapy, have achieved overall survival rates of 85% and event-free survival of 75% at five years (Denton et al., 2012). However, AHSCT in SSc carries particular complexity due to the multisystem nature of the disease. Key risk factors include a low pretransplant estimated glomerular filtration rate (eGFR < 65–75 mL/min/1.73 m^2), which significantly increases transplant-related morbidity and mortality. All treating centers report complications during conditioning, including cardiac toxicity, scleroderma renal crisis, and interstitial pneumonitis. Consequently, corticosteroid premedication and meticulous renal function monitoring throughout the conditioning phase are considered essential components of safe transplant delivery in this population (Ismail et al., 2024).

Systemic lupus erythematosus (SLE) represents a more complex and less uniformly successful indication for AHSCT. Approximately 50% of transplanted patients with SLE remain disease-free at five years, a response rate that, while meaningful, is lower than that observed in MS. Treatment-related mortality in SLE ranges from 4% to 12% depending on center experience, patient selection, and conditioning intensity, reflecting both the severity of the underlying disease and the comorbidities associated with longstanding SLE, including renal impairment, cytopenias, and prior cumulative immunosuppressive exposure (Farge et al., 2010). Immunological studies have documented TCR repertoire renewal and thymic reactivation following AHSCT in SLE patients, confirming that the fundamental immune resetting mechanisms operate in this disease. Regimen selection in SLE requires balanced consideration of the specific

pattern of organ involvement, as patients with significant renal or cardiac disease may be at elevated risk for conditioning-related toxicity (Jain et al., 2016).

Other autoimmune diseases for which AHSCT has been applied include rheumatoid arthritis, Crohn's disease, neuromyelitis optica spectrum disorders, and autoimmune cytopenias. Patient numbers in these indications remain smaller, and the evidence base is correspondingly less robust. Regimen selection in these conditions is guided primarily by organ function and comorbidities, disease severity, prior treatment history, and extrapolation from more extensively studied indications. Some centers have employed reduced-intensity protocols such as cyclophosphamide-fludarabine-ATG combinations in patients with significant comorbidities or compromised organ function, accepting a potentially lower depth of immune ablation in exchange for improved tolerability (Jain et al., 2016; Ismail et al., 2024).

Metabolic and Electrolyte Considerations During Conditioning

High-dose cyclophosphamide conditioning, a cornerstone of AHSCT protocols for autoimmune diseases, produces significant metabolic and electrolyte disturbances that require systematic monitoring and proactive clinical management. These alterations, while often overshadowed by the hematological and immunological effects of conditioning, can result in clinically significant complications if unrecognized or inadequately managed.

A prospective study conducted in 75 patients with multiple sclerosis undergoing AHSCT with a nonmyeloablative protocol consisting of cyclophosphamide 200 mg/kg combined with rituximab 1,000 mg (referred to as the "Mexican method") systematically characterized the metabolic consequences of conditioning. Significant changes in both serum and urinary electrolyte concentrations were documented following cyclophosphamide delivery. Notably, 16% of patients developed hyponatremia during the conditioning period, with two patients experiencing hyponatremia-induced seizures requiring emergency hospitalization and intensive electrolyte correction. Drug-induced hyperglycemia and elevated serum uric acid concentrations were also observed as consistent metabolic perturbations. Serial monitoring demonstrated statistically significant decreases in serum calcium, sodium, and potassium concentrations following cyclophosphamide administration, likely reflecting a combination of direct renal tubular effects, inappropriate antidiuretic

hormone secretion, and dilutional mechanisms associated with the high-volume intravenous hydration required to prevent hemorrhagic cystitis. Importantly, no evidence of permanent renal function damage was detected at day 0 of stem cell infusion, suggesting that these metabolic disturbances are largely transient and reversible with appropriate supportive care (Méndez-Laureano et al., 2023).

Cardiac toxicity represents another important consideration during high-dose cyclophosphamide conditioning, particularly at the cumulative doses employed in AHSCT protocols. An innovative approach to mitigating this risk is the split-cyclophosphamide protocol, in which the total cyclophosphamide dose is divided into two administration blocks separated by a rest interval rather than delivered over consecutive days. This approach has demonstrated an excellent cardiac safety profile, avoiding the peak myocardial exposure and associated cardiotoxicity that can occur with the standard four-day continuous administration schedule. The split-Cy protocol preserves the total immunoablative dose while distributing the cardiac metabolic burden more favorably over time (Olivares-Gazca et al., 2022).

The clinical implications of these findings are significant for transplant practice. Close monitoring of serum electrolytes, metabolic parameters, and cardiac function throughout the conditioning phase is mandatory for all patients undergoing AHSCT with cyclophosphamide-containing regimens. Supportive care protocols must be tailored to the specific comorbidities associated with each autoimmune disease, recognizing that patients with systemic sclerosis may have pre-existing cardiac and renal compromise, while patients with SLE may present with baseline electrolyte abnormalities related to prior nephritis or chronic corticosteroid use. Standardized monitoring and management protocols, incorporating lessons from prospective metabolic studies, represent an important component of safe and effective conditioning regimen delivery (Méndez-Laureano et al., 2023; Olivares-Gazca et al., 2022).

Synthesis and Future Directions

The evidence reviewed in the preceding sections converges on a central conclusion: no single, universally superior conditioning regimen exists for AHSCT across all autoimmune disease indications. The heterogeneity of autoimmune diseases in their pathobiology, organ involvement, and response to immune ablation necessitates

a fundamentally individualized approach to conditioning regimen selection, guided by multiple interdependent clinical and biological factors.

Regimen selection must be individualized based on a comprehensive assessment of five key determinants: (1) the specific autoimmune disease type and its current phase of activity, recognizing that inflammatory and degenerative phases may respond differentially to immune ablation; (2) organ function and existing comorbidities, particularly cardiac, renal, and hepatic reserve, which directly influence the tolerability of conditioning chemotherapy; (3) prior treatment history and cumulative immunosuppressive exposure, which may affect bone marrow reserve and infectious risk; (4) center expertise and transplant volume, which correlate with treatment-related mortality and overall outcomes; and (5) patient age and performance status, which modulate both the feasibility of intensive conditioning and the capacity for immune reconstitution following transplantation (Ismail et al., 2024; Greco et al., 2025).

The progressive shift away from myeloablative and TBI-containing conditioning regimens toward intermediate-intensity protocols based on Cy-ATG or BEAM-ATG reflects the field's improved understanding of the toxicity-efficacy balance in AHSCT for autoimmune diseases. This evolution has been driven by the recognition that effective immune resetting can be achieved without full myeloablation, provided that the conditioning protocol incorporates adequate lymphoablative and serotherapeutic components to eliminate autoreactive clones and facilitate de novo immune regeneration (Bonnin et al., 2023). Anti-thymocyte globulin remains indispensable in contemporary conditioning protocols, and the emergence of rituximab as an adjunctive agent reflects the growing appreciation of the B-cell compartment's contribution to autoimmune pathogenesis.

Notwithstanding this progress, standardization of ATG dosing and administration schemes across transplant centers remains an open challenge. The EBMT survey documented substantial variability in ATG product selection, total dose, fractionation schedule, and timing relative to stem cell infusion, variability that likely contributes to heterogeneity in transplant outcomes (Ismail et al., 2024). The influence of pharmacokinetic factors, particularly the relationship between pre-conditioning lymphocyte counts and effective ATG exposure, suggests that fixed weight-based dosing

may be suboptimal and that pharmacokinetics-guided individualized dosing could improve consistency of immune ablation across patients.

Several priority areas for future investigation emerge from this analysis. Pharmacokinetics-guided ATG dosing represents a promising avenue for optimizing conditioning intensity while minimizing toxicity. Prospective randomized controlled trials directly comparing Cy-ATG and BEAM-ATG across multiple autoimmune indications are urgently needed to replace the current reliance on retrospective registry data. Biomarker-based patient stratification, incorporating pre-transplant immune profiling and disease activity metrics, may enable more precise matching of conditioning intensity to individual patient risk profiles. Finally, the continued development of collaborative multicenter registries, exemplified by the EBMT Autoimmune Diseases Working Party, remains critical for generating the large-scale, standardized outcome data required to refine evidence-based guidelines for conditioning regimen selection in this evolving therapeutic landscape (van Rhijn-Brouwer et al., 2018; Greco et al., 2025).

Conclusion. The selection of conditioning regimens for autologous hematopoietic stem cell transplantation in patients with autoimmune diseases represents a multidimensional clinical decision that must integrate disease-specific pathobiology, patient-level risk factors, and center-level expertise to optimize both therapeutic efficacy and safety. This narrative review has identified the intermediate-intensity protocols—cyclophosphamide plus anti-thymocyte globulin (Cy-ATG) and BEAM plus ATG (BEAM-ATG)—as the current standard of care, having replaced the earlier myeloablative and TBI-containing regimens that carried unacceptable treatment-related mortality. Comparative evidence from large registry analyses demonstrates that Cy-ATG and BEAM-ATG achieve comparable efficacy in the most extensively studied indication, relapsing-remitting multiple sclerosis, while Cy-ATG offers a significantly superior safety profile with lower rates of severe adverse events and shorter hospitalization. These findings support the preferential use of Cy-ATG in this patient population, pending confirmation from prospective randomized controlled trials.

References:

1. Bonnin, A., Terriou, L., Beuvon, C., Tudesq, J., Puyade, M., Pugnet, G., Maria, A., Castilla-Llorente, C., Lansiaux, P., Cacciatore, C., Badoglio, M., Yakoub-Agha, I.,

Farge-Bancel, D., & Marjanovic, Z. (2023). Mobilization and conditioning protocols actualization for autologous stem cell transplantation for autoimmune diseases: Guidelines from MATHEC-SFGM-TC. Bulletin du Cancer, 110(10). https://doi.org/10.1016/j.bulcar.2023.09.002

2. Burman, J., Tolf, A., Hägglund, H., & Askmark, H. (2024). BEAM or cyclophosphamide in autologous haematopoietic stem cell transplantation for multiple sclerosis. Bone Marrow Transplantation, 59. PMC11530369.

3. Burt, R. K., Traynor, A. E., Pope, R., Schroeder, J., Cohen, B., Karlin, K., Lobeck, L., Goolsby, C., Rowlings, P., Davis, F. A., Stefoski, D., Terry, C., Keever-Taylor, C., Rosen, S., Vesole, D., Fishman, M., Brush, M., Mujias, S., Villa, M., & Burns, W. H. (1998). Treatment of autoimmune disease by intense immunosuppressive conditioning and autologous hematopoietic stem cell transplantation. Blood, 92(10), 3505–3514. https://doi.org/10.1182/BLOOD.V92.10.3505.422K48_3505_3514

4. Denton, C., Hawkey, C., Peters, C., Farge, D., Mancardi, G., Moore, J., Passweg, J., Snowden, J., van Laar, J., Allez, M., Labopin, M., Rabusin, M., Rovira, M., Arnold, R., Cervera, R., Martin, R., Saccardi, R., & Ardizzone, S. (2012). Haematopoietic SCT in severe autoimmune diseases: Updated guidelines of the European Group for Blood and Marrow Transplantation. Bone Marrow Transplantation, 47(6), 770–775. https://doi.org/10.1038/bmt.2011.185

5. Farge, D., Labopin, M., Tyndall, A., Fassas, A., Mancardi, G. L., Van Laar, J., Ouyang, J., Kozak, T., Moore, J., Marmont, A. M., Saccardi, R., & Gratwohl, A. (2010). Autologous hematopoietic stem cell transplantation for autoimmune diseases: An observational study on 12 years' experience from the European Group for Blood and Marrow Transplantation Working Party on Autoimmune Diseases. Haematologica, 95(2), 284–292. https://doi.org/10.3324/haematol.2009.013458

6. Greco, R., Saccardi, R., Ponzano, M., Badoglio, M., Helbig, G., Śmiłowski, M., Mariottini, A., Burman, J., Carlson, K., Kazmi, M., Muraro, P., Gabriel, I., Withers, B., Massey, J., Varaldo, R., Inglese, M., Sanz, J., Gil-Perotín, S., Sharrack, B., Roldan, E., Nozzoli, C., Signori, A., Sormani, M. P., Alexander, T., & Snowden, J. A. (2025). BEAM/ATG or cyclophosphamide/ATG as conditioning regimen in autologous haemopoietic stem cell transplantation for multiple sclerosis: A retrospective

analysis of the EBMT Autoimmune Diseases Working Party. Bone Marrow Transplantation. https://doi.org/10.1038/s41409-025-02715-x

7. Ismail, A., Nitti, R., Sharrack, B., Badoglio, M., Labopin, M., Ambron, P., Greco, R., & Alexander, T. (2024). ATG and other serotherapy in conditioning regimens for autologous HSCT in autoimmune diseases: A survey on behalf of the EBMT Autoimmune Diseases Working Party (ADWP). Bone Marrow Transplantation, 59, 1614–1617. https://doi.org/10.1038/s41409-024-02383-3
8. Jain, S., Ramaswamy, S., & Ravindran, V. (2016). Hematopoietic stem cell transplantation for autoimmune rheumatic diseases. World Journal of Transplantation, 6(1), 199–212. https://doi.org/10.5500/wjt.v6.i1.199
9. Méndez-Laureano, B. J., Gallardo-Pérez, M., Minutti-Zanella, C., & Ruiz-Argüelles, G. J. (2023). Serum electrolyte and metabolic changes during conditioning of autologous hematopoietic stem cell transplantation in patients with autoimmune diseases: A prospective study in a single institution. Mediterranean Journal of Hematology and Infectious Diseases, 15(1). https://doi.org/10.56875/2589-0646.1106
10. Olivares-Gazca, J. C., Guerrero-Pesqueira, F., Murrieta-Alvarez, I., Cantero-Fortiz, Y., León-Peña, A., Priesca-Marín, M., Gómez-Almaguer, D., Gómez-De-León, A., Ruiz-Delgado, G. J., & Ruiz-Argüelles, G. J. (2022). Cyclophosphamide split in two blocks apart renders an excellent cardiac safety profile during conditioning regimen for autologous hematopoietic stem cell transplantation for multiple sclerosis and other autoimmune disorders. Transplantation and Cellular Therapy, 28(3). https://doi.org/10.1016/s2666-6367(22)00462-6
11. Oliveira, G. L. V., Lima-Júnior, J. R., de Azevedo, J. T. D., Malmegrim, K. C. R., Arruda, L. C. M., & Oliveira, M. C. (2018). Autologous hematopoietic stem cell transplantation for autoimmune diseases: From mechanistic insights to biomarkers. Frontiers in Immunology, 9, 2602. https://doi.org/10.3389/fimmu.2018.02602
12. Polushin, A., Lopatina, E., Tsynchenko, A., Zalyalov, Y. R., Skiba, I., Shegurova, A. V., Totolyan, N. A., Kulagin, A., Ionova, T., Nikitina, T. P., Porfirieva, N., & Skoromets, A. A. (2024). Quality of life of patients with multiple sclerosis after high-dose immunosuppressive therapy with autologous hematopoietic stem cell transplantation. Russian Neurological Journal, 29(1), 25–35. https://doi.org/10.30629/2658-7947-2024-29-1-25-35

13. van Rhijn-Brouwer, F. C. C., van Wijk, F., Spierings, J., van Laar, J. M., & Lutter, L. (2018). Resetting the T cell compartment in autoimmune diseases with autologous hematopoietic stem cell transplantation: An update. Frontiers in Immunology, 9, 767. https://doi.org/10.3389/fimmu.2018.00767
14. Yang, G., Wei, J., Guo, L., Song, Q., Wang, R., Huang, R., Yang, S.-J., Zhang, X., Wang, X., Xu, Y., & Hu, Z. (2024). Advances in hematopoietic stem cell transplantation for autoimmune diseases. Heliyon, 10(20), e39302. https://doi.org/10.1016/j.heliyon.2024.e39302
15. Gazkhanovna, M. A., Makhmatovich, A. K., & Utkirovich, D. U. (2022). Clinical efficacy of extracorporeal and intravascular hemocorrection methods in psoriasis. Academicia: An International Multidisciplinary Research Journal, 12(2), 313-318.
16. Madasheva, A. G., & Abdiev, K. M. (2023). Blood transfusion therapy in patients with vitamin B12 deficiency anemia after resection of 2/3 of the stomach. Science and Education, 4(5), 407-412.
17. Мадашева, А. Г., & Жураева, М. З. (2019). Биохимические показатели и комплексное лечение больных псориазом с лечебным плазмаферезом. Достижения науки и образования, (10 (51)), 78-82.
18. Мадашева, А., Бергер, И., Махмудова, А., Абдиев, К., & Амерова, Д. (2025). Лабораторная диагностика. восточная европа. лабораторная диагностика, 14(1), 87-96.
19. Мадашева, А. Г. (2022). Клинико-неврологические изменения у больных гемофилией с мышечными патологиями. Science and Education, 3(12), 175-181.
20. Мадашева, А. Г. (2022). Коррекция диффузной алопеции при железодефицитной анемии. Science and Education, 3(12), 231-236.
21. Мадашева, А. Г., Дадажанов, У. Д., Абдиев, К. М., Маматкулова, Ф. Х., & Махмудова, А. Д. (2019). Динамика электронейромиографических показателей и эффективность электрической стимуляции мышц у больных гемофилией с мышечными атрофиями. Достижения науки и образования, (10 (51)), 26-30.