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Safety and Efficacy of Stem Cell Therapy on the Treatment for Multiple Sclerosis

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ABSTRACT

Background: *Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system characterized by inflammation, axonal injury, and progressive neurological decline. Current disease-modifying therapies (DMTs) reduce relapse rates but remain insufficient for halting neurodegeneration or promoting repair, particularly in progressive MS. Stem cell–based therapies have emerged as promising strategies by integrating immunomodulation, neuroprotection, and remyelination.*

Objective: *This review critically evaluates the therapeutic potential, mechanisms of action, clinical evidence, and translational challenges of stem cell–based interventions for MS.*

Methods: *A comprehensive synthesis of preclinical and clinical studies was performed, emphasizing randomized controlled trials, systematic reviews, and meta-analyses evaluating autologous hematopoietic stem cell transplantation (aHSCT), mesenchymal stem cells (MSCs), neural stem/progenitor cells (NSPCs), and induced pluripotent stem cells (iPSCs).*

Results: *aHSCT achieves durable immune "resetting" and superior relapse and disability outcomes compared with high-efficacy DMTs in aggressive relapsing MS, albeit with significant procedure-related risks. MSCs exhibit favorable safety and potent paracrine immunomodulatory and neuroprotective actions; however, efficacy signals across trials remain inconsistent, underscoring the need for standardized dosing, delivery routes, and larger multicenter studies. Early investigations of NSPCs and iPSC-derived oligodendrocyte progenitors demonstrate feasibility and remyelinating potential but remain preclinical or early phase. Across modalities, mechanistic studies highlight immunoregulation, trophic support, microglial modulation, and restoration of metabolic resilience as central pathways. Emerging biomarkers, including neurofilament light (NfL), glial fibrillary acidic protein (GFAP), and advanced imaging metrics, are being integrated to establish causal links between biological effect and clinical outcome.*

Conclusions: *Stem cell therapies represent a transformative avenue for MS treatment, offering potential beyond immunosuppression to promote central repair. aHSCT provides high-potency immune reconstitution but at higher procedural risk, while MSCs deliver safer, paracrine-driven neurorepair with unresolved efficacy. Translation to clinical practice will require harmonized manufacturing*

standards, long-term efficacy data, biomarker integration, and equitable access frameworks. Rigorous phase 3 trials are critical to define safety, efficacy, and positioning within MS care paradigms.

Keywords
Multiple Sclerosis, Stem Cell.

Introduction

Multiple sclerosis (MS) is an autoimmune disorder characterized by immune-mediated damage to the myelin sheath of central nervous system axons, leading to neurological dysfunction [1]. Although inflammation is the primary driver of demyelination, reduced oxygen availability has also been observed in affected brain regions, where it exacerbates injury by reinforcing a bidirectional cycle with neuroinflammation [2]. While remyelination can partially restore function, demyelinated axons remain highly susceptible to degeneration, particularly under hypoxic conditions, contributing to progressive and irreversible disability. Current disease-modifying therapies (DMTs) effectively reduce relapse rates and inflammatory activity in relapsing-remitting MS, but their benefits are limited in progressive disease, and they fail to halt long-term neurodegeneration or disability progression [3]. Moreover, variable patient responses and risks such as infection and systemic toxicity further constrain their utility [4]. These limitations underscore the urgent need for therapeutic approaches that go beyond immunosuppression to promote neuroprotection, enhance remyelination, and leverage endogenous tissue responses to hypoxia during repair.

Preclinical and early translational studies suggest that stem cell–based approaches hold promise in MS by combining immunomodulatory and regenerative mechanisms. Among these, autologous hematopoietic stem cell transplantation (aHSCT) has shown the capacity to induce durable immune "resetting," with early-phase clinical trials in both relapsing-remitting and progressive MS demonstrating reduced inflammatory activity, stabilization of disability, and improvement in selected functional outcomes [5]. In parallel**,** mesenchymal stem cells (MSCs) derived from bone marrow, adipose tissue, or umbilical cord exhibit potent immunomodulatory and neuroprotective effects, mediated in part by trophic factor secretion that promotes oligodendrocyte survival, differentiation, and remyelination in experimental demyelination models [6]. Neural progenitor cells (NPCs) from the subventricular zone also show the ability to generate new oligodendrocytes and restore myelin in preclinical studies, while umbilical cord–derived MSCs are of particular interest for their enhanced proliferative capacity and translational potential [7]. Together, these modalities illustrate the multifaceted potential of stem cell–based therapies to not only recalibrate aberrant immunity but also foster structural repair, positioning them as leading candidates to address the dual challenges of inflammation and neurodegeneration in MS.

In addition to their remyelinating potential, MSCs exert protective effects on neurons by reducing oxidative stress and inflammatory cascades, mechanisms that may mitigate progressive axonal degeneration and secondary tissue loss [8,9]. Early-phase clinical studies in relapsing-remitting and progressive MS have reported encouraging signals, reduced inflammatory activity, stabilization of disability, and improvements in selected functional outcomes [10,11]. Expanded cord tissue–derived umbilical MSCs are being investigated for their enhanced proliferative capacity and potential clinical applicability [12].

Despite these advances, stem cell therapy for MS remains investigational. Current evidence underscores the need for long-term efficacy data (≥5–10 years), standardized protocols for delivery and dosing, and multicenter randomized controlled trials to establish safety, reproducibility, and cost-effectiveness [13,14]. Until such evidence is available, stem cell–based approaches should be considered experimental and delivered within controlled research environments.

Stem Cell Modalities in MS Treatment

Autologous Hematopoietic Stem Cell Transplantation (aHSCT)

aHSCT aims to "reset" adaptive immunity by cytotoxic conditioning (e.g., cyclophosphamide, ATG ± busulfan) followed by autologous $CD34^+$ hematopoietic rescue, thereby extinguishing autoreactive clones that drive inflammatory disease activity in MS. Several factors are known to be influenced on the successful rate of aHSCT in patients with MS. Muraro and colleagues evaluated long-term cohort and registry reports from a multicenter series (n=281; predominantly progressive MS) observing 5-year progression-free survival ~46% and 100-day transplant-related mortality (TRM) 2.8%, quantifying durable benefit alongside early risks in historical practice eras [15]. In the randomized MIST trial (NCT00273364; n=110), with the primary end point disease progression, defined as an EDSS score increase after at least 1 year of 1.0 point or more on 2 evaluations, nonmyeloablative aHSCT significantly prolonged time to disease progression vs continued high-efficacy disease-modifying therapy (hazard ratio ≈0.07) [16]. In a study to compare the efficacy and safety of aHSCT and alemtuzumab in aggressive relapsing-remitting MS [17], Boffa, et al. concluded aHSCT superior to alemtuzumab in inducing complete disease control and in promoting short-term disability improvement. aHSCT significantly reduced the risk of relapse, MRI activity, and the annualized relapse rate at 36 months was significantly lower in the aHSCT group. A significant effect of aHSCT in promoting Expanded Disability Status Scale (EDSS) improvement compared with alemtuzumab was also noted. Analysis of single-group phase 2 data using near-complete immunoablation described sustained relapse/MRI suppression over ~7.5 years in aggressive MS, supporting the immune-reset paradigm [18]. Ongoing rater-masked RCTs (e.g., BEAT-MS) are directly comparing aHSCT with "best available therapy" to clarify positioning, safety, and health-economic impact in contemporary practice. Safety considerations remain central (i.e., cytopenias, severe infections, regimen-related toxicities) necessitating accredited centers, standardized protocols, and EBMT/ECTRIMS-aligned selection criteria and supportive care pathways.

While aHSCT provides proof-of-concept that resetting immune tolerance can yield durable disease control in MS. However, its use remains constrained by regimen-related risks, specialized infrastructure, and stringent eligibility requirements. This has fueled parallel investigation of alternative cell-based strategies with potentially broader applicability and improved safety. Among these, MSC therapy has emerged as a leading candidate, leveraging immunomodulatory and neuroprotective mechanisms distinct from the cytotoxic/reconstitution approach of transplantation.

MSC Therapy

MSCs (bone marrow, adipose, or umbilical sources) exert potent paracrine immunomodulation (e.g., T-cell anergy, Treg induction; microglial biasing), neuroprotection, and pro-remyelination support of oligodendrocyte lineage cells, motivating clinical translation [19]. In the multicenter (15 sites, 9 countries), randomized, double-blind, crossover MESEMS phase 2 trial, intravenous autologous bone-marrow MSCs were safe and well tolerated (n=144) [20]. Two-hundred thirteen adverse events (AE) were similarly distributed between groups. The most frequent adverse events reported were infection and infestations, with a total of 54 (25%) of 213 AEs. Nine serious adverse events were reported in seven patients treated with placebo versus none in the MSC group. However, MSC treatment did not meet the primary endpoint of efficacy on the total number of gadolinium-enhancing lesions (GELs) accumulated from baseline to week 24 and exploratory efficacy signals were inconsistent. These findings underscored the need for larger, uniformly powered trials and optimized dosing/routes. Riorden, et al. [21] conducted a safety and feasibility study using of umbilical cord MSC (UCMSC; NCT02034188) in a 1-year study, in which participants received seven intravenous infusions of over 7 days. No serious AEs were reported. Symptom improvements were most notable 1 month after treatment and EDSS scores significantly improved, in addition to bladder, bowel, and sexual dysfunction, in non-dominant hand average scores, in walk times and general perspective of a positive health change and improved quality of life. MRI scans of the brain and the cervical spinal cord showed inactive lesions in 15/18 (83.3%) subjects after 1 year indicating safety, and potential therapeutic benefits should be further investigated.

Visual impairment represents a significant component of overall disability in MS. Earlier controlled and open-label studies provided mixed efficacy readouts from MSC therapy in visual pathways. The MSCIMS phase 2a study in 2011 in secondary progressive MS reported improvements on visual pathway outcomes consistent with neuroprotection, while remaining non-definitive for global disability [22]. Alternative delivery and phenotype strategies are in evaluation. Harris, et al., conducted an open-label phase I trial of intrathecal MSC-derived neural progenitors (MSC-NPs) in progressive MS (n=20) showing acceptable safety and disability improvements in a subset, warranting randomized confirmation [23]. Meta-analyses and recent systematic reviews across MS trials conclude that MSC therapy has a safety profile that is favorable, yet efficacy remains inconclusive pending larger placebo-controlled studies with harmonized endpoints and longer follow-up [24]. A systematic review and meta-analysis of safety profiles, including nine RCTs that met the inclusion criteria (n = 540 patients), reported MSCs delivered intrathecally relative to controls, were associated with an increased probability of AEs of musculoskeletal and connective tissue disorders [25]. Further, random-effects meta-regress modeling suggested that fresh MSCs increased the probability of occurrence of AEs compared to cryopreserved MSCs yet the multiple-dose, decreased the probability of AEs by 36% compared to single doses. They also reported univariate random effects meta-regression models did not demonstrate a significant association between the occurrence of AEs from MSCs intrathecal delivery and each covariate. As such, the authors concluded that IT delivery of MSCs was associated with a slight increase in AEs associated with musculoskeletal and connective tissue disorders, albeit without serious AEs, implying adequate safety profile for patients with neurological conditions. A more recent systematic review [26] of 34 studies that met the inclusion criteria, covering both preclinical and clinical investigations, indicated that MSC therapy contributed to neuroprotection, immunomodulation, and functional recovery. Short-term safety profiles were favorable. However, long-term efficacy and optimal administration protocols remain uncertain. Variations in cell sources, administration methods, and patient responses demonstrate the importance of standardized protocols, highlighting the need for large-scale, long-term studies are essential to confirm efficacy, optimize treatment strategies, and assess potential risks.

Trial (Year)	Design / Phase	Cell Type & Route	n	Primary Endpoint	Outcome
MESEMS (2021)	Phase II, randomized, double-blind, crossover (multicenter)	Autologous BM-derived MSCs, IV	144	Number of gadolinium-enhancing MRI lesions over 24 weeks	Safe and well tolerated; no effect on MRI lesion count[27]
MSC-NP IT (2024)	Phase II, randomized, double-blind, crossover (single center)	Autologous MSC-derived neural progenitors, IT	54	EDSS-Plus (composite of EDSS, T25FW, 9-HPT)	Primary endpoint not met; improvements in walking (T25FW/6MWT), bladder function, gray matter atrophy, and MRI/CSF biomarkers in subgroup[28]
NG-01 IT (2024, interim analysis)	Phase II open-label extension	Autologous MSCs (NG-01), IT	≈23	Serum biomarkers (NfL, GFAP), neurological function	Significant reductions in NfL (~33%) and GFAP (~22%), improvements in cognition/walking reported[29]
Repeated MSC injections (2021)	Open-label, prospective long-term follow-up	Autologous MSCs, IV and/or IT	24	Long-term safety and clinical/immunological effects	Safe, with indications of clinical and immunological benefit over extended follow-up[29]

Other Stem Cell Types (NSPCs/OPCs, iPSCs)

Neural stem/progenitor cells (NSPCs) and oligodendrocyte progenitor cells (OPCs) are conceptually suited to remyelination and local immunomodulation. Early human experience remains limited but growing: a recent phase I intracerebroventricular human neural stem cell study in secondary progressive MS primarily established feasibility and safety, with efficacy endpoints exploratory. In an analysis of one year data (NCT03282760), Leone, et al. [30] reported no treatment-related deaths nor serious adverse events (AEs). All participants displayed stability of clinical and laboratory outcomes and longitudinal metabolomics and lipidomics of biological fluids identified time- and dose-dependent responses with increased levels of acyl-carnitines and fatty acids in the cerebrospinal fluid (CSF), highlighting the translational gap from robust preclinical remyelination to reproducible clinical benefit.

Induced Pluripotent Stem Cell (iPSC)

While MSCs and aHSCT have advanced into clinical trials for MS, induced pluripotent stem cell (iPSC)–derived approaches remain preclinical and investigational. iPSCs offer a theoretically limitless, patient-specific source of neural and glial progenitors, making them an attractive option for cell replacement strategies aimed at remyelination [31,32]. Differentiation protocols have been developed to generate bona fide oligodendrocyte progenitor cells (OPCs), astrocytes, and neurons from human iPSCs, with studies demonstrating functional myelin repair in rodent demyelination models [33,34]. iPSC-derived OPCs can migrate to demyelinated lesions, differentiate into myelinating oligodendrocytes, and restore conduction velocity in experimental autoimmune encephalomyelitis (EAE) and cuprizone models. Unlike MSCs, which primarily act via paracrine modulation, iPSC-derived OPCs are intended to serve as direct cellular replacements for lost myelin-forming cells [35]. Additionally, iPSCs enable the creation of patient-specific models of MS pathology, allowing *in vitro* exploration of susceptibility pathways, drug screening, and personalized therapeutic testing [36]. Despite these advantages, translation of iPSC-derived therapies into the clinic faces substantial safety and manufacturing hurdles. For example, residual pluripotent cells carry a risk of teratoma formation, necessitating stringent purification and quality control [37,38]. Although iPSCs can be autologous, culture-induced mutations and epigenetic drift may elicit immune rejection even in "self" products [39,40]. In addition, differentiation into lineage-stable OPCs requires lengthy, technically demanding protocols, limiting scalability and reproducibility [41]. As iPSCs are classified as advanced therapy medicinal products (ATMPs), they must meet rigorous GMP standards that remain challenging for academic laboratories to achieve, introducing potential regulatory challenges.

Contemporary efforts focus on gene-edited "universal donor" iPSCs, where HLA engineering reduces immunogenicity [42], and on rapid OPC differentiation pipelines that shorten manufacturing timelines [43]. Advances in single-cell sequencing and lineage tracing are improving quality assurance and reducing heterogeneity [44]. In parallel, iPSC-derived extracellular vesicles (EVs) have shown early promise in preclinical models as cell-free mediators of neuroprotection and remyelination, potentially sidestepping tumorigenicity risks [45]. At present, iPSC-based OPC transplantation in MS remains preclinical, with no completed human trials. The next critical step will be rigorously designed early-phase clinical studies assessing safety, biodistribution, and preliminary efficacy in progressive MS, where cell replacement needs are greatest. Until then, iPSCs remain primarily a platform for mechanistic discovery and disease modeling, while MSCs and aHSCT continue to lead the translational pipeline.

Mechanisms of Action

Across cellular modalities, immunomodulation is a unifying mechanism for controlling focal inflammatory activity in MS. aHSCT eliminates peripheral lymphocytes with high-intensity conditioning followed by immune reconstitution that skews toward a less autoreactive repertoire, particularly in highly active relapsing MS selected early and appropriately [46,47]. By contrast, MSCs operate primarily through paracrine immune re-programming rather than direct lymphodepletion. MSCs and their derivatives dampen Th1/Th17 polarization, bolster regulatory circuits, and modulate antigen presentation via secreted factors and extracellular vesicles (EVs), yielding reductions in inflammatory cascades that seed new lesions [48,49]. As noted in the MESEMS trial, route/product choices and target phenotype matter. EV-centric approaches are advancing as cell-free surrogates that retain immunomodulatory/trophic cargo and may simplify manufacturing and delivery.

Beyond inflammation control, neuroprotection and remyelination are active targets of cellular therapies. MSC-conditioned secretomes and MSC-NPs supply trophic support to oligodendrocyte lineage cells (e.g., BDNF, IGF-1, VEGF), attenuate oxidative and excitotoxic stress, and polarize microglia/macrophages toward pro-repair states that facilitate debris clearance and remyelination [50,51]. *In vivo* demyelination models show that microglial polarization dynamics, with reparative phenotypes dominating during remyelination, are integral to lesion repair, providing a mechanistic substrate that matches the MSC/MSC-NP mode of action [52,53]. As previously noted, early human data with NSPC transplants also suggest neuroprotective effects, including gray-matter atrophy reduction in first-in-human experiences and interpretive clinical commentaries; rigorous randomized testing is ongoing.

Emerging work highlights mitochondrial and metabolic deficits across neural and immune compartments in MS, implicating redox imbalance, impaired oxidative phosphorylation, and bioenergetic stress in axonal degeneration and oligodendroglial dysfunction [54,55]. Cell therapies plausibly re-tune metabolic/antioxidant pathways via cargoed miRNAs, enzymes, and mitochondria-targeted signals, thereby improving redox tone and injury resilience in recipient cells [56,57]. While biologic plausibility and preclinical evidence are strong, definitive human biomarker–outcome linkages (e.g., coupling shifts in metabolic signatures to slowed atrophy or disability) remain an unmet need for the field.

To translate mechanisms into patient-level benefit, fluid and imaging biomarkers are essential. Neurofilament light (NfL) and glial fibrillary acidic protein (GFAP) now serve as sensitive readouts of neuro-axonal injury and astroglial activation in MS trials [58]. Reductions in these markers have been reported and are being prospectively integrated into next-generation cell-therapy studies. State-of-the-art reviews in 2024–2025 codify NfL/GFAP as actionable endpoints for disease activity and treatment response, while encouraging alignment with MRI (lesion load, gray-matter/NAWM metrics) and quantitative disability composites (EDSS-Plus) [59]. Taken together, aHSCT provides a high-potency immune reset for selected patients with aggressive relapsing disease, with durable suppression of new inflammatory activity but procedure-linked risks requiring specialized centers. MSCs and derivatives enact paracrine immune re-programming and neurorepair via multimodal trophic, anti-oxidative, and microglial-modulating effects. IT delivery and lineage-primed products (MSC-NPs) currently show the most compelling signals in progressive MS, warranting Phase 3 confirmation with harmonized products, dosing, and endpoints [60,61]. EV/exosome strategies may ultimately deliver the "active ingredients" with improved scalability and safety. Across platforms, embedding mechanism-linked biomarkers (NfL, GFAP, MRI atrophy/remyelination metrics) into trials is paramount to establish causal bridges from cellular mechanisms to patient-relevant outcomes.

Comparative Context and Challenges

Cellular therapies for MS occupy distinct positions on the spectrum of risk and potential efficacy. aHSCT has demonstrated durable suppression of inflammatory activity and relapses in appropriately selected patients with aggressive relapsing forms of MS. In some cohorts, long-term outcomes rival or exceed those achieved with high-efficacy DMTs. However, aHSCT requires myeloablative or lymphoablative conditioning, with attendant risks of infection, infertility, and treatment-related mortality, though recent registry analyses suggest that mortality has declined to <1% in specialized programs. By contrast, MSCs and their derivatives demonstrate a more favorable safety profile across routes of administration (IV, intrathecal), with consistent evidence of tolerability in both early-phase trials and pooled safety analyses. Nonetheless, efficacy signals remain variable and context-dependent. This risk–benefit contrast underscores the trade-off between aHSCT's potency (at higher risk) and MSCs' safety (with uncertain efficacy).

Practical barriers are substantial. In the United States, the FDA requires Investigational New Drug (IND) authorization and rigorous trial oversight for both aHSCT protocols and MSC products. Professional societies emphasize that these interventions should be restricted to accredited centers and controlled trials until reproducible efficacy and long-term safety are established. aHSCT demands multidisciplinary transplant infrastructure, prolonged hospitalization, and access to conditioning regimens, limiting its availability to specialized centers with transplant accreditation. MSC therapies, while logistically simpler, face manufacturing and standardization hurdles: donor variability, product heterogeneity (bone marrow vs umbilical cord vs adipose), and lack of consensus on dose and route. Regulatory agencies have issued warnings regarding unproven commercial "stem cell clinics", highlighting the need for formal oversight to protect patients from unsafe or untested interventions. Cost further compounds these challenges as both aHSCT and MSC-based approaches remain resource-intensive compared with conventional DMTs.

High-complexity, high-cost therapies raise questions of equity and access. aHSCT is currently available only at specialized transplant centers, often concentrated in high-income regions. Even within trial frameworks, eligibility criteria (e.g., aggressive relapsing phenotype, younger age, preserved functional reserve) restrict broader applicability. MSC trials frequently rely on academic or research infrastructures for GMP-grade manufacturing, and most have not transitioned to commercially scalable platforms. This limits access outside of investigational protocols and contributes to global disparities in availability.

Equity challenges extend to insurance coverage and healthcare policy. aHSCT for MS remains non-standard of care in many jurisdictions, and reimbursement is inconsistent. For MSCs, lack of FDA approval precludes coverage, placing the financial burden on patients or limiting participation to those who can access research centers. Without deliberate planning, cellular therapies risk widening treatment gaps between patients in resource-rich and resource-limited settings. Reviews increasingly emphasize the need for equitable trial design, cost modeling, and policy engagement to ensure that successful therapies translate into broad patient benefit.

Future Directions

The next phase of cellular therapy development in MS requires expansion across disease phenotypes, with a particular emphasis on progressive forms where DMTs have limited efficacy. While aHSCT has demonstrated potency in relapsing MS, the unmet need lies in progressive disease, where MSC-derived products and neural stem/progenitor cell approaches are being increasingly tested. The inclusion of diverse patient populations, longer follow-up intervals, and harmonized outcome measures will be critical for defining efficacy across the full MS spectrum. Future research must also focus on optimizing MSC biology. Source heterogeneity (bone marrow, adipose, umbilical cord) yields variability in immunomodulatory potency and trophic factor secretion. Comparative studies and standardization of culture/manufacturing protocols are essential to reduce variability. Intrathecal delivery has shown stronger biologic activity in progressive MS compared with intravenous infusion, but dose, schedule, and durability of effect require rigorous testing. Concurrently, scaling up controlled, multicenter trials with consistent manufacturing standards is paramount for clinical translation. Cellular therapies may achieve maximal benefits when integrated into multimodal care paradigms, such as DMTs for controlling peripheral immune activity alongside cell therapies that provide central repair and immunomodulation, rehabilitation and neurorehabilitation strategies to exploit neuroplasticity triggered by trophic support, and lifestyle interventions (exercise, diet, sleep optimization) to

enhance neuroprotection and reduce systemic inflammation. Such combination strategies align with precision medicine approaches and reflect the multidimensional nature of MS pathophysiology.

A major frontier is the incorporation of mechanistic biomarkers into clinical trial design to enable response stratification and precision medicine. NfL and GFAP are increasingly validated as markers of neuroaxonal injury and astroglial activity, respectively, and are now being integrated as trial endpoints. Imaging markers of remyelination, gray-matter atrophy, and functional MRI connectivity provide additional resolution on therapeutic impact. Immunologic biomarkers can complement imaging and fluid biomarkers, enabling mechanistic alignment between biological effect and clinical response.

Stem cell therapies hold transformative potential to halt disease progression in carefully selected MS populations. For MSCs, the appeal lies in their favorable safety profile, scalability of donor-derived products, and breadth of paracrine actions. Yet efficacy validation remains incomplete, requiring larger and more definitive trials. The contrast between the high-risk, high-reward profile of aHSCT and the lower-risk, potentially incremental efficacy of MSCs underscores the need for tailored patient selection and risk–benefit balancing. The path to mainstream applicability requires robust clinical trials coupled with regulatory harmonization. Current FDA designations consider both aHSCT and MSC-based therapies investigational, demanding rigorous oversight and GMP compliance. Addressing access challenges (i.e., cost, insurance coverage, geographic disparities in specialized center availability) will be essential to ensure equity. Without deliberate policy planning, cellular therapies risk exacerbating disparities in MS care.

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