Graft-versus-host disease (GvHD) remains one of the most significant complications following allogeneic hematopoietic stem cell transplantation (HSCT), contributing substantially to morbidity and mortality despite advances in conditioning regimens, donor selection, and prophylactic strategies. Understanding the etiopathogenesis of acute and chronic GvHD is essential for improving risk stratification, tailoring prophylaxis, and designing novel targeted therapies. Acute GvHD (aGvHD) typically develops within the first 100 days post-transplant and arises from a multi-step immunopathological cascade. Conditioning regimens induce extensive tissue damage, releasing danger-associated molecular patterns (DAMPs) and pro-inflammatory cytokines such as TNF-α, IL-1, and IL-6, which activate host antigen-presenting cells (APCs). Activated APCs prime donor T cells, leading to the expansion of alloreactive effector T cells. These T cells infiltrate target organs—most prominently the skin, gastrointestinal tract, and liver—mediating tissue destruction via cytotoxic molecules (perforin, granzyme) and further amplification of the inflammatory milieu. Regulatory T cell (Treg) dysfunction, microbial translocation from intestinal damage, and loss of epithelial integrity amplify these effects. Emerging evidence highlights the contribution of innate immune cells, the microbiome, and cytokine networks in shaping the severity and trajectory of aGvHD. Chronic GvHD (cGvHD), in contrast, is a complex, multifactorial syndrome that shares features with autoimmune and fibrotic disorders. It generally manifests beyond day 100, although temporal overlap with aGvHD is increasingly recognized. The pathogenesis of cGvHD involves sustained immune dysregulation, including aberrant thymic recovery, impaired central and peripheral tolerance, and persistence of autoreactive and alloreactive T and B cells. B cell hyperactivity, autoantibody production, and activation of germinal center–like reactions contribute to chronic inflammation. Crosstalk between T follicular helper cells, pathogenic B cells, and fibroblasts drives tissue remodeling and fibrosis. Key target organs include the skin, lungs, liver, eyes, and mucous membranes, with progressive organ dysfunction severely impacting quality of life. Recent studies underscore the importance of profibrotic cytokines (e.g., TGF-β, PDGF) and aberrant tissue repair pathways in perpetuating cGvHD. Advances in molecular and cellular profiling have provided novel insights into both acute and chronic disease mechanisms. High-throughput sequencing, proteomic analyses, and microbiome studies have identified candidate biomarkers for early diagnosis, disease monitoring, and therapeutic stratification. These findings are paving the way toward precision medicine approaches, including selective inhibition of JAK/STAT pathways, B cell depletion strategies, adoptive Treg therapy, and microbiota modulation. Despite these promising developments, challenges remain in balancing graft-versus-host effects with graft-versus-leukemia (GvL) activity, underscoring the need for therapeutic interventions that preserve antitumor immunity while mitigating alloreactivity. In summary, both acute and chronic GvHD arise from complex, overlapping yet distinct immunopathological processes that reflect dysregulated interactions between donor-derived immune cells, host tissues, and the microenvironment. Ongoing research continues to refine our understanding of GvHD biology, which is critical for developing innovative therapies and improving long-term outcomes in allogeneic HSCT recipients.

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Abstract 027

CHELATION THERAPY IN THALASSEMIA

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Thalassemia major is a severe hereditary hemoglobinopathy characterized by ineffective erythropoiesis and transfusion-dependent anemia. Regular red blood cell transfusions remain the cornerstone of supportive treatment; however, they inevitably result in progressive iron overload due to the absence of physiological mechanisms for iron excretion. Iron accumulation predominantly affects the liver, heart, and endocrine organs, leading to cirrhosis, cardiomyopathy, arrhythmias, and multiple endocrinopathies. Consequently, iron chelation therapy constitutes a fundamental component of long-term management in patients with thalassemia major. The first clinically available chelating agent was deferoxamine (DFO) promotes urinary and fecal iron excretion. Long-term use of DFO has significantly improved survival by reducing iron-related cardiac mortality. Nevertheless, its administration—via subcutaneous or intravenous infusion for 8–12 hours on most days of the week—poses substantial challenges to adherence, particularly in pediatric and adolescent populations. To address these limitations, oral chelators were developed. Deferiprone (DFP) is effective in reducing myocardial iron burden and preventing cardiac dysfunction, although it carries the risk of agranulocytosis, requiring strict hematological monitoring. Deferasirox (DFX) has demonstrated efficacy in maintaining negative iron balance and reducing hepatic iron concentration, thereby improving adherence and overall patient satisfaction. In cases of severe or refractory iron overload, combination therapy has been employed. The concurrent use of DFO and DFP exhibits synergistic effects, particularly in the clearance of cardiac iron. Emerging data also support the potential benefits of combining DFO with DFX in select clinical scenarios. These strategies allow for individualized treatment based on iron burden, organ involvement, and patient tolerance. Monitoring of chelation efficacy is essential. Serum ferritin is widely utilized as a surrogate marker of body iron, though it may be confounded by inflammation or hepatic injury. T2-star magnetic resonance imaging provides a more reliable and non-invasive quantification of cardiac and hepatic iron, enabling timely therapeutic adjustments and prevention of irreversible organ damage. Chelation therapy has transformed the prognosis of thalassemia major, shifting the natural history from early mortality to survival into adulthood with improved quality of life. Nevertheless, challenges persist, including variability in drug availability, treatment adherence, and adverse event profiles. Future perspectives include optimization of chelation regimens, development of safer agents, and curative

approaches such as gene therapy and hematopoietic stem cell transplantation, which may ultimately reduce or eliminate the lifelong requirement for transfusion and chelation.

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Abstract 028

RELAPS/REFRACTORY MANTLE CELL LYMPHOMA TREATMENT

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Mantle cell lymphoma (MCL) is a rare and aggressive subtype of non-Hodgkin lymphoma (NHL) characterized by the overexpression of cyclin D1 due to the chromosomal translocation t(11;14)(q13;q32). Despite advances in therapeutic approaches, MCL remains a significant clinical challenge, particularly in relapsed and refractory (R/R) cases. Relapse occurs when the disease reappears after an initial response to therapy, while refractory MCL refers to cases where the disease fails to respond adequately to standard treatment regimens. Both conditions are associated with poor prognosis and limited treatment options, reflecting the need for novel therapeutic strategies. Relapsed MCL is characterized by clonal evolution and the emergence of more aggressive phenotypes, including resistance to previously administered therapies. Refractory cases, on the other hand, exhibit intrinsic or acquired resistance mechanisms, such as mutations in the B-cell receptor (BCR) signaling pathway, TP53 abnormalities, and alterations in DNA damage response genes. Recent therapeutic advances have improved outcomes for R/R MCL patients. Targeted therapies, including Bruton's tyrosine kinase (BTK) inhibitors such as ibrutinib, acalabrutinib, and zanubrutinib, have demonstrated significant efficacy by disrupting BCR signaling. Ibrutinib, the first BTK inhibitor approved for R/R MCL, has shown durable responses in clinical trials, although resistance to BTK inhibitors is a growing concern. Lenalidomide, an immunomodulatory agent, and venetoclax, a BCL-2 inhibitor, have also shown promise in heavily pretreated patients. Furthermore, chimeric antigen receptor (CAR) T-cell therapy targeting CD19, such as brexucabtagene autoleucel, represents a groundbreaking approach for patients with chemorefractory disease. While these therapies offer hope, their application is often limited by adverse events, accessibility, and high costs. Biological heterogeneity within MCL further complicates the management of R/R cases. The proliferation index (Ki-67), TP53 mutation status, and the presence of blastoid or pleomorphic variants are critical prognostic factors influencing treatment decisions. Additionally, the integration of next-generation sequencing (NGS) and molecular profiling enables the identification of actionable mutations and pathways, paving the way for personalized medicine. Despite these advancements, challenges remain in optimizing the sequencing of therapies, managing toxicities, and overcoming resistance. Clinical trials continue to explore novel agents, including bispecific antibodies, proteasome inhibitors, and checkpoint inhibitors, as well as combination strategies to enhance efficacy and minimize resistance. Moreover, the role of minimal residual disease (MRD) monitoring in guiding treatment remains an area of active investigation. In conclusion, relapsed and refractory MCL represents a complex clinical entity with significant unmet needs. While recent therapeutic innovations have improved outcomes, the heterogeneity of the disease necessitates a personalized approach to treatment. Future research should focus on elucidating resistance mechanisms, refining therapeutic strategies, and improving access to novel treatments to enhance the prognosis for this challenging patient population.

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Abstract 029

SUMMARY: OPTIMIZATION OF TREATMENT IN PHILADELPHIA CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA (PH+ ALL)

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Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) is a high-risk subtype of ALL, historically associated with poor outcomes. The introduction of tyrosine kinase inhibitors (TKIs) has dramatically changed its therapeutic landscape. Current optimization strategies focus on integrating TKIs with chemotherapy, immunotherapy, and, in selected cases, allogeneic stem cell transplantation (allo-HSCT), while tailoring treatment according to minimal residual disease (MRD) status and patient characteristics. Induction therapy now commonly consists of a TKI combined with corticosteroids and/or reduced-intensity chemotherapy, aiming to achieve remission with lower toxicity compared to traditional intensive regimens. Commonly used TKIs include imatinib, dasatinib, and ponatinib, with the latter being preferred in cases with the T315I mutation due to its broader activity. Consolidation therapy is designed to eradicate residual disease. Achieving MRD negativity is the primary goal, as it strongly predicts long-term survival. Strategies include continued TKI administration combined with short chemotherapy blocks or novel agents such as blinatumomab, a CD19-targeted bispecific T-cell engager. Allo-HSCT remains an important option for younger, fit patients, especially those with persistent MRD or high relapse risk. However, accumulating evidence suggests that deep and durable remissions may be achievable without transplantation when combining TKIs with immunotherapies. Maintenance therapy typically involves prolonged TKI treatment, often for at least two to three years, with ongoing MRD monitoring to guide adjustments. In the relapsed or refractory setting, therapeutic options expand to include next-generation TKIs such as ponatinib, immunotherapies including blinatumomab and the CD22-targeted antibody-drug conjugate inotuzumab ozogamicin, and chimeric antigen receptor T-cell (CAR-T) therapies targeting CD19, which have shown promising results in heavily pretreated patients. The core principles of treatment optimization in Ph+ ALL include: 1. MRD-directed decision-