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

Damla Ortaboz

Sultan Abdulhamid II Training and Research Hospital, Türkiye

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)

Demet Çekdemir

İstanbul Acibadem Health Group, Türkiye

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-