malignancies due to high mortality rates and limited treatment options. In this context, Chimeric Antigen Receptor T (CAR-T) cell therapy has emerged as a promising approach for patients with refractory or relapsed disease. CAR-T cells are generated by genetically engineering the patient's T cells to express synthetic receptors targeting specific tumor-associated antigens. In ALL, CD19-targeted CAR-T cell therapies have demonstrated complete remission (CR) rates of 70–90%. For AML, ongoing research is exploring alternative targets. Clinical Studies and Outcomes ELIANA Trial The ELIANA trial, the largest global multicenter study of CD19-targeted CAR-T therapy, focused on pediatric and young adult ALL patients Tisagenlecleucel was infused into 75 ALL patients and evaluated for efficacy. The overall remission rate at 3 months was 81%, and all patients who responded to treatment were found to be negative for minimal residual disease by flow cytometry. Event-free survival and overall survival rates were 73% and 90% at 6 months and 50% and 76% at 12 months, respectively. Median duration of remission was not achieved. Tisagenlecleucel persisted in the blood for up to 20 months. Grade 3 or 4 adverse events thought to be related to tisagenlecleucel occurred in 73% of patients. Cytokine release syndrome occurred in 77% of patients, 48% of whom received tocilizumab. Neurological events occurred in 40% of patients and were managed with supportive care, and no brain edema was reported. ZUMA-3 Trial The ZUMA-3 an international, multicentre, single-arm, open-label study evaluating the efficacy and safety of the autologous anti-CD19 CAR-T-cell therapy KTE-X19 in adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia. KTE-X19 was administered to 55 (77%) patients. At a median follow-up of 16.4 months (13.8-19.6), 39 patients (71%; 95% CI 57-82, p<0.0001) had CR or CRi and 31 (56%) achieved CR. Median duration of remission was 12.8 months (95% CI 8.7 - not estimable), median relapse-free survival was 11.6 months (2.7-15.5) and median overall survival was 18.2 months (15.9 - not estimable). Among responders, median overall survival was not reached and 38 (97%) patients had MRD negativity. Ten (18%) patients received allo-SCT consolidation after KTE-X19 infusion. The most common adverse events of grade 3 or higher were anemia (27 [49%] patients) and pyrexia (20 [36%] patients). 14 (25%) patients had grade 3 or higher infections. Two grade 5 KTE-X19-related events occurred (cerebral herniation and septic shock). Grade 3 or higher cytokine release syndrome occurred in 13 (24%) patients, and grade 3 or higher neurologic events occurred in 14 (25%) patients. AML Target Studies AML poses unique challenges due to its heterogeneous cell populations. Early-phase studies of CD33-targeted CAR-T cells have shown promising tumor burden reductions in specific patient cohorts. However, these studies are still in the clinical validation phase. Future Perspectives Next-generation CAR-T cell designs aim to enhance target specificity and minimize adverse effects, improving the therapy's safety and efficacy profile. Allogeneic CAR-T platforms and universal CAR-T cell technologies are also under development, potentially increasing accessibility for a broader range of patients. In conclusion, CAR-T cell therapy represents a transformative step in personalized treatment strategies for acute leukemias. Continued advancements in clinical trials and translational research will further unlock the potential of this innovative approach in hematology.

https://doi.org/10.1016/j.htct.2024.11.102

21

## PRECISION MEDICINE IN MULTIPLE MYELOM

Elif Aksoy

*İstanbul University, Faculty of Medicine*

Precision medicine, an approach tailored to individual patient characteristics and disease profiles, has become increasingly important in the treatment of multiple myeloma (MM). Conventional MM treatment often yields variable results because the biological and clinical course of MM is heterogeneous. One of the main strategies in precision medicine for MM is genetic profiling. Certain genetic mutations such as t(4;14), t (14;16) and del(17p) are associated with a higher risk of aggressive disease. In addition, copy number alterations involving the long arm of chromosome 1 (1q) predict worse survival. In addition to cytogenetics, differential gene expression profile (GEP) signatures are independent prognostic factors for both PFS and OS, thus providing an additional method to identify high risk. By identifying these markers early, clinicians can classify patients into risk categories and tailor treatment accordingly. High-risk patients may receive more intensive treatments, while standard-risk patients may benefit from less aggressive regimens that preserve quality of life. Targeted therapies are another critical component of precision medicine in MM. Unlike conventional chemotherapy, which affects both cancerous and healthy cells, targeted therapies are designed to act specifically on the molecular pathways that drive MM cell growth. Drugs such as proteasome inhibitors, immunomodulatory agents and monoclonal antibodies are designed to attack key mechanisms in MM cells. For example, proteasome inhibitors disrupt protein excretion pathways in cancer cells, leading to cell death, while monoclonal antibodies can mark MM cells for immune destruction. These therapies offer more effective and tolerable treatment options when matched to patients whose disease characteristics are compatible with the drug's mechanism. CAR-T cell therapy and bispecific antibodies are promising options for relapsed/refractory MM and offer significant disease reduction for patients with limited options. Precision medicine also plays a role in monitoring minimal residual disease (MRD), which refers to the small number of cancer cells that can remain after treatment and potentially cause relapse. Multiparameter flow cytometry (MFC) and next-generation sequencing (NGS) are the most common and standardised methods. Whole body MRI and PET/CT provide better assessment for extramedullary disease. Patients with MRD-negative status generally have better long-term outcomes, so precision medicine approaches can tailor treatment to MRD status, aiming for complete eradication of disease in patients with evidence of remaining cancer cells. Finally, clinical trials are essential to develop precision medicine in MM. Studies focused on biomarker-driven therapies and novel agents give

patients access to cutting-edge treatments that may be more effective for specific disease profiles. As genomic data and biomarker research progress, trials are increasingly focused on matching patients with therapies based on individual molecular characteristics, increasing the likelihood of a favourable outcome. AI is supporting precision medicine in MM by improving diagnostic accuracy, risk stratification and treatment matching, potentially transforming personalised oncology care. Overall, precision medicine in MM, supported by AI insights, aims to optimise treatment efficacy, promote longer-lasting remission and improve quality of life by tailoring therapies to each patient's unique disease profile.

https://doi.org/10.1016/j.htct.2024.11.103

22

## SUPPORTIVE CARE AND QUALITY OF LIFE IN MDS: ESSENTIAL MANAGEMENT STRATEGIES

Metban Mastanzade

*Istanbul University Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Hematology*

Supportive care is critical for patients with Myelodysplastic Syndromes (MDS), aiming to enhance quality of life (QoL) amidst this chronic, hematologic disorder. MDS management focuses on alleviating symptoms of ineffective hematopoiesis and preventing complications like infections and cardiovascular disease. Managing Anemia and Transfusion Dependence: Anemia is prevalent in MDS, often requiring blood transfusions. However, frequent transfusions can lead to iron overload, risking damage to organs like the heart and liver. Iron chelation therapy mitigates this risk by reducing iron buildup, crucial for transfusion-dependent patients. Erythropoiesis-stimulating agents (ESAs) are effective in lower-risk MDS patients, reducing transfusion needs, while the recent COMMANDS Trial highlights luspatercept as an alternative to epoetin alfa, showing promising results in managing anemia and improving QoL. Addressing Thrombocytopenia and Bleeding Risks: Patients with MDS frequently experience thrombocytopenia, which increases bleeding risk. Thrombopoietin receptor agonists, like eltrombopag and romiplostim, aid platelet production, though long-term safety and efficacy require further research. For severe cases, prophylactic platelet transfusions are essential, with tailored transfusion thresholds improving patient outcomes. In addition, antifibrinolytic agents, such as tranexamic acid, are used adjunctively to manage bleeding. Infection Prophylaxis: Due to compromised immunity, MDS patients face high infection risks. Antimicrobial prophylaxis and vaccinations against common pathogens are critical. Prophylactic measures are especially relevant for patients with neutropenia, where antibiotics, antifungals, and antivirals provide protection. Vaccinations further support infection prevention, although immune responses in MDS patients may require adjustments. Nutritional and Metabolic Support: Malnutrition is common in MDS and correlates with poor prognosis. Regular nutritional assessments help address deficiencies, and supplements, particularly of B vitamins and folate, are beneficial in sustaining hematopoiesis. Recent findings suggest vitamin C's potential in supporting hematologic function through DNA demethylation, though optimal dosages are still under study. Cardiovascular and metabolic complications are also common, emphasizing lifestyle modifications and careful management of comorbidities like hypertension and diabetes. Psychological and Palliative Care: Chronic symptoms and disease progression often lead to depression and anxiety among MDS patients. Psychosocial support, including therapy and support groups, can significantly enhance emotional resilience. For those in advanced stages, palliative care, emphasizing dignity and comfort, is essential. Pain management and non-pharmacological approaches for symptoms like fatigue help improve end-of-life quality. Role of Technology and Geriatric Assessments: Telemedicine offers a means for remote monitoring, enhancing access to care for elderly or immobile patients. Geriatric assessments guide treatment decisions, balancing efficacy and tolerance, especially in older patients who may face higher treatment-related risks. In conclusion, MDS supportive care integrates various strategies, from anemia management to infection control, tailored for physical, emotional, and psychosocial well-being. Multidisciplinary approaches and emerging tools like telemedicine continue to improve outcomes, underscoring supportive care's pivotal role in MDS management.

https://doi.org/10.1016/j.htct.2024.11.104

23

## HARMONIZATION OF TREATMENT APPROACHES: DRAWING INSPIRATION FROM PEDIATRIC TREATMENTS IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY

Ferda Can

*Ankara Bilkent City Hospital Divisium of Hematology*

Age, genetic characteristics, comorbidities, and minimal residual disease determine prognosis in patients with Acute Lymphoblastic Leukemia (ALL). Advanced age, the presence of adverse genetic markers and reduced treatment intensity typically lead to poorer outcomes, with disease-free survival and remission rates decreasing with age. In adult patients, disease remission rates are around 35%. In recent years, there has been a growing focus on applying treatment protocols developed for pediatric age groups to adult ALL patients. In pediatric ALL protocols, the main factor that enhances treatment success is the dose intensity. These protocols involve higher doses and more frequent dosing intervals of L-asparaginase, vincristine, methotrexate and steroids compared to adult ALL protocols. In recent years, it has been shown that treatment regimens applied to young adult/adolescent ALL patients have an independent impact on outcomes. Various retrospective studies have shown that complete response rates in the 15-20 age group were similar between adult and