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.

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

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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.

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

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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

pediatric protocols, but disease-free survival was significantly higher with pediatric protocols. There is no consensus about age range for the young adult/adolescent group. In some protocols, these protocols can be applied up to the age of 35 to 50 years. Rather than age, the intensity of chemotherapy can be determined according to patients' comorbidities and performance status. Current guidelines recommend pediatric-based chemotherapy protocols for young adult/adolescent patients with no comorbidities. These protocols include CALGB 10403, DFCI Protocol 00-01 and PETHEMA ALL-96. According to the prospective study results using the CALGB 10403 protocol, for ALL patients aged 17-39 years, the median event-free survival (EFS) was 78.1 months (historical control: 30 months); the 3-year EFS was 59%; and the median overall survival (OS) was not reached. The estimated 3-year OS was 73%, with a low treatment-related mortality rate of 3%. In a study by the Dana-Farber Cancer Institute (DFCI) group in adult ALL patients aged 18-50 using pediatric-based chemotherapy protocols, 85% of patients achieved complete remission (CR) after one month of intensive induction therapy. With a median follow-up of 4.5 years, the 4-year disease-free survival (DFS) for patients who achieved CR was 69%, and the 4-year OS was 67%. In the PETHEMA group's data for ALL patients aged 15-30 treated with a pediatric-based chemotherapy protocol, the CR rate was 98%. The 6-year EFS and OS were 61% and 69%, respectively. Other protocols recommended for ALL patients under 65 include the dose-adjusted CALGB 8811 Larson, MRC UKALLXII/ECOG 2993, GRAALL-2005, dose-adjusted HyperCVAD, USC/MSKCC ALL regimen based on the CCG-1882 regimen and the Linker 4-drug regimen. Studies using these protocols, CR rates were reported between 85% and 95%. Median survival was 36 months, with 3-year OS ranging from 50% to 70%, and 5-year OS ranging from 30% to 40%. Chemotherapy-related mortality is reported at approximately 5%. In conclusion, pediatric-based chemotherapy protocols offer higher CR rates compared to low-intensity treatments. Despite the lack of a significant increase in treatment-related mortality, the advantage of prolonged OS means that pediatric-based chemotherapy should be applied to all eligible adult ALL patients, whenever appropriate.

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ONGOING CLINICAL TRIALS IN MULTIPLE MYELOMA

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a) BCMA-Targeted Therapies: I. CAR-T Cell Therapies: 1- KarMMa-3 Trial: This is a multicenter, randomized, open-label, Phase 3 study comparing the efficacy and safety of ide-cel versus standard regimens in subjects with R/R multiple myeloma. Ide-cel therapy significantly prolonged progression-free survival and improved response as compared with standard regimens. 2- CARTITUDE-4 Trial: The purpose of this study is to compare the efficacy of ciltacabtagene autoleucel (cilta-cel) with standard therapy, either PVd or DPd. A single cilta-cel infusion resulted in a lower risk of disease progression or death than standard care in lenalidomide-refractory patients. II. Bispesific Antibodies: 1- MajesTEC-1 Trial: The purpose of this study is to evaluate the efficacy of teclistamab at the recommended Phase 2 dose. Teclistamab resulted in a high rate of deep and durable response in patients with triple-class–exposed relapsed or refractory multiple myeloma. 2- MagnetisMM-3 Trial: The purpose of the study is to evaluate whether single-agent Elranatamab can provide clinical benefit in participants with R/R multiple myeloma. Elranatamab induced deep and durable responses with a manageable safety profile. III. Drug-Antibody Conjugates: 1- DREAMM-7 Trial: This is a Phase 3, randomized, open-label study designed to evaluate safety and efficacy of belantamab mafodotin in combination with bortezomib/dexamethasone (Arm A) versus daratumumab in combination with bortezomib/dexamethasone (Arm B). BVd therapy conferred a significant benefit with respect to progression-free survival among patients who had R/R multiple myeloma after at least one line of therapy. b) Selinexor Combinations: 1- Updated Results Of Boston Trial By Prior Therapies: Stratified subgroup data from longer follow-up in the BOSTON trial confirm the PFS benefit of SVd over Vd in patients. 2- STOMP Trial: This study will independently assess the efficacy and safety of 11 combination therapies in 12 arms, in dose-escalation/-evaluation and expansion phases, for the treatment of patients with R/R multiple myeloma and newly diagnosed multiple myeloma. X–containing regimens are potent and achieve durable responses with numerically higher overall response and clinical benefit rates, as well as median progression free survival c) Venetoclax Combinations: 1- CANOVA Trial: A study designed tocompare progression-free survival (PFS) in participants with t (11;14)-positive MM treated with venetoclax in combination with dexamethasone versus pomalidomide in combination with dexamethasone. Patients with $BCL2^{high}$ or gain(1q) had numerically improved clinical efficacy with VenDex versus PomDex. d) CELMoDs (Cereblon E3 Ligase Modulation Drugs): 1- CC-92480-MM-001 Trial: This is an open-label, multi-center, international, Phase 1/2 study to assess the safety, PK and efficacy of mezigdomide monotherapy and in combination with dexamethasone in subjects with relapsed and refractory multiple myeloma (RRMM). The all-oral combination of mezigdomide plus dexamethasone showed promising efficacy in patients with heavily pretreated multiple myeloma, with treatment-related adverse events consisting mainly of myelotoxic effects. 2- CC-220-MM-001 Trial: This is a multicenter, multi-country, open-label, Phase 1b/2a dose-escalation study. Iberdomide plus dexamethasone was generally safe and showed meaningful clinical activity in heavily pretreated patients with multiple myeloma, including in disease that was refractory to immunomodulatory drugs.

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