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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