expression levels. AVE9633, another anti-CD33-maytansin conjugate, has shown promising results in Phase I trials with relapsed/refractory AML patients. Targeting CD123 with ADCs and exploring NK cell therapies offer hope for AML with measurable residual disease (MRD) or high-risk forms. **Bispecific T-Cell Engagers (BiTEs):** Bispecific T-cell engagers (BiTEs), such as AMG330 and AMG673, redirect T-cells or NK cells to AML cells, yielding a 20-30% response rate, though they are associated with significant side effects like cytokine release syndrome. These therapies may benefit MRD-positive AML patients in remission. T-cell immunotherapies, including flotetuzumab (FLZ), enhance T-cell activation and MHC-independent killing of AML cells, showing promise in overcoming chemotherapy resistance. **Checkpoint Inhibitors:** Immune checkpoint inhibitors targeting PD-1/PD-L1 are being explored in AML and Myelodysplastic Syndromes (MDS). Preclinical studies suggest potential benefits, but challenges remain in identifying biomarkers and optimizing combination therapies. Magrolimab, an anti-CD47 monoclonal antibody, has shown a 71% response rate and 45% complete remission (CR) when combined with azacitidine in TP53-mutant AML. **CAR-T Cell Therapies:** The success of CAR-T cell therapies in hematologic cancers has sparked interest in applying this approach to AML. Preclinical studies show that CAR-T cells targeting AML surface proteins, such as CD33 and CD123, can effectively eliminate AML cells. However, off-target toxicity due to antigen expression on healthy stem cells remains a concern. **NK Cell-Based Therapies:** Natural killer (NK) cells are being explored as an alternative to allogeneic cell therapies. NK cells can recognize and kill AML cells without causing graft-versus-host disease or cytokine release syndrome, offering a potentially safer treatment approach. **Conclusion:** In conclusion, with accumulating data, new treatment standards are being developed for AML, particularly for younger and older patients, including induction, consolidation, hematopoietic stem cell transplantation (HSCT), and maintenance therapy.

https://doi.org/10.1016/j.htct.2024.11.110

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ADVANCES IN THE ASSESSMENT OF MINIMAL RESIDUAL DISEASE (MRD) IN ALL

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General Information: A “positive” or “negative” MRD test result indicates whether measurable disease is detected above certain thresholds that may vary by test and laboratory. It is important to recognize that a negative MRD result does not necessarily indicate eradication of disease, but rather represents disease below the test threshold in the tested sample, and patients may still experience relapse. **MRD Methods:** ELN identifies multiparametric flow cytometry (MFC) and quantitative polymerase chain reaction (qPCR) among useful methods suitable for detecting MRD. Recently, innovative techniques such as digital PCR (dPCR), next-generation sequencing (NGS), and next-generation flow cytometry (NGF) have also been applied in the detection of MRD. **MRD in ALL:** In the study by Yilmaz et al., it was seen that earlier MRD negativity in Ph(-) B-ALL was associated with higher survival. The best results were obtained with Flow Cytometry MRD negativity after the 1st cycle (i.e. CR time). The 3-year relapse rate in early MRD negativity was still approximately 25%. Short NJ et al investigated the effect of CMR in Ph (+) B ALL. In 85 Ph+ ALL patients who were treated with Hyper-CVAD plus TKI and did not undergo HSCT in CR1, the median OS was 127 months in the group achieving CMR; OS was 38 months in those without CMR (P=0.009). CMR at 3 months was seen as the only prognostic factor for OS. In the study by Sasaki K et al. evaluating the effect of TKI selection on achieving 3-month CMR; 84 Ph+ ALL patients were treated with Hyper-CVAD plus TKI and CMR was achieved at 3 months. 5-year OS was found to be 84% with ponatinib. 5-year OS was found to be 60-65% with other TKIs. Ponatinib treatment was the only prognostic factor for PFS or OS. Ghobadi A et al found no benefit from allogeneic SCT in patients with Ph+ ALL who achieved CMR. Short NJ et al. compared the correlation and prognostic impact of NGS MRD and MFC MRD in Ph(-) ALL. NGS MRD (-) 5-year OS: 90%; NGS MRD (+) 5-year OS: 61%; MFC MRD (-) NGS MRD (+) 5-year OS: 62% were seen. 46% of the MFC MRD (-) group was NGS MRD (+). Blinatumomab for MRD in B-Cell ALL showed MRD negativity rate = 78% after 1 cycle in BLAST Study. Pulsipher MA et al viewed pretransplantation NGS MRD status as prognostic in pediatric ALL. Prospective follow-up for posttransplantation MRD was superior with NGS. Liang EC et al assessed NGS MRD up to 1 year after SCT for 139 patients after allogeneic SCT. Muffly L et al evaluated the correlation of NGS MRD with Peripheral Blood and Bone Marrow. Strong correlation (r=0.87; P<0.0001) was seen between PB and BM NGS MRD. MRD was detected in PB in 100% of those who relapsed after SCT and in 85% of those who relapsed after CAR T. Pulsipher MA et al. study, MRD assessment after CAR T Cell for ALL was considered prognostic. NGS-detectable MRD after tisagenlecleucel was independently predictive of EFS and OS in multivariate analysis. Short NJ et al evaluated the effect of NGS MRD for IG/TR in Ph+ ALL. The study enrolled adults with Ph+ ALL receiving first-line therapy. Disagreements between MRD assessment by PCR and MRD assessment by NGS are relatively common. RT-PCR for BCR::ABL1 is not prognostic in patients who achieve NGS MRD negativity. Ph+ ALL patients who achieve NGS MRD negativity have good outcomes regardless of PCR response. Flow cytometry in T-ALL has been validated in T ALL, including ETP. Good agreement between bone marrow and peripheral blood. NGS has not been validated in T ALL because the cells have not yet undergone a TCR rearrangement. **MRD Follow-up Periods:** In first-line ALL, MRD from bone marrow should be measured after the end of induction, during early consolidation (after approximately 3 months of therapy), and then approximately every 3 months for at least 3 years (5 years for patients with Ph-positive ALL in first remission who do not undergo HSCT). In patients undergoing HSCT, MRD should be assessed immediately before HSCT; serial MRD measurements should be performed after HSCT (approximately every 3 months).”

https://doi.org/10.1016/j.htct.2024.11.111