AMLGlobalPortal

NPM1, FLT3

MFC-MRD may stratify outcomes of standard risk AML patients

Cynthia Umukoro | Apr 10, 2018

Multiparameter flow cytometric - measurable residual disease (MRD) assessment may be able to predict outcomes among younger adult acute myeloid leukemia (AML) patients, according to a study published in the March issue of the Journal of Clinical Oncology by Sylvie D. Freeman from Birmingham Medical School, Birmingham, UK, and Robert K. Hills from Cardiff University, Cardiff, UK, and colleagues.

In this study, 6,539 bone marrow or peripheral blood samples from 2,450 younger adult patients with AML or high-risk myelodysplastic syndrome who were enrolled in the National Cancer Research Institute trial (ISRCTN55675535) was prospectively analyzed for MFC-MRD at diagnosis and following each of two induction courses.

Responses after the first course of induction (C1) were categorized as complete remission (CR) or CR with an incomplete neutrophil count below 1000/μL or thrombocytopenia less than 100,000/μL (CRi), partial remission (PR) and resistant disease (RD). Patients in CR/CRi were further stratified into MRD-positive (MRD+) and MRD-negative (MRD-) groups. Patients lacking high-risk factors including *FLT3-ITD* wt/*NPM1*-wt, received a second course of induction therapy (C2) with daunorubicin plus cytosine arabinoside, while patients with high-risk factors received an intensified course.

Key findings:

- 5-year overall survival (OS) in all patients in CR/CRi MRD-, CR/CRi MRD+, PR and RD were 63%, 44%, 35% and 24% respectively, $P < 0.0001$
- 5-year OS in good and standard-risk patients in CR/CRi MRD-, CR/CRi MRD+, PR, and RD were 70%, 51%, 48% and 27% respectively, $P < 0.0001$
- Post-course C1, significant differences were observed in OS between RD and PR/MRD+ in good and standard risk patients: HR = 2.28, $P < 0.001$
- There was no difference between PR and MRD+ in good and standard risk patients post-course C1: HR = 1.32, $P = 0.4$
- MFC-MRD status on relapse (HR = 1.88, $P < 0.001$) and OS (HR = 1.77, $P < 0.001$) was more prognostic at C2 compared to C1
- *NPM1*-wt standard-risk subgroup,
    - Post-C2 MRD+ was significantly associated with poorer OS (5-year OS rate, MRD+ 33% *vs*63% MRD-, $P = 0.003$) and higher relapse incidence
- The advantage of transplant was more apparent in patients with MRD+ (HR = 0.72) than those with MRD− (HR =1.68)

In summary, standard risk patients with detectable MFC-MRD in CR/CRi post C1 have similar survival outcomes particularly patients with good and standard-risk disease. Additionally, assessment of MFC-MRD post C2 appears to provide additional discrimination to C2.

The authors concluded by stating that “MFC-MRD can improve outcome stratification by extending the definition of partial response after first induction and may help predict *NPM1*-wt standard-risk patients with poor outcome who benefit from transplant in the first CR.”

References

1. Freeman S. D., Hills R. K. *et al*. Measurable Residual Disease at Induction Redefines Partial Response in Acute Myeloid Leukemia and Stratifies Outcomes in Patients at Standard Risk Without NPM1 Mutations. J Clin Oncol. 2018 Mar 30. DOI: 10.1200/JCO.2017.76.3425. [Epub ahead of print].