HEMATOLOGY

Complete remissions in AML

Elderly patients with acute myeloid leukemia (AML) often fail to respond to standard chemotherapy agents and have a dismal prognosis—with a median survival of less than 1 year. A study by Fehniger *et al.* published in the journal *Blood* reports sustained, complete remissions in two elderly patients with AML who had a particularly poor-risk profile.

The poor outcome in older patients with AML is because of the existence of comorbidities and the unfavorable tumor biology associated with this disease. Novel biomarkers and drugs to treat AML are, therefore, needed. Lenalidomide showed promising activity in several hematological malignancies and has been approved for the treatment of patients with low-risk myelodysplastic syndrome who have failed previous treatment or relapsed.

Responses to lenalidomide in patients with myelodysplastic syndrome suggested that this agent might be efficacious in patients with AML. Lenalidomide can cause myelosuppression in patients with myelodysplastic syndrome and so the dose is often limited to 10 mg daily; however, because treatment of myelosuppression in AML is routine, Fehniger *et al.* investigated whether a higher dose (50 mg daily) of lenalidomide could improve the outcomes in patients over the age of 60 with AML. They report sustained, cytogenetic, complete remission in two elderly patients with AML who harbored the trisomy 13 genetic abnormality, which is an extremely rare abnormality associated with a very poor prognosis.

The precise mechanism of action of lenalidomide is not known. Previous reports have shown that the 5q chromosomal abnormality is strongly associated with clinical and cytogenetic responses in patients with myelodysplastic syndrome treated with lenalidomide. The authors speculate that extrinsic effects such as natural killer activation or T-cell activation, antiangiogenesis, or cytokine modulation might contribute to its clinical activity.

"To our knowledge, this is the first report of high-dose lenalidomide inducing morphologic and cytogenetic complete remission in AML or any other myeloid disorder with trisomy 13 as the sole chromosomal abnormality," the authors commented. Both patients achieved a morphologic and cytogenetic complete remission after receiving high-dose lenalidomide.

In patients with myelodysplastic syndrome clinical responses have been noted in those with the 5q chromosomal abnormality. Retrospective analyses of data from patients with AML revealed a strong association of trisomy 13 with mutations of the *AML1 (RUNX1)* gene and with increased expression of the

tyrosine kinase FLT3, which is located on chromosome 13. These data indicate potential targets that might be relevant to the lenalidomide activity observed.

The authors conclude that, "Further analysis of lenalidomide activity in additional trisomy 13 AML patients may ultimately lead to a better understanding of myeloid leukemogenesis and aid in the development of new targeted therapeutic approaches for AML."

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Original article Fehniger, T. A. *et al.* Single-agent lenalidomide induces complete remission of acute myeloid leukemia in patients with isolated trisomy 13. *Blood* **113**, 1002–1005 (2009).