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Teaching an old dog new trick: Genetic profiling predicts response in elderly acute myeloid leukemia treated with old/new drugs combos

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Older patients with acute myeloid leukemia (AML) have poor outcome; new effective therapies are needed. We hypothesized that the addition of tosedostat, a new amino peptidase inhibitor, or lenalidomide, to low dose cytarabine may improve response over what expected with chemotherapy or tosedostat alone. 66 patients were treated with lenalidomide/araC, 33 with tosedostat/araC (sample sizes according to MiniMax design). The primary outcome was complete remission rate (CR+CRi). To identify sensitivity biomarkers, global gene expression profiling (GEP) was performed on purified AML cells. Lena/araC combo: CR rate was 36.3% (24/66 patients), with an overall response rate (ORR) of 39.3% (26/66). Responding patients had a longer median overall survival than non-responders (375 vs. 70.5 days, $P < 0.0001$). A molecular signature was identified, including 306 genes and 3 miRNA associated with the clinical response, predictable with high accuracy. Concerning the second combo, CR rate was 48.5% with an overall response rate of 54.6%. Responding patients (CR+PR) had a longer median overall survival than non-responders ($P = 0.018$). GEP identified a molecular signature associated with the clinical response, efficiently predicted (overall accuracy exceeding 90%). In conclusion, these data are promising in view of producing companion tests for therapies in elderly AML; and intriguing when thinking at the potential interactions of older drugs with new molecules on gene expression and response to therapy

Biography

Giuseppe Visani, MD, graduated in Medicine from Bologna University Medical School, Italy. After Training at the University Hospital in Bologna, he became Specialist in Hematology and, later, in Oncology. He was Research Fellow in 1986 and 1989 at the Daniel den Hoed Cancer Center–Research Hematology Laboratory, directed by Prof. Bob Lowenberg. He was Aggregate Professor in Hematology at the Institute of Hematology, University of Bologna, Italy, focusing on research and clinical applications in the transplant field, in particular in lymphomas and in acute leukemia. Currently, he is the Head of Hematology and Stem Cell Transplant Center, AORMN Marche Nord, Pesaro, Italy. He is a National Principal Investigator for trials of new drugs in leukemias and lymphomas, with particular interest for conditioning regimens in transplantation in lymphomas. As well, genomics, discovery and clinical application of biomarkers in hematology area are his main focus of activity. He has published more than 350 papers on international, peer reviewed journals.

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