patients in these studies deemed fit, had donors, and were referred for transplant. **Conclusions:** Approximately 40% of elderly AML patients may be cured by allo-SCT.

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Genetic alterations in Guatemalan acute myeloid leukemia patients

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Context: Acute myeloid leukemia (AML) is a cancer in which the three hematopoietic lines are altered: erythroid, myeloid and megakaryocytic line. In this type of leukemia, we have found a variety of genetic markers that allow better management of the disease. The translocation t (8; 21) (q22; q22), which causes the transcript AML1-ETO, the t (15; 17) (q22; q21), which causes the transcript PML-RARA and inv (16) (p13; q22) that leads to the transcribed CBFB-MYH11; have good prognosis. Even the presence of the PML-RARA transcript directed to a specific treatment, that is the combination of trans- retinoic acid with chemotherapy.

Furthermore mutations in FLT3 and cKIT genes; and monosomies on chromosome 7 and 5; confer a poor prognosis when they are present in acute myeloid leukemia. **Objective:** The main aim of this study was to assess the frequency of the main genetic alterations that have been found worldwide related to acute myeloid leukemia in Guatemalan population. **Design and Patients:** We collected 129 bone marrow samples from patients with a diagnosis of AML referred from different national hospitals. Every patient signed the informed consent form approved by the local ethics committee. For the identification for all the genetic alterations, we use a combination of various techniques such as PCR, SANGER sequencing and FISH. **Results:** The PML-RARA transcript was the most frequent alteration found in our population (14%) and was found in 87% of patients with AML M3; as it has been reported in other countries. This was followed by the AML1-ETO transcript, which was found in 9%. The third most frequent was the FLT3 internal tandem duplication mutation in 10% of patients. We have found only two patients with the V826 mutation in exon 17 of c-KIT; two patients with monosomy 7 and one patient with the inv(16) (p13q22).

Additionally, we have found several co-expressions: two patients who have PML-RARα transcript and FLT3 ITD mutation; two patients with PML-RARα and FLT3 D835 mutation, one patient with the AML1-ETO transcript and c-KIT exon 17 mutation; and one patient with monosomy 7 and AML1-ETO presence. These co-expressions have been reported with low incidence in other countries. **Conclusion:** The genetic alteration co-expressions in AML are rare events that can occur in this pathology. We found 6 patients with two genetic markers, one of good prognosis and one poor prognosis. **Keywords:** genetic, alteration, acute, myeloid, leukemia.

Table 1 Genetic Alterations In Guatemalan Acute Myeloid Leukemia Patients

Genetic Alteration	Total	Percentage
t(15;17)(q22;q11-12) PML-RARα transcript	18	14
t(8;21)(q22;q22) AML1-ETO transcript	11	9
inv(16)(p13q22) CBFB/MYH11	1	1
monosomy of chromosome 7	2	2
FLT3 Internal tandem duplication	10	8
FLT3 D835 MUTATION	2	2
c-KIT exon 17 mutation	2	2
c-KIT exon 8 mutation	0	0
negatives	83	64
Total	129	100

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HEXIM1 induction mechanistically contributes to anti-AML activity of BET protein bromodomain antagonist

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BET protein bromodomain antagonists (BA), including JQ1, disrupt the binding of the BET proteins, e.g., BRD4, to acetylated histones and exert lethal activity against AML cells, especially those harboring genetic alterations in NPM1, MLL, FLT3, IDH2 or EVI1. Treatment with BA inhibits BRD4-mediated recruitment of the positive transcription elongation factor b (pTEFb), a heterodimer of CDK9 and Cyclin T1, which inhibits the phosphorylation of RNA polymerase-II (RNAP2) on its C-terminal serine-2. This abrogates the pause-release of RNAP2, thereby attenuating the mRNA transcript elongation and inhibiting the expression of oncogenes, including Myc, BCL2 and CDK4/6. Conversely, treatment with JQ1 increases the mRNA and protein expression of hexamethylene bisacetamide-inducible protein 1 (HEXIM1), associated with growth inhibition and apoptosis of human AML blast progenitor cells (BPCs). HEXIM1 binds to Cyclin T1, thereby sequestering pTEFb in an inhibitory complex, which reduces the free pTEFb available for phosphorylating and activating RNAP2. This raises the question whether HEXIM1-induction is mechanistically involved in BA-mediated RNAP2 inhibition, leading to growth inhibition, differentiation and apoptosis of AML cells. Parenthetically, we determined that HEXIM1 mRNA overexpression is almost mutually exclusive with MYC overexpression in the TCGA AML samples. Here, we demonstrate that the knockdown of HEXIM1 (HKD) increased MYC expression and cell growth, as well as causes significant attenuation of JQ1- or panobinostat (HDAC inhibitor, PS)-induced differentiation and apoptosis in the AML MOLM13-HKD cells. In contrast, tetracycline-inducible,