Efficiency of blinatumomab in a t(8;21) acute myeloid leukemia expressing CD19

Acute myeloid leukemia (AML) blast cells frequently express clusters of differentiation from different cell lineages, a phenomenon known as leukemia associated immunophenotype (LAIP). This phenomenon is widely used to confirm the diagnosis or track minimal residual disease (MRD) by flow cytometry, but has currently not been considered as a therapeutic target.

In AML driven by the t(8;21) translocation, leading to the RUNX1-RUNX1T1 (AML1-ETO) fusion transcript expression, CD19 B-cell antigen is aberrantly expressed in around 80% of the cases.[1] Interestingly, the expression of the CD19 antigen is also detected in the $CD34^+CD38^-$ population, which is enriched in leukemic stem cells.[2] This AML subtype has a rather good prognosis with an intensive chemotherapy regimen, but relapses occur in around 40% of the patients and new therapeutic options are needed for these patients.[3] We describe a patient with a CD19 positive relapsed t(8;21) AML, who achieved a complete molecular response after blinatumomab, a bi-specific antibody engaging T-cell lymphocytes against CD19 expressing cells.

A 62-year-old man was referred to our hospital with relapsed t(8;21) AML 15 months after the start of the induction chemotherapy (Figure 1, panel A). After a salvage regimen based on gemtuzumab, ozogamycin and aracytine, he received a myeloablative conditioning regimen followed by transplantation of hematopoietic stem cells from a 10/10 matched unrelated donor. A molecular relapse occurred 13 months later, which evolved to an overt hematological relapse (30% of bone marrow blasts) despite one donor lymphocyte infusion (DLI). Given the expression of CD19 on the leukemic bulk and also on the more immature $CD34^+CD38^-$ compartment of the relapsed AML (Figure 1B), we hypothesized that targeting this LAIP could have a therapeutic impact. Due to the lack of alternative therapeutic options, the patient gave his consent to receive three courses of blinatumomab following the administration regimen described for lymphoblastic leukemias.[4] A complete remission was obtained after the first course, with no detectable MRD by flow cytometry (Figure 1, panel B) and a deep response at the molecular level. As the molecular MRD level started to rise after three months, a preemptive DLI was performed at the same time as the third course of blinatumomab, leading to undetectable molecular MRD. At the last follow-up eight months after the start of blinatumomab, the patient was in molecular complete response with a total donor chimerism without graft *versus* host disease.

This report suggests that the aberrant expression of CD19 by AML blasts might represent an interesting tar-

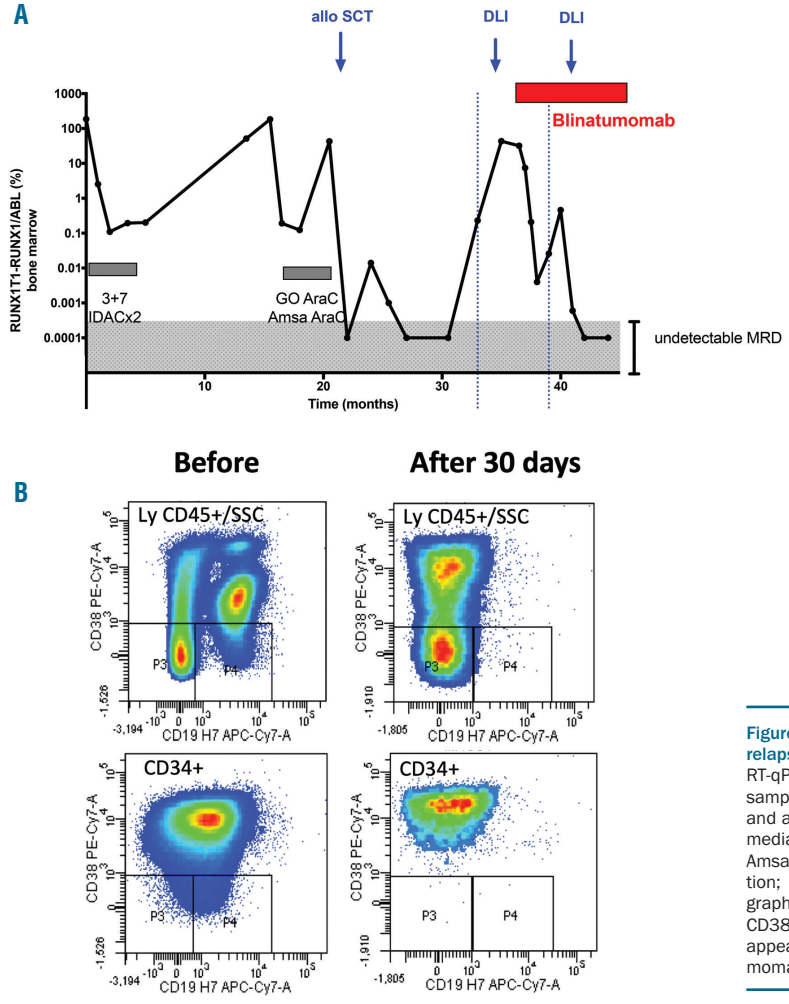

Figure 1. Efficiency of blinatumomab in CD19 positive AML relapse. (A) Evolution of the leukemic burden as evaluated by RT-qPCR of the RUNX1-RUNX1T1/ABL1 ratio in bone marrow samples. 3+7: induction chemotherapy with daunorubicine and aracytine ; IDAC: consolidation chemotherapy with intermediate doses of aracytine; GO: Gemtuzumab ozogamycin; Amsa: amsacrine; Allo-SCT: allogeneic stemcell transplantation; DLI: donor lymphocyte infusion. (B) Flow cytometry graphs showing the presence of leukemic stem cells ($CD34^+$ $CD38^-$) expressing the CD19 antigen (left panel); and the disappearance of this population after one course of blinatumomab (right panel).

get, which warrants rigorous evaluation in prospective clinical trials.

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