



## Cure of Leukemia by Cooperative Research

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### Editorial

In view of the still high mortality of patients with leukemia, progress with leukemia research is urgently needed. Last December, after a 2-year Corona break, the European LeukemiaNet (ELN) resumed meeting overseas cooperation partners by organizing the traditional ELN breakfast symposium at the ASH congress on Sunday mornings from 6 to 10 to promote cooperative leukemia research. The outcome was overwhelming, in part as a rebound effect, but also indicating the unbroken interest in continuing international collaboration in leukemia research thereby supporting the mission of ELN to make the leukemias curable by cooperative research.

In this context, it may be worthwhile to briefly update what progress has been made in leukemias in recent years.

Important advances have been made possible by the precise genetic and molecular characterization of cellular targets, the inhibition of which with specific kinase inhibitors or monoclonal antibodies can be used to target leukemias and which indicate whether therapy has been successful or must be continued because of residual disease.

- In Acute Myeloid Leukemia (AML, 35% to 40% of all leukemias), about half of younger patients (age under 60) can be cured with intensive chemotherapy with or without stem cell transplantation as consolidation. Measurable residual disease status can inform consolidation treatment. ELN recommendation concerning MRD has recently been updated [1]. Patients over 60, who represent the majority of patients, have a median life expectancy of little more than one year despite therapy. There is an urgent need for research in this area. The new ELN recommendations for treating AML prepared under the leadership of Hartmut Döhner will help here [2].

- In Acute Promyelocytic Leukemia (APL, 3% to 5% of all leukemias), a special form of AML, cures without chemotherapy are achieved in 80% of patients only with a vitamin A analog and arsenic [3]. One problem is timely detection and therapy.

- Acute Lymphoblastic Leukemia (ALL, about 15% of all leukemias) has a cure rate of 80% in childhood. In adulthood, the prognosis has improved significantly under intensive chemotherapy and stem cell transplantation with the addition of a tyrosine kinase inhibitor in the particularly unfavorable Philadelphia chromosome positive ALL [4] and by a chemotherapy-free approach with dasatinib and the bispecific CD19 and CD3 targeting monoclonal antibody blinatumomab [5] to a cure rate of 60% to 70%.

- In Chronic Myeloid Leukemia (CML, about 15% of all leukemias), which was inevitably fatal until 25 years ago, almost all patients now achieve a normal life expectancy when treated with a specific tyrosine kinase inhibitor [6]. Currently, therapy-free cures are being pursued [7]. New ELN recommendations for treating CML are being prepared.

- In Chronic Lymphocytic Leukemia (CLL, 35% to 40% of all leukemias), patients who need treatment can now benefit from new targeted BTK or BCL2 inhibitors to significantly prolong life expectancy to levels similar to the unaffected population, at least for the elderly patients [8]. The challenge is how to reduce and optimize the duration of treatment to limit adverse events and clonal evolution. Combinations of these novel drugs look promising. Ongoing research will unravel how the Traditional Predictive markers (TP53 and IGHV mutational status) can still help to stratify patients at the time of starting therapy and whether minimal residual disease might become part of clinical monitoring [9].

The cure of leukemia will depend on continued research, but also on the appropriate dissemination of research results in scientific journals. The American Journal of Leukemia Research helps by informing the leukemia community and the public on research advances to the benefit of patients with leukemia.

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