

CML – where do we stand in 2015?

The progress with CML treatment continues at a rapid pace. Treatment of choice is targeted therapy with tyrosine kinase inhibitors (TKI). Five-year survival ranges around 91% and 10-year survival around 84% up from 11% with Busulfan 30 years ago. More CML patients meanwhile die from other causes than from CML, and survival approaches that of the general population.

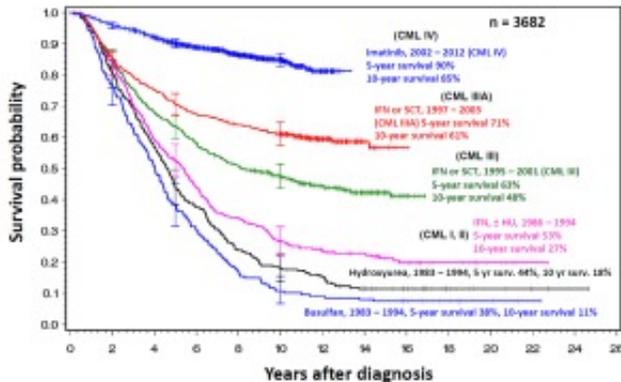


Fig. 1. Survival with CML over time. German CML Study Group, update 2015

Figure 1 gives an overview what has been achieved over the past 30 years. An important early measure of treatment success is the disappearance of leukemia cells from blood and marrow as measured by cytogenetics (no Philadelphia (Ph) chromosomes detectable anymore) or molecular testing (BCR-ABL fusion transcripts, the molecular correlate of the Ph chromosome, greatly reduced). Figure 2 illustrates the depth of molecular response achieved over the years with the TKI imatinib.

Experience over the last few years has shown that treatment can be successfully discontinued in patients that have been treated long enough and have achieved a sufficiently deep molecular remission over a sufficiently long period of time. Treatment goal for CML is no longer palliation or prolongation of survival, but discontinuation of therapy or cure.

Due to the almost normal life span of CML patients, the number of patients (prevalence) is increasing worldwide posing economic problems due to the high TKI costs. The availability of generic imatinib from 2016 onwards is likely to decrease costs substantially. The special CML issue of the Annals of Hematology summarizes in 15 state-of-the-art reviews current knowledge on CML. There are multiple options to improve 1st and 2nd line treatment on the basis of now 6 different TKI (imatinib, dasatinib, nilotinib, bosutinib, ponatinib and radotinib).

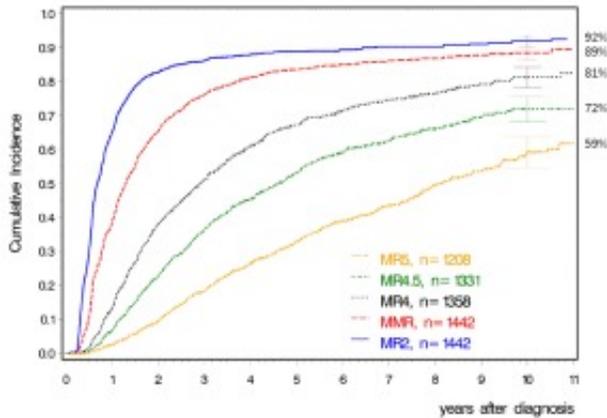


Fig. 2. Molecular response achieved with imatinib over time. Kalmanti et al., Leukemia (2015)

Management recommendations of the European LeukemiaNet facilitate a personalized approach to individual patients that considers comorbidities, adverse drug effects and special situations such as pregnancy and fertility preservation.

Blast crisis has become rare, but is still a problem if it occurs. Stem cell transplantation and investigational agents can be tried. Most important is adequate treatment monitoring. Lack of adherence to treatment is probably the most important reason for suboptimal outcomes. The baseline of the current situation in CML is that we have achieved much, but that still 6-10% of CML patients die of CML. Due to the necessity of life-long treatment of most CML patients, the high treatment costs and the need for regular monitoring CML remains a public health issue. Optimization of treatment and progress with discontinuation will help, but probably not solve the problem. We have not yet reached our goal of cure for every patient with CML.

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