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HAEMATOLOGICAL CANCER

# Deep molecular response predicts survival in CML

New research has shown that a majority of patients with chronic myeloid leukaemia (CML) who are treated with the tyrosine kinase inhibitor imatinib can achieve a deep molecular response (≥4.5-log reduction in *BCR–ABL* fusion gene transcript levels; $MR^{4.5}$) and that $MR^{4.5}$ is predictive of survival.

Major molecular response (MMR; ≥3-log reduction in *BCR–ABL* transcript levels) is currently used to assess prognosis. However, mounting evidence has shown that deeper molecular responses (that is, $MR^{4.5}$ or higher) might correlate better with long-term outcomes. The CML–Study IV trial is the first to evaluate correlations between $MR^{4.5}$ and long-term outcomes; molecular monitoring was performed for all patients in the study from the beginning.

More than 1,500 patients were enrolled and were assigned to several different imatinib-based regimens in terms of dosing or combination with other therapies (namely, IFN-α, cytarabine or alone). The median observation time was 67.5 months.

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"Deep molecular response is a prestage of cure of CML," explains lead investigator Rüdiger Hehlmann, from the University of Heidelberg, Germany. "We found that a deep response level can be achieved in the majority of imatinib-treated patients with CML." Indeed, after 9 years, 70% of patients achieved $MR^{4.5}$. Furthermore, this level of response was more common in patients who were treated with the highest doses of imatinib (800 mg per day, tolerability-optimized). "It is also interesting that $MR^{4.5}$ is achieved faster in these patients than those receiving 400 mg imatinib," comments Hehlmann. Additionally, $MR^{4.5}$ at 4 years independently predicted survival and, in turn, high-dose imatinib and early MMR predicted $MR^{4.5}$.

These results suggest that $MR^{4.5}$ can be used to guide treatment cessation in patients with CML, with treatments selected that can achieve an early deep molecular response.

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