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Cure of chronic myeloid leukemia by tyrosine kinase inhibitors

ABL tyrosine kinase inhibitor, imatinib mesylate (GlivecTM) has drastically changed the prognosis of chronic myeloid leukemia (CML). However, it had been believed that CMP patients could not stop imatinib because it had no effects on CML stem cells. Recently, French group reported that imatinib could be discontinued without molecular relapse at least in some CML patients when complete molecular response (CMR) sustained more than two years with imatinib. However, little is known about whether the assumption could be exploitable for the second-generation ABL-tyrosine kinase inhibitor, dasatinib (SprycelTM) which was more potent than imatinib. Thus, we conducted a prospective, multicenter clinical trial, named Dasatinib Discontinuation (DADI) to assess whether dasatinib could be discontinued without molecular relapse in CML patients in CMR. In total, 88 patients were pre-registered at 41 participating institutions in Japan. Among them, a total of 64 patients who maintained stable CMR for one year after pre-registration were enrolled for the dasatinib-discontinuation stage. Among 62 patients evaluated, the estimated molecular relapse free survival at 6 months was 48.3%. Reintroduction of dasatinib to the relapsed patients showed rapid molecular responses in all of them. These findings suggested that dasatinib could be safely discontinued in a proportion of CML patients with stable CMR for at least one year, provided that frequent molecular monitoring is performed. In this session, the author will summarize the current status of "Cure of CML with tyrosine kinase inhibitors" including our other ongoing studies.

Biography

Shinya Kimura has completed his MD from Jichi Medical School and Postdoctoral studies from the Walter and Eliza Hall Institute and Frankfurt University. He is the Director of Cancer Centre of Saga University Hospital. He has published more than 130 papers mostly in the fields of clinical hematological malignancies and novel targeted therapies for BCR-ABL positive leukemias. He developed a novel ABL/LYN inhibitor, bafetinib and a fully automated ABL mutation detection system (i-densyTM). He also serves on the editorial board of Recent Patents on *Anti-Cancer Drug Discovery, International Journal of Clinical Oncology and Open Journal of Hematology*.

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