Evolution of CML treatment

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Chronic myeloid leukemia (CML) is a hematopoietic malignancy caused by the Philadelphia chromosome, which is formed by reciprocal translocation of chromosomes 9 and 22. The prognosis for CML patients has improved dramatically since the introduction of imatinib mesylate, an ATP competitive type tyrosine kinase inhibitor (TKI), in 2001. However, approximately one-third of CML patients become resistant and/or intolerant to imatinib mesylate. To overcome this, second-generation TKIs dasatinib, nilotinib, and bosutinib were developed. These second-generation TKIs cause faster and deeper remission, and all three are now available as a first-line treatment. However, these TKIs are ineffective against the T315I mutation. Thus, a third-generation TKI, ponatinib, was developed. Use of these five TKIs means that the life-expectancy of CML patients is almost the same as that of healthy individuals [1]. Furthermore, many clinical trials show that a certain number of CML patients do not develop molecular relapse, even after discontinuing TKIs [2]. CML is a hematological malignancy that benefits from the most advanced treatments; therefore, the knowledge gained from studying CML is extremely useful not only in the context of other hematological malignancies but also in the context of other cancers.

So, I plan to use CML as a topic for the Progress in Hematology Review Series. To eliminate bias with respect to country, and to further internationalize the *International Journal of Hematology*, I invited contributors from the United States, Canada and Japan.

The group of Dr. Koji Sasaki (The University of Texas MD Anderson Cancer Center) gave a presentation entitled “Current status and novel strategy of CML”. Dr. Sasaki is a Japanese clinical hematologist who leads the section of

CML at MD Anderson Cancer Center, and is, therefore, the most appropriate person to write about the present and future status of CML [3].

The group of Dr. Dennis Kim (Princess Margaret Cancer Centre, University of Toronto) wrote a review entitled “Target Spectrum of the BCR-ABL Tyrosine Kinase Inhibitors in Chronic Myeloid Leukemia”. Dr. Kim has worked as a clinical hematologist in both Korea and Canada and has published many clinical reports and basic research papers on CML [4].

Dr. Hiroshi Ureshino (Saga University) wrote a review article entitled “Treatment-free remission and immunity in chronic myeloid leukemia”. Although total cell kill by TKIs is impossible, some patients sustain treatment-free remission (TFR) after stopping TKIs. This is thought to be due to the immune system. Dr. Ureshino has been studying the importance of immunity in TFR at his institution and in multicenter trials [5].

Dr. Kazuhito Naka (Hiroshima University) has been conducting basic research on hematopoietic stem cells for a long time and has published many excellent papers [6]. Since TKIs cannot eliminate CML stem cells, residual CML stem cells are a major obstacle to the maintenance of a molecular response after TKI discontinuation. Thus, more research on CML stem cells is needed to bring more patients to TFR. Dr. Naka has summarized the latest findings in the field of CML stem cell research as “New Routes to Eradicating Chronic Myelogenous Leukemia Stem Cells by Targeting Metabolism”.

I hope that these four review articles will be of interest to readers, and improve clinical practice and research in the field of CML.

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