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Drug induced inhibition of kinases activity and immunological surveillance in patients with hematological malignancies

Andrzej Lange
Polish Academy of Sciences, Poland

The current description of leukemia and lymphoma is based on molecular analysis of the neoplastic cells. Mutation of some genes increases the activity of serine/threonine and tyrosine (T/S) kinases, which drives the proliferation potential of malignant cells. In clinical practice several small-molecules are in use to block the enhanced kinases activity. The immune system plays a role in the surveillance of leukemia, providing the recognition of leukemic cells by lymphocytes what facilitates the administration to patients kinases inhibitors able to moderate tumor burden to avoid high-dose antigen tolerance. This will be discussed in some detail based on the model situations: (i) Flt-3 + acute myeloid leukemia, (ii) bcr/abl+ acute lymphoblastic leukemia relapsing post alloHSCT and (iii) JAK2 V617F + myelofibrosis. The use of T/S kinases inhibitors helped in the induction of remission. The role of the immune system surveillance including the graft-versus-leukemia effect in maintaining the remission will be discussed on the basis of the analysis of lymphocytes colonizing the marrow spontaneously or as an effect of donor lymphocytes infused intravenously or directly to the leukemic bone lesions in a relapsing patient. The data presented support the view that the use of some T/S kinases inhibitors by slowing down the expansion potential of leukemia facilitates the initiation of a spontaneous or induced graft-versus-leukemia effect.

Biography

Andrzej Lange is a Professor of the Institute of Immunology and Experimental Therapy, and the Founder and Head of the Lower Silesian Centre for Cellular Transplantation, Wrocław, Poland. He was a Research Fellow and lectured at several European and American universities. His pioneering work on immunological and genetic consequences of asbestos and aromatic hydrocarbons exposure earned him international recognition. He published 212 papers in peer-reviewed journals, mostly devoted to immunogenetic and clinical aspects of leukaemia treatment, including Hematopoietic Stem Cell Transplantation. Recently he has been involved in a study on regenerative medicine and cellular therapy post HSCT.

lange@dctk.wroc.pl