Cytogenetic landscape and impact in blast phase of chronic myeloid leukemia in the era of tyrosine kinase inhibitor therapy

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The landscape of additional chromosomal alterations (ACAs) and their impact in chronic myeloid leukemia, blast phase (CML-BP) treated with tyrosine kinase inhibitors (TKIs) have not been well studied. Here, we investigated a cohort of 354 CML-BP patients treated with TKIs. We identified +8, an extra Philadelphia chromosome (+Ph), 3q26.2 rearrangement, −7 and I (17q) as the major-route changes with a frequency of over 10%. In addition, +21 and +19 had a frequency of over 5%. These ACAs demonstrated lineage specificity: +8, 3q26.2 rearrangement, I (17q) and +19 were significantly more common in myeloid BP and −7 more common in lymphoid BP; +Ph and +21 were equally distributed between two groups. Pearson correlation analysis revealed clustering of common ACAs into two groups: 3q26.2 rearrangement, −7 and I (17q) formed one group and other ACAs formed another group. The grouping correlated with risk stratification of ACAs in CML, chronic phase. Despite, the overall negative prognostic impact of ACAs, stratification of ACAs into major vs minor-route changes provided no prognostic relevance in CML-BP. The emergence of 3q26.2 rearrangement as a major-route change in the TKI era correlated with a high frequency of ABL1 mutations, supporting a role for TKI resistance in the changing cytogenetic landscape in CML-BP.

Biography
Shimin Hu is currently a Faculty Member at The University of Texas MD Anderson Cancer Center. He has received his MD from Peking University and PhD from University of Michigan. He did his Pathology Residency training at Hartford Hospital, CT and Hematopathology Fellowship training at The University of Texas MD Anderson Cancer Center. He has published about 60 papers during past three years in highly-regarded journals, including many in Blood and Leukemia.

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