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Recent advances in treatment of childhood cancer : role of targeted therapy

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Editorial

Advances in the basic science of cancer, genetic studies, molecular biology and different modalities of therapy including chemotherapy, radiotherapy, surgery and supportive care have occurred in the last few decades. Improvement in histological, immunological and cytogenetic techniques has made the diagnosis and classification more accurate. The development of multiple-agent chemotherapy, targeted and pharmacogenetic therapies as well as hematopoietic stem cell transplantation hold great promise for the future. Molecular HLA-typing techniques and the international donor registries have solved the problem of finding appropriate donors for transplantation. In addition, progress in palliative care has provided a degree of comfort for patients undergoing chemotherapy, radiotherapy and surgery.

Recently targeted cancer therapy has made a good impact in treatment of childhood chronic myeloid leukemia (CML) and Philadelphia positive acute lymphoblastic leukemia (Ph+ ALL). The Ph+ is due to reciprocal translocation of the long arms of chromosomes 9 and 22, t (9:22) (q34; q11), which results in a fusion gene BCR-ABL, encoding a constitutively active tyrosine kinase. The BCR-ABL tyrosine kinase inhibitor (TKI), imatinib, is now used in treatment of Pediatric CML as well as Ph+ALL. It selectively inhibits the tyrosine kinase domain in the Abelson proto-oncogene (ABL) and targets the tyrosine kinase C-kit and platelet – derived growth factor receptor (PDGF-R) which causes the mutations found in both myeloid and lymphoid malignancies.[1, 2] As a result, phosphorylation of ABL-tyrosine kinase substrates fails to occur and prevent activation of leukemogenic signal transduction. It was approved in 2001 for treatment of CML and in 2013 for treatment of Pediatric Ph+ALL.

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A report from the children's Oncology group has recorded success in treatment of de-novo chronic phase CML in children in 80% of cases.[3] CML comprises 2-3% of all childhood leukemia. Response to treatment with imatinib appears to be better in children than in adults.[4, 5, 6] Recently, the use of imatinib alone in treating CML in children is considered when no HLA-identical donor for stem cell transplantation is available.

The high-risk Ph+ALL represents 3-5% of childhood ALL.[7] The use of chemotherapy alone in its treatment results in less than 30% event-free survival rates.[8] Children Oncology Group (COG) reported improved outcomes of children with Ph+ALL treated with imatinib and chemotherapy.[9] Its role in pre-and post-hematopoietic stem cell transplantation is still under study and evaluation.[10] In conclusion, the targeted imatinib therapy dramatically improved the outcomes of children with CML and Ph+ALL.

Currently, several novel targeted therapeutic strategies are being investigated. They include Troxacitabine (a nucleoside analogue), Decitabine (a hypomethylating agent), R15777 SCH66336 (farnesyl transferase inhibitor), Homoharringtone (a plant alkaloid), PS-341 (a proteosome inhibitor), PR1 vaccine, polyethylene glycol IFN-α preparations, and inhibitor of heat shock protein 90 (a molecular chaperone required for stability of signal proteins). Success of these novel drugs will add a major advance in combating malignancy.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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(Dr. Youssef Al-Tonbary is an editorial board member of International Journal of Cancer Therapy and Oncology)

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