Contemporary Treatment of Pediatric Ph+ ALL

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Ph+ ALL represents approximately 2.5% of all pediatric ALL cases and was until recently considered to be one of the highest risk subgroups of pediatric ALL. The introduction of tyrosine kinase inhibitor agents in combination with ALL therapy has resulted in a significant improvement in the outcomes of pediatric Ph+ ALL in the last 15 years. These advances have been a result of standardized clinical trials performed by the North American based Children’s Oncology Group (COG) and European-based EsPhALL group. These studies helped us to develop a roadmap for the integration of targeted therapies in combination with chemotherapy for other pediatric malignancies as well. A number of controlled trials have been completed and an international COG-EsPhALL study is current accruing the largest cohort of pediatric Ph+ ALL patients worldwide. We have learned a number of things regarding the tolerability of TKIs with backbone chemotherapy, the role of MRD in predicting the outcome of Ph+ ALL therapy, and additional biological risk factors that impact outcome of Ph+ ALL chemotherapy with TKI. Large biology studies have also identified that a large number of Ph- very high risk pre-B ALL have a BCR-ABL-like molecular pattern and are amenable to identical strategies as used for classic Ph+ ALL. The role of hematopoietic stem cell transplantation (HSCT) and other immune based therapies such as bispecific antibodies and CAR T cells continue to be re-evaluated and their role is evolving. In addition, there remain a number of unanswered questions regarding the use of TKIs after completion of chemotherapy and HSCT, and in BCR-ABL-like pre-B ALL.

Objectives:

a. To learn of the results of the past and current COG and EsPhALL therapeutic and biology studies and their impact on the outcomes of pediatric Ph+ ALL.

b. To present the state-of-the-art therapies for pediatric Ph+ ALL and BCR-ABL-like ALL and contrast these results to outcomes in adult Ph+ ALL.

c. To discuss controversies and unanswered questions regarding the role of minimal residual disease, backbone chemotherapies, cell based and monoclonal based immune therapies, and hematopoietic stem cell transplant in the era of TKIs for Ph+ ALL.