

Remaining Challenges in Childhood Cancer and Newer Targeted Therapeutics



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KEYWORDS

- Targeted therapy • Personalized medicine • Pediatric cancer drug development
- Innovative clinical trials • Preclinical testing

KEY POINTS

- There are only a limited number of druggable molecular targets identified to date in childhood cancers. Nonetheless, evaluation of inhibitors of those that have been identified is warranted in relevant tumor types and subsets of patients.
- The principle of integration of active targeted therapy with best-available therapy has been established and will likely be the basis for future investigations and hopefully advances.
- Strong biologic rationale and preclinical data, particularly from in vivo testing, are central to effective prioritization of agents for clinical evaluation.
- Prioritization of “same-in-class” products will be a persistent challenge, but is essential for effective pediatric cancer drug-development strategies.
- Increased, effective communication and collaboration among clinical investigators, industry, and international regulatory agencies are essential for the development of successful clinical research plans and improved drug-development opportunities.

INTRODUCTION

The remaining challenges for childhood cancer research are best understood in the context of past advances. Treatment of childhood cancer was one of the important success stories of twentieth century medicine as exemplified by the conversion of pediatric acute lymphoblastic leukemia (ALL) from an incurable disease in the 1950s to one in which more than 90% of children survived 5 years from diagnosis, with most of these children cured of their leukemia.¹ Other cancers also have 5-year survival

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rates approaching or exceeding 90%, including Wilms tumor, non-Hodgkin lymphoma (NHL), Hodgkin lymphoma, and germ cell tumors. Importantly, the decline in childhood cancer mortality that began in the 1960s continued through the first decade of the twenty-first century.¹ Research advances averted more than 45,000 childhood cancer deaths from 1975 to 2010.¹

Despite the successes in identifying effective treatments for many children with cancer, approximately 2000 children and adolescents die of their disease each year in the United States.¹ Fig. 1 shows the distribution of childhood cancer mortality for children and adolescents, highlighting the contribution of leukemias, brain cancers, and neuroblastoma in younger children and the contribution of leukemias and brain cancers, along with sarcomas and lymphomas, in adolescents. Additionally, for some cancers, progress has been very limited (eg, diffuse intrinsic brainstem gliomas, high-grade gliomas, and metastatic sarcomas). Beyond the number of children who die each year, there is also the burden of long-term morbidity that diminishes quality of life for some childhood cancer survivors.

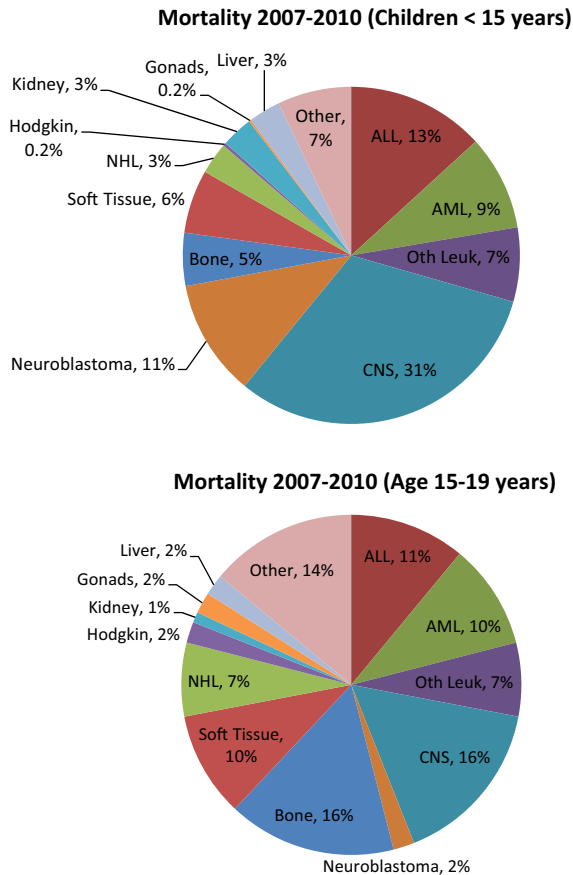


Fig. 1. Patterns of mortality for children and adolescents younger than 15 years and 15 to 19 years for 2007 to 2010. CNS, central nervous system; Oth Leuk, other leukemia. (Adapted from Smith MA, Altekruze SF, Adamson PC, et al. Declining childhood and adolescent cancer mortality. *Cancer* 2014;120(16):2500; with permission.)

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