Targeted Therapies in Pediatric Oncology

The optimization of treatment strategies in pediatric oncology has massively improved survival rates of children with cancer over the last decades. In recent years, however, it became clear that further intensification of conventional treatment modalities may not necessarily lead to additional advancements in outcome, or may be limited by their toxicities. High hopes have therefore been raised on the advent of targeted therapies in pediatric oncology. As a prototypic example, implementation of the kinase inhibitor imatinib directed against *BCR-ABL1* fusions in clinical practice has revolutionized treatment of adult and pediatric chronic myeloid leukemia patients, leading to dramatically improved outcome with limited toxicities. While great efforts are being made to establish similar strategies in other pediatric malignancies, a number of challenges have to be overcome to achieve the goal of personalized therapies in children with cancer. First, characterization of genomic alterations in pediatric tumors by massively parallel sequencing revealed that the mutation rate in these tumors is low, compared to adult malignancies, and that the mutation spectrum is heterogeneous in most entities. Taking also the low incidence of pediatric tumors into account, the resulting low patient numbers pose a challenge to establishing clinical trials, in which the potential benefit of such therapies can be examined. Second, many of the genomic mutations that are known to be drivers in pediatric cancers are currently not actionable by available drugs, such as alterations of *MYCN* or *TERT*. Third, ethical and economic considerations hamper the transfer of novel targeted drugs from adult oncology to pediatrics. While it is plausible that the safety and tolerability of novel drugs is usually investigated in adult patients first, the transfer of these drugs to pediatric patients is often impaired by economic considerations, which may be due to the low numbers of patients eligible for such therapies. To overcome these hurdles, intensive collaboration between pediatric oncologists, cancer geneticists, pathologists, and pharma industry is needed to ultimately reach the goal of improving patient outcome by personalized therapies in pediatric oncology.

Conflict of Interest

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