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Immunotherapy in pediatric oncology: Opportunities and challenges.

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Introduction

Over the past decade, immunotherapy has emerged as a transformative approach in oncology, harnessing the body's own immune system to detect and destroy cancer cells. While adult oncology has witnessed significant strides with immune checkpoint inhibitors, CAR-T cell therapies, and cancer vaccines, pediatric oncology poses a distinct set of biological, clinical, and ethical considerations. The development and application of immunotherapeutics in children hold immense promise but are also fraught with unique challenges requiring innovative solutions and collaborative frameworks [1].

Unlike adult cancers, pediatric malignancies often arise from developmental abnormalities and are less likely to be associated with environmental exposures or mutations accumulated over time. Pediatric tumors—such as acute lymphoblastic leukemia (ALL), neuroblastoma, and Wilms tumor—typically exhibit: Low mutational burden, leading to fewer neoantigens for immune recognition. High heterogeneity and rapid proliferation. Unique tumor microenvironments, sometimes less infiltrated by immune cells [2].

Ethical concerns in enrolling pediatric patients, necessitating careful trial design and informed consent processes. Low neoantigen load in pediatric tumors reduces immunogenicity: Requires engineering novel targets or using bispecific antibodies to overcome antigen limitations. Advanced immunotherapies are expensive and not readily available in low- and middle-income countries: Raises questions about global equity, policy frameworks, and resource allocation. This distinct biology affects the responsiveness of pediatric tumors to immune-based therapies. Despite these challenges, several immunotherapy modalities have shown promise: Chimeric Antigen Receptor (CAR) T-cell therapy has revolutionized treatment for relapsed/refractory B-cell ALL in children: CD19-targeted CAR-T cells have achieved complete remission rates exceeding 80% in clinical trials. Offers curative potential for patients unresponsive to conventional chemotherapy. Monoclonal antibodies directed against tumor-specific antigens are effective in neuroblastoma: Anti-GD2 antibody therapy combined with cytokines improves survival and reduces recurrence risk [3].

Although still exploratory, vaccines based on tumor antigens and genetically engineered viruses have shown immunostimulatory effects and potential in pediatric gliomas. Checkpoint blockade targeting PD-1/PD-L1 or CTLA-4 remains under investigation in pediatric settings: Some success in lymphomas and sarcomas, though responses are variable due to the immunologically “cold” nature of pediatric tumors. Advancements in genomic and transcriptomic profiling now allow personalized strategies in pediatric immunotherapy: Tumor mutational burden (TMB) and immune cell infiltration guide patient selection [4].

Children are a vulnerable population; immunotherapy must respect developmental, psychological, and ethical dimensions: Long-term effects of immune modulation on developing systems are not well understood. Fertility preservation, growth impacts, and immune system maturation require longitudinal follow-ups. Equitable involvement of pediatric patients and families in clinical decisions is essential. Circulating tumor DNA (ctDNA) and immune signatures serve as non-invasive biomarkers for monitoring response and relapse. Integration of AI-

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based analytics helps stratify patients for tailored immunotherapy regimens. Several hurdles limit widespread application and effectiveness: Immune therapies may trigger cytokine release syndrome (CRS) or neurotoxicity, which are especially concerning in children: Pediatric physiology and immune development require age-specific toxicity monitoring [5].

Conclusion

Immunotherapy in pediatric oncology offers transformative potential but must be approached through a lens of biological nuance, ethical sensitivity, and collaborative innovation. As our understanding of child-specific immune mechanisms grows, and as clinical trial infrastructures evolve, immunotherapeutic approaches will increasingly provide safer, more effective, and accessible cures for childhood cancers.

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