CLIPPINGS

Combination therapy with anti-pd-1 or pd-1 antibody alone in Asian pediatric patients with relapsed or refractory cancer (*Front Immunol. 2021;647733*)

Prognosis for recurrent/progressive solid tumors in children remains unfavorable, with a 10-year OS and PFS of 24.5% and 18.4%, respectively. Many novel targeted therapies have come up in the recent years, inhibitors of PD-1, pembrolizumab and nivolumab have been extensively explored. The results indicated that they are tolerated well in pediatric patients and have shown benefit in lymphomas, especially in HL.

In this study, twenty-two pediatric patients with cancer who received PD-1 inhibitors between 2017 and 2020 were enrolled. Nine patients (6 with Hodgkin's lymphoma, 2 with Malignant melanoma and one with Burkitt's Lymphoma) received monotherapy with Anti PD-1. Amongst these, the Hodgkin's Lymphoma patients responded well. For PD-1 antibody combined with other standard chemotherapy regimens, no significant benefit was observed. Interestingly, among the patients treated with PD-1 antibody combined with decitabine, the effect was significant. The hypomethylating agent decitabine is suggested to increase tumor T-cell infiltration and the antitumor response, ultimately restoring immunosurveillance. Both the groups (monotherapy and combination therapy) tolerated Anti PD-1 well with minimal adverse events. Thus, combinatorial approaches are likely to be used in the future and have the potential to achieve therapeutic success, especially in relapse/refractory setting.

The phase 3 pediatric anticoagulant era (*Blood.2020;135:459-60*)

A phase 3 trial was done on patients from 3 months to 18 years with a history of provoked VTE (i.e. VTE associated with a clinical trigger such as central venous catheterization, etc) in whom 1 or more prothrombotic risk factors persisted after completion of a conventional course of anticoagulation and also patients with recurrent unprovoked VTE. The median duration of dabigatran administration (adjusted for age and body weight) in this study was 8 months. The investigators observed significant bleeding in only 2.5% of patients (5 of 203) and recurrent VTE in 1% (2 of 203) with no deaths reported.

These findings were consistent with studies on Riva-roxaban (Factor Xa inhibitor) in EINSTEIN Jr phase 3 trial of acute VTE in children. In this group clinically relevant bleeding was found in 3% of patients, and symptomatic recurrent VTE was found in 1%. Post throm-botic syndrome was observed by Brandão and colleagues in 1% of the children receiving extended anticoagulation with a DOAC. These studies suggest that dabigatran and Rivaroxaban are safe for extended VTE treatment in children and do not require routine laboratory monitoring. However, issues such as the optimal duration of antico-agulant therapy for pediatric VTE and the relationship between antiphospholipid antibodies and outcomes in young patients yet need to be evaluated.

2021 Update on clinical trials in β-thalassemia (*Am J Hematol.2021;96:1518-31*)

The treatment of β-thalassemia patients has witnessed a swift evolution from transfusions alone to novel targeted therapies, yet several unmet needs continue to persist.

Interim analysis of ongoing phase 3 trials using a refined transduction process showed transfusion independence in 30/34 (88.2%) evaluable patients (6/7 [85.7%] β0/β0 and 24/27 [88.9%] non-β0/β0) on receiving cells transduced ex-vivo with the LentiGlobinBB305 vector based gene therapy product betibeglogene autotemcel in 2019. Genome editing approaches are developed to inhibit BCL11A through enzymes like CRISPR-Cas9, transcrip-tion activator-like effector nucleases (TALENS), and zinc finger nucleases (ZFN). A phase 2 trial is underway in adults for PDE9 inhibitor IMR-687, which increases intracellular cGMP levels and stimulates the production of HbF. Erythroid maturation agents - Luspatercept (ACE-536) is a recombinant fusion protein of the human activin receptor type IIB fused to the Fc domain of human IgG1 which blocks SMAD2/3 signaling, and enhances erythroid maturation. The BELIEVE and BEYOND trial in adults have shown significant reduction in transfusion requirement. Pediatric trials on luspatercept are also underway. These therapies are promising but the key challenges to wide implementation are cost and the need for specialized centers and clinical expertise for application.

Palliative care in paediatric oncology: An update (*Curr Oncol Rep. 2022;24:175-86*)

Palliative care provides active, holistic care for children and young people with life-limiting illnesses, from the point of a child's diagnosis, throughout the child's life, death, and bereavement. Many deficiencies were realized while providing treatment to pediatric oncology patients in even tertiary care centers. Pain is a common symptom which is often not addressed adequately. Families felt that continuous communication between parents, family caregivers, and health care providers is lacking and they often felt unprepared to deal with their child's death.

Globally, children with cancer were infrequently referred to palliative care or referred late in the illness. Problems in low and middle income countries like limited access to opioids, lack of interdisciplinary care, and families less empowered to participate in decision-making; worsens the situation.

Palliative care input bettered end-of-life care support to children and their families. It facilitated less invasive diagnostic and therapeutic interventions at the end of life. The families appreciated the healthcare system's support beyond usual clinical management, also in terms of managing finances and assistance to manage the child's needs at home.

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