Supplemental Table 1. Immunotherapeutic Approaches Tested in Clinical trials for Pediatric Solid Tumors at the Crossroads

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| --- | --- | --- | --- |
| Immunotherapeutic Approach | Target | Disease Evaluated | Ref |
| mAb | HER2 (Trastuzumab) | Osteosarcoma | (1) |
| mAb | Anti-glycoprotein non-metastatic B (CDX-011) | Osteosarcoma | (2) |
| mAb | Tumor necrosis factor related apoptosis-inducing ligand (lexatumumab) | Pediatric sarcomas | (3) |
| mAb | Insulin-like growth factor 1 receptor (cixutumumab) | Pediatric sarcomas | (4) |
| CAR-T | GD2 (3rd generation) | Neuroblastoma | (5) |
| CAR-T | HER2 (2nd generation) | Pediatric sarcomas | (6) |
| ICI | CTLA4 (ipilimumab) | Pediatric solid tumors | (7) |
| ICI | PD-1 (nivolumab) | Pediatric solid tumors | (8) |
| ICI | PD-1 (pembrolizumab) | Pediatric solid tumors /lymphoma | (9) |
| ICI | PD-L1 (atezolizumab) | Pediatric solid tumors | (10) |
| Vaccine therapy | Wilms tumor gene 1 | Pediatric tumors | (11) |
| Vaccine therapy | NeuGcGM3 (racotumomamb) | Neuroblastoma and other pediatric tumors | (12) |
| Vaccine therapy | Dendritic cell vaccines (Review) | Pediatric tumors | (13) |

Supplemental Table 2. Promising Immunotherapeutic Approaches Beyond Traditional Checkpoint Blockade with Examples of Successful Clinical Application in Adult Solid T umors

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| --- | --- | --- | --- |
| Biologic Approach | Target / Modality  | Agents utilized  | Clinical Application (Ref) |
| T cell based therapies | Co-inhibitory pathways  | Anti-LAG3; anti-TIM-3; anti-TIGIT | (14) |
| T cell based therapies | Tumor reactive (TCR-driven) T cells | Viral specific T cells (i.e. autologous EBVSTs); Autologous and normal donor-specific T cells; Autologous TAA-specific T cells; T cells with vaccines; TILs enriched for mutation-specific T cells | (15) |
| T cell based therapies | CAR-T cells | CAR-T cells | (16) |
| NK cells | NK cells | NK cells | (17) |
| Vaccine therapy | Vaccine therapy  | Synthetic peptides, messenger RNA, DNA plasmids, viral vectors, engineered attenuated bacterial vectors, ex vivo antigen-loaded dendritic cells | (18) |
| TME | Vasculature, hypoxia | Anti-angiogenics (i.e. anti-VEGF); anti-hypertensives targeting the renin-angiotensin system; anti-CXCR4 agents | (19,20) |
| TME | Regulatory T cells (Tregs) | Depletion of Tregs (anti-CD25, anti-CCR4); Reprogramming of Tregs (OX40, GITR, IDO1 inhibitors)  | (21) |
| TME | Myeloid cells  | Tumor associated macrophage reprogramming agents (i.e. Anti-CSF-1/R+, CCL2, IL-6, CD40) | (22) |

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