Hematopoietic cell transplantation after CD19-directed CAR T-cell therapy for remission consolidation or relapse treatment in pediatric acute lymphoblastic leukemia

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DATA SUPPLEMENT

Supplemental Methods

Transplant Approach

Bone marrow grafts from HLA-matched related donors (MRDs) were used when available. Alternative donors were otherwise selected based on donor availability and recipient clinical status: 9- or 10-allele matched unrelated donor (URD) unmanipulated bone marrow (BM) or peripheral stem cells (PSC), or mismatched related donor (MMRD) PSCs. All PSCs underwent *ex vivo* partial T cell depletion using the CliniMACS Plus device (NCT02356653, NCT02323867, NCT03810196).[1,2]

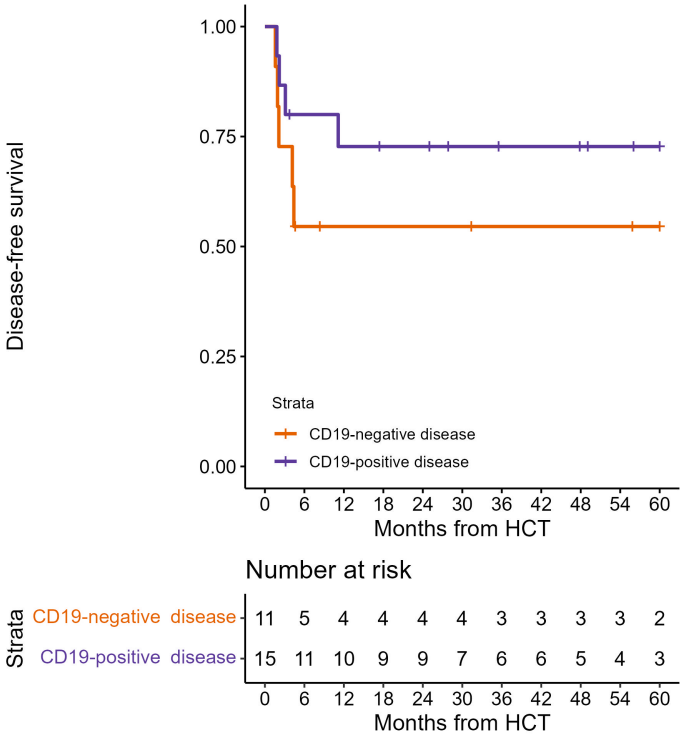
All patients had pre-HCT disease restaging to confirm adequate remission [<0.1% marrow blasts by multiparameter flow cytometry (MFC), central nervous system (CNS)-1]. All received myeloablative conditioning with total body irradiation (TBI; 1200 cGy), cyclophosphamide and thiotepa with the exception of children <3 years of age, who received clofarabine, thiotepa and melphalan.[3,4] Thymoglobulin (9mg/kg) was added for URD BMTs or MMRD PSCTs. GVHD prophylaxis included a calcineurin inhibitor +/- methotrexate for BMTs, [5] or a calcineurin inhibitor (in cases of CD3 or CD45RA-depleted addback) or no prophylaxis for partially T cell-depleted PSCTs.

All patients received bacterial, fungal and *Pneumocystis jirovecii* prophylaxis. Prophylactic acyclovir was used for patients with herpes simplex or varicella virus seropositivity, foscarnet or letermovir for patients with positive cytomegalovirus (CMV) serology, and rituximab for Epstein-Barr virus (EBV) seropositivity after serotherapy or *ex vivo* T cell depletion. CMV, adenovirus, and EBV were monitored weekly by polymerase chain reaction. Cellular immune reconstitution was assessed at 4, 8, 12 and 24 months. Immunoglobulin G (IgG) was followed monthly with replacement for serum levels <400mg/dL.

Definitions of Toxicity Endpoints

1. Neutrophil engraftment was defined as the first of 3 successive days with an absolute neutrophil count ≥500/μL.[6]
2. Acute and chronic GVHD were defined by the modified Glucksberg scale or the National Institute of Health consensus criteria, respectively.[7,8]
3. VOD/SOS was defined and graded by the European Society for Blood and Marrow Transplantation criteria for children[9] and further classified as VOD/SOS with or without other organ failure.

Figure S1. Disease-free survival among patients who underwent HCT for post-CAR19 relapse, stratified by relapse immunophenotype.



Disease-free survival, defined as time from transplant to relapse or death from any cause.

CAR19, CD19-directed chimeric antigen receptor T-cell therapy; HCT, hematopoietic cell transplant.

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