Cytomegalovirus Triplex vaccine in pediatric hematopoietic stem cell transplant patients at high risk for cytomegalovirus complications: evaluation of vaccine safety, immunogenicity and impact on viremia requiring antivirals

Authors

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Cytomegalovirus Triplex vaccine in pediatric hematopoietic stem cell transplant patients at high risk for cytomegalovirus complications: evaluation of vaccine safety, immunogenicity and impact on viremia requiring antivirals

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Supplementary data

Table 1S. HCT recipients demographics, clinical characteristics, and treatments

HCT recipient	Age	Gender	Diagnosis	HCT donor type/ cell source	Conditioning regimen	HCT donor CMV serostatus	Letermovir prophylaxis	Triplex DL	Start day of CMV antiviral therapy
COH001	19	M	ALL	MRD/BMT	Myeloablative	Positive	Yes	DL1	None
COH002	17	M	ALL	MUD/BMT	Myeloablative	Negative	No	DL1	Day 44
COH009	18	F	AML	HAPLO/PB	Myeloablative	Negative	Yes	DL1	None
COH010	12	F	AML	MRD/BMT	Myeloablative	Positive	Yes	DL2	None
COH011	21	M	ALL	MUD/PB	Myeloablative	Positive	Yes	DL2	Day 216
COH012	8	F	ALL	MUD/BMT	Myeloablative	Positive	Yes	DL1	None
COH013	13	F	ALL	HAPLO/PB	Myeloablative	Negative	Yes	DL2	None
COH014	3	M	SAA	HAPLO/BMT	Reduced intensity	Negative	Yes	DL1	None
COH015	9	F	SAA	MUD/BMT	Reduced intensity	Positive	Yes	DL1	None

HCT = hematopoietic stem cell transplant; CMV = cytomegalovirus; DL = dose level: DL1 = 10^8 PFU, DL2 = 5 x 10^8 PFU; M = male; F = female; ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; SAA = severe aplastic anemia; MRD = matched related donor; MUD = matched unrelated donor; HAPLO = haploidentical; BMT = bone marrow transplant; PB = peripheral blood stem cell transplant.

Figure 1S.

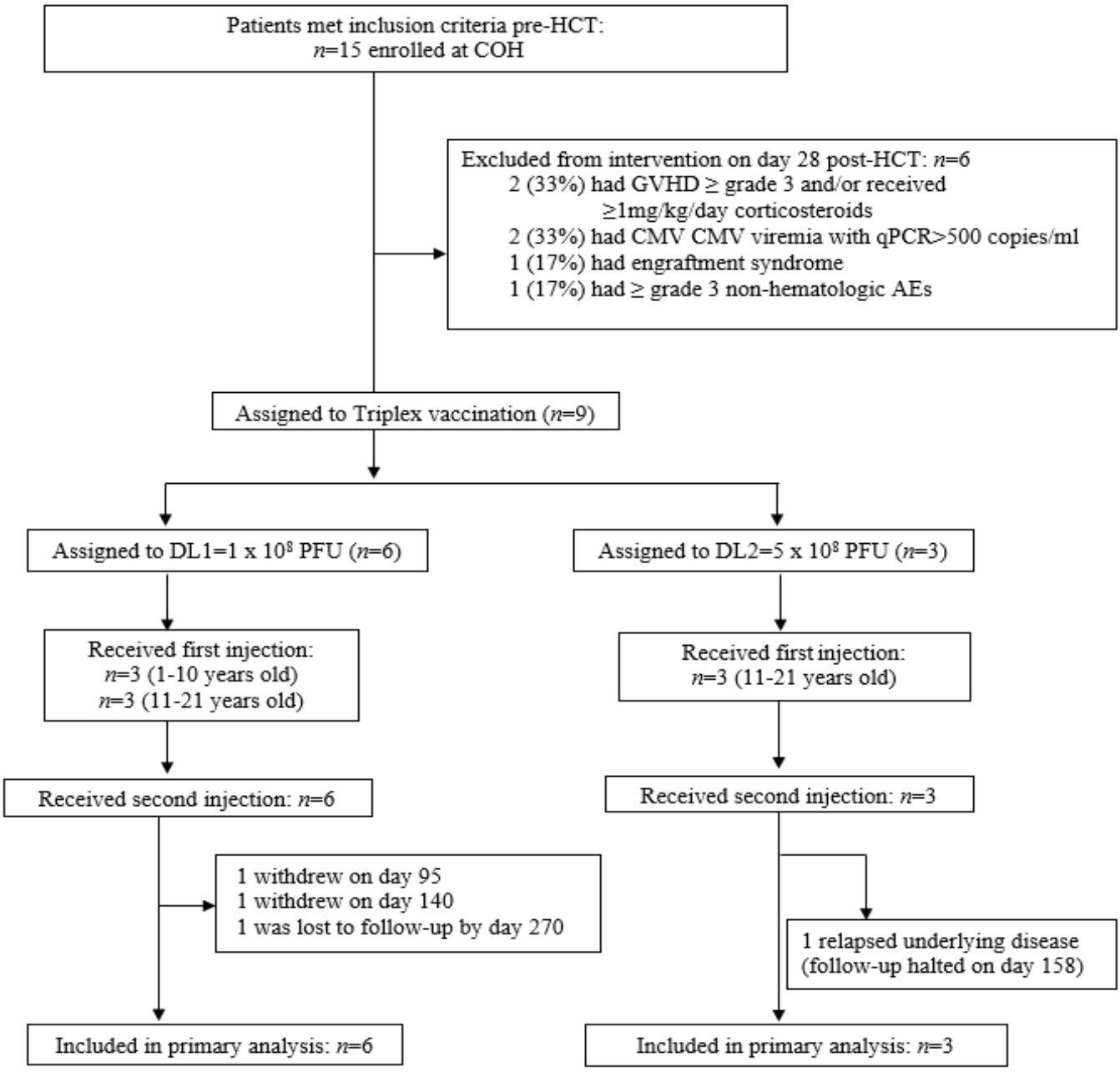
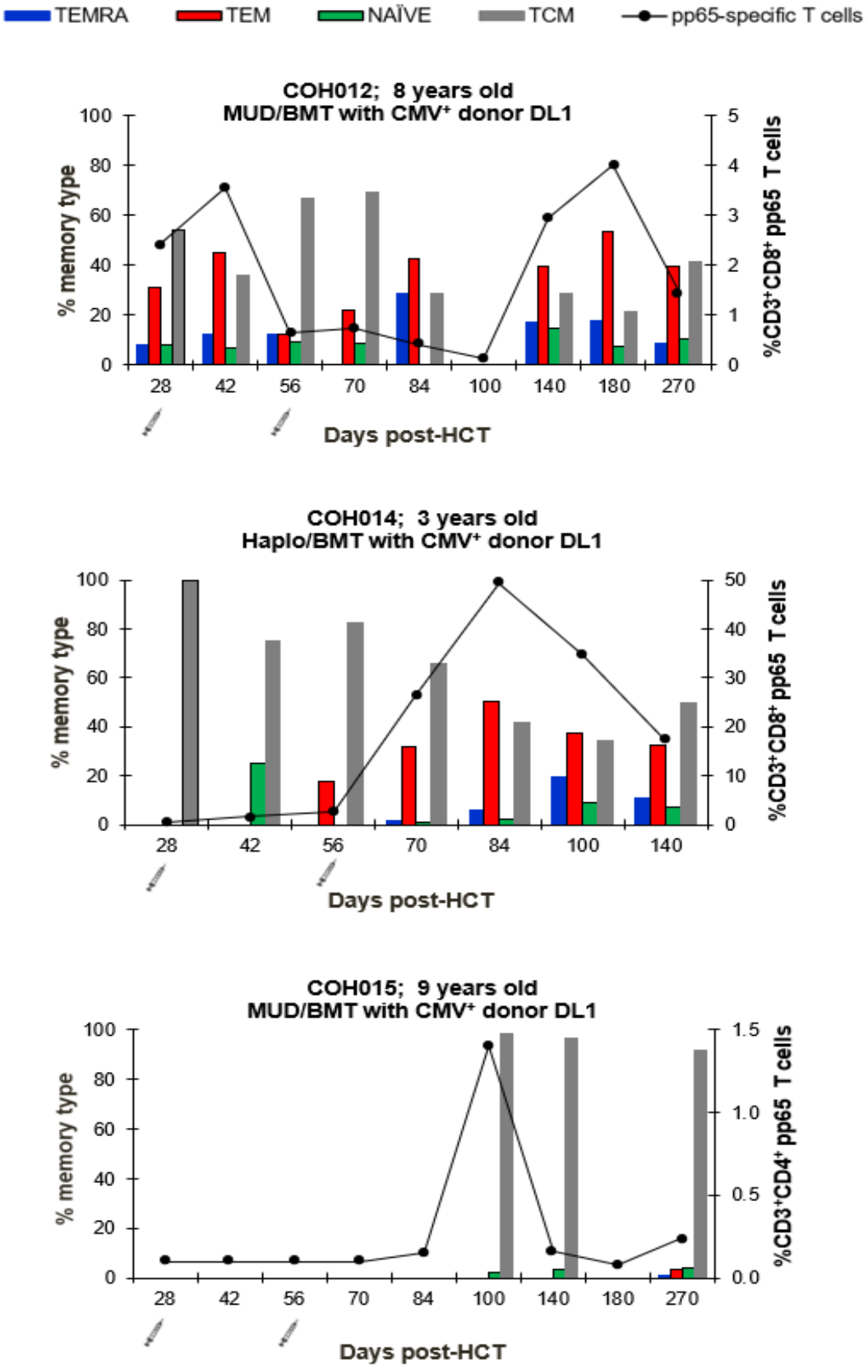

Patients met inclusion criteria pre-HCT:
n=15 enrolled at COH
Excluded from intervention on day 28 post-HCT: *n*=6
2 (33%) had GVHD ≥ grade 3 and/or received ≥1mg/kg/day corticosteroids
2 (33%) had CMV CMV viremia with qPCR>500 copies/ml
1 (17%) had engraftment syndrome
1 (17%) had ≥ grade 3 non-hematologic AEs
Assigned to Triplex vaccination (*n*=9)
Assigned to DL1=1 x 10^8 PFU (*n*=6)
Assigned to DL2=5 x 10^8 PFU (*n*=3)
Received first injection:
n=3 (1-10 years old)
n=3 (11-21 years old)
Received first injection:
n=3 (11-21 years old)
Received second injection: *n*=6
Received second injection: *n*=3
1 withdrew on day 95
1 withdrew on day 140
1 was lost to follow-up by day 270
1 relapsed underlying disease
(follow-up halted on day 158)
Included in primary analysis: *n*=6
Included in primary analysis: *n*=3

Figure 2S


TEMRA
TEM
NAÏVE
TCM
pp65-specific T cells
COH012; 8 years old
MUD/BMT with CMV+ donor DL1
% memory type
%CD3+CD8+ pp65 T cells
Days post-HCT
COH014; 3 years old
Haplo/BMT with CMV+ donor DL1
% memory type
%CD3+CD8+ pp65 T cells
Days post-HCT
COH015; 9 years old
MUD/BMT with CMV+ donor DL1
% memory type
%CD3+CD4+ pp65 T cells
Days post-HCT

Legend

Figure 1S. Enrollment and assignment of patients. Details regarding eligibility and exclusion criteria are provided in the manuscript. HCT = hematopoietic stem cell transplant; CMV = cytomegalovirus; COH = City of Hope; GVHD = graft versus host disease; AE = adverse event; DL = dose level.

Figure 2S. Frequency and memory phenotypes of functional pp65-specific T cells in Triplex vaccinated children recipients. Longitudinal immunogenicity profiles of children (<12 years old) recipients as specified on each plot. Right y axes report the percentages of $CD137^+CD3^+$ $CD8^+$ (COH012 and COH014) and $CD4^+$ T cells (COH015) specific for pp65. The left y axes indicate the percentage of specific memory phenotypes (histograms) in function of time (reported as Days post-HCT). The syringe symbol shows post-HCT day of Triplex injections. The legend specifies (from left to right) the following phenotypes: TEMRA (effector "revertant" T-cells, re-expressing the RA isoform of the CD45 surface marker; blue bars); TEM ($CD45RA^-$ $CD28^-$ effector T -cells; red bars); naïve ($CD45RA^+CD28^+$ naïve T cells, green bars) TCM ($CD45RA^-$ $CD28^+$ central memory T cells; gray bars). Memory analysis was performed when $CD3^+CD8^+CD137^+$ T-cell or $CD3^+CD4^+CD137^+$ T cell populations were ≥0.2%. MUD = matched unrelated donor; Haplo=haploidentical; BMT=bone marrow transplant; DL= dose level.