LONGITUDINAL IMMUNE RECONSTITUTION PROFILING SUGGESTS ANTI-VIRAL PROTECTION AFTER TRANSPLANTATION WITH OMIDUBICEL: A PHASE 3 SUBSTUDY

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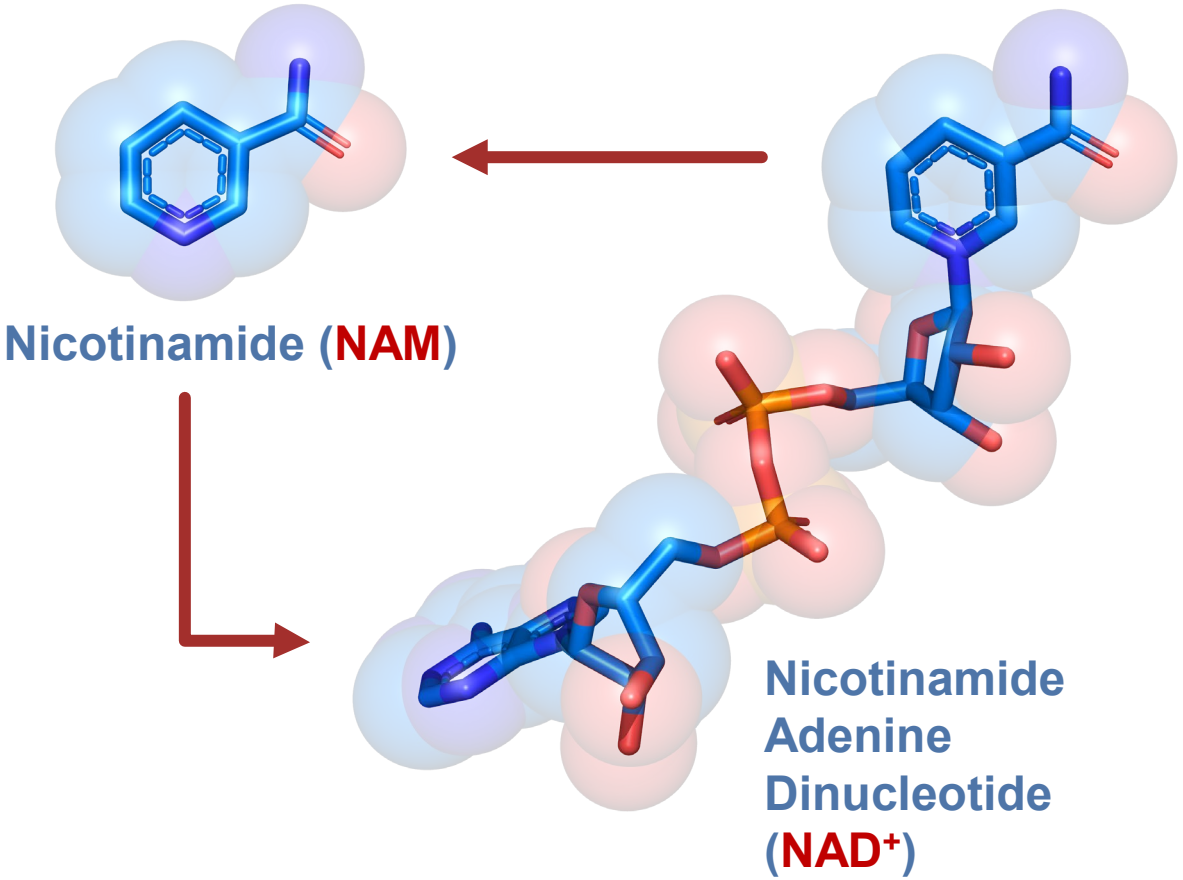
PRESENTING AUTHOR DISCLOSURES

- Positions:
  - Medical Director, Gamida Cell Ltd. Cell Therapy Technologies
  - Head, Clinic Of Histiocytic Neoplasms, Institute Of Hematology, Assuta Medical Center

- Patents:
  - Antibodies for the treatment of cancer. Il285313 02-aug-2021
  - Antibodies, peptides and combinations of same for the treatment or prevention of coronavirus infection. Il280340 21-jan-2021

NICOTINAMIDE (NAM) PROMOTES STEM CELL EXPANSION & PRESERVES STEMNESS



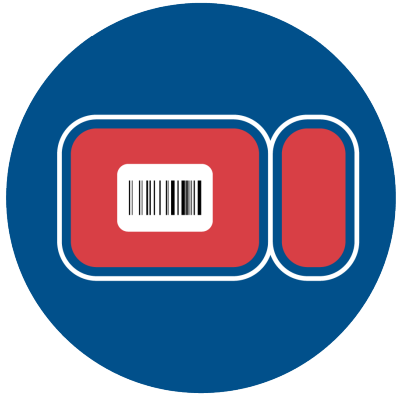
NAM-based manufacturing of UCB-derived stem cells leads to:

- **Preservation of stemness**
- Enhanced bone marrow homing
- Retained engraftment capacity
- Reduction in cellular stress
- Decreased apoptotic & inflammatory signatures
- Down-regulation of signaling pathways that are typically activated upon removal of HSCs from their natural environment

HSC, hematopoietic stem cell; NAD, nicotinamide adenine dinucleotide; NAM, nicotinamide; UCB, umbilical cord blood.

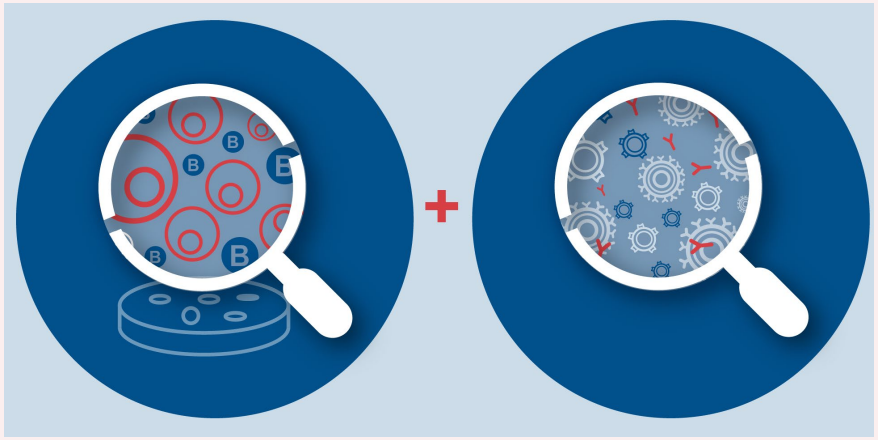
Peled T, et al. *Exp Hematol.* 2012;40(4):342-355.

OMIDUBICEL MANUFACTURING



CBU selected by treating physician from public cord blood bank

Omidubicel



NAM-Expanded Cells*

Stem cells cultured using proprietary NAM technology

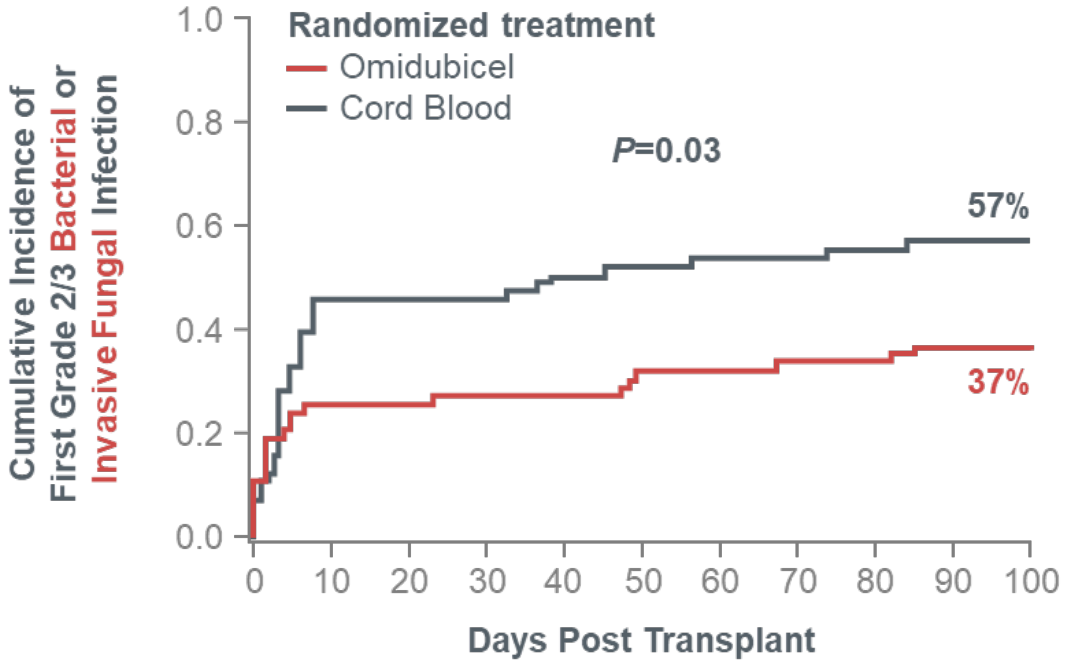
Non-cultured Fraction*

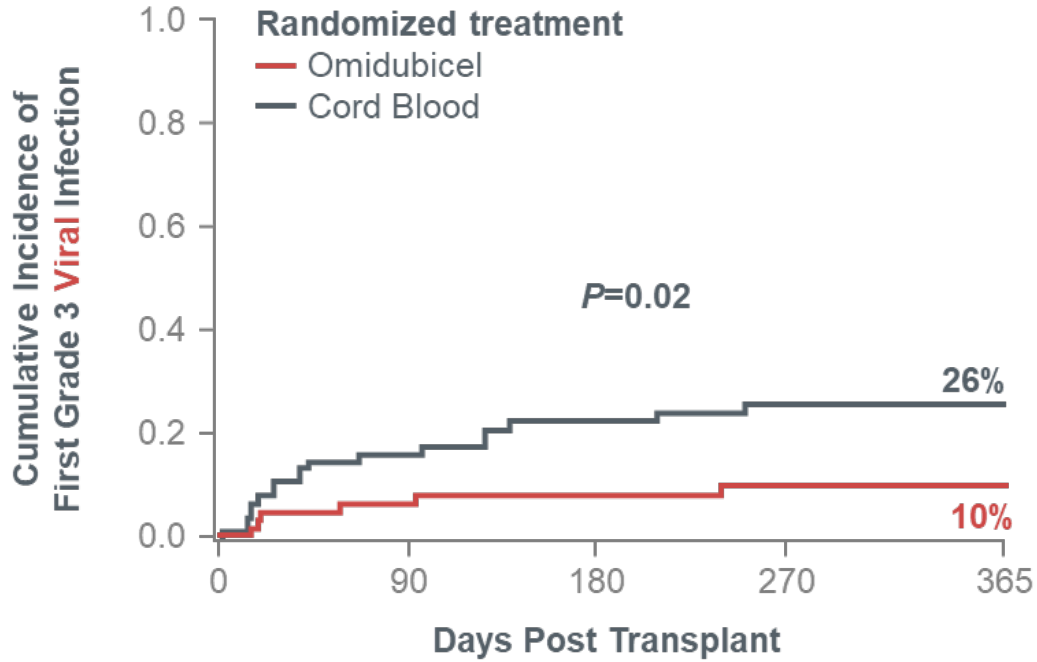
Immune cells, including T cells

Omidubicel Infusion

*Fractions are cryopreserved for transport and thawed prior to infusion.
CBU, cord blood unit; NAM, nicotinamide.

PHASE 3 DATA:
TRANSPLANTATION WITH OMIDUBICEL REDUCES THE RISK FOR BACTERIAL, FUNGAL, AND VIRAL INFECTIONS





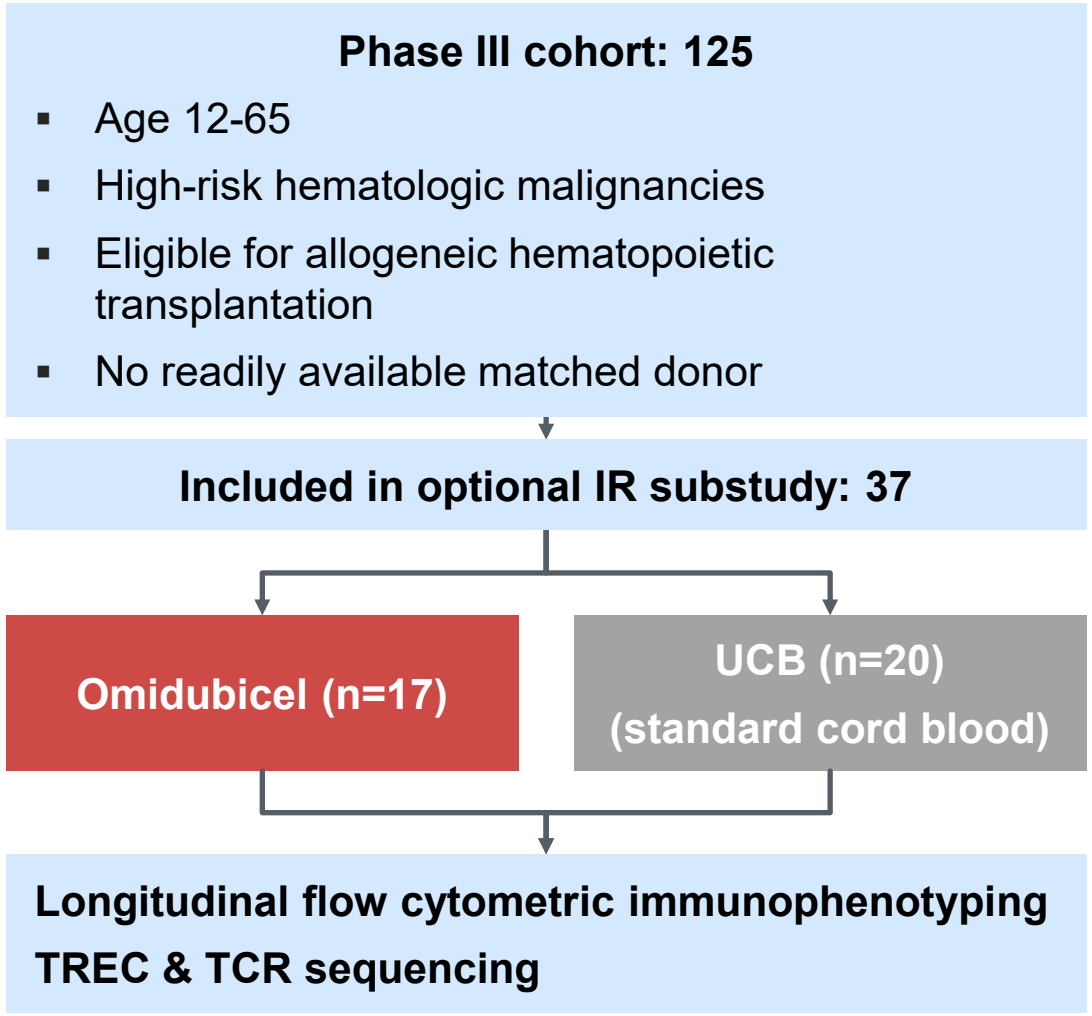
Plausible mechanistic explanation:

Faster post-HCT lymphocyte reconstitution → superior anti-viral immunity?

HCT, hematopoietic cell transplantation.

Horwitz ME, et al. *Blood*. 2021;138(6):1429-1440.

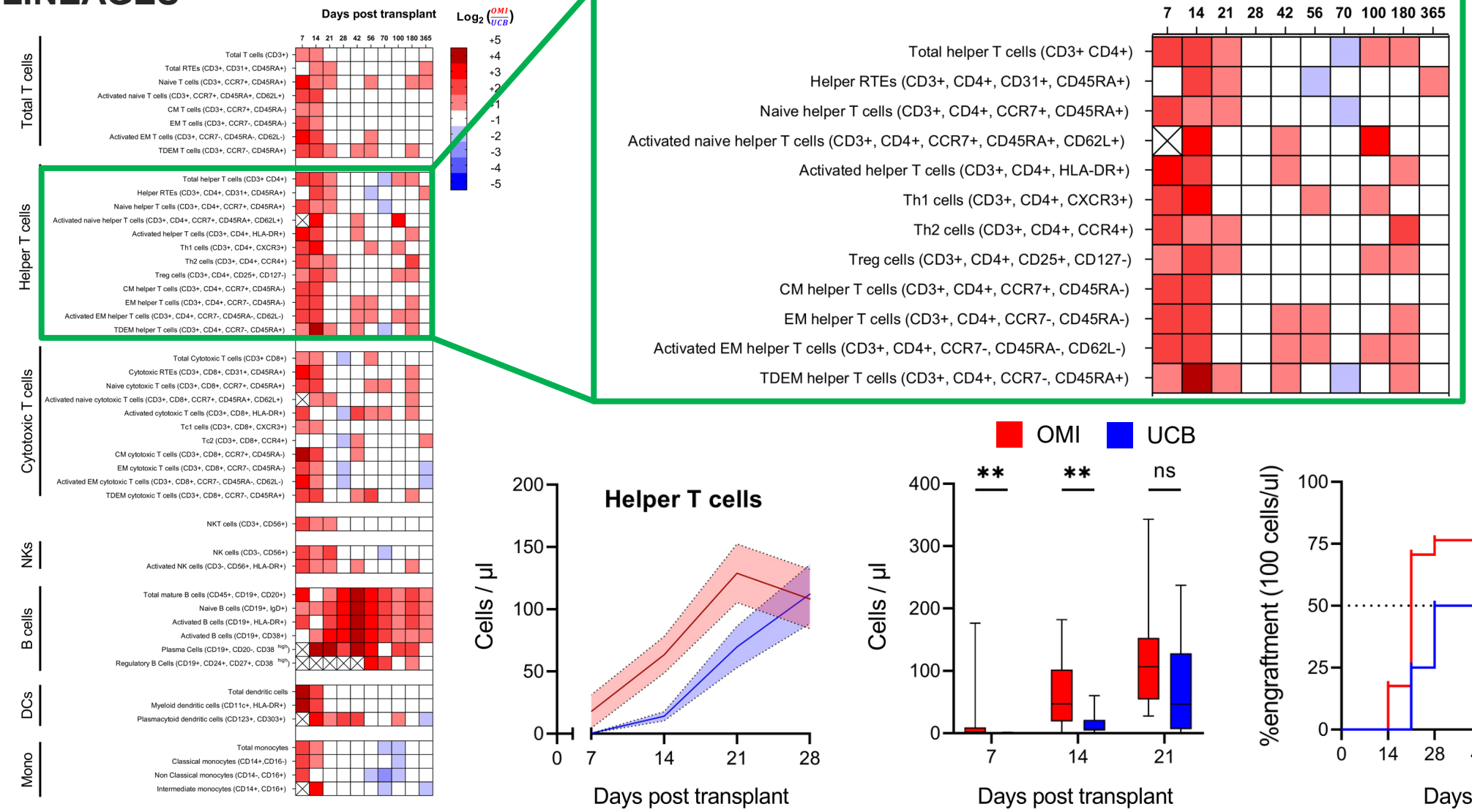
OMIDUBICEL VS. STANDARD UCB TRANSPLANTATION: AN OPTIONAL PHASE 3 IMMUNE RECONSTITUTION SUB-STUDY



IR, immune reconstitution; TCR, T cell receptor; TREC, T cell receptor excision circle; UCB, umbilical cord blood.

Horwitz ME, et al. *Blood*. 2021;138(6):1429-1440.

OMIDUBICEL FACILITATES RAPID RECONSTITUTION OF THE LYMPHOID AND MYELOMONOCYTIC LINEAGES



**$P \leq 0.01$.

CCR7, chemokine (C-C motif) receptor [7]; CM, central memory; DC, dendritic cell; EM, effector memory; HLA, human leukocyte antigen; Mono, monocytes; NK, natural killer; ns, not significant; OMI, omidubicel; RTE, recent thymic emigrant; TDEM, terminally differentiated effector memory; UCB, umbilical cord blood.

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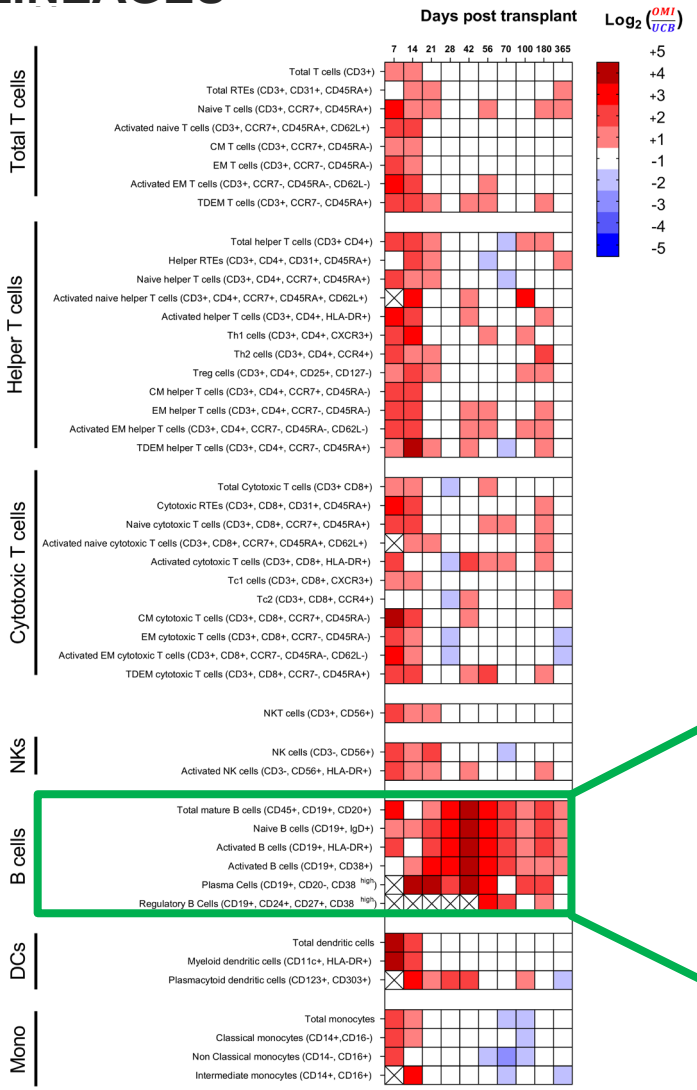

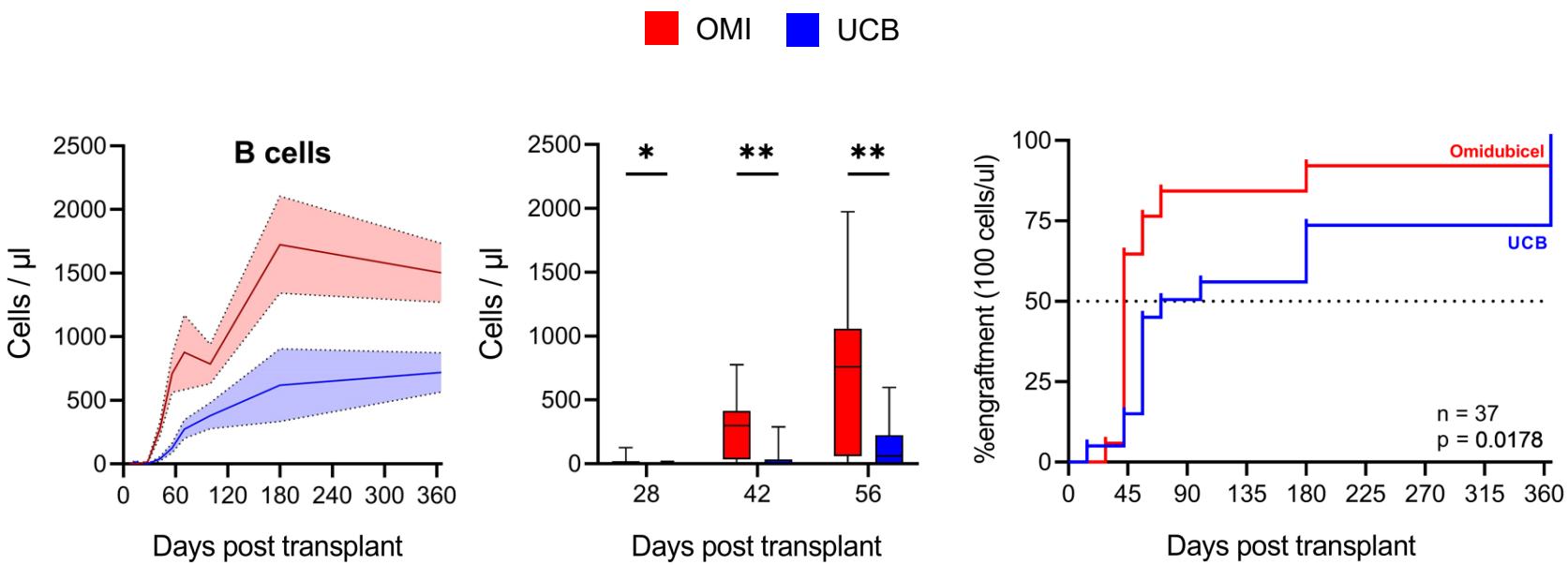

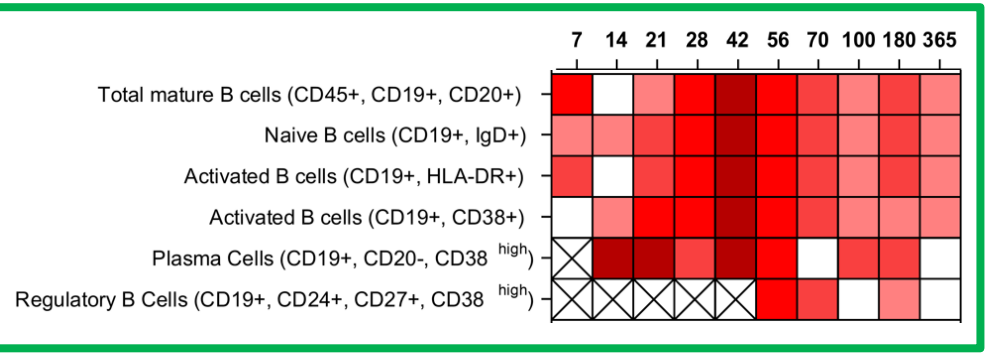

*$P \leq 0.05$; **$P \leq 0.01$.

CCR7, chemokine (C-C motif) receptor 7; CM, central memory; DC, dendritic cell; EM, effector memory; HLA, human leukocyte antigen; Mono, monocytes; NK, natural killer; OMI, omidubicel; RTE, recent thymic emigrant; TDEM, terminally differentiated effector memory, UCB, umbilical cord blood.

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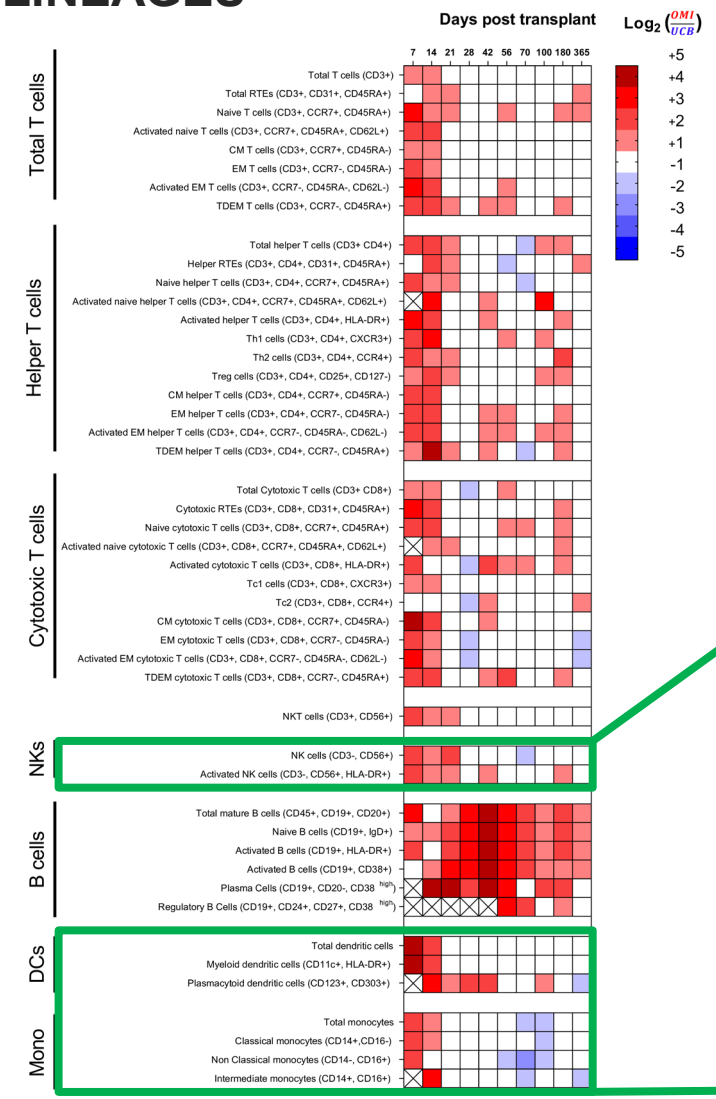
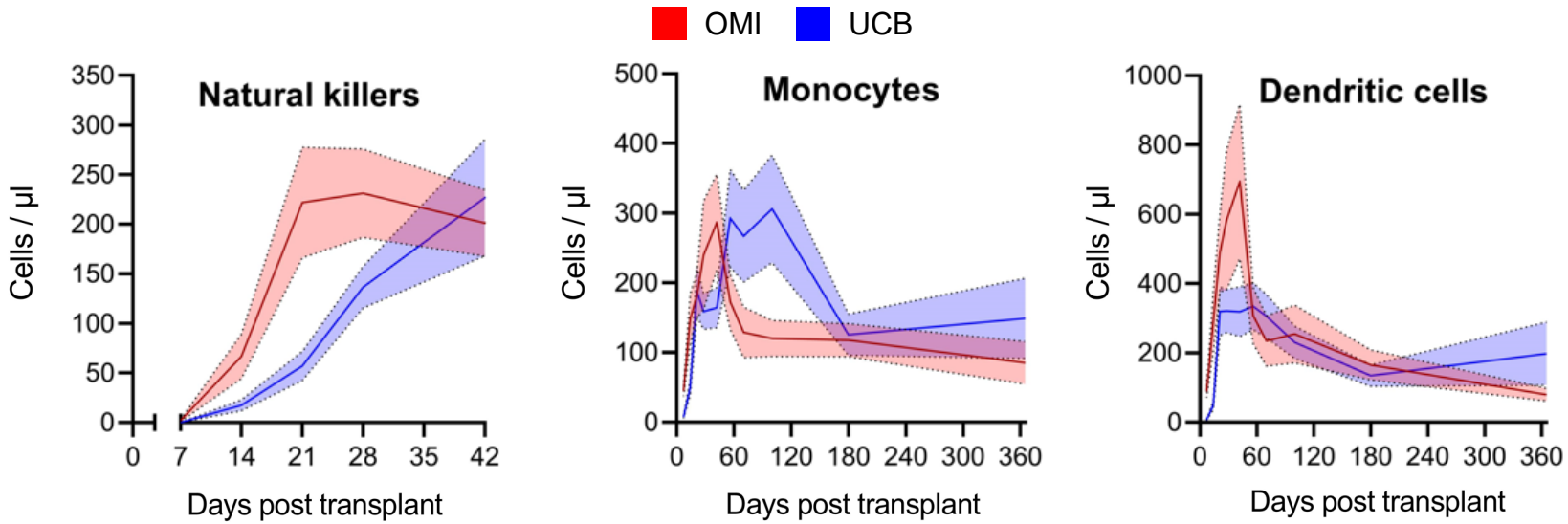
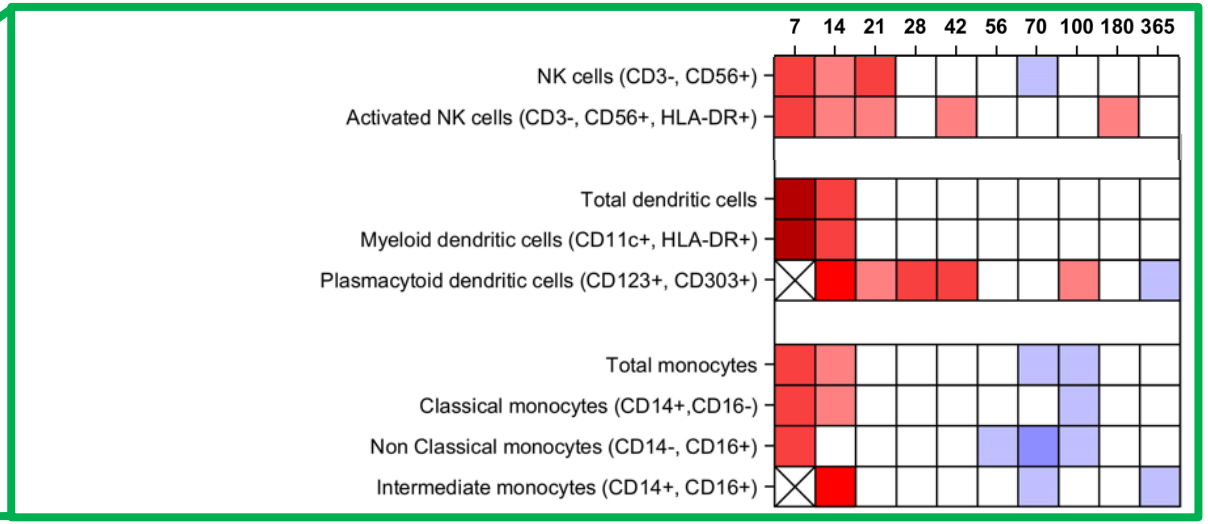
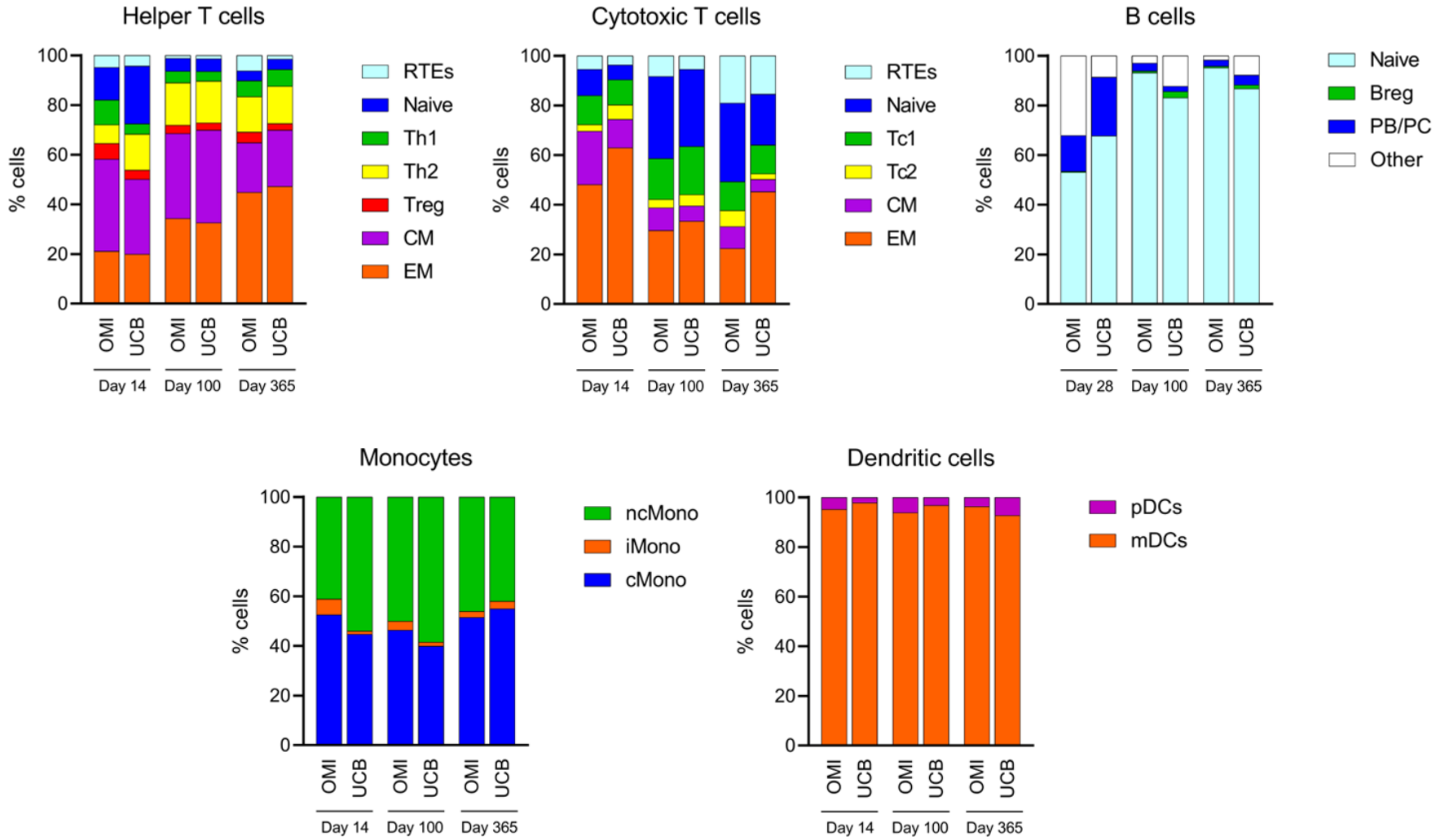






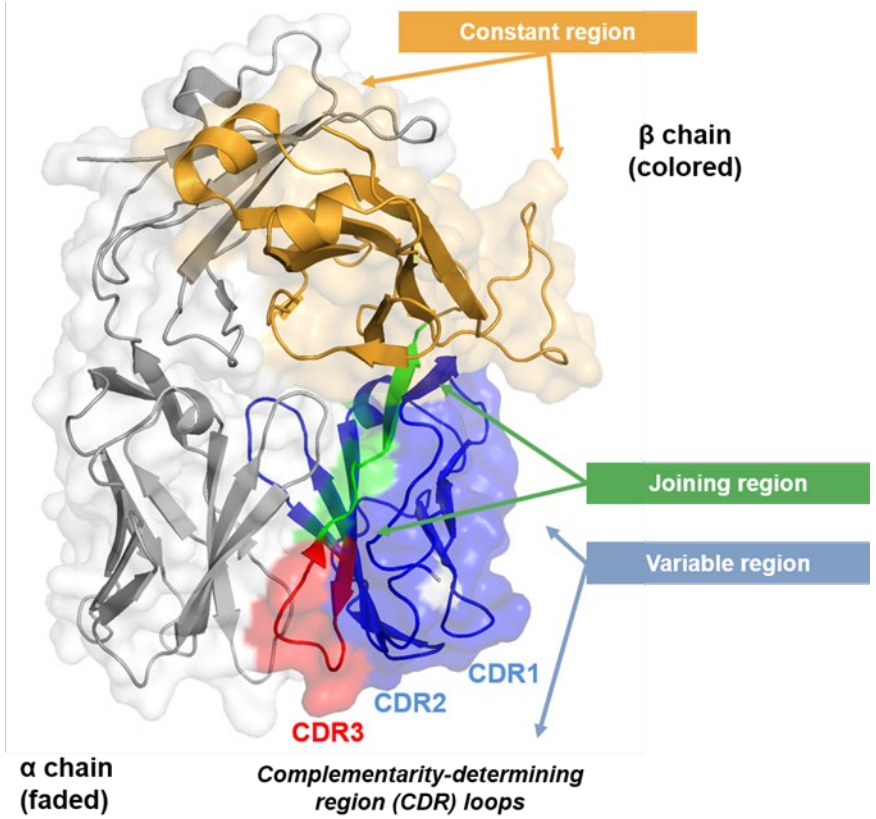
CCR7, chemokine (C-C motif) receptor 7; CM, central memory; DC, dendritic cell; EM, effector memory; HLA, human leukocyte antigen; Mono, monocytes; OMI, omidubicel; NK, natural killer; RTE, recent thymic emigrant; TDEM, terminally differentiated effector memory; UCB, umbilical cord blood.

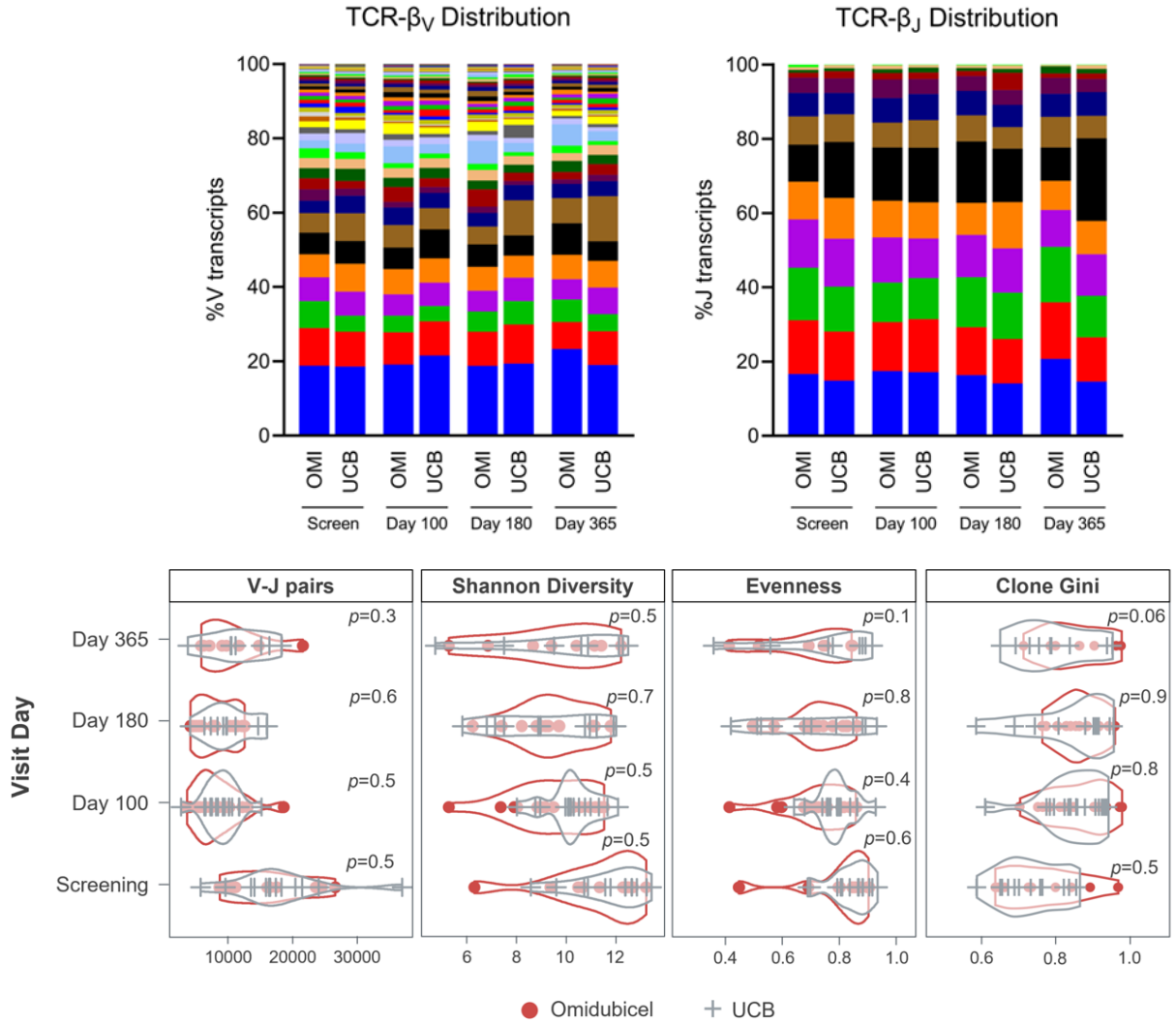
IMMUNOLOGICAL RECOVERY FOLLOWING OMIDUBICEL RETAINS MONONUCLEAR CELLULAR PROPORTIONS



B-reg, B regulatory cells; CM, central memory; cMono, classical monocytes (CD14+, CD16-); EM, effector memory; iMono, intermediate monocytes (CD14+, CD16+); mDCs, myeloid dendritic cells; ncMono, non-classical monocytes (CD14-, CD16+); OMI, omidubicel; PB/PC, plasma blasts/plasma cells; pDCs, plasmacytoid dendritic cells; RTE: recent thymic emigrant; Tc, cytotoxic T cells; Th, helper T cells; Treg, T regulatory cells; UCB, umbilical cord blood.

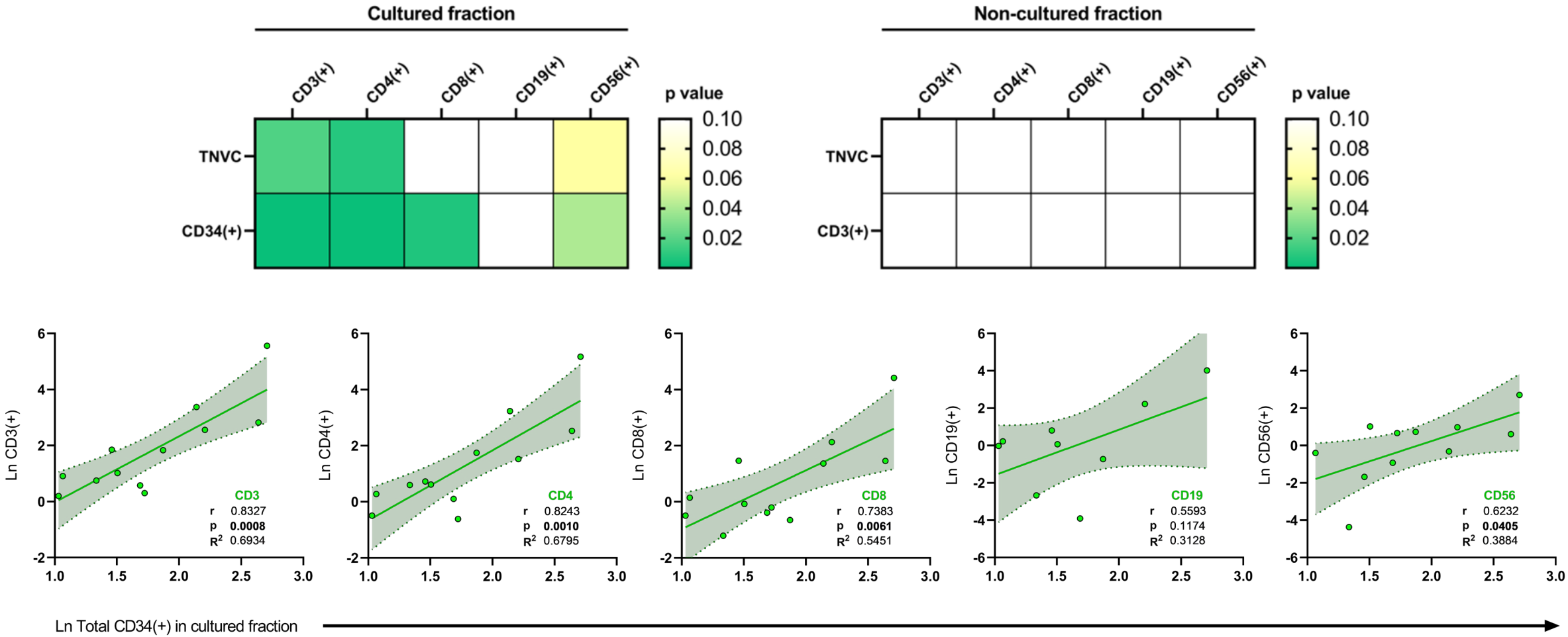
IMMUNOLOGICAL RECOVERY FOLLOWING OMIDUBICEL RETAINS T CELL REPERTOIRE DIVERSITY





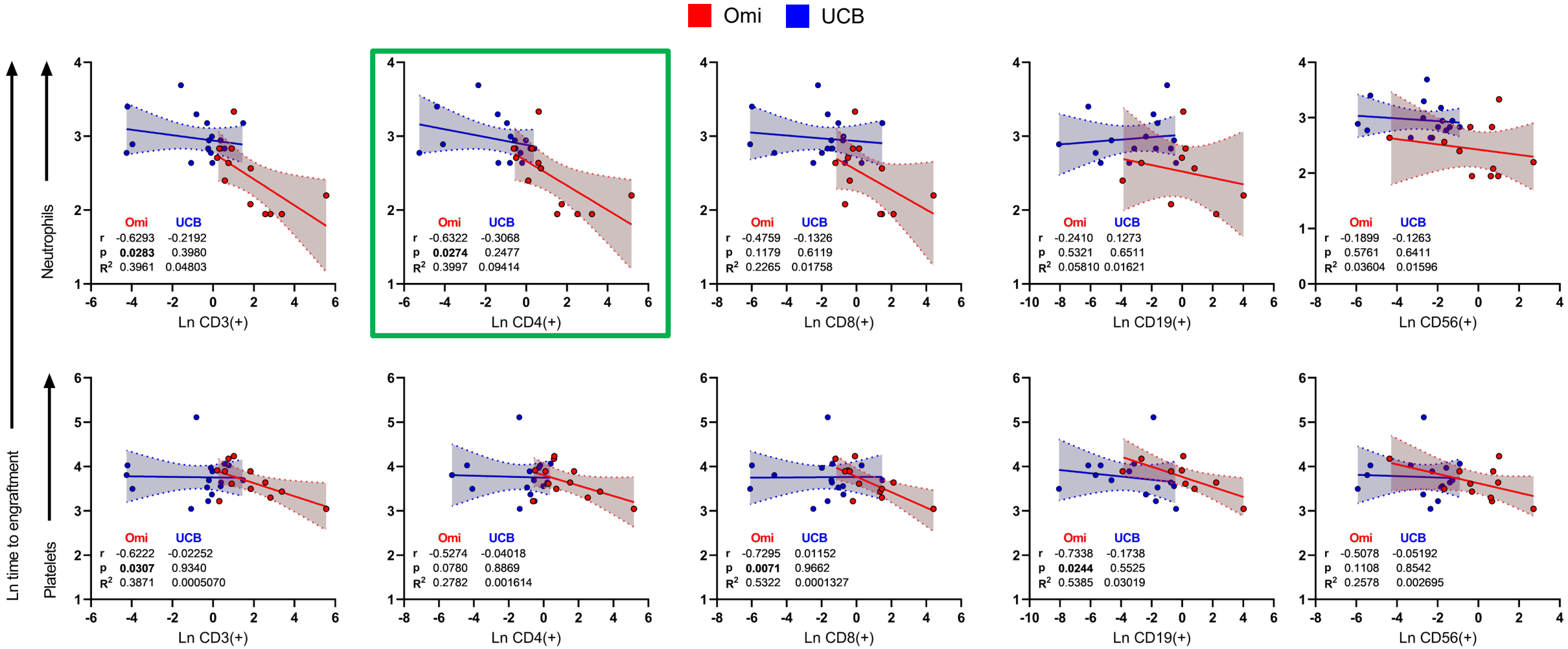
CDR, Complementarity Determining Region; OMI, omidubicel; TCR, T cell receptor; UCB, umbilical cord blood.

OMIDUBICEL RECIPIENTS EXHIBIT DOSE-DEPENDENT CORRELATIONS BETWEEN THE CD34(+) CELL CONTENT AND EARLY T & NK CELL RECONSTITUTION



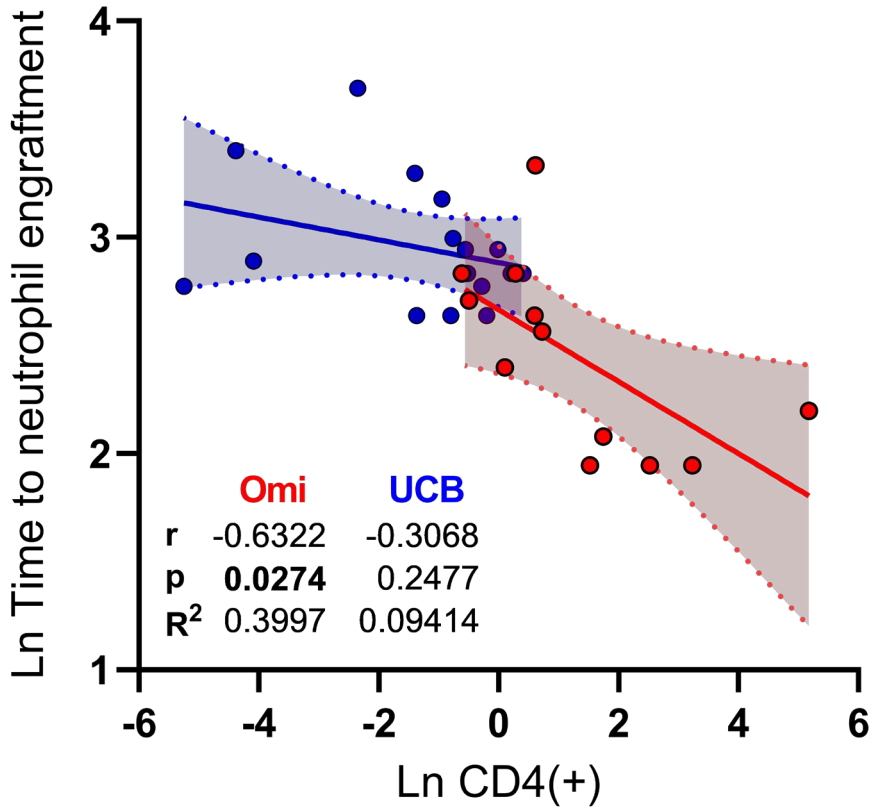
NK, natural killer; TNVC, total number of viable cells.

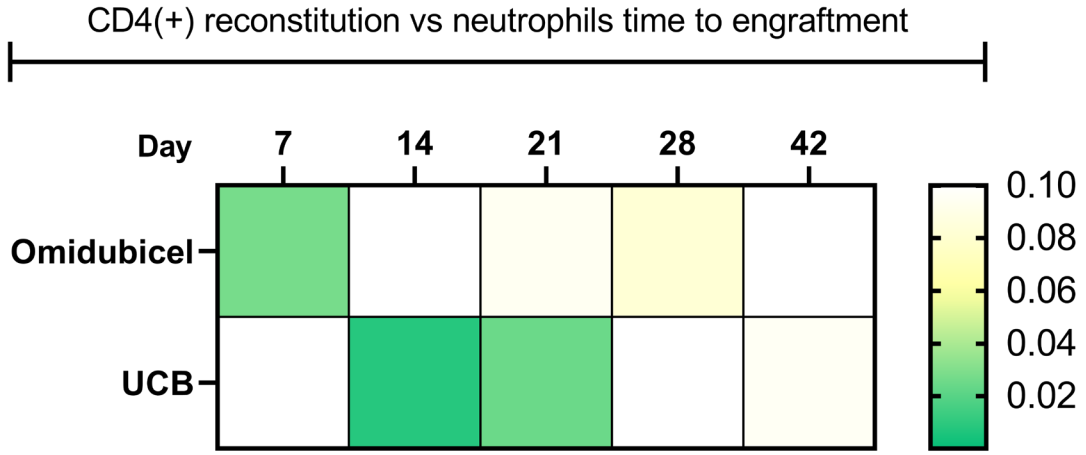
EARLY HELPER T CELL RECOVERY IN OMIDUBICEL TRANSPLANTED PATIENTS CORRELATES WITH FASTER NEUTROPHIL ENGRAFTMENT



Omi, omidubicel; UCB, umbilical cord blood.

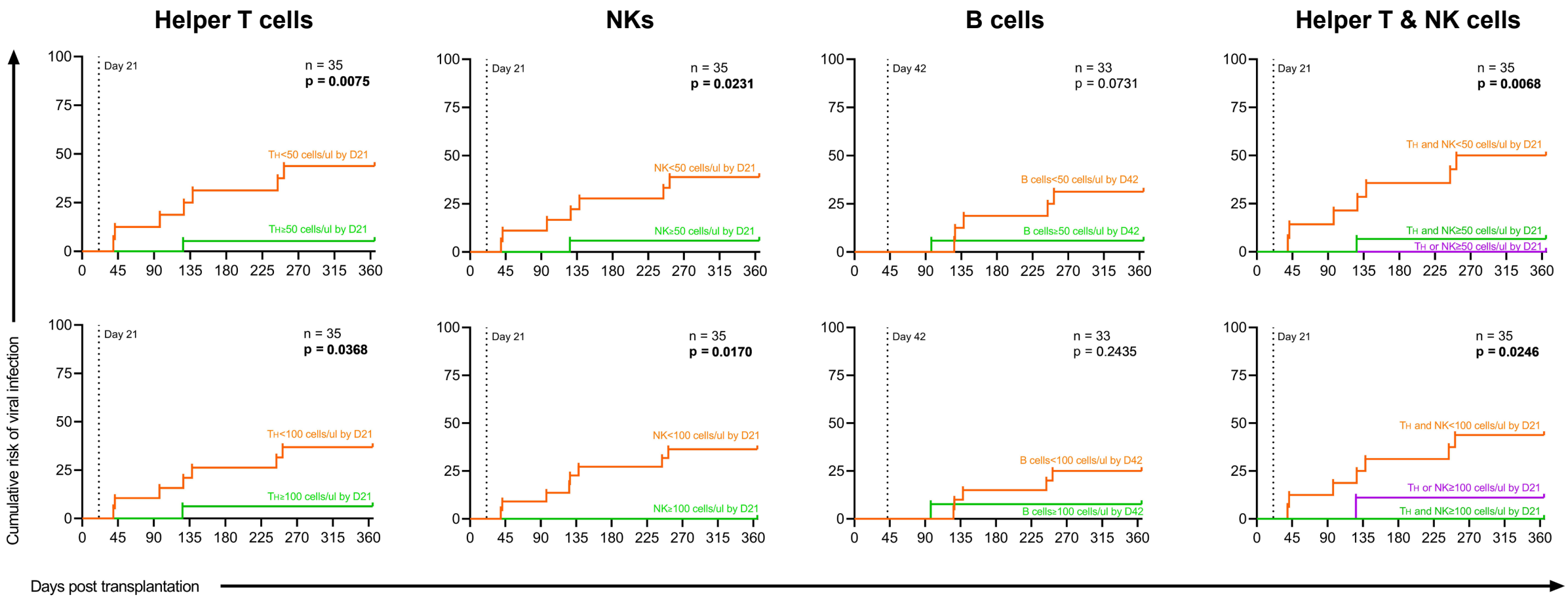
SUPERIOR EARLY HELPER T CELL RECOVERY IN OMIDUBICEL TRANSPLANTED PATIENTS CORRELATES WITH FASTER NEUTROPHIL ENGRAFTMENT





Omi, omidubicel; UCB, umbilical cord blood.

SHORT TERM NK AND T HELPER RECONSTITUTION COINCIDES WITH A DECREASED RATE OF SEVERE POST-TRANSPLANT VIRAL INFECTIONS



NK, natural killer; TH, helper T cells.

CONCLUSIONS:

- Patients transplanted with omidubicel exhibit early and robust immune reconstitution across multiple cell populations as early as **7 days post transplant**
- Immunological recovery following omidubicel retains mononuclear cellular proportions and TCR repertoire diversity
- Omidubicel **CD34+ progenitor cell dose** correlates with **faster immune reconstitution** one week after transplant, which in turn coincides with **faster hematopoietic recovery**
- Early NK and helper T cell reconstitution correlates with **superior antiviral immunity** post-transplant

NK, natural killer; TCR, T cell receptor.