

Solid Organ Transplantasyonunda Hücresel Tedaviler

Böbrek Nakli Güncelleme Sempozyumu-IV
27.09.2025

Mesut YİĞİT, M.D.
PhD Candidate in Immunology

Principal Investigator (PI)
Prof. Dr. Caner Süsal



Funded by
the European Union



1-Mixed Kimerizm

2-Regulatory macrophages (M regs)

3-Poliklonal Treg

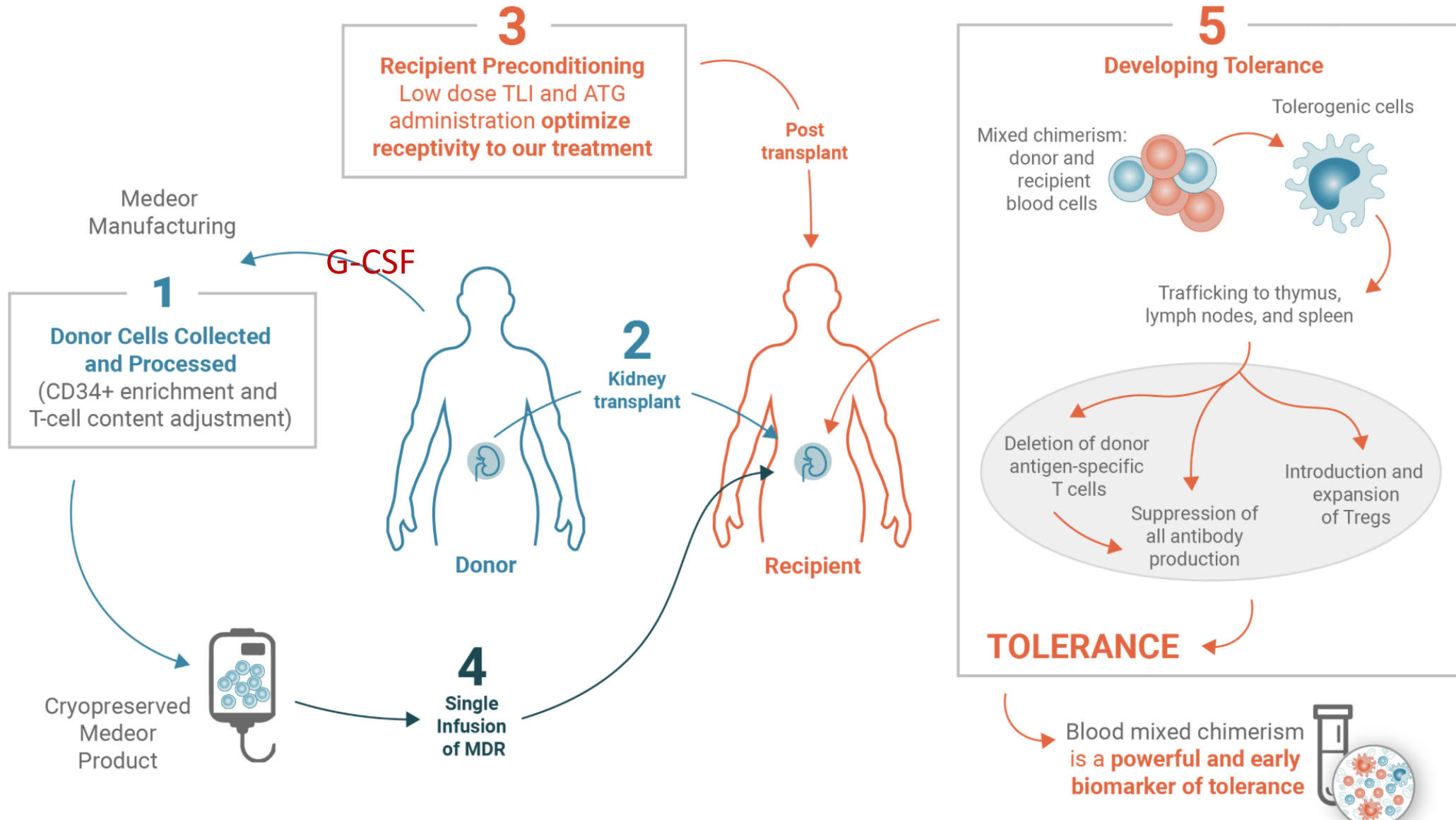
4-Donor antigen-specific regulatory T cell Treg (Dar-Treg)

5-HLA-A2 CAR-Treg

6-Production of HLA-Silenced Pluripotent Stem Cells



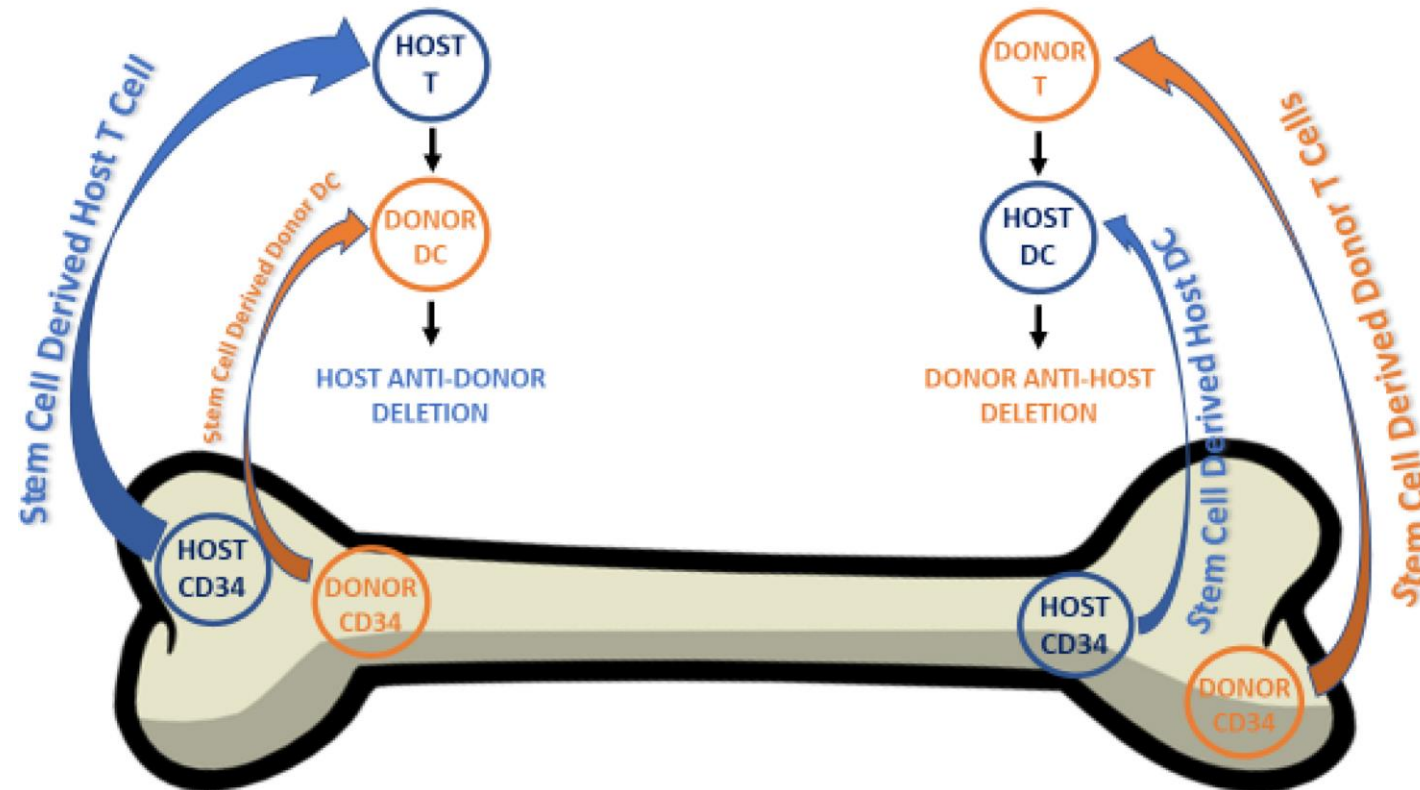
1-Mixed Kimerizm





1-Mixed Kimerizm

Intrathymic Clonal Deletion





1-Mixed Kimerizm

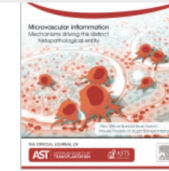
American Journal of TRANSPLANTATION

Induction of immune tolerance in living related human leukocyte antigen–matched kidney transplantation: A phase 3 randomized clinical trial

[Dixon B. Kaufman](#)¹   · [Sanjeev K. Akkina](#)² · [Mark.D. Stegall](#)³ · [James B. Piper](#)⁴ · [A. Osama Gaber](#)⁵ · [William S. Asch](#)⁶ · [Stephan Busque](#)⁷ · [Erik Stites](#)⁸ · [Michael De Vera](#)⁹ · [Titte R. Srinivas](#)¹⁰ · [Diane Alonso](#)¹⁰ · [Ashesh Shah](#)¹¹ · [Anup Patel](#)¹² · [Martin L. Mai](#)¹³ · [Kenneth D. Chavin](#)¹⁴ · [Meelie DebRoy](#)¹⁴ · [Arksarapuk Jittirat](#)¹⁴ · [Nadiesda Costa](#)¹⁵ · [Matthew Cooper](#)¹⁵ · [Gayle Vranic](#)¹⁵ · [Mark R. Laftavi](#)¹⁶ · [Reza F. Saidi](#)¹⁶ · [Suzon Collette](#)¹⁷ · [Daniel C. Brennan](#)¹⁸ on behalf of the [MDR-101-MLK Study Group](#) [Show less](#)

[Affiliations & Notes](#)  [Article Info](#)  [Linked Articles \(1\)](#) 

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- 18 Medeor Therapeutics, South San Francisco, California, USA

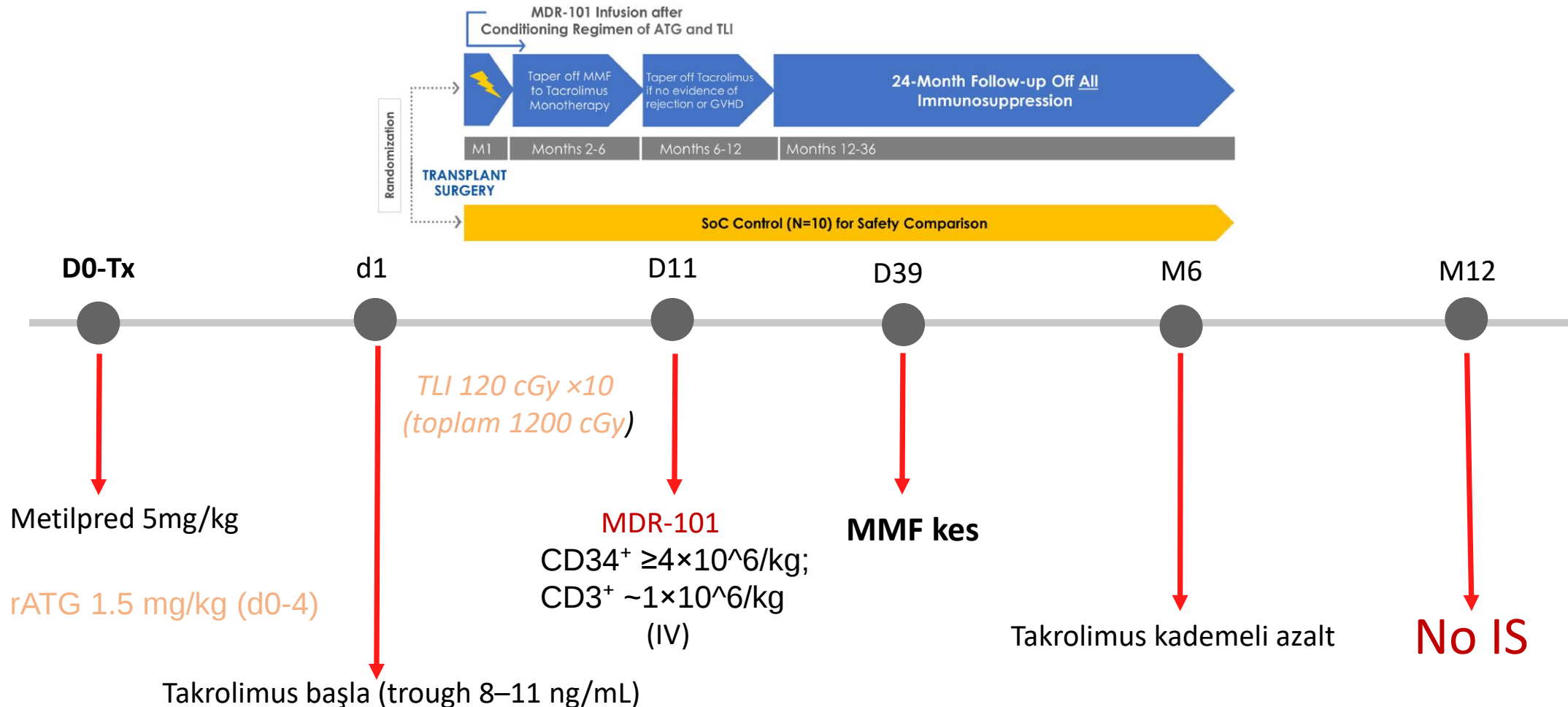




1-Mixed Kimerizm

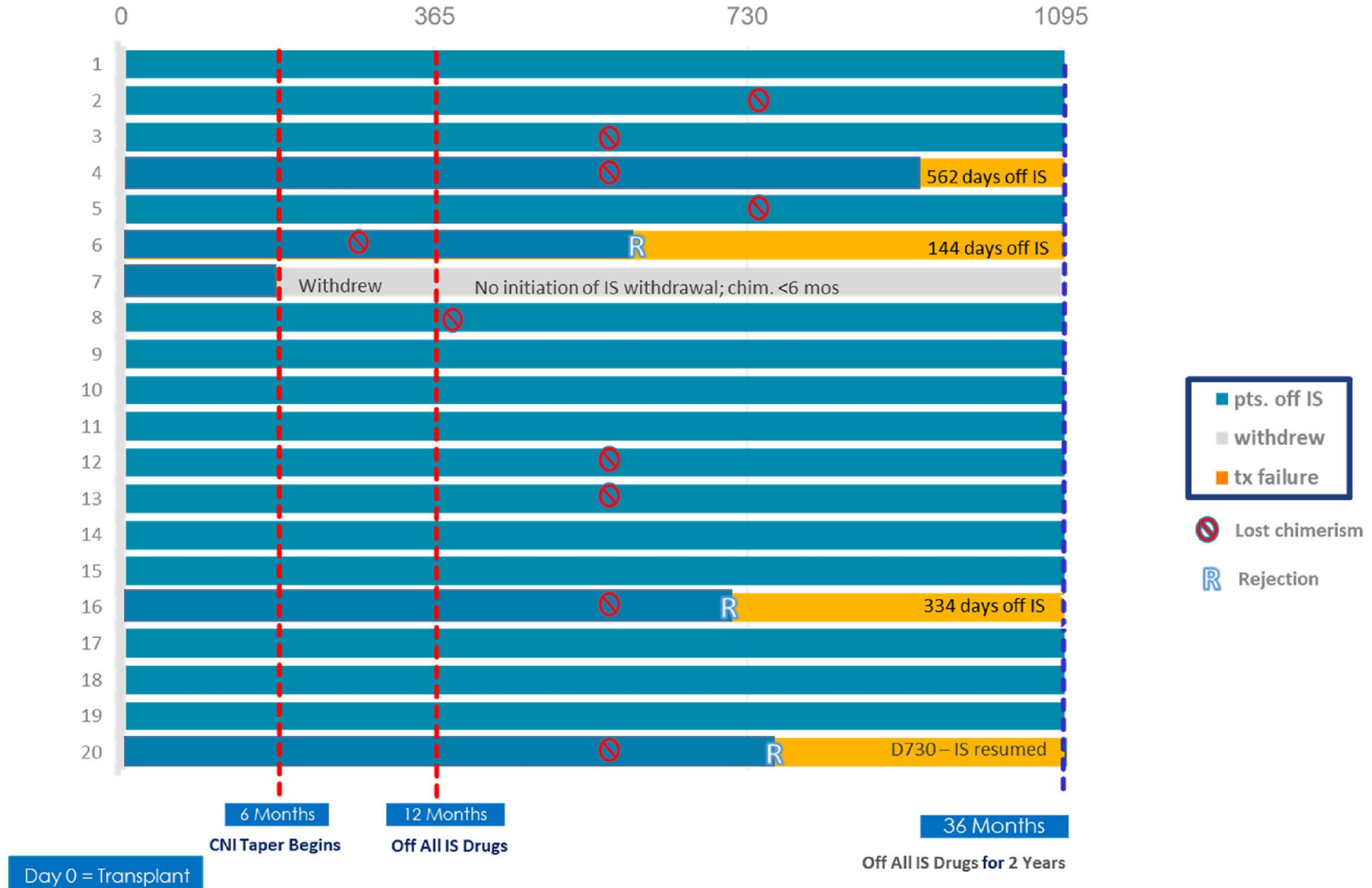
MDR-101: Pivotal Phase 3 Trial Design

Open Label, 2:1 Randomization
Treatment (N=20) versus Standard of Care (N=10)





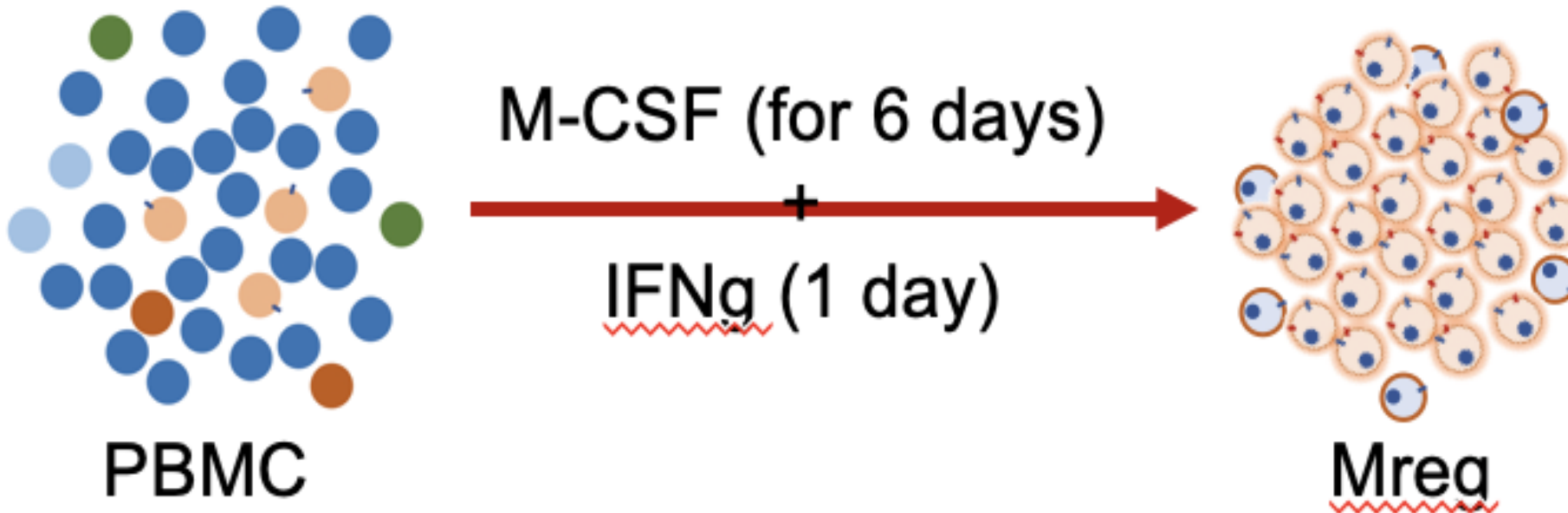
1-Mixed Kimerizm





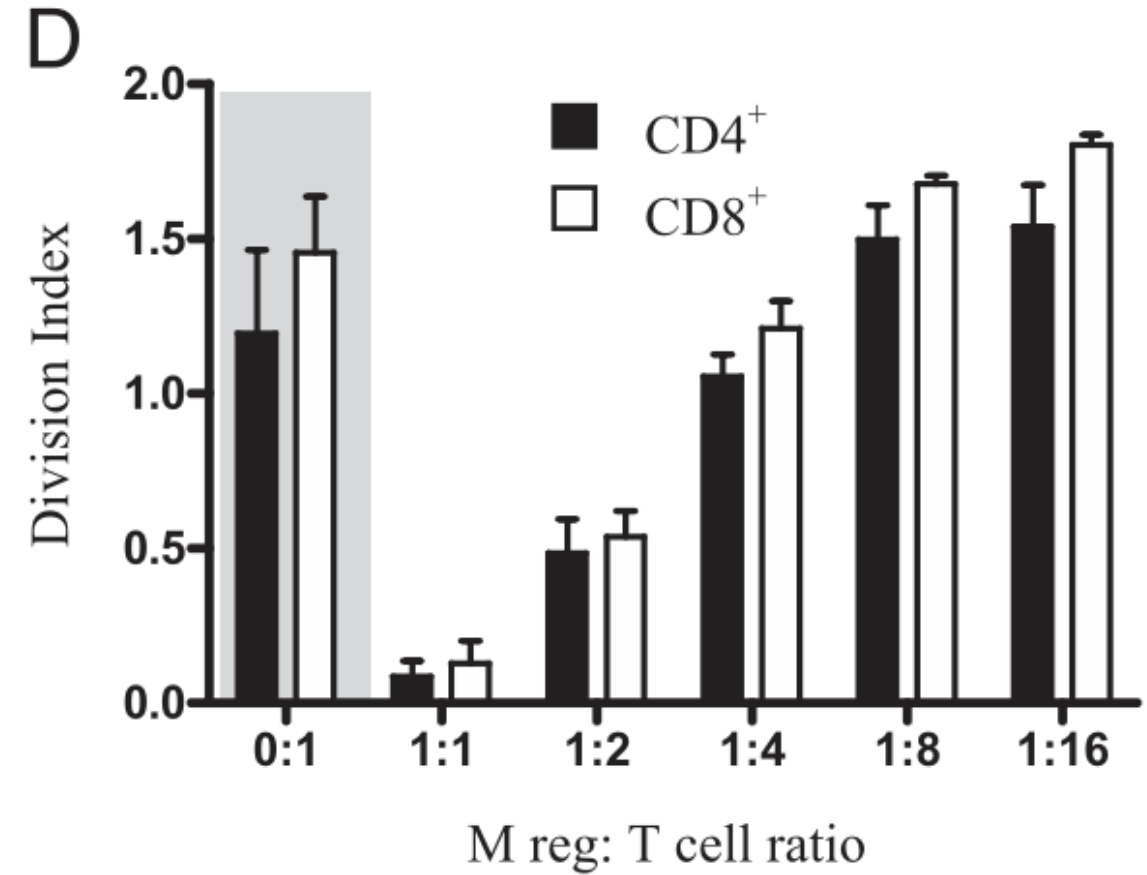
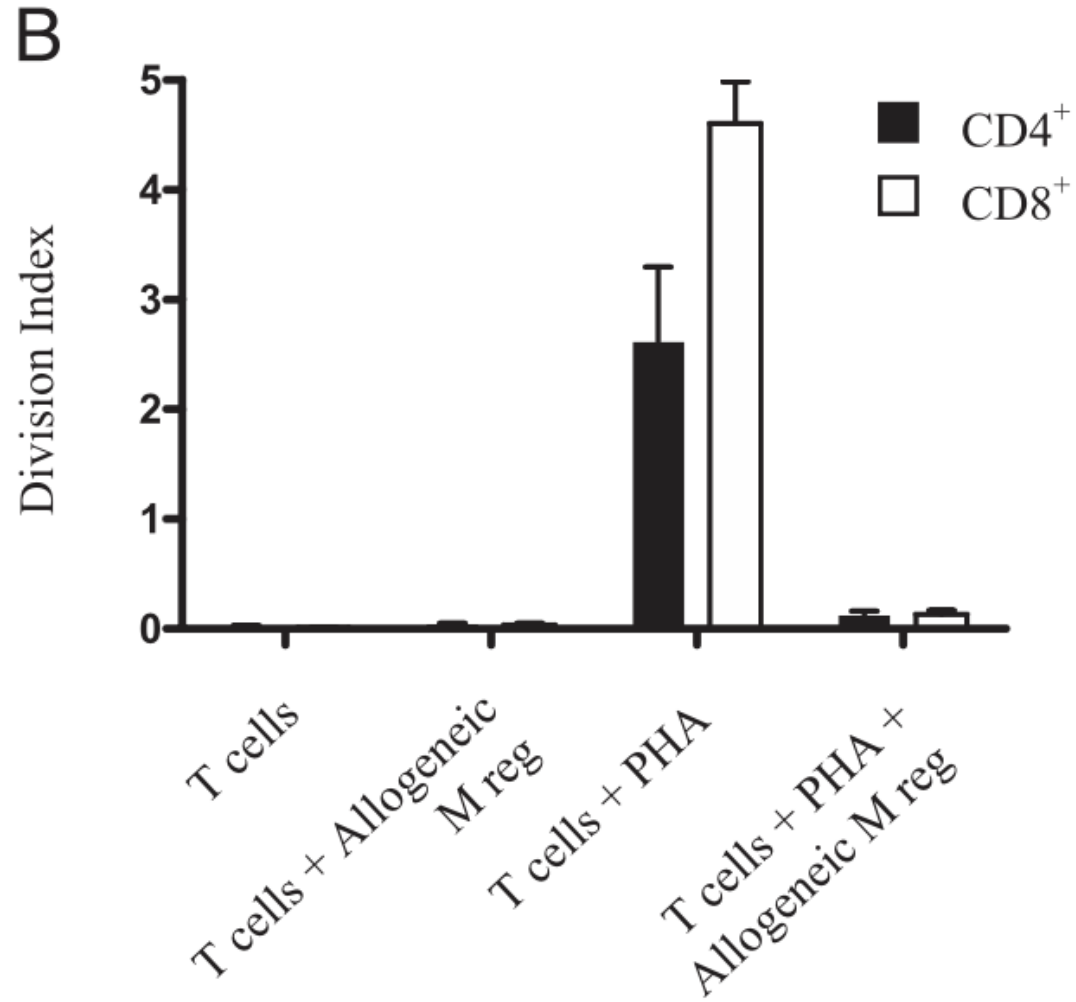
2-Regulatory macrophages (M regs)

188 Hutchinson et al.





2-Regulatory macrophages (M regs)





2-Regulatory macrophages (M regs)

Cutting Edge

THE JOURNAL OF
IMMUNOLOGY

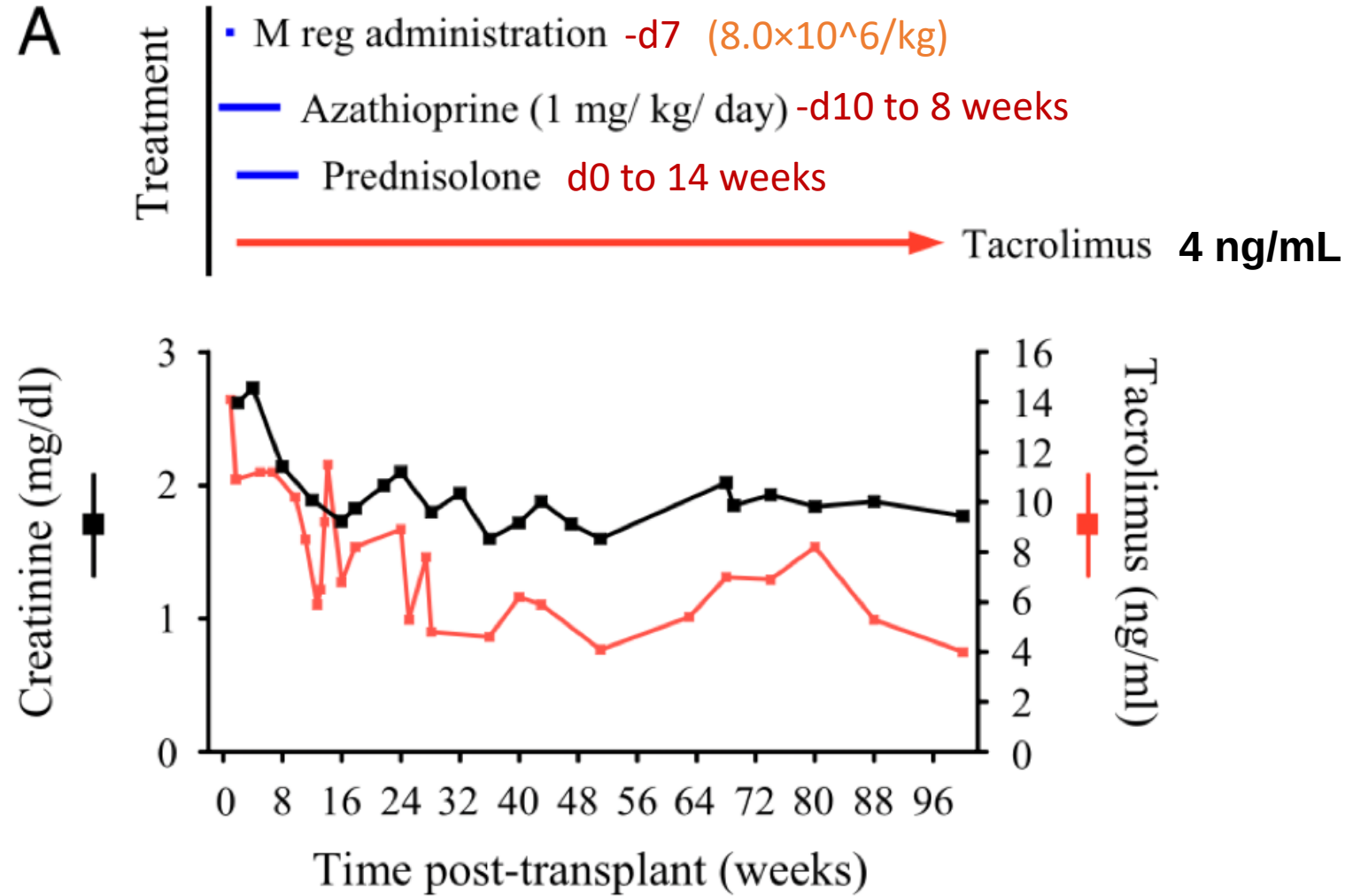
Cutting Edge: Immunological Consequences and Trafficking of Human Regulatory Macrophages Administered to Renal Transplant Recipients

James A. Hutchinson,^{*,†} Paloma Riquelme,^{*,†} Birgit Sawitzki,^{†,‡} Stefan Tomiuk,^{†,§}
Patrick Miqueu,^{†,¶} Maaz Zuhayra,^{||} Hans H. Oberg,[#] Andreas Pascher,^{**} Ulf Lützen,^{||}
Uwe Janßen,^{†,§} Christiane Broichhausen,^{*} Lutz Renders,^{††} Friedrich Thaiss,^{‡‡}
Ernst Scheuermann,^{§§} Eberhard Henze,^{||} Hans-Dieter Volk,^{†,‡} Lucienne Chatenoud,^{†,¶¶}
Robert I. Lechler,^{†,|||} Kathryn J. Wood,^{†,##} Dieter Kabelitz,[#] Hans J. Schlitt,^{*}
Edward K. Geissler,^{*,†} and Fred Fändrich^{†,***}

*Laboratory for Transplantation Research, Department of Surgery, University Hospital Regensburg, Regensburg 93053, Germany, **2011**



2-Regulatory macrophages (M regs)



47 M, Fully HLA-mismatched

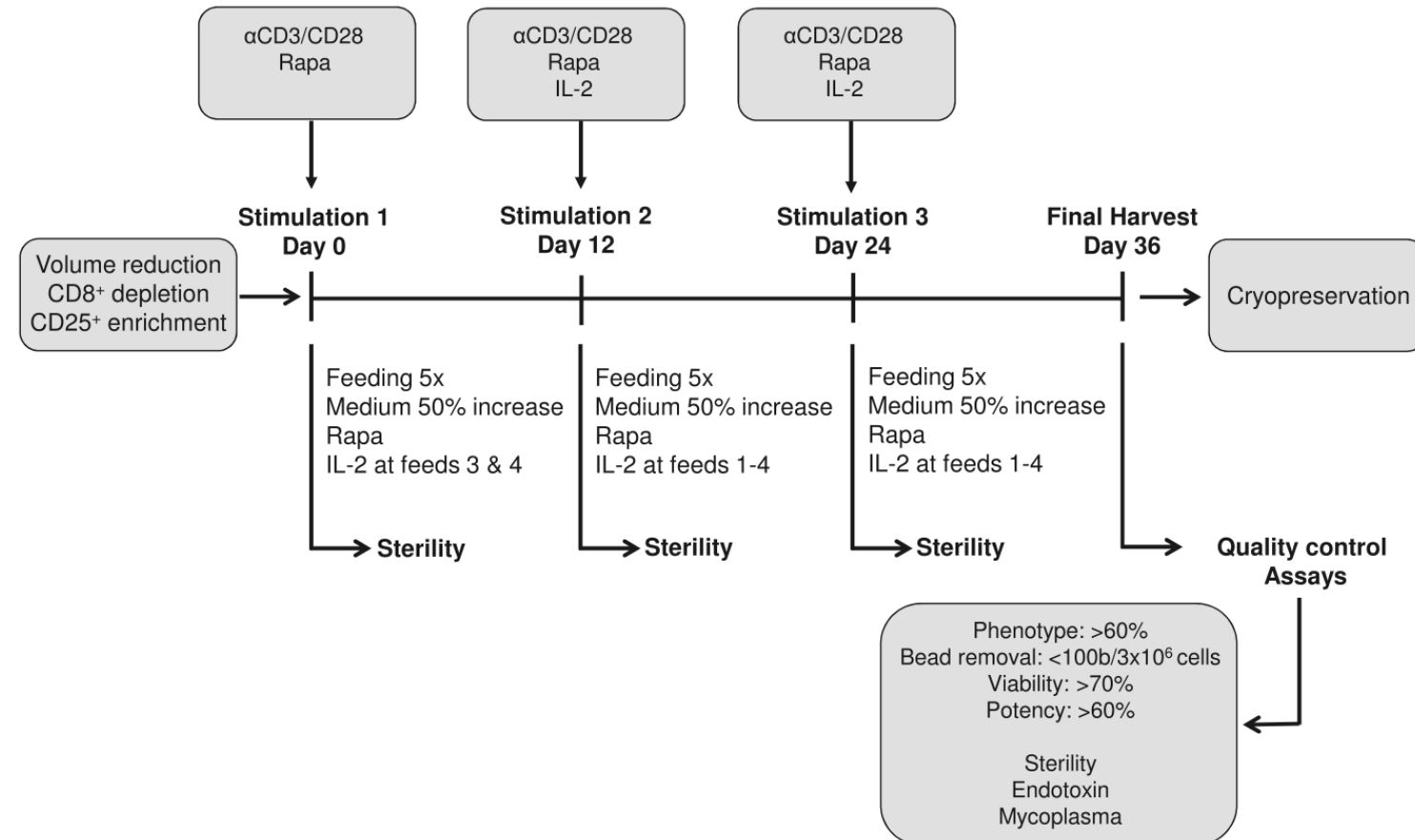


3-Poliklonal Treg

A Rapamycin-Based GMP-Compatible Process for the Isolation and Expansion of Regulatory T Cells for Clinical Trials

Henrieta Fraser,^{1,5} Niloufar Safinia,^{1,5} Nathali Grageda,¹ Sarah Thirkell,¹ Katie Lowe,¹ Laura J. Fry,¹ Cristiano Scottá,¹ Andrew Hope,¹ Christopher Fisher,¹ Rachel Hilton,² David Game,² Paul Harden,³ Andrew Bushell,⁴ Kathryn Wood,⁴ Robert I. Lechler,¹ and Giovanna Lombardi¹

¹Division of Transplantation, Immunology and Mucosal Biology, King's College London, London, UK; ²The Department of Nephrology and Transplantation, Guy's Hospital, Guy's and St. Thomas NHS Foundation Trust; ³Oxford Transplant Centre, Oxford, UK; ⁴Transplantation Research Immunology Group, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK





3-Poliklonal Treg



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Volume 21, Issue 4, April 2021, Pages 1603-1611



BRIEF COMMUNICATION

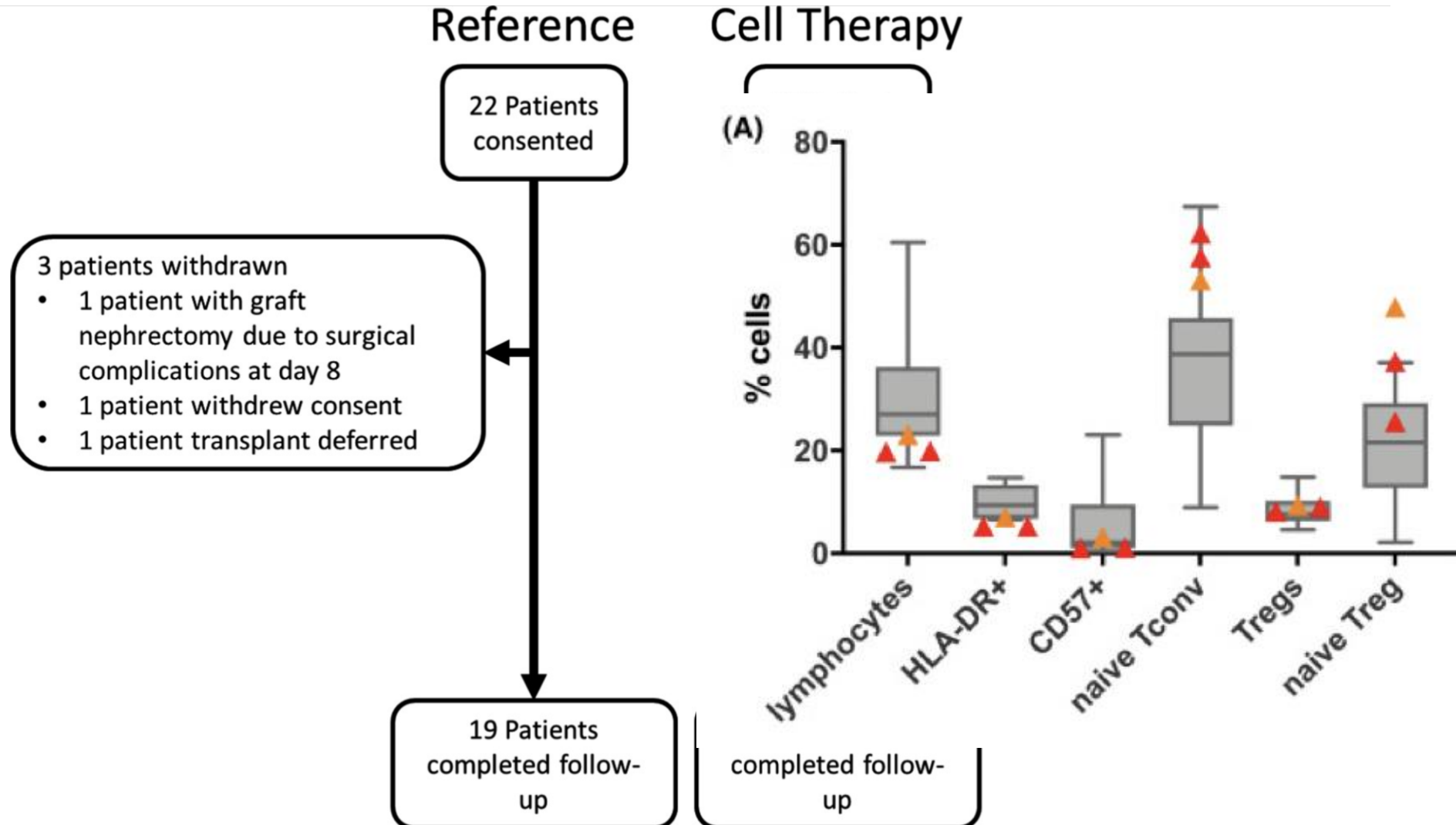
Feasibility, long-term safety, and immune monitoring of regulatory T cell therapy in living donor kidney transplant recipients

Paul N. Harden¹  , David S. Game², Birgit Sawitzki³, Jeroen B. Van der Net¹, Joanna Hester⁴, Andrew Bushell⁴, Fadi Issa⁴, Matthew O. Brook^{1 4}, Alaa Alzhrani⁴, Stephan Schlickeiser³, Cristiano Scotta⁵, William Petchey¹, Mathias Streitz⁶, Gilles Blancho⁷, Quizhi Tang⁸, James Markmann⁹, Robert I. Lechler⁵, Ian S.D. Roberts¹⁰, Peter J. Friend¹, Rachel Hilton², Edward K. Geissler¹¹, Kathryn J. Wood⁴, Giovanna Lombardi⁵

¹ Oxford Transplant Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, UK



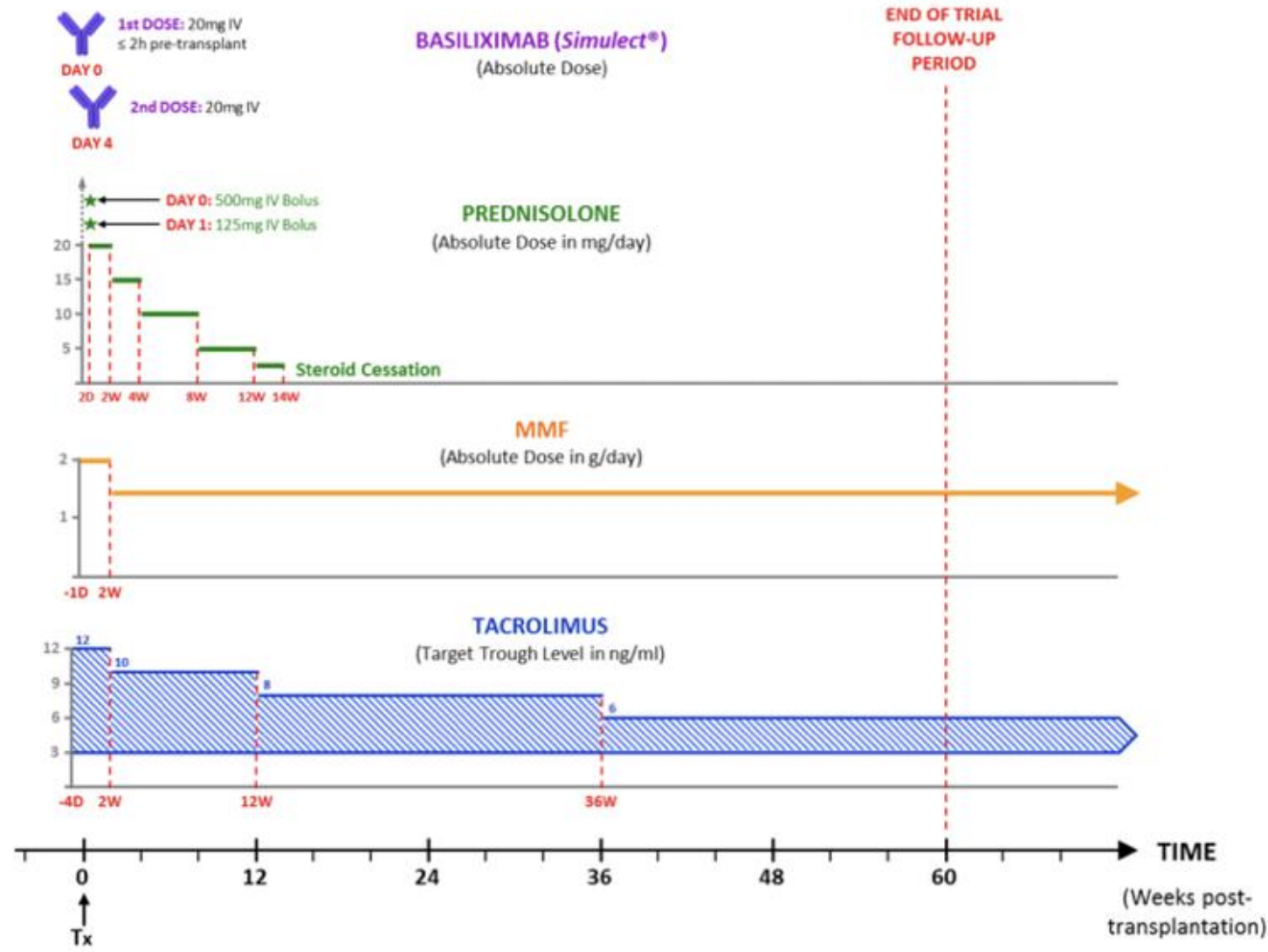
3-Poliklonal Treg





3-Poliklonal Treg (apTreg)

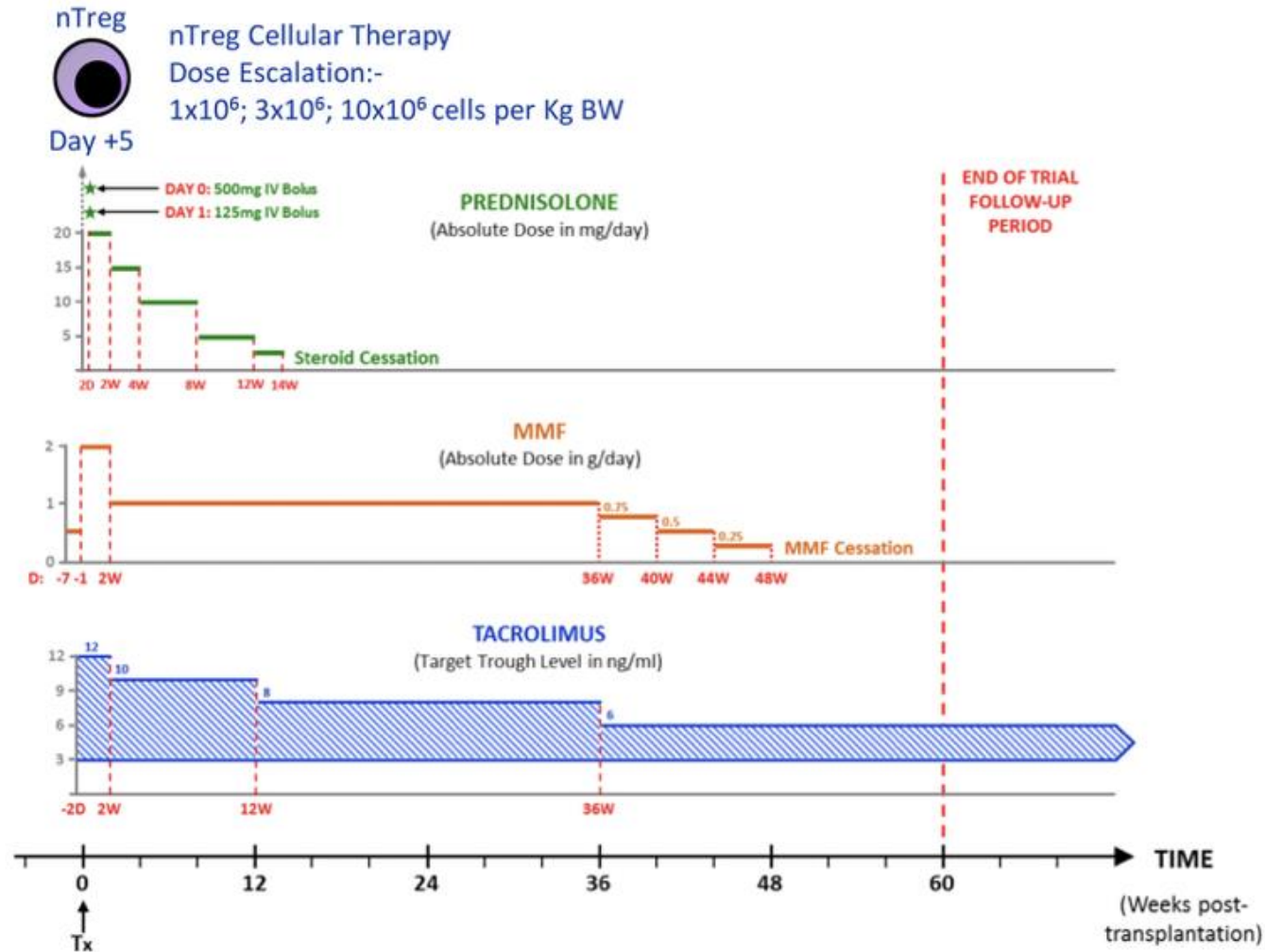
Reference Group





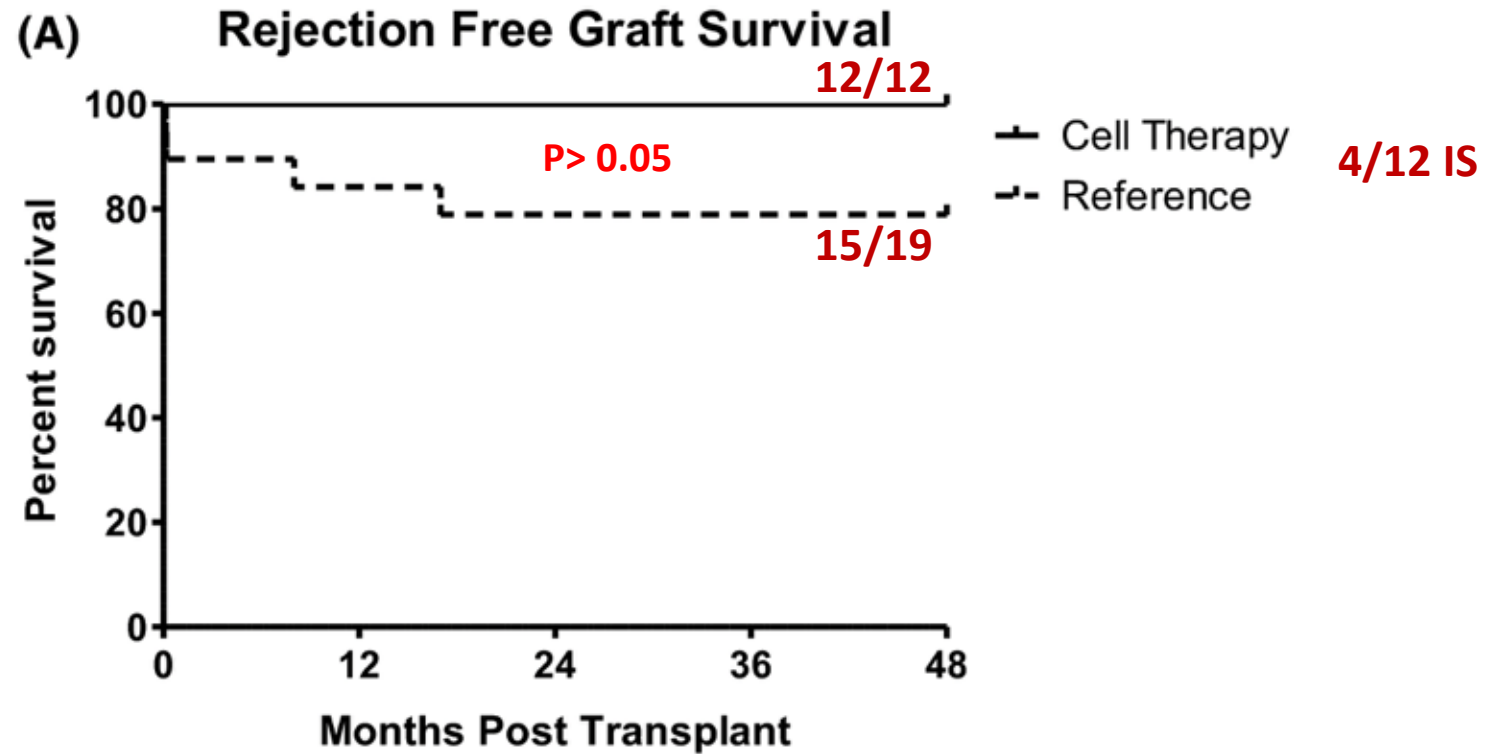
3-Poliklonal Treg

Cell Therapy Group



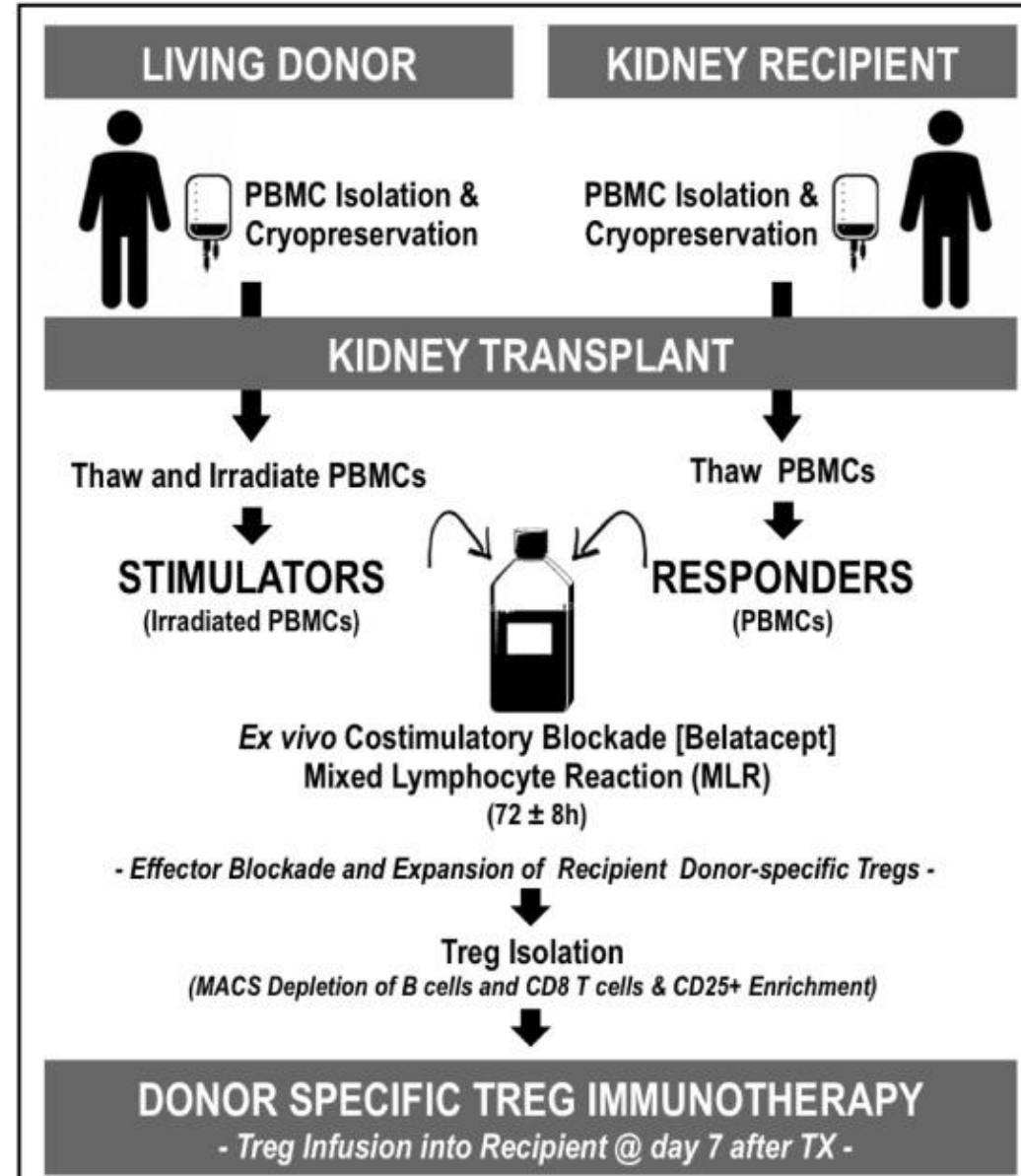


3-Poliklonal Treg





4-Donor antigen-specific regulatory T cell Treg (Dar-Treg)





4-Donor antigen-specific regulatory T cell Treg (Dar-Treg)

American Journal of TRANSPLANTATION

ORIGINAL ARTICLE · Volume 23, Issue 12, P1872-1881, December 2023 · [Open Archive](#)

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Donor antigen-specific regulatory T cell administration to recipients of live donor kidneys: A ONE Study consortium pilot trial

[Eva C. Guinan](#)^{1,†} · [Laura Contreras-Ruiz](#)^{1,†} · [Kerry Crisalli](#)² · [Charles Rickert](#)² · [Ivy Rosales](#)² · [Robert Makar](#)³ · [Robert Colvin](#)² · [Edward K. Geissler](#)⁴ · [Birgit Sawitzki](#)⁵ · [Paul Harden](#)⁶ · [Qizhi Tang](#)⁷ · [Giles Blanco](#)⁸ · [Laurence A. Turka](#)² · [James F. Markmann](#)² [Show less](#)

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¹ Department of Radiation Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts, USA



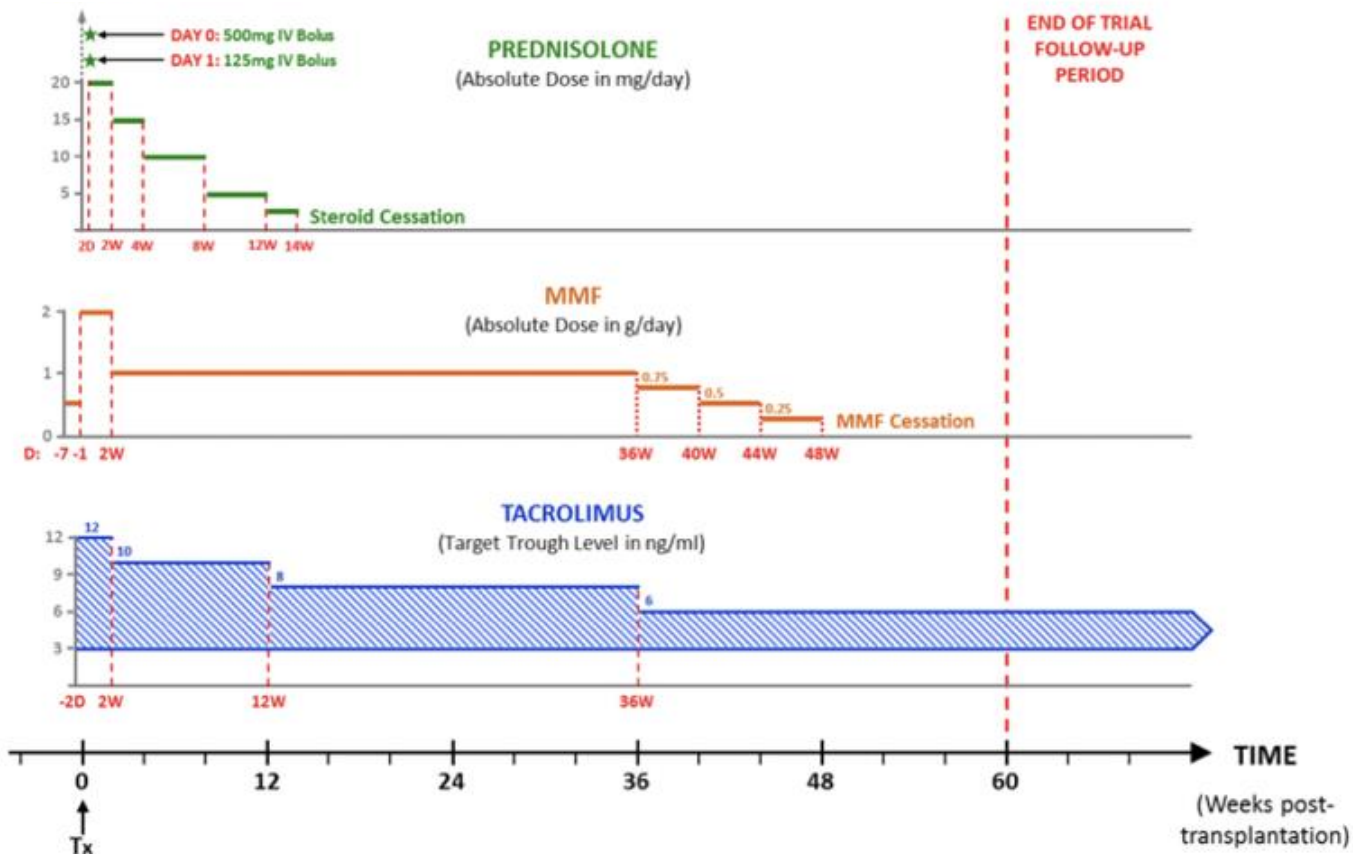
4-Donor antigen-specific regulatory T cell Treg (Dar-Treg)

Cell Therapy Group

DarTreg Cellular Therapy

Dose: $1-3 \times 10^4$

Day +7





4-Donor antigen-specific regulatory T cell Treg (Dar-Treg)

Table 1

Recipient and donor-patient characteristics.

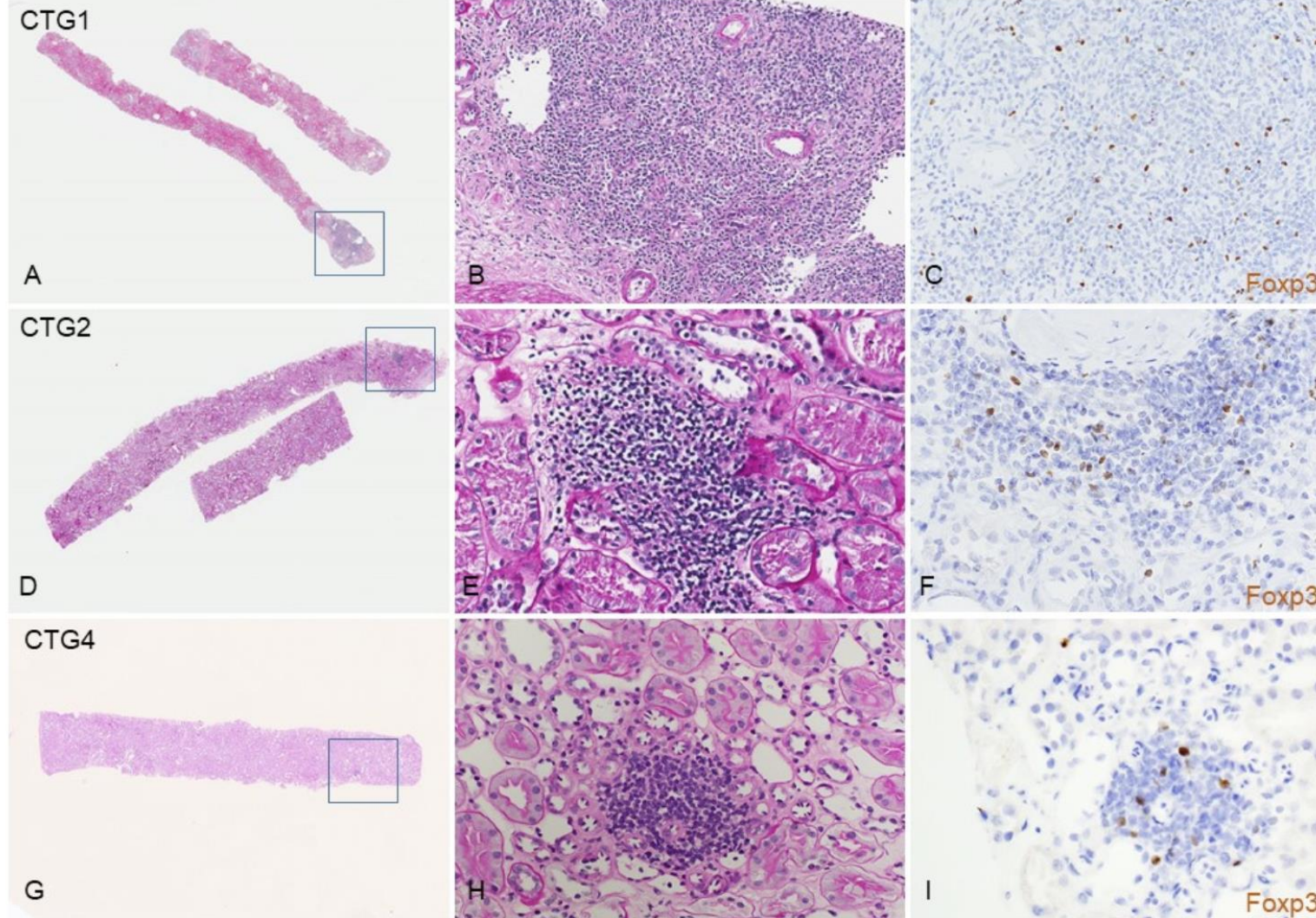
Group	Subject	Age (y)/sex	Cause of ESRD	Donor	HLA match
Reference group trial	RGT1	37/M	Diabetes Mellitus Type 1	Related (Sibling) Male	2/6
	RGT2	66/M	Diabetes Mellitus Type 2	Unrelated Female	0/6
	RGT3	46/M	Dysplasia	Unrelated Female	0/6
Cell therapy group	CTG1	48/M	Fibrillary GN	Unrelated Female	1/6
	CTG2	53/M	IgA Nephropathy	Unrelated Female	0/6
	CTG4	57/M	Polycystic Kidney Disease	Unrelated Female	0/6

ESRD, end-stage renal disease; GN, glomerulonephritis, HLA, human leukocyte antigen; M, male.



4-Donor antigen-specific regulatory T cell Treg (Dar-Treg)

6 yıllık Takip

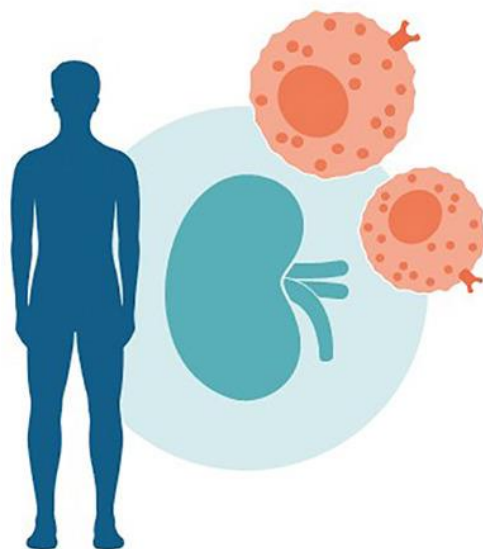




4-Donor antigen-specific regulatory T cell Treg (Dar-Treg)

Donor antigen-specific regulatory T cell administration to recipients of live donor kidneys:
A ONE Study consortium pilot trial

How does infusion of donor antigen reactive regulatory T cells (dar-Treg) impact outcomes for living donor kidney Tx recipients?



Single-center
safety / feasibility study



3 kidney recipients
received dar-Treg
infusions 3-7 days
posttransplant



No induction
immunosuppression



Initial maintenance
immunosuppression
(Tac + MMF + steroids)
was tapered to
Tac monotherapy
by month 13



No acute rejection or
serious adverse events
were observed within the
first 6 years posttransplant

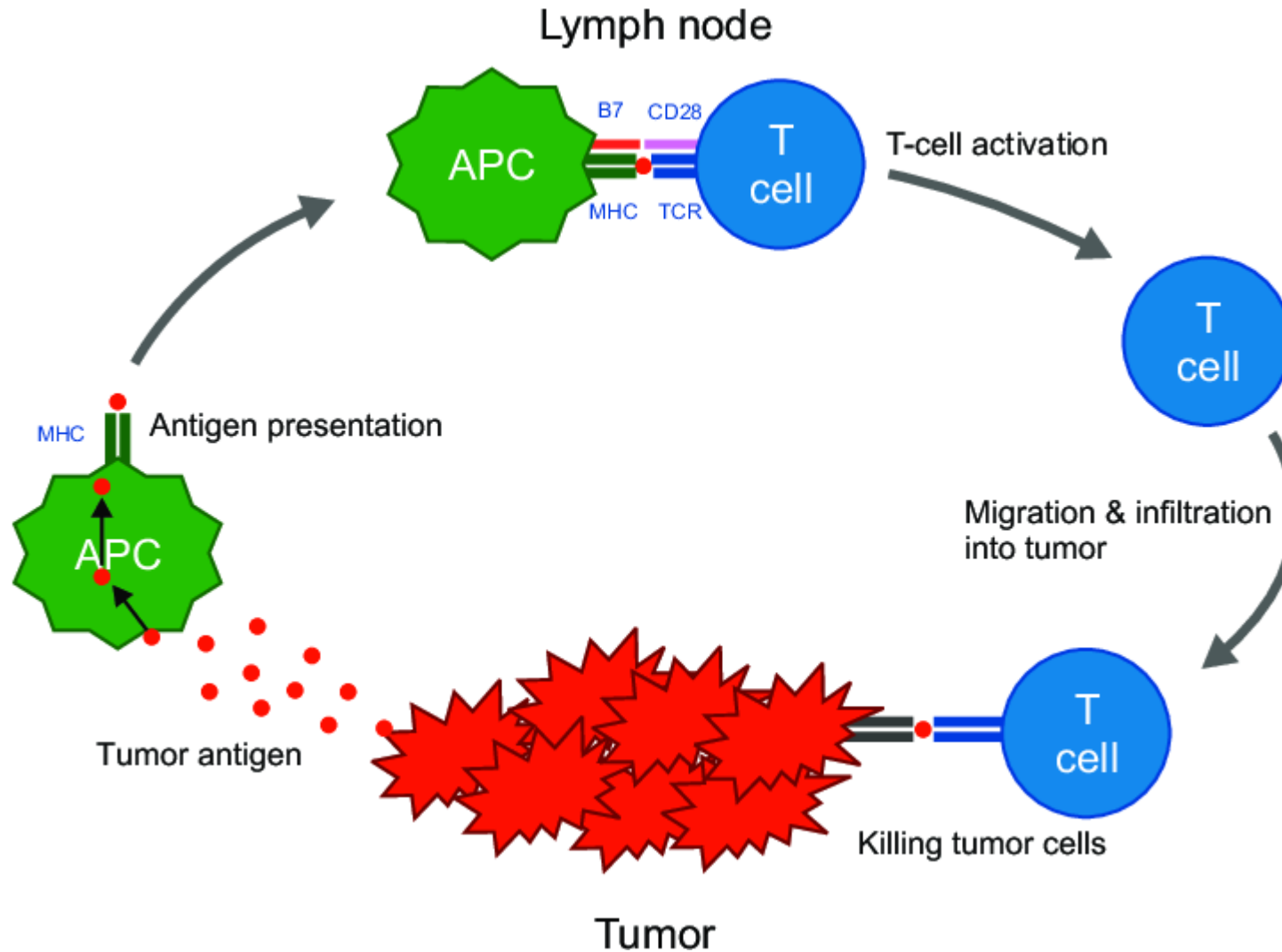


All patients had
Treg-containing lymphoid
aggregates
on biopsy

AJT

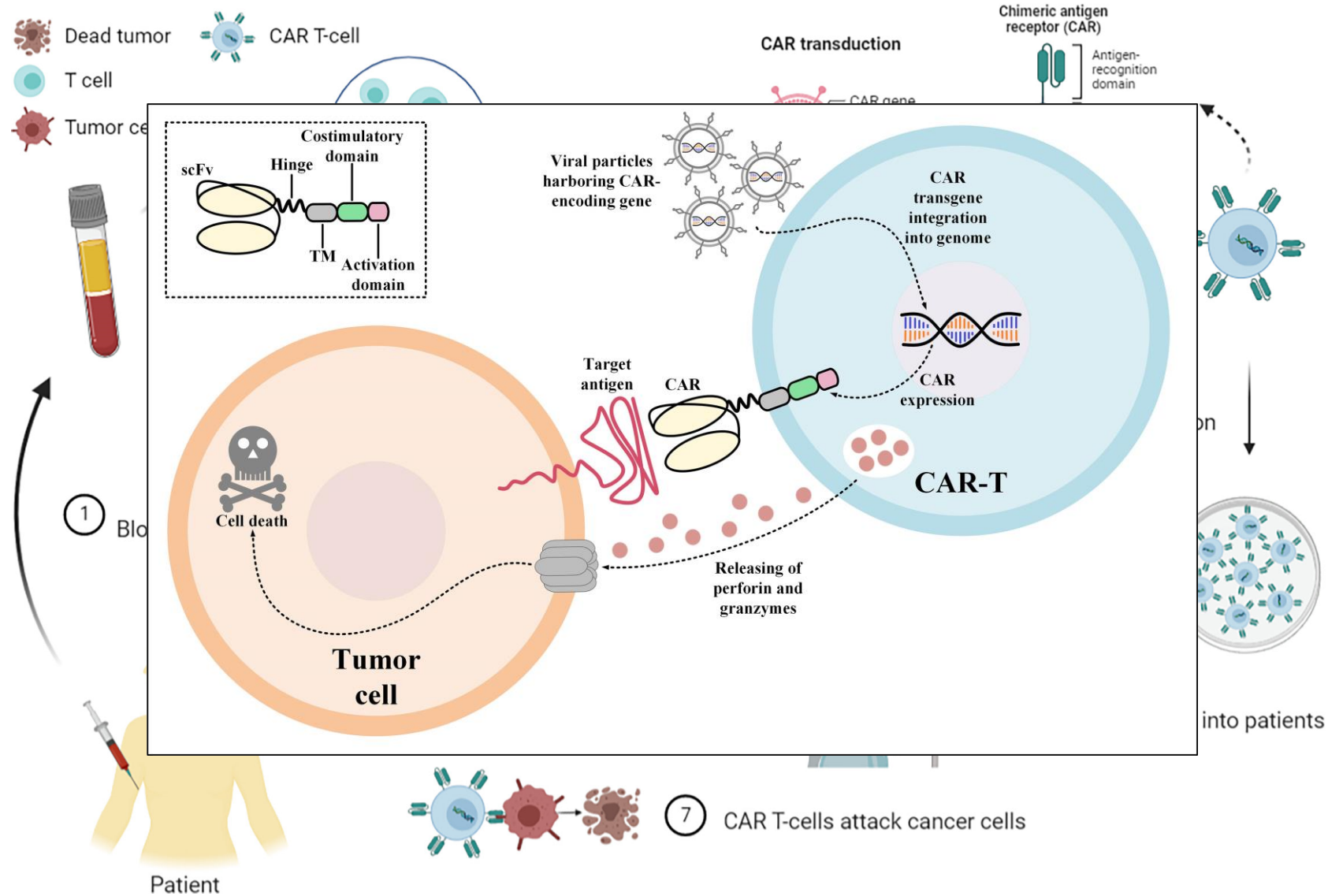


5-HLA-A2 CAR-Treg



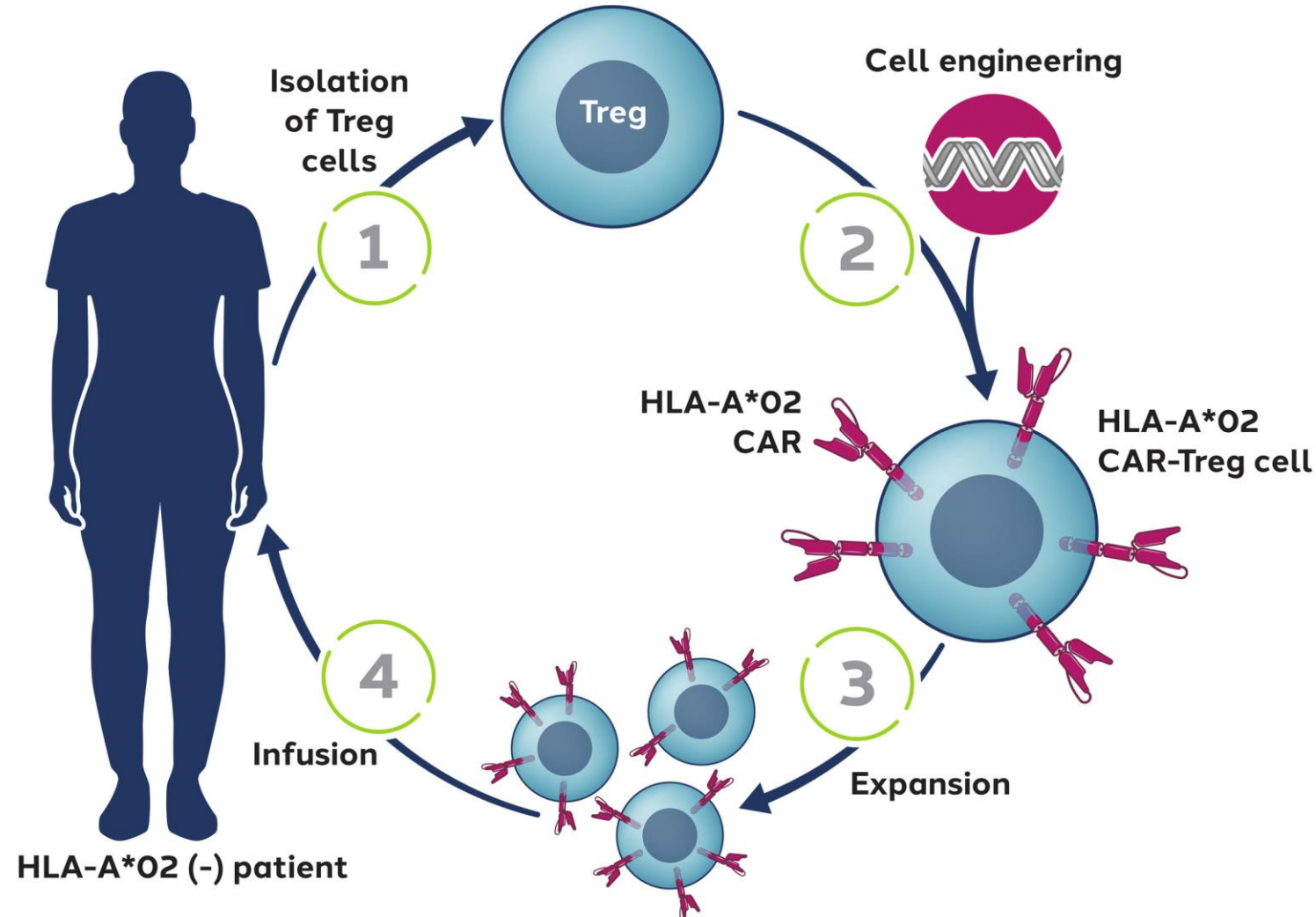


5-HLA-A2 CAR-Treg



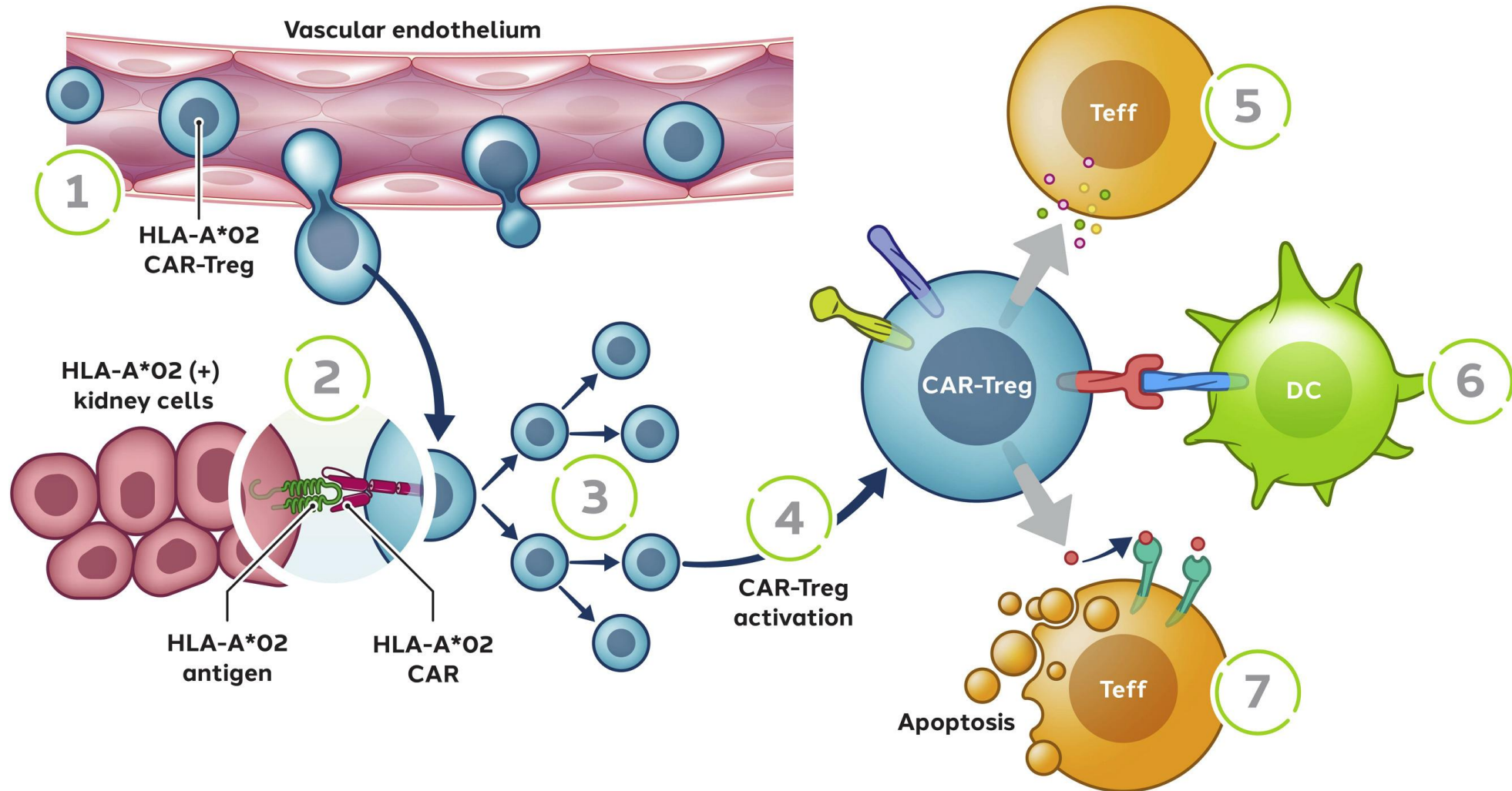


5-HLA-A2 CAR-Treg





5-HLA-A2 CAR-Treg





5-HLA-A2 CAR-Treg



WTC 2025
World Transplant Congress
San Francisco, USA | August 2-6



STEADFAST Study Update: A Phase I/II Clinical Trial of Regulatory T Cells Expressing a Chimeric Antigen Receptor Directed Towards HLA-A2 in Renal Transplantation

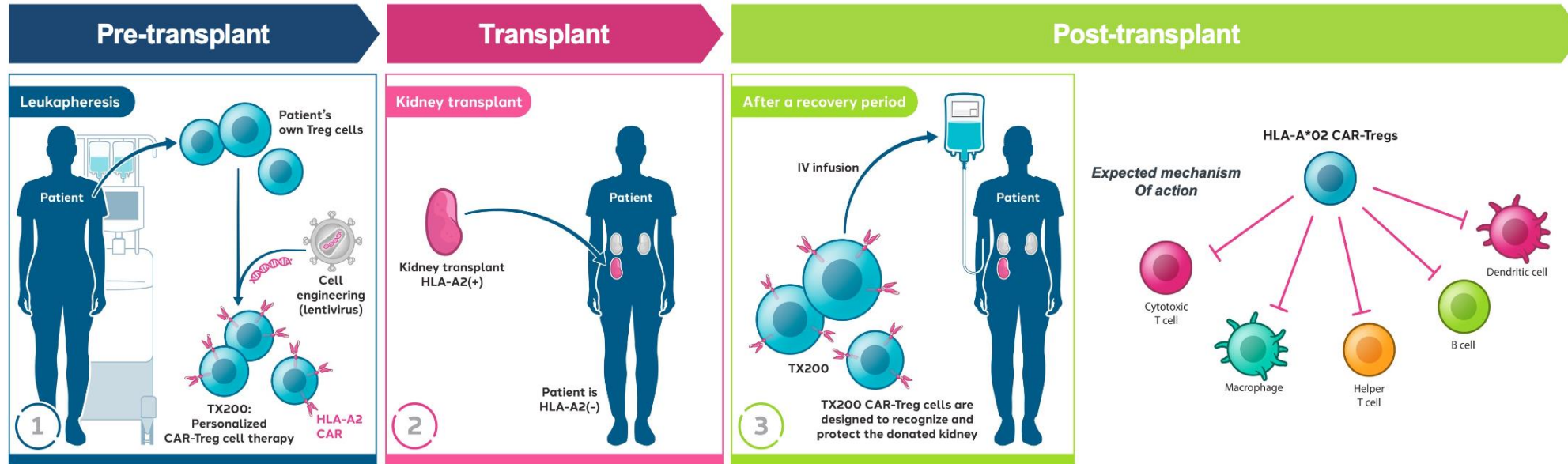
Katharina Schreeb¹, Gillian Atkinson¹, Claire Chapman¹, Liching Cao², Yanmei Lu², Kathleen Meyer², Michael Chen², Dirk Kuypers³, Johannes-Stephanus Sanders⁴, Aiko deVries⁵, Dennis Hesselink⁶, and **Paul Harden⁷**

Presented August 6, 2025 at the World Transplant Congress 2025

¹ Sangamo Therapeutics, United Kingdom; ² Sangamo Therapeutics Inc, CA; ³ Nephrology and Renal Transplantation, UZ Leuven, Belgium; ⁴ University Medical Center, Groningen, Netherlands; ⁵ Leiden University Medical Center, Netherlands; ⁶ Erasmus Medical Center Rotterdam, Netherlands; ⁷ Oxford University Hospital, United Kingdom



5-HLA-A2 CAR-Treg

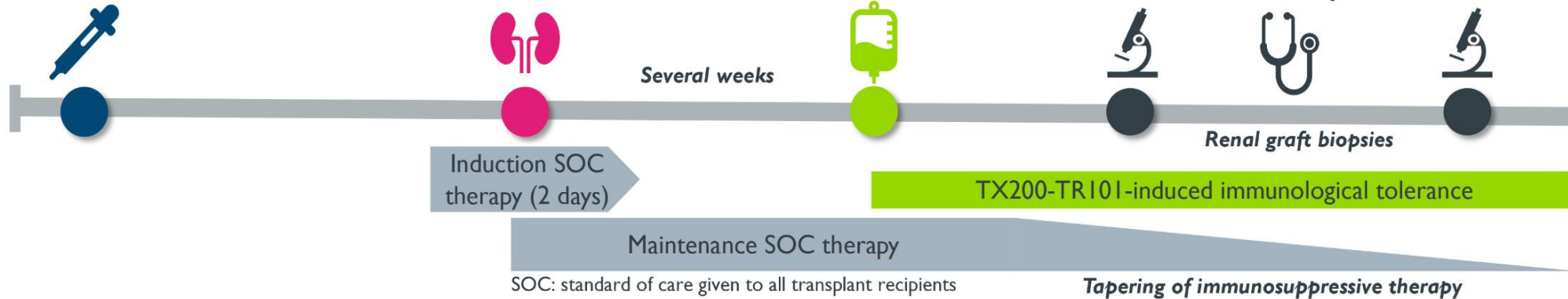


Leukapheresis & Manufacturing

Transplantation surgery

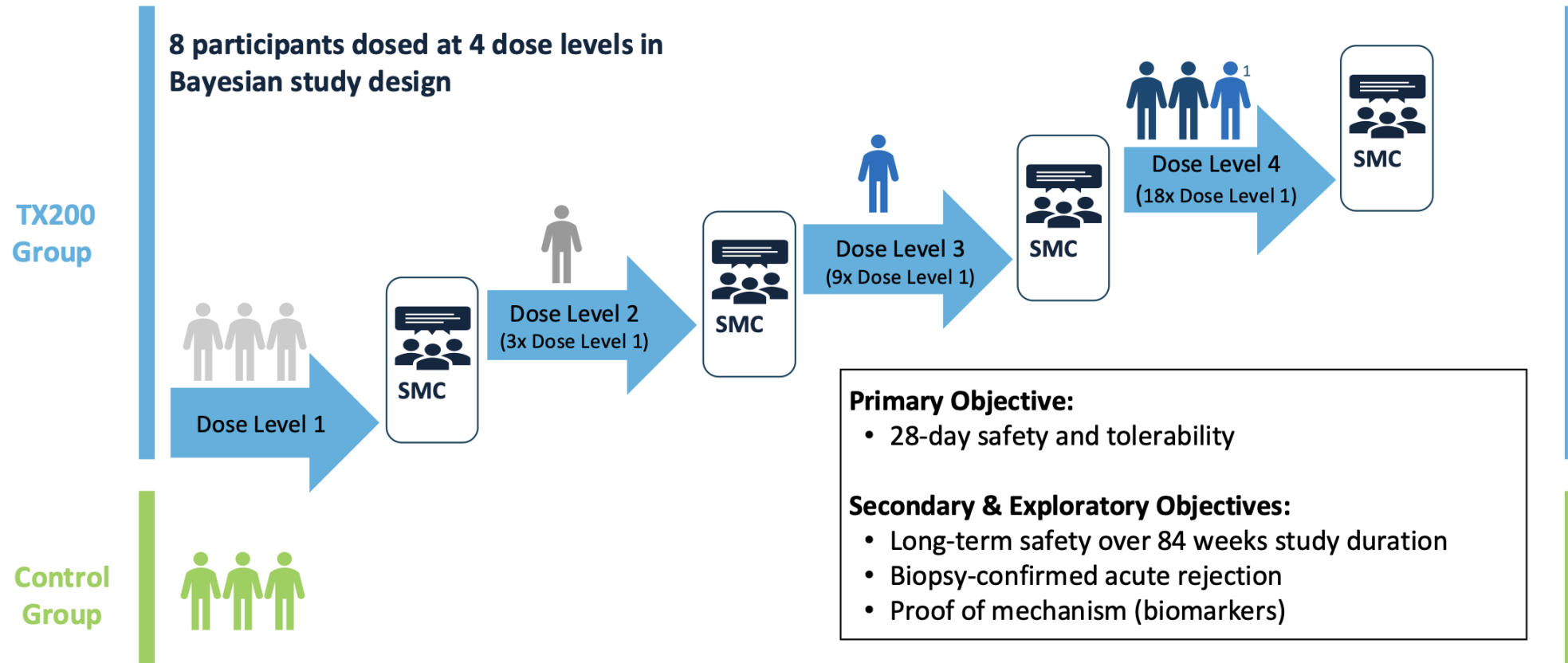
TX200 infusion

Follow-up





STEADFAST: A first-in-human Phase I/II study of CAR-Treg therapy in living donor renal transplant patients



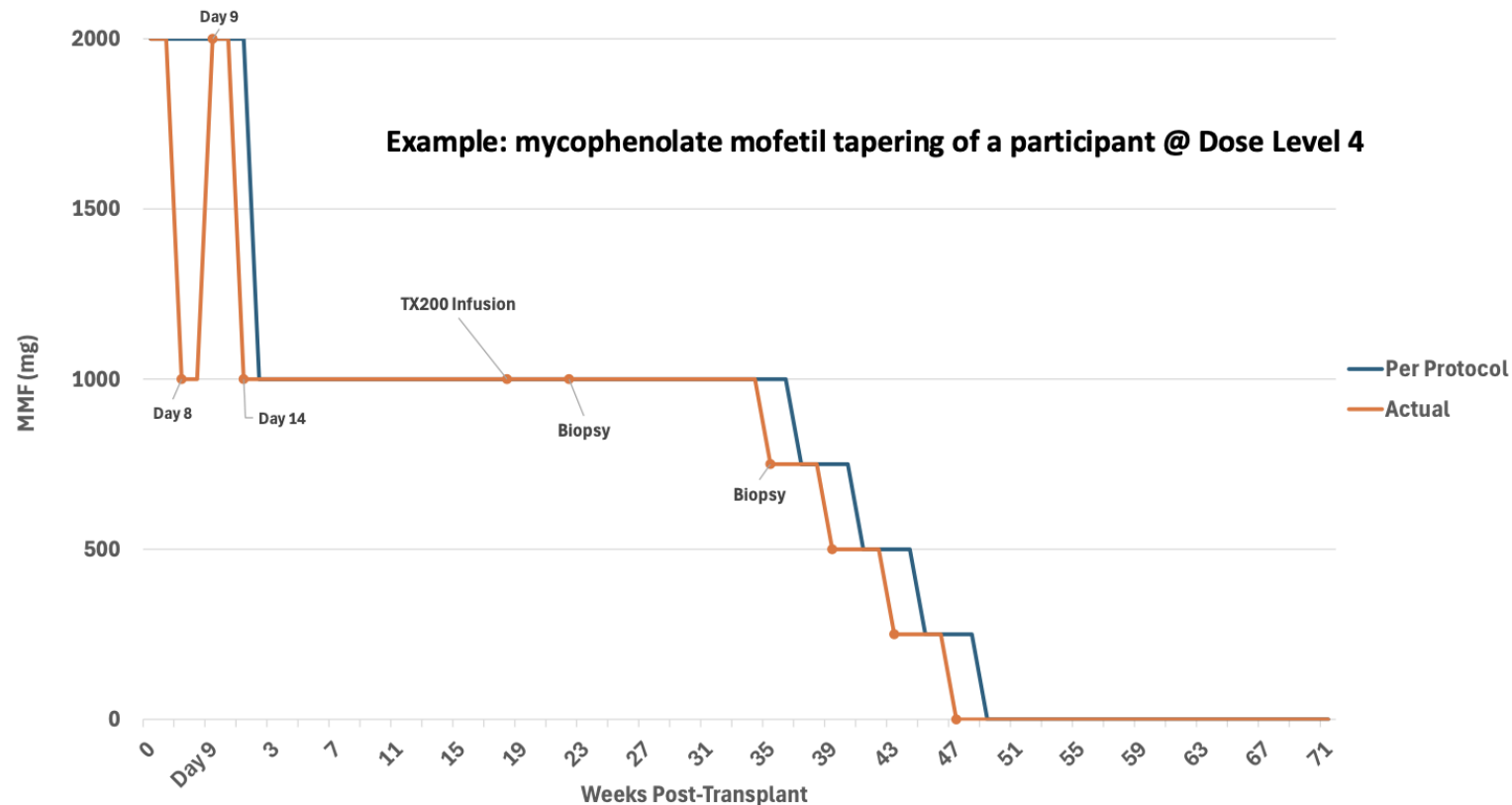
N = number; SMC = Safety Monitoring Committee.

¹Received a reduced number of CAR Treg cells, similar to dose level 3



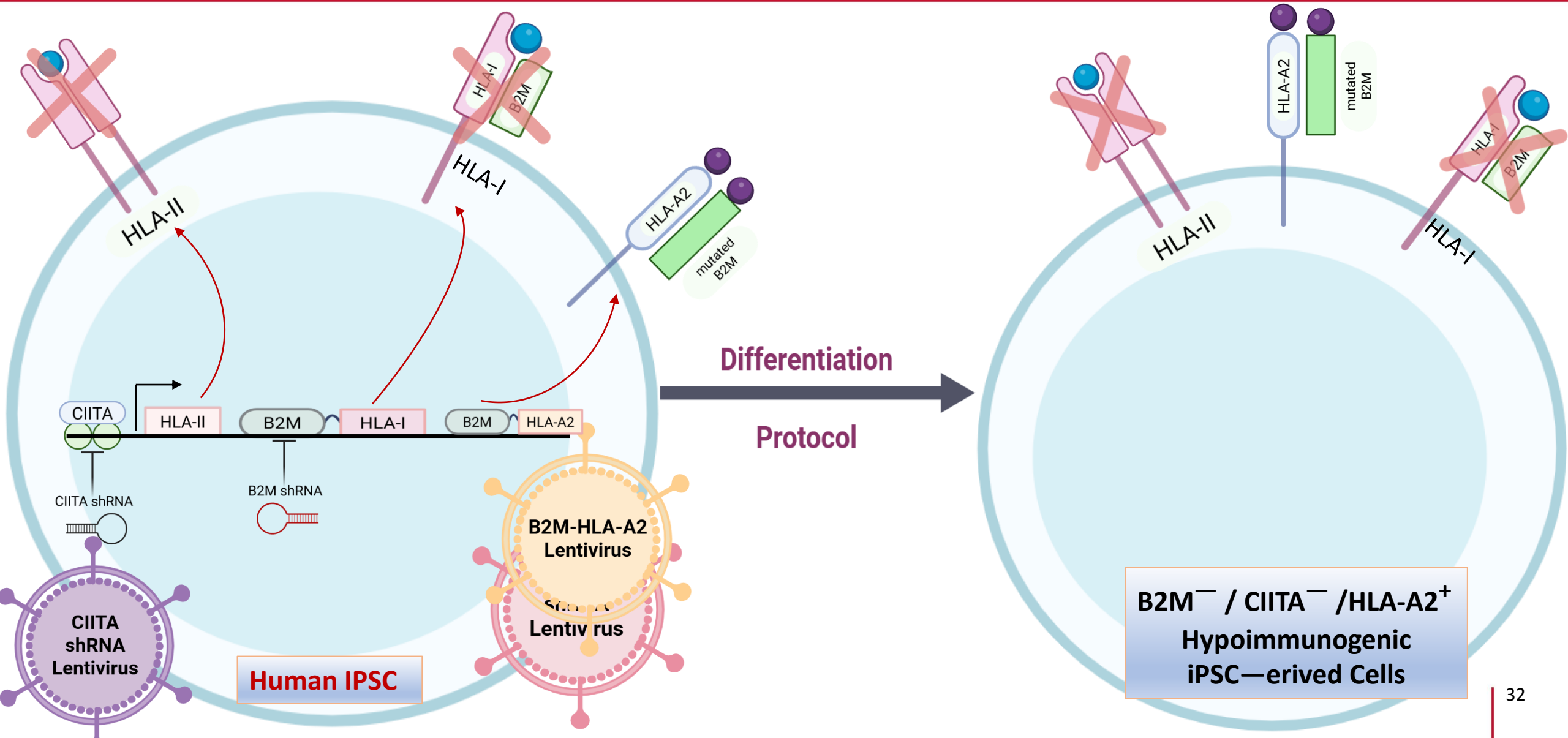
Reduction of immunosuppression post-TX200 with no significant inflammatory findings on kidney biopsies

- As of 28 May 2025 data cut, 4 of the 5 participants at Dose Levels 2, 3 and 4 had titrated down to tacrolimus monotherapy.
- No events of Biopsy Confirmed Acute Rejection have been reported for any participant.



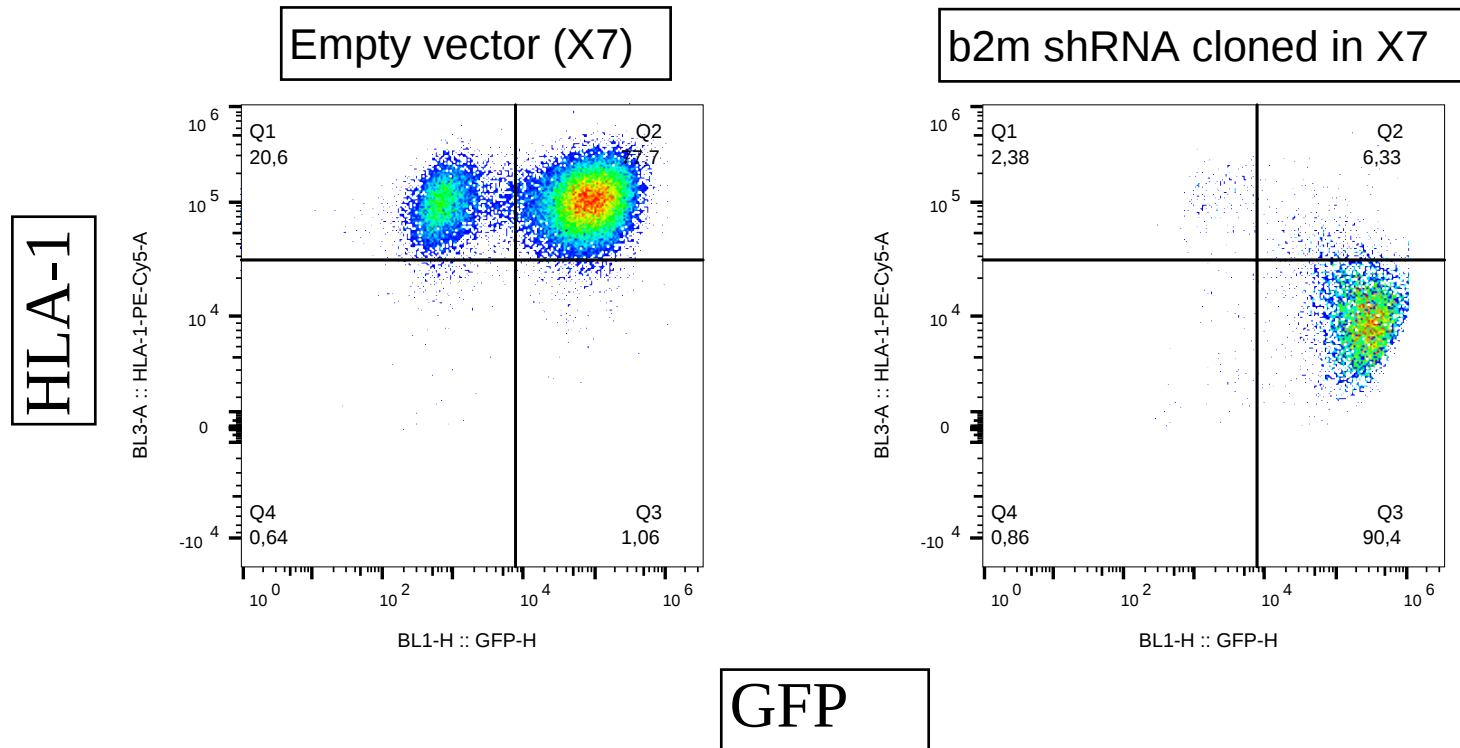


6-Production of HLA-Silenced Pluripotent Stem Cells





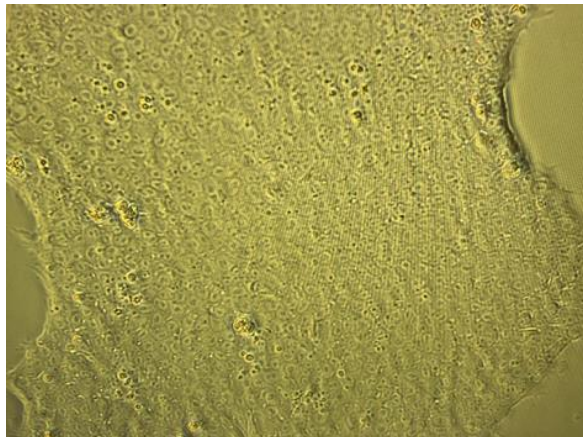
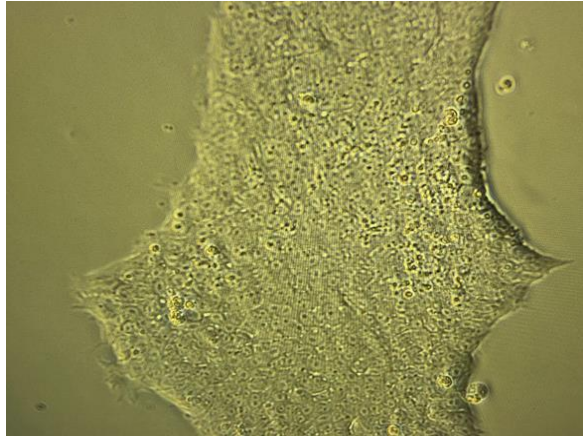
6-Production of HLA-Silenced Pluripotent Stem Cells



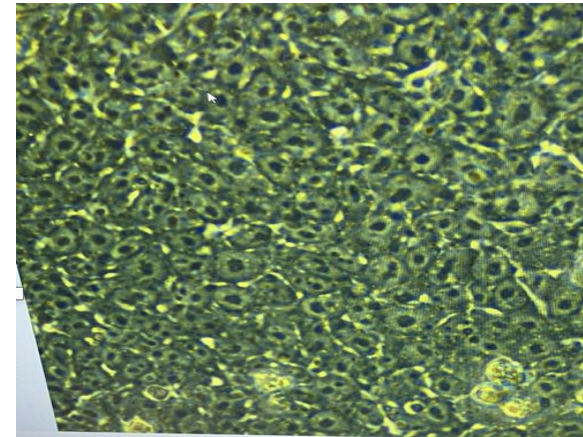
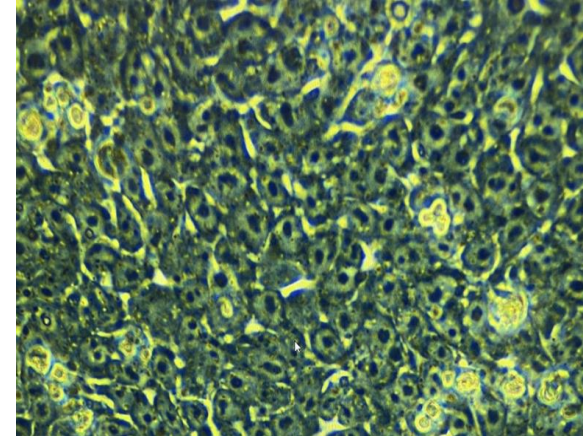


6-Production of HLA-Silenced Pluripotent Stem Cells

Day 1



P2D1





Teşekkür ederim...

