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Fc-Modified Anti-CD154 Mab Induced Long Term Renal Allograft Survival without Thromboembolic Complications

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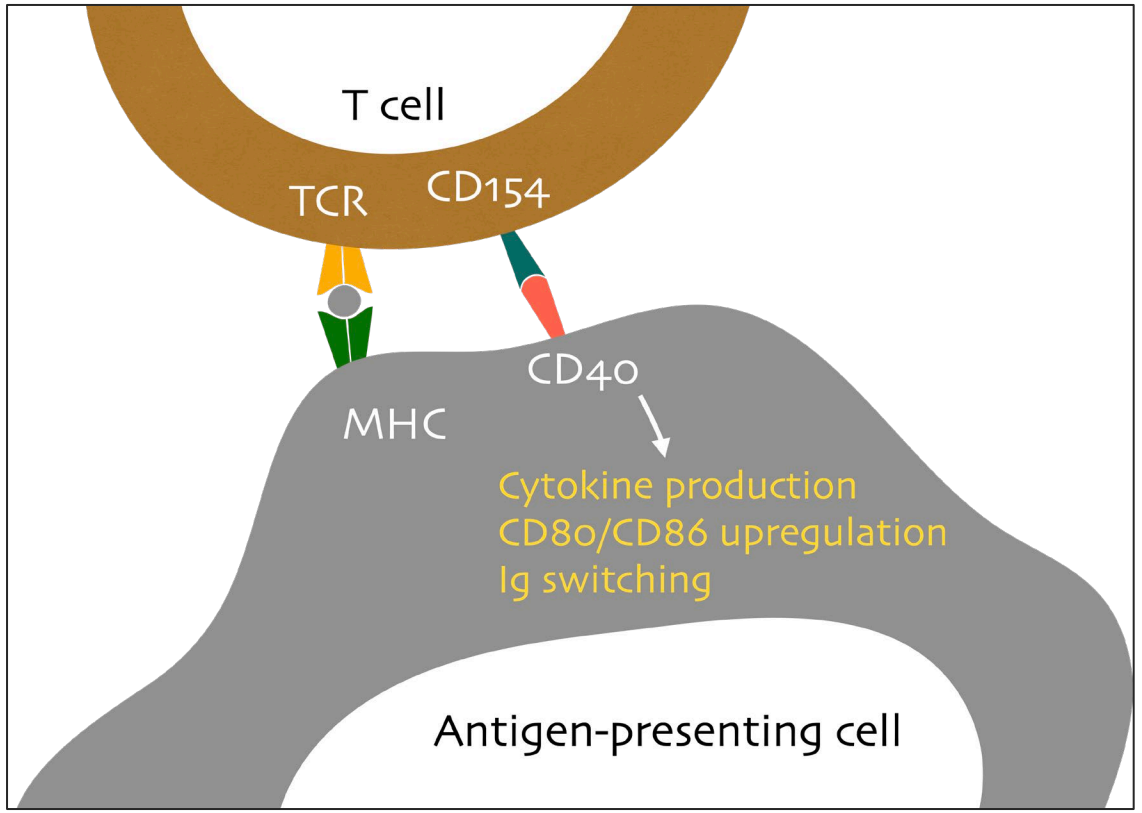
I have no financial relationships with commercial interests to disclose.

AND

My presentation does not include discussion of off-label or investigational use.

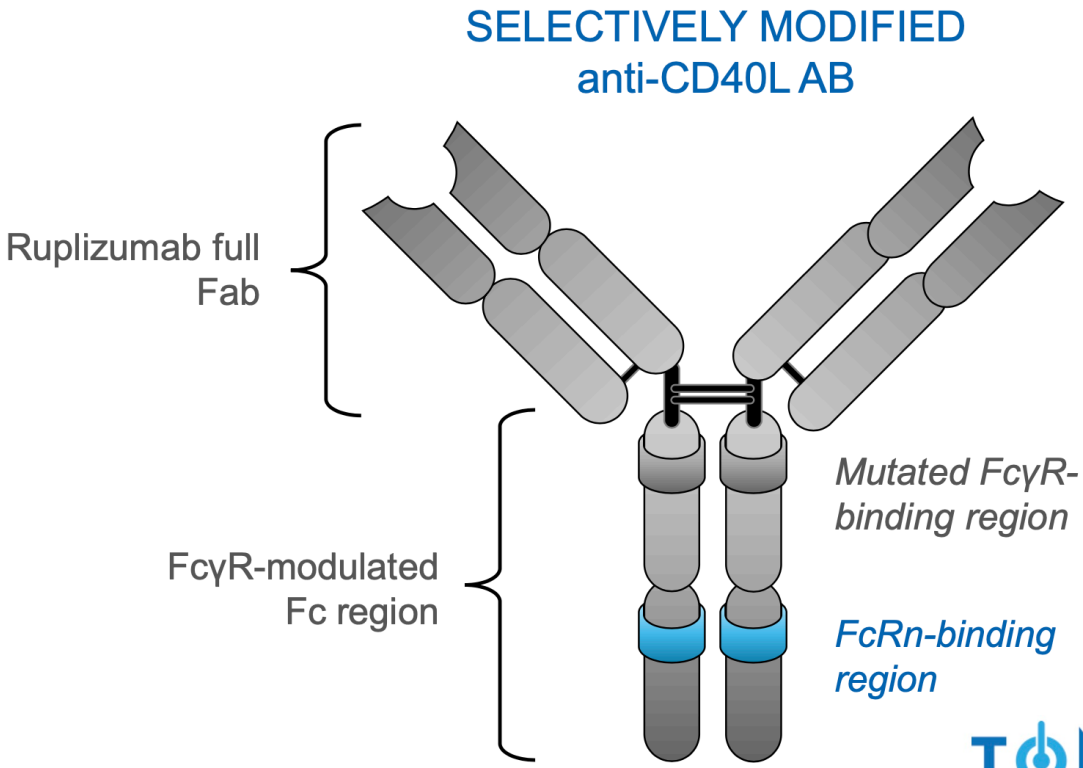
Biology of CD154

- CD154 is expressed on various types of cells, including activated T cells.
- Through interactions with its receptor, CD40, CD154 plays an important role in regulating interactions between T cells and antigen-presenting cells and thus affects several important functional events thought to be involved in allograft rejection.



TNX-1500: next generation anti-CD154 monoclonal antibody

TNX-1500 is engineered to target CD154 therapeutically while reducing Fc-receptor binding to overcome previously reported thrombogenicity.



TONIX PHARMACEUTICALS

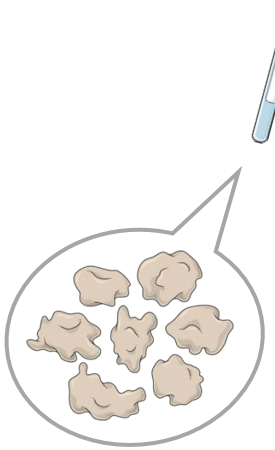
*TNX-1500 is an investigational new drug and has not been approved for any indication

Aims of the study

In this study, we compared **TNX-1500** with **conventional anti-CD154 antibodies** in terms of platelet activation *in vitro* and evaluated the efficacy of TNX-1500 to prevent kidney allograft rejection in an NHP kidney transplantation model.

Assay for platelet activation

NHP
whole blood



Platelets

5C8
alone

or

5C8=CD154
immune
complex

hu5C8
alone

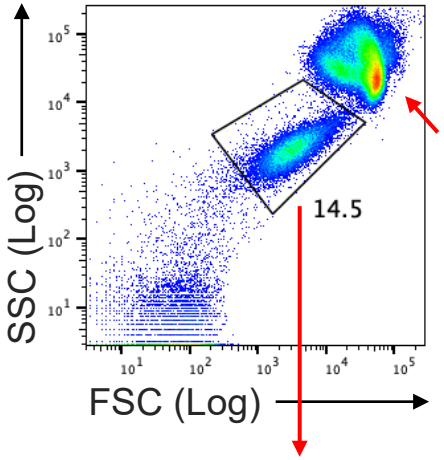
or

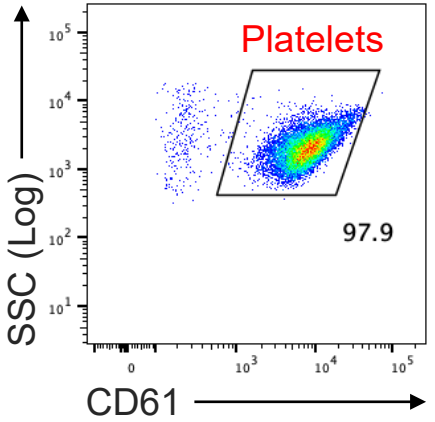
hu5C8=CD154
immune
complex

TNX-1500
alone

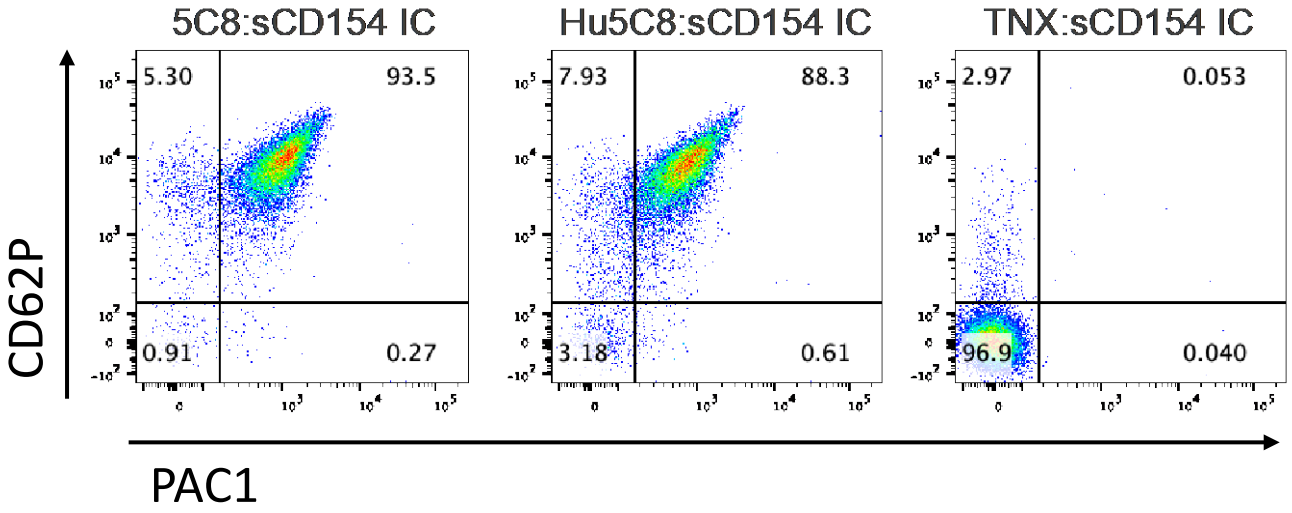
or

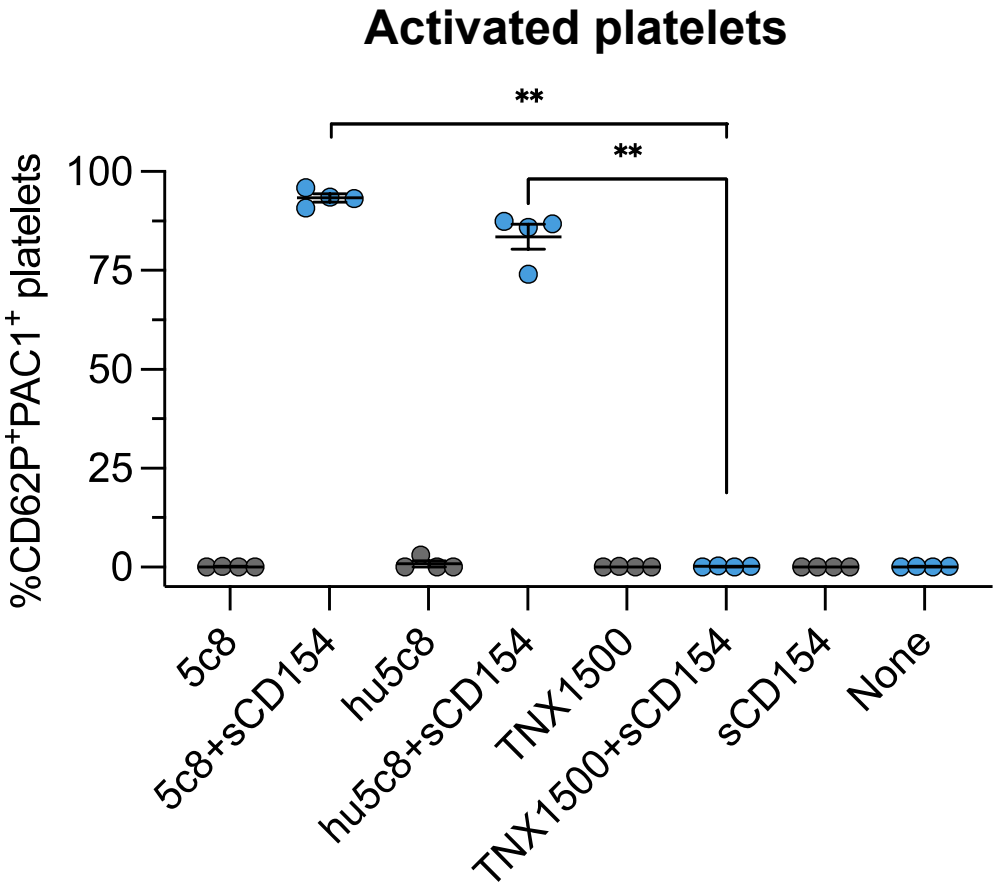
TNX-1500=CD154
immune
complex



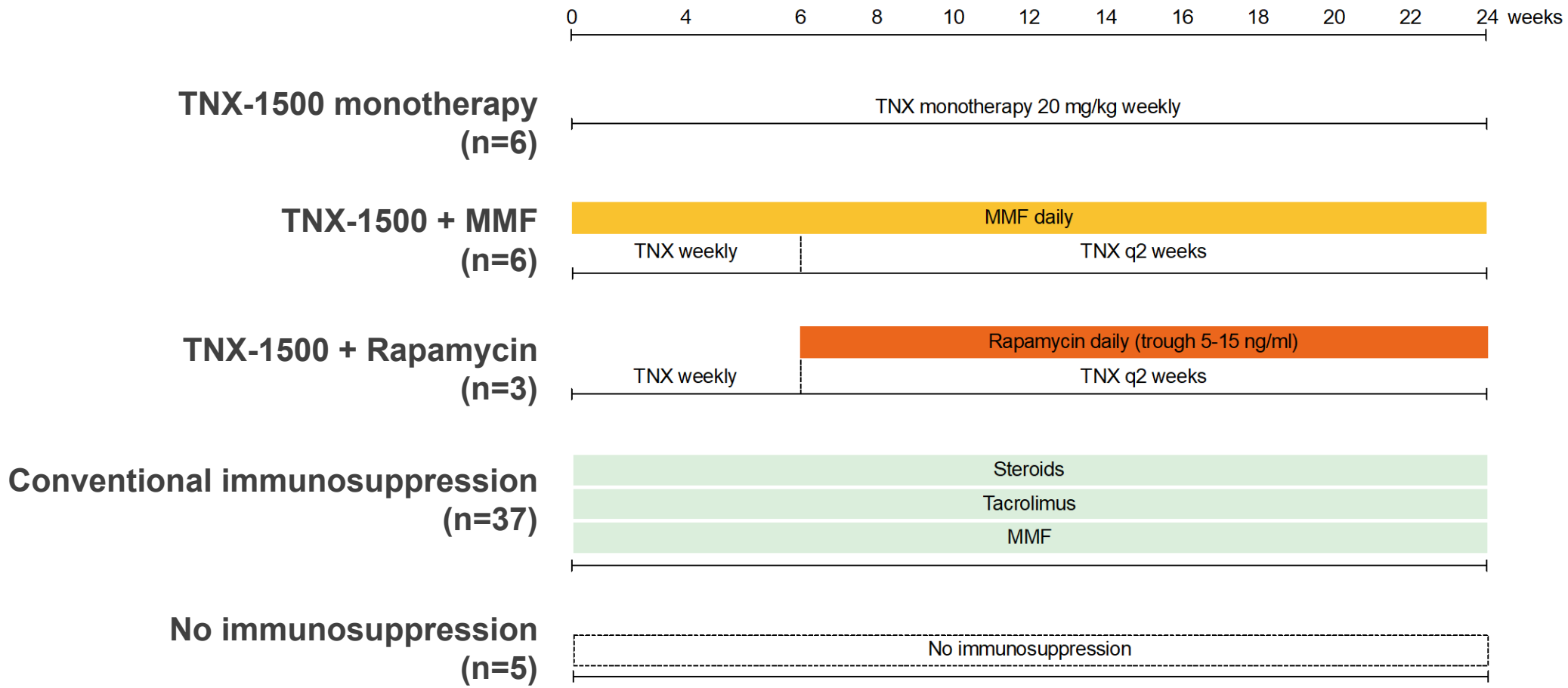


Platelet activation after exposure to anti-CD154 immune complex

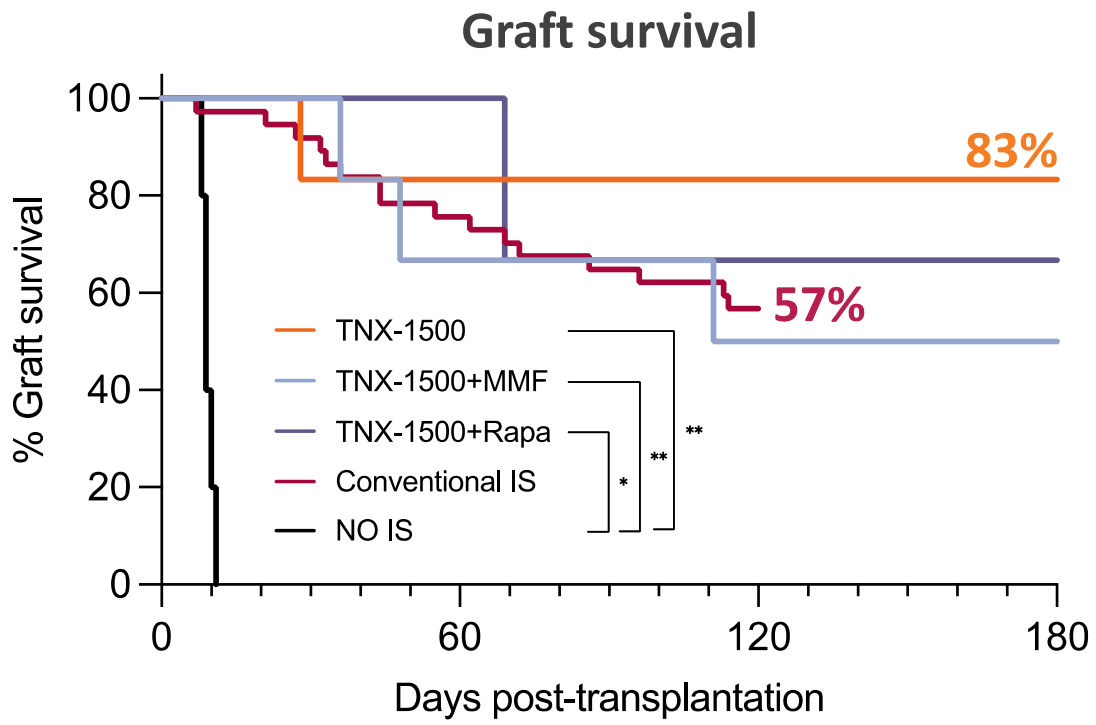


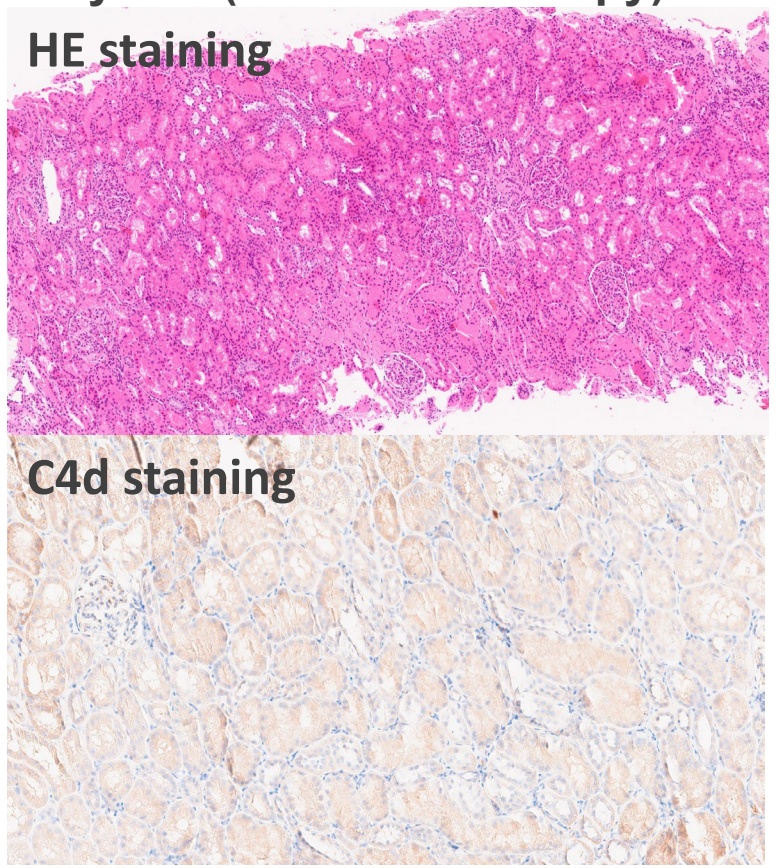


Treatment regimens for NHP kidney transplantation



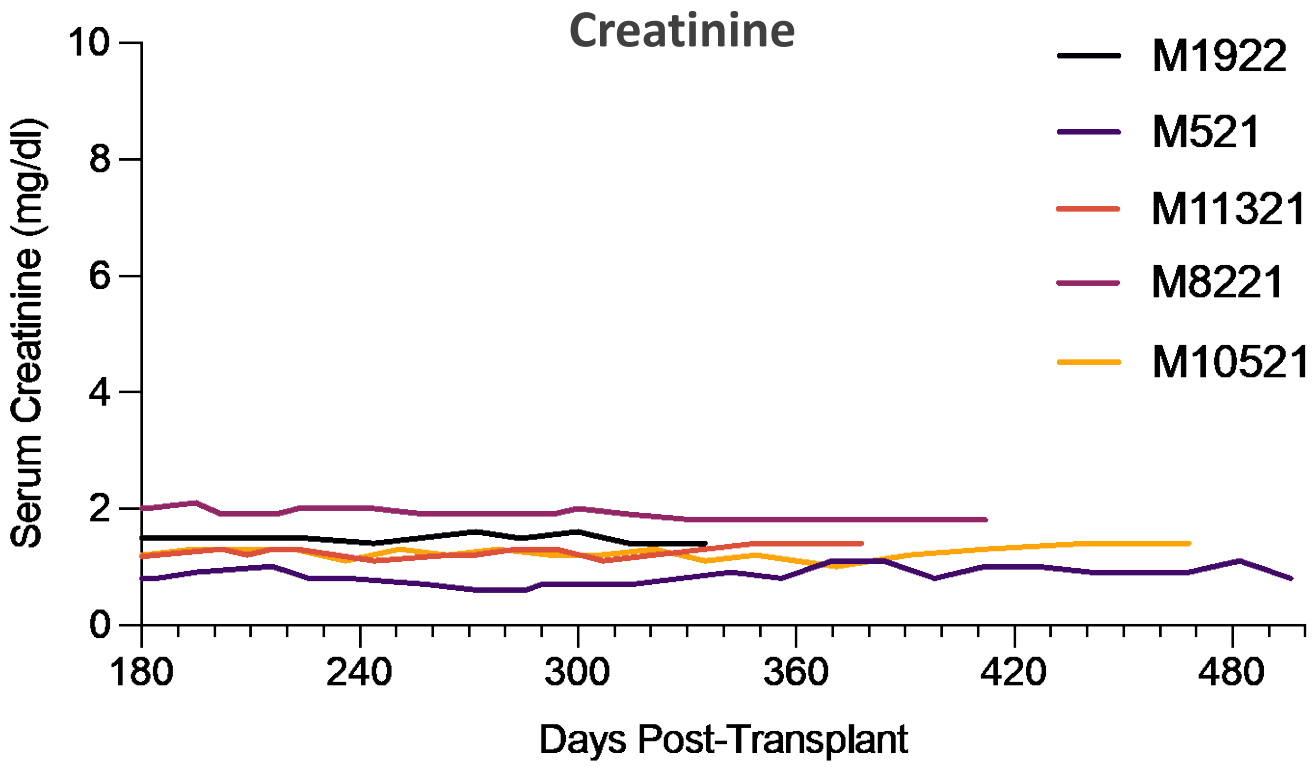
Kidney allograft survival





No thrombosis-related complications were observed.

Long-term observation beyond 180 days



ID	POD	TNX admin.	Combination
M10521	>497	Q4 weeks	Mono → MMF
M521	>665	Q4 weeks	MMF
M11321	>422	Q4 weeks	MMF
M8221	>450	Q4 weeks	MMF
M1922	>350	Q4 weeks	Rapa → MMF

No thrombosis-related complications were observed in long-term survivors.

Conclusion

- Fc-modification effectively prevented platelet activation
- TNX-1500 inhibited renal allograft rejection without thromboembolism in NHPs
- TNX-1500 can be an effective alternative to conventional immunosuppression therapy in kidney transplantation
- Optimal dosage for clinical application remains to be clarified

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