ATC2022 JUNE 4–8, 2022 / BOSTON, MA
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TNX-1500, an Fc-modified Anti-CD154 Antibody, Prolongs Nonhuman Primate Cardiac Allograft Survival

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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.

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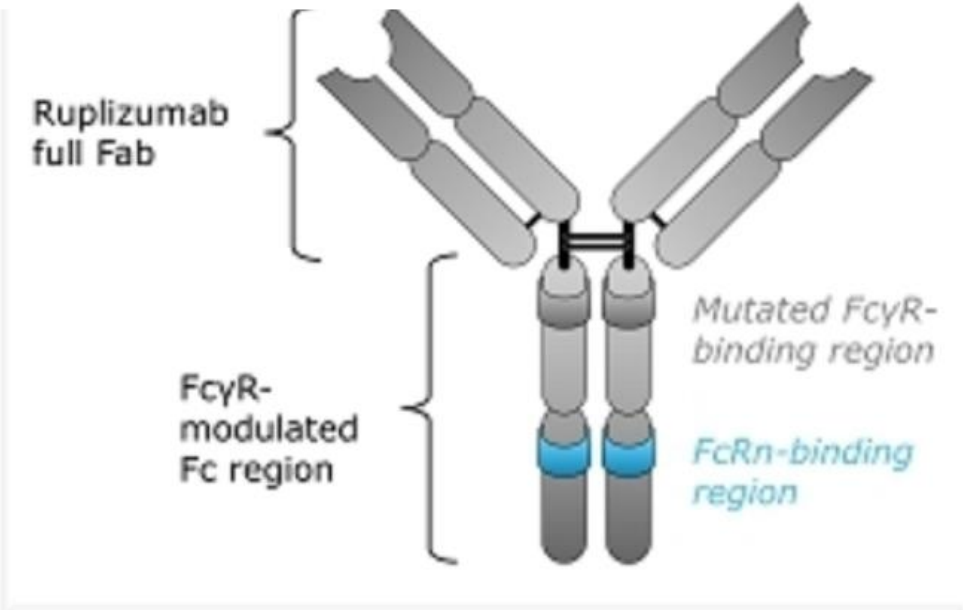
Background TNX-1500,* a novel Fc-Modified-anti CD154 mAb

TONIX PHARMACEUTICALS



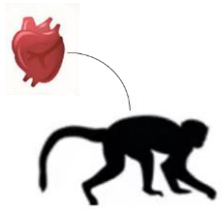
- The development of humanized 5c8 (ruplizumab) was halted due to thrombotic complications seen in human clinical trials, associated with anti-CD154 Abs to an Fcγ receptor-binding.
- Several Abs engineered to down-modulate FcγR-binding, successfully avoided thrombosis, however, reduced Fc functionality was associated with reduced efficacy as monotherapy in NHP kidney transplant models.

  Ferrant, et al. International Immunology 2004
  Kim, et al. AST 2017
- We evaluated the preserved functional ability of TNX-1500 (TNX), containing the hu5c8 Fab and an IgG4 Fc region engineered to reduce FcγR-binding associated with the risk of thrombosis in a NHP heart transplant model.

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

Methods

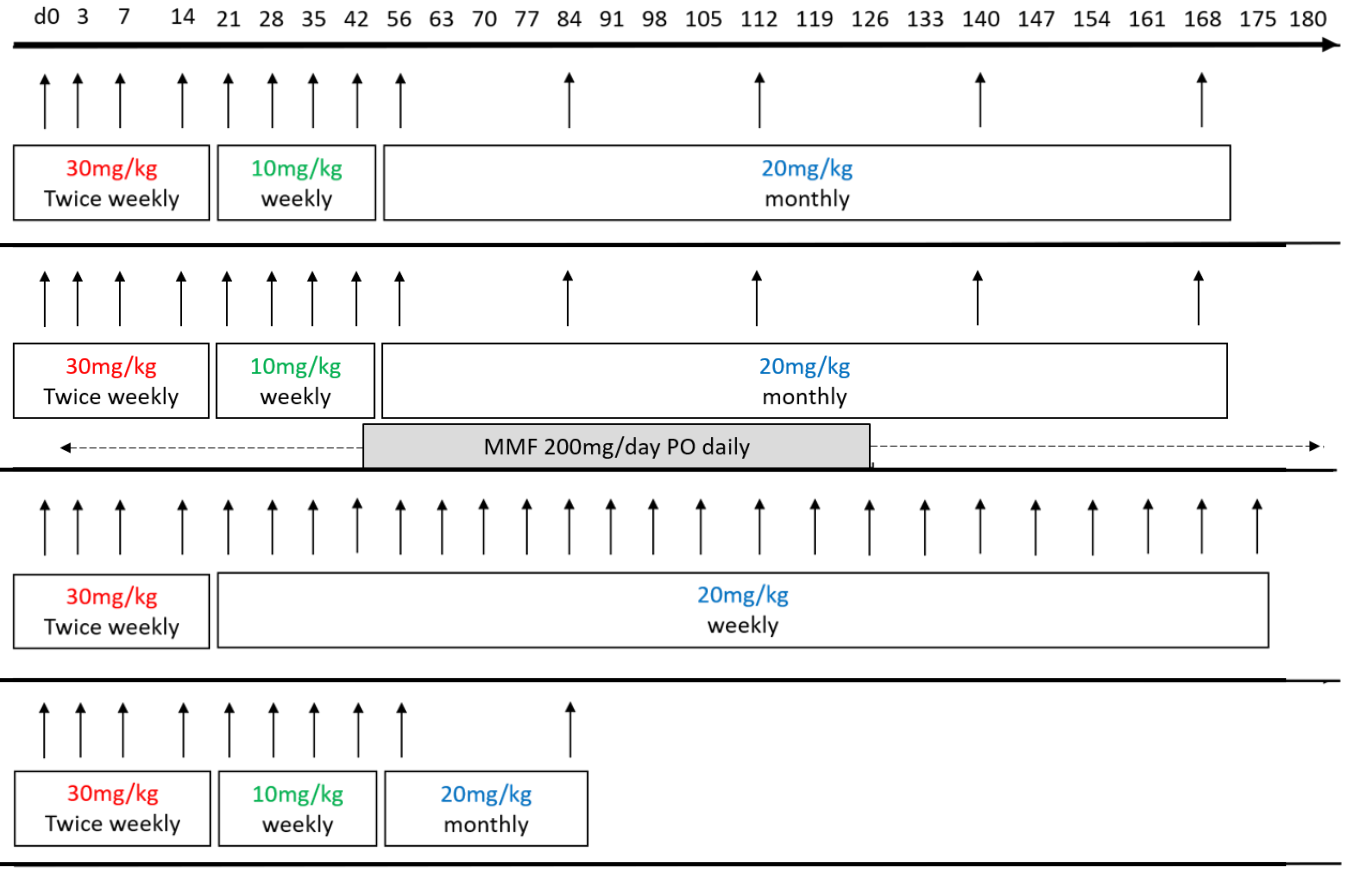
Heterotopic abdominal allo-heart Tx



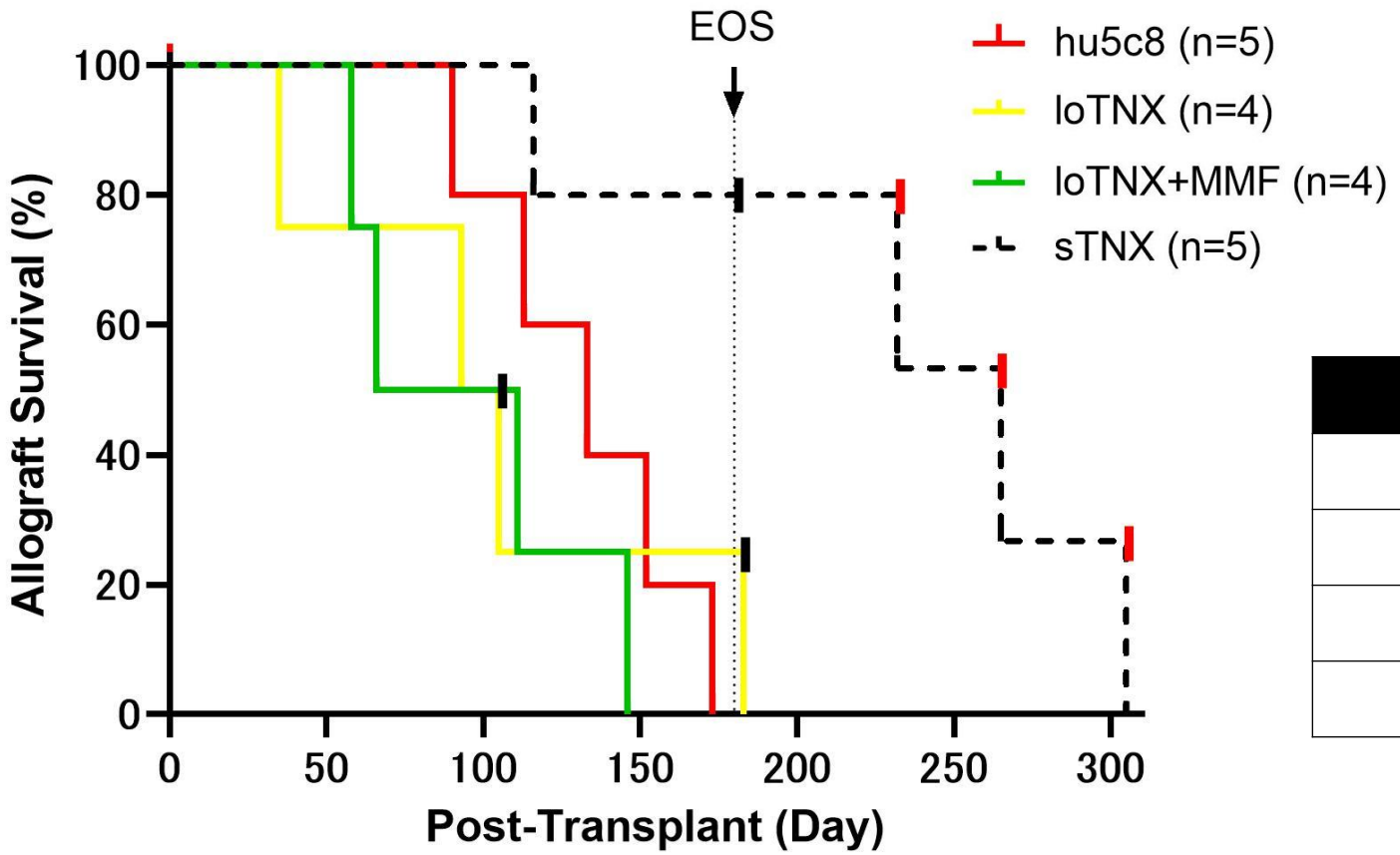
Protocol biopsies : POD 45 and 90

EOS : POD 180

Treatment Group



Results-1 Allograft Survival



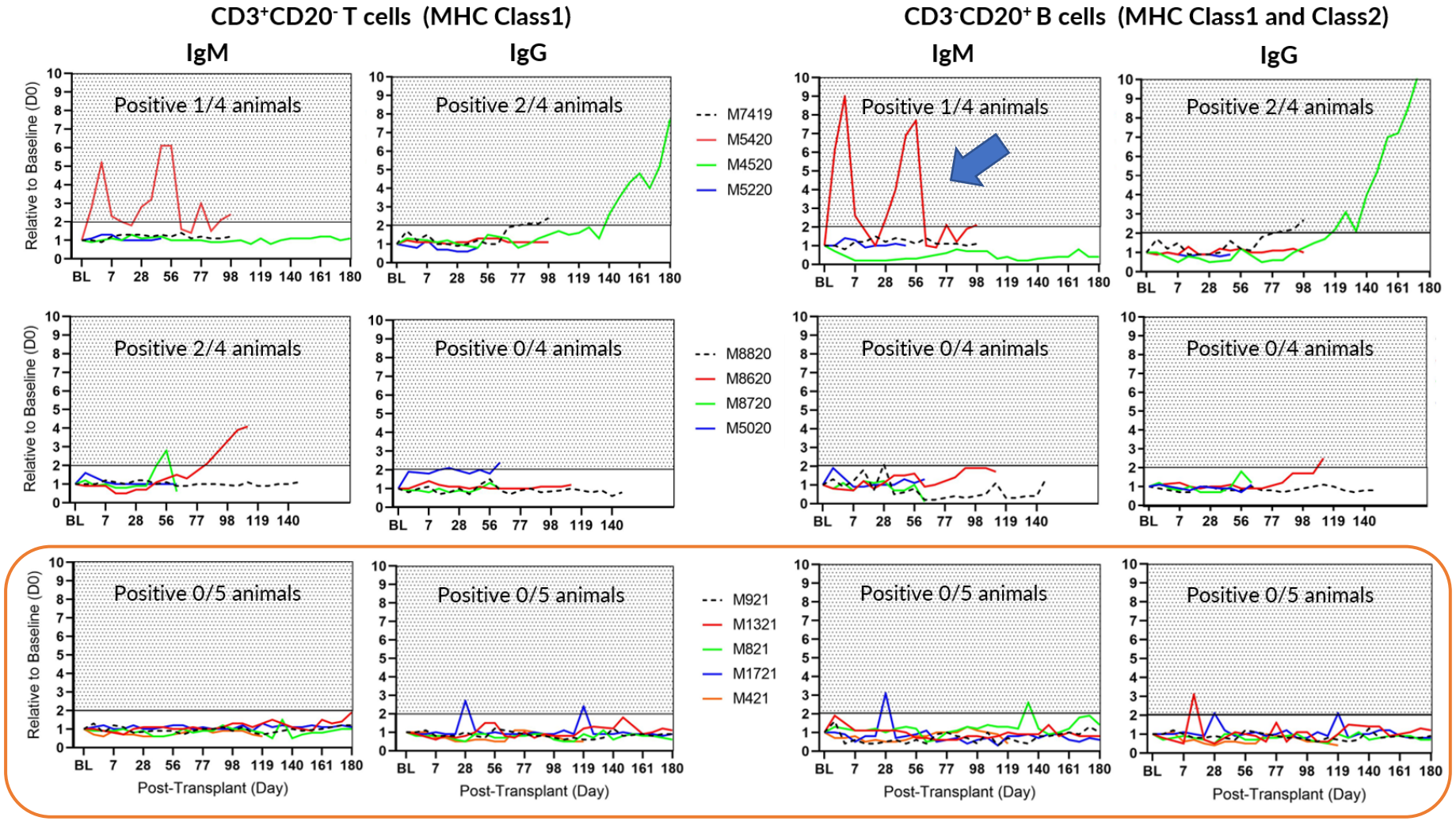
Explant of beating graft

Rejection after cessation of sTNX treatment

Treatment Group	MST (range)
hu5c8	133 days (90-173)
loTNX	99 days (35-183)
loTNX + MMF	88 days (58-146)
sTNX	>265 days (116-305)

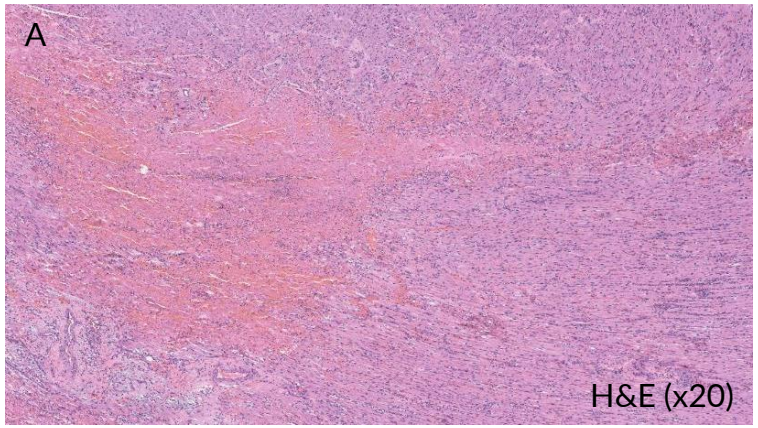
P<0.05 for all comparisons against sTNX

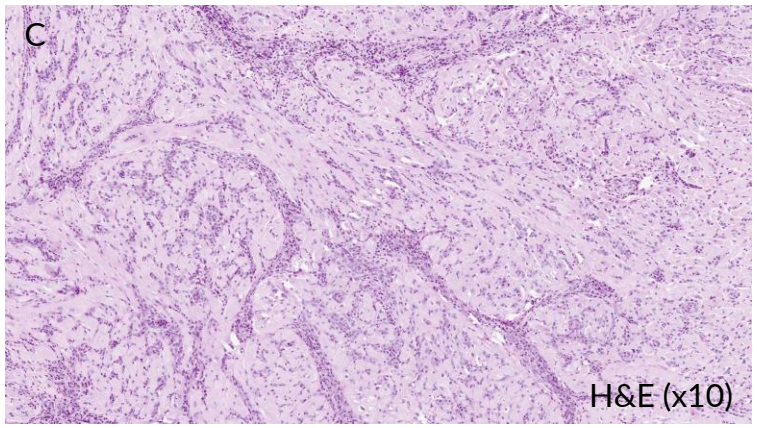
Results-2 Anti-donor-alloantibody elaboration

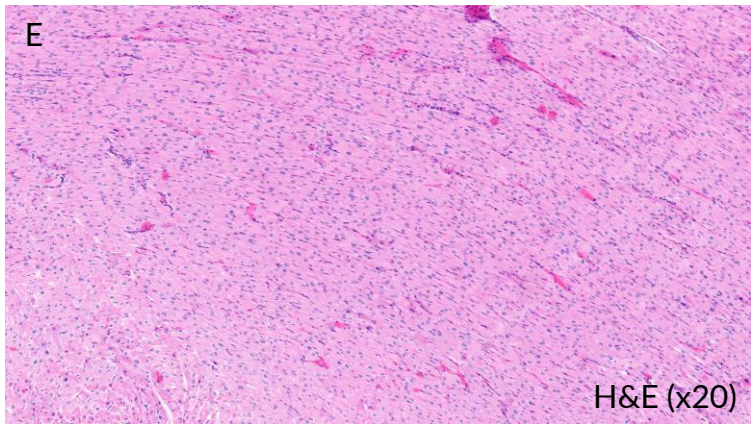


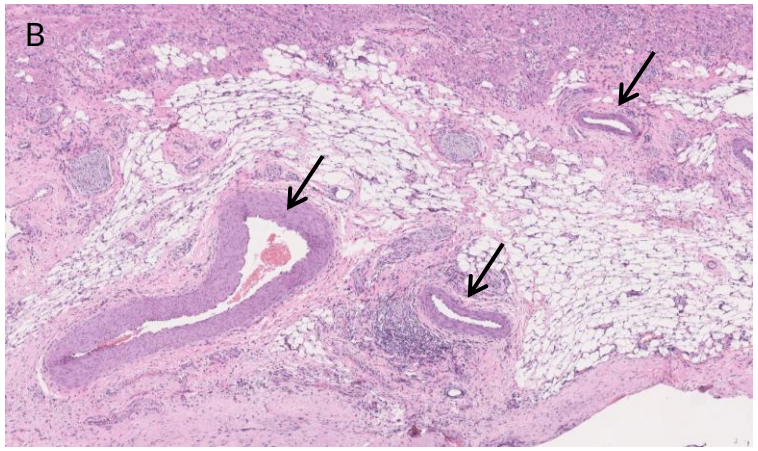
Results-3 Representative cardiac pathology at explant

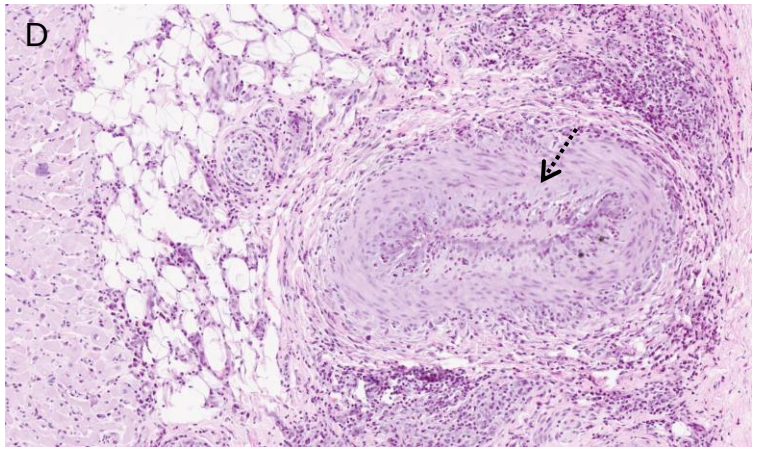
LoTNX monotherapy | **LoTNX + MMF** | **sTNX monotherapy**

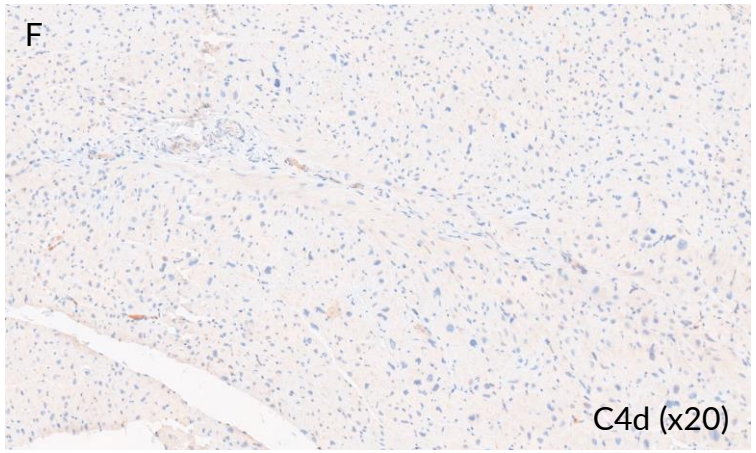








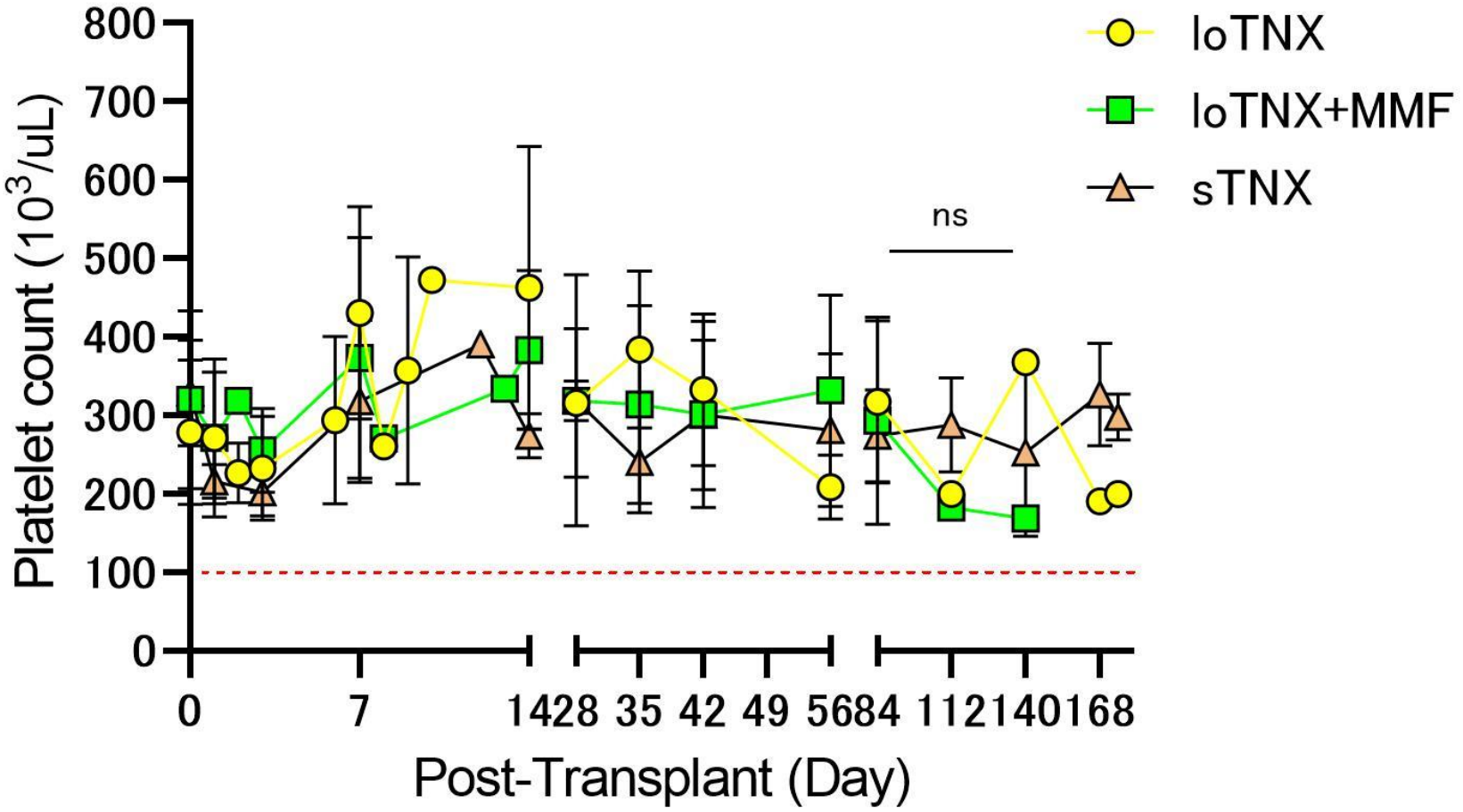




Day 93 | **Day 111** | **Day 181**

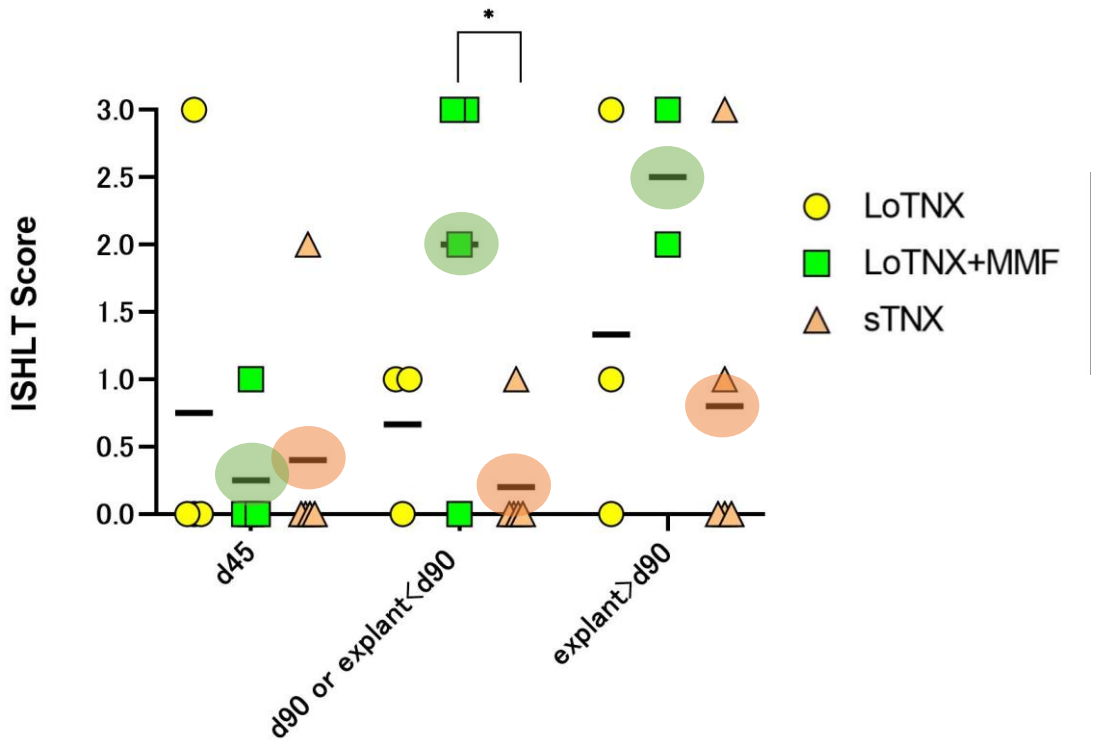
Results-4 Platelet counts

No thromboembolic complications were observed.

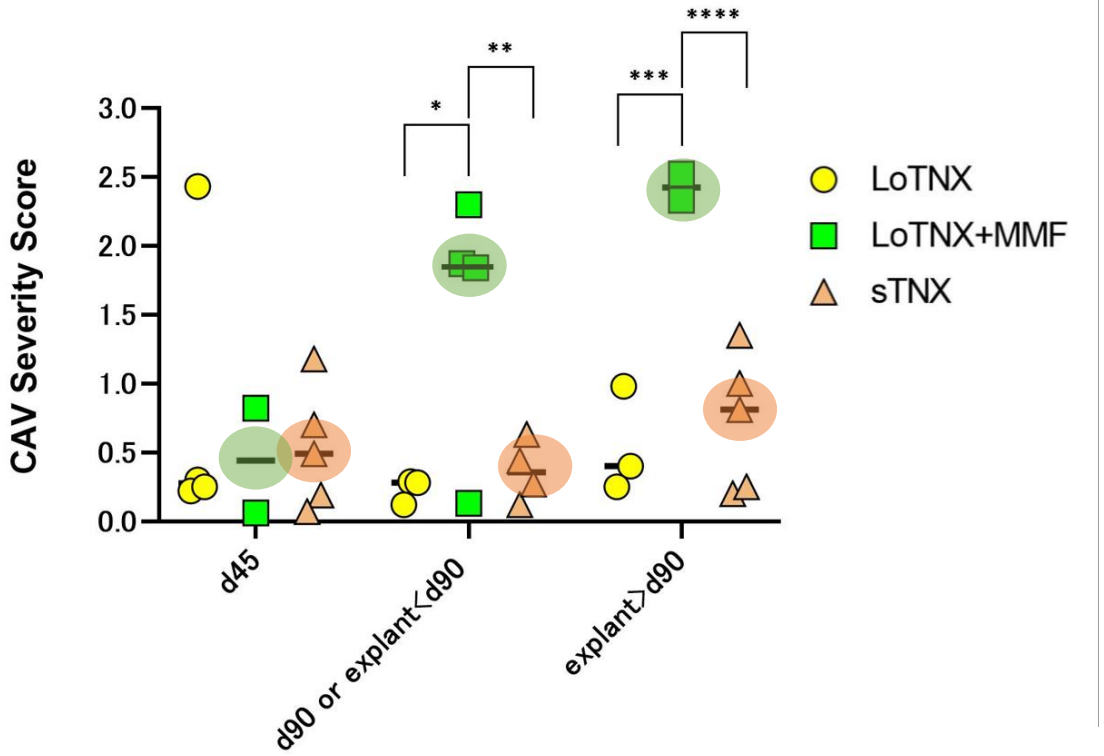


Results-5

ISHLT scores



CAV severity scores



Conclusion

- Blockade of CD154 with TNX-1500 monotherapy consistently and safely prevented pathologic alloimmunity in a NHP cardiac allograft model at least as effectively as hu5c8 monotherapy, without clinical thrombotic events.

- "Standard-dose" TNX-1500 regimen was associated with prolonged allograft survival relative to "low-dose" maintenance regimen, with or without MMF, as supported by prevention of antidonor alloAb elaboration, reduced ISHLT and CAV severity scores.