THE SCIENCE OF TOMORROW STARTS TODAY

AMERICAN TRANSPLANT CONGRESS ATC20222 JUNE 4–8, 2022 / BOSTON, MA JOHN B. HYNES CONVENTION CENTER

atcmeeting.org / #ATC2022Boston

atcmeeting.org

Financial Disclosures

• Funding is provided for these studies via NIH Grants and Tonix Pharmaceuticals Inc.



Long-term rejection free renal allograft survival with Fc-modified anti-CD154 antibody monotherapy in nonhuman primates.

Grace Lassiter, Takayuki Hirose, Ashley D'Attilio, Ryo Otsuka, Ahmad Karadagi, Toshihide Tomosugi, Tatsuo Kawai



CENTER FOR TRANSPLANTATION SCIENCES

atcmeeting.org

Background

- Current immunosuppressive regimens have significant side effects
 - Nephrotoxicity
 - Steroid induced diabetes
 - Cytopenia
 - Increased risk of infection
 - etc...
- Belatacept is currently the only FDA approved costimulatory blockade alternative to calcineurin inhibitors.
 - Higher rate of acute cellular rejection compared to conventional immunosuppression

atcmeeting.org

aCD154 / CD40L



- In 1999 Allan Kirk et al. tested a novel monoclonal antibody blocking the costimulatory signal in nonhuman primates (hu5c8 aCD154)
- This therapy progressed to a phase IIb clinical trial but was halted due to increased incidence of thromboembolic events



CD154 mAb-sCD154 immune complex can activate platelets



Selectively Modified Anti-CD40L Ab

- To date, there has not been a fully human or humanized aCD154 antibody that can effectively prevent transplant rejections, inflammatory conditions or autoimmune conditions with an acceptable level of side effects
- Tonix Pharmaceuticals Inc. has developed an Fc-Modified aCD154 with low binding to FcγRIIa (TNX-1500)

atcmeeting.org

Twelve Transplants have been Completed & Compared with Historical Results





Group A Immunosuppressive Regimen



Group B Immunosuppressive Regimen





atcmeeting.org

Conventional Immunosuppressive Regimen





Kidney Transplant

Methylprednisolone 1mg IM Daily

Mycophenolate Mofetil 100mg PO BID (25mg/kg)

Tacrolimus 0.1mg/kg IM daily (titrated)



atcmeeting.org

No Immunosuppressive Regimen







Renal Allograft Survival



- --- Group A (n=6)
- Group B (n=6)
- Conventional I.S. (n=20)

atcmeeting.org

--- No I.S. (n=4)



atcmeeting.org



Group A NHP (1) biopsy at day 180 post transplant C4d negative



Group A NHP (2) biopsy at day 169 post transplant C4d negative

- No increased incidence of thrombosis seen
- No other evidence of end organ damage noted on Necropsy



Group	TNX-1500	MMF	Тас	Pred	Renal allograft survival (days)
A	weekly	-	-	-	>180,>180, >180, >180, >160, 28
В	weekly for 6 weeks, followed by every 2 weeks	daily	-	-	>180, >167, >125, 111, 36, 48
Conventional I.S.	-	daily	daily	daily	>120, >120, >120, >120, >120, >120, >120, >120, >120, >120, >120, >120, 114, 106, 84, 69, 68, 65, 55, 43, 27
No I.S.	-	-	-	-	11,10, 9, 9, 8

Group	TNX-1500	MMF	Тас	Pred	Renal allograft survival (days)
Α	weekly	-	-	-	>180,>180, >180, >180, >159, 28 Rapid rejectors
В	weekly for 6 weeks, followed by every 2 weeks	daily	-	-	>180, >166, >124, 111, 36, 48
Conventional I.S.	-	daily	daily	daily	>120, >120, >120, >120, >120, >120, >120, >120, >120, >120, >120, >120, >120, 114, 106, 84, 69, 68, 65, 55, 43, 27
No I.S.	-	-	-	-	11,10, 9, 9, 8

TNX-1500 Levels



• Long term survivor

atcmeeting.org

Rapid Rejector

Conclusion

• Fc-Modified aCD154 is well tolerated and can be an effective alternative to conventional immunosuppression therapy in nonhuman primates.

- TNX-1500 in combination with MMF resulted in an increased rate of graft failure compared to monotherapy
- Optimal dosage remains to be defined

Questions?

Special Thanks to these wonderful people

Takayuki Hirose Ryo Otsuka Ahmad Karadagi Toshi Tomosugi Kohei Kinoshita Abbas Dehnadi Cindy Miller Jane O Franzi Pollok R.N. Pierson, III A.Benedict Cosimi Tatsuo Kawai

Knight Surgery Research Laboratory Jessica Burke Anet Calisir Nick Deluca Nelson Marquez Carvajal Eli Smith Michael Duggan

<u>MGH Pathology</u> Ivy Rosales Robert Colvin Catherine Stevens