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I have financial relationship with:
BioFire Diagnostics:
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My presentation includes discussion of an investigational product, FCR001.

Identification of a Unique and Mechanistic Urinary Cell mRNA Signature in Tolerant Kidney Transplant Recipients Conditioned with FCR001 Facilitating Cells

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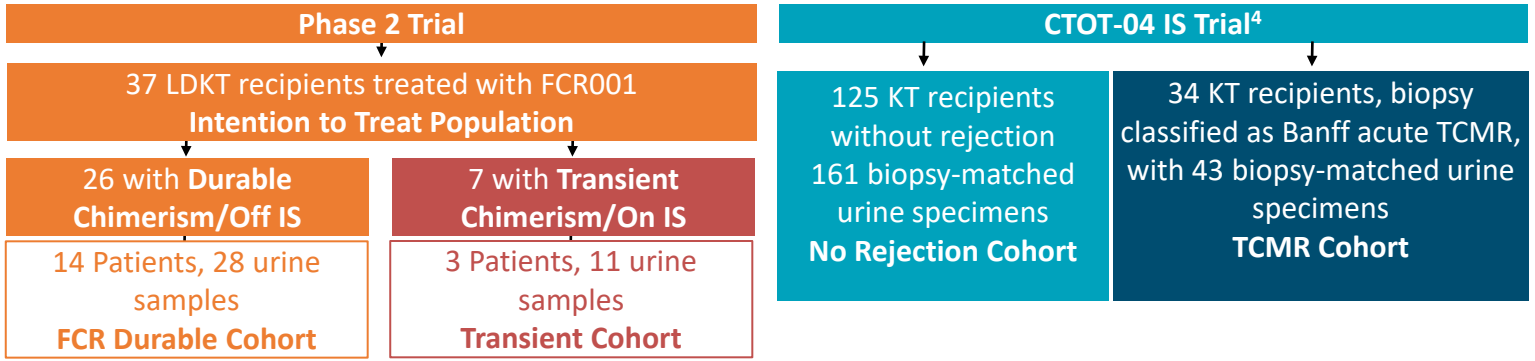
Transplant, Allogeneic Tolerance, and Chimerism

- The benefits of kidney transplantation (KT) for patients with end-stage kidney disease are tempered by the adverse effects of chronic immunosuppression (IS)[1]
- Alternative therapies that minimize or eliminate the need for IS are a high-priority unmet need
- Donor-specific transplant tolerance established by hematopoietic chimerism could prevent organ rejection without the use of lifelong IS
- FCR001 is an investigational allogeneic cell therapy derived from donor-mobilized peripheral blood cells that may induce chimerism and establish immune tolerance in highly HLA-mismatched donor-recipient pairs[2]
- An open-label, single-arm, phase 2 trial of FCR001 in 37 adult living donor kidney transplant (LDKT) patients treated with FCR001 found that durable chimerism was induced in 26 of 37 patients (70%) and allowed complete discontinuation of IS without any organ rejection for the duration of their follow-up (median of 6 years)[3]

1. Leventhal JR, et al. *Sci Transl Med*. 2012. 2. Leventhal et al. *Hum Immunol*. 2018. 3. Leventhal et al., 2021. American Transplant Congress. 21(suppl 3): Abstract 685.

Method and Objective

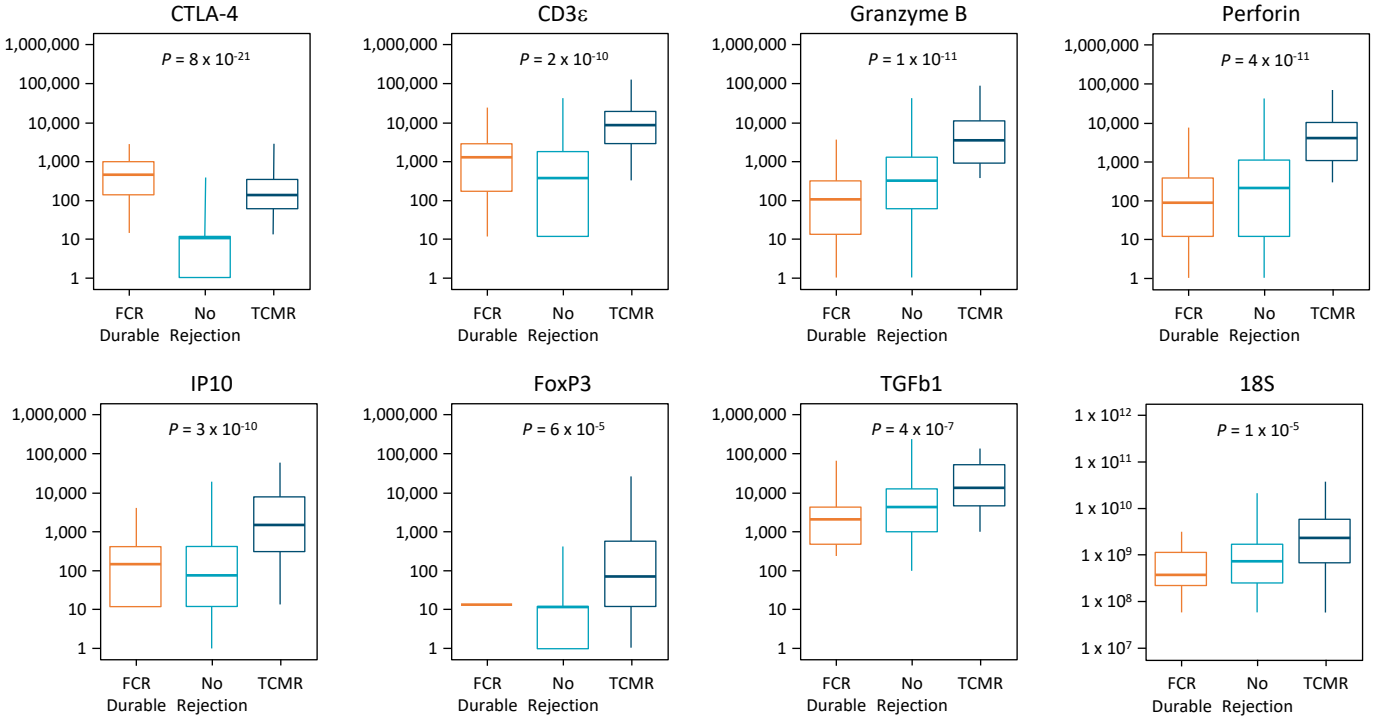
- We measured a hypothesis-based custom panel of urinary cell mRNAs in biopsy-matched urine specimens from a subgroup of patients in the Phase 2 FCR001 study (FCR Durable Cohort) and compared this panel to two standard-of-care cohorts from the Clinical Trials in Organ Transplantation-04 (CTOT-04)[1] study:



- The objective was to identify a urinary cell mRNA signature in tolerant KT recipients conditioned with FCR001 facilitating cells and correlate it with donor chimerism

4. Suthanthiran M, et al. *N Engl J Med*. 2013.

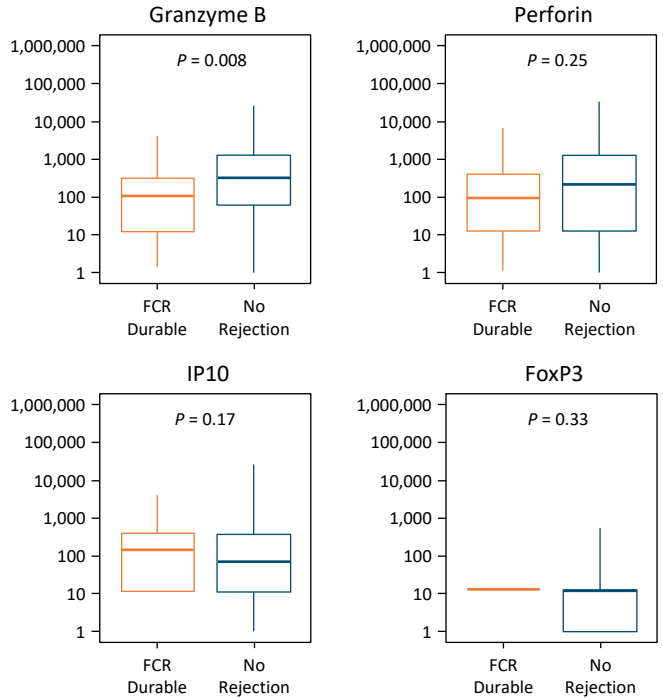
Contrasting Urinary Cell mRNA Profiles Between the FCR Durable Cohort and the CTOT-04 Cohorts



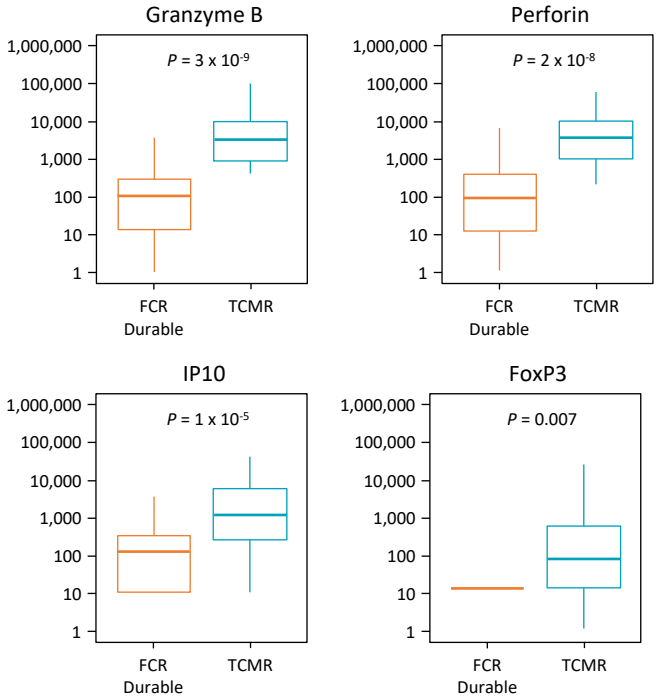
mRNA copy number per microgram of total RNA and 18S rRNA copy number per microgram of total RNA. *P*-values at the top of each box are based on Kruskal-Wallis test comparing the three cohorts, using mRNA copy numbers as the dependent variable.

FCR001 Patients Have a Quiescent Profile Compared to KT with TCMR

FCR Durable vs. No Rejection



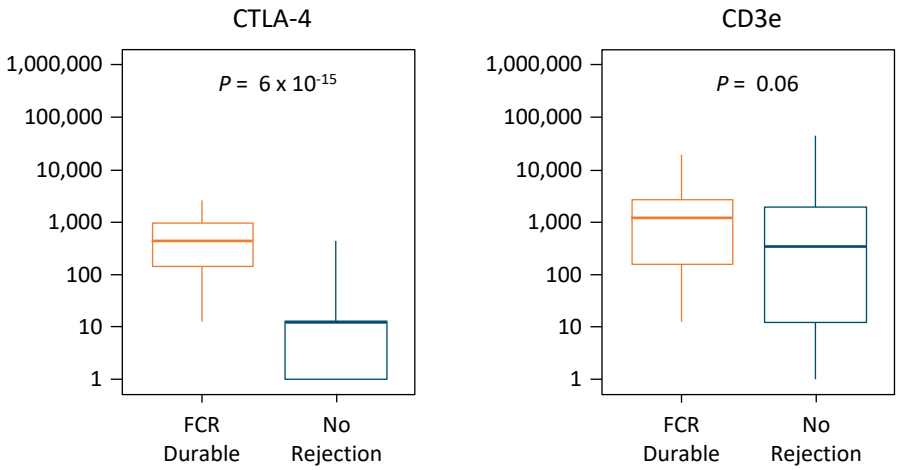
FCR Durable vs. TCMR



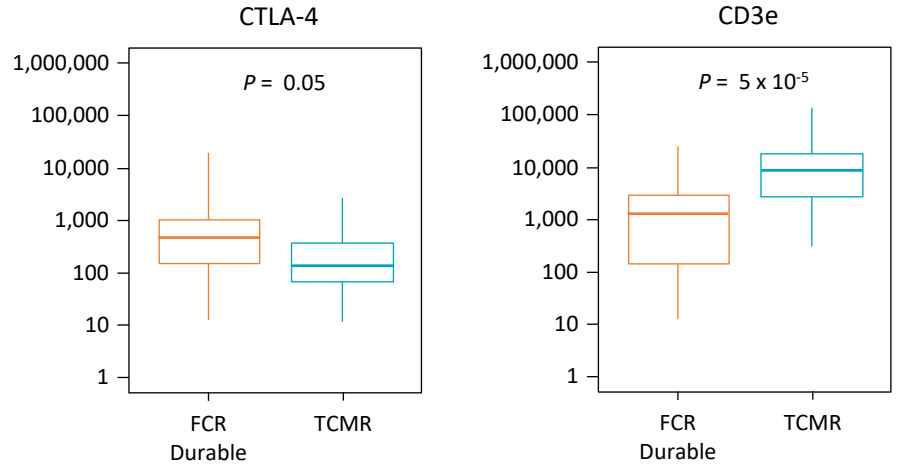
mRNA copy number per microgram of total RNA and 18S rRNA copy number per microgram of total RNA. *P*-values at the top of each box are based on Wilcoxon rank sum test comparing the two cohorts, using mRNA copy numbers as the dependent variable.

Urinary Cell mRNA Profiles from FCR001 Durable Patients Have a Unique CTLA-4 mRNA Signature

FCR Durable vs. No Rejection



FCR Durable vs. TCMR

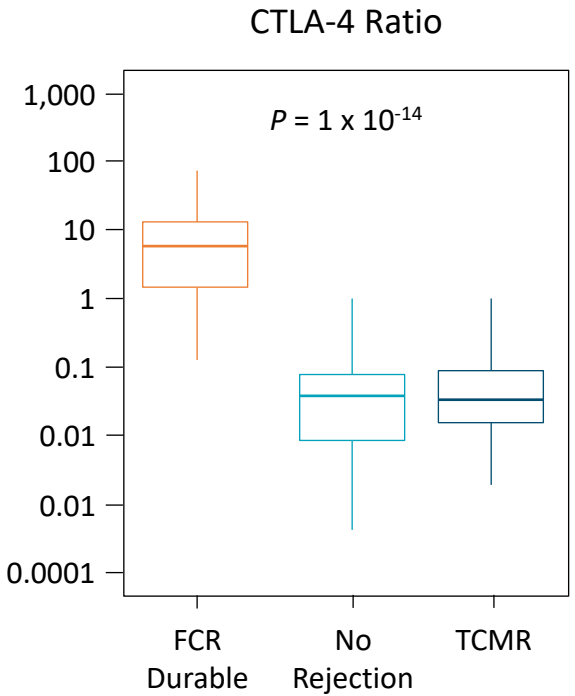


- CTLA-4 urinary mRNA in the FCR Durable Group was significantly higher than in the No Rejection Group and the TCMR Group

mRNA copy number per microgram of total RNA and 18S rRNA copy number per microgram of total RNA. *P*-values at the top of each box are based on Wilcoxon rank sum test comparing the two cohorts, using mRNA copy numbers as the dependent variable.

Significantly Higher Ratio of CTLA-4 mRNA to Granzyme B mRNA in the FCR001 Durable Patients

- The ratio of CTLA-4 mRNA to granzyme B mRNA was significantly higher in the FCR Durable Cohort than the TCMR Cohort and the No Rejection Cohort (Kruskal Wallis $P = 1 \times 10^{-14}$). Pair-wise comparison showed that the ratio was higher in the FCR Durable Cohort than the TCMR Cohort (5.62 vs 0.03, $P = 6 \times 10^{-16}$, Wilcoxon rank sum test) and the ratio in the FCR Durable Cohort was also higher than in the No Rejection Cohort (5.62 vs 0.04, $P = 7 \times 10^{-15}$)



Conclusions

- We have identified a unique and mechanistic urinary cell mRNA signature that is consistent with immune quiescence, defined by the ratio of CTLA-4 to granzyme B mRNA in tolerant kidney allograft recipients
- Urinary cell levels of several other mRNAs did not differ between FCR001 treatment and the No Rejection Cohort and were significantly lower than the levels in the TCMR cohort
- This signature may help to identify FCR001 patients who could safely discontinue chronic immunosuppression