Tutivia Molecular Risk Scores In Relation To BK Viral Activity, BK Virus Nephropathy, And Rejection Phenotypes In Kidney Transplant Recipients

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Abstract D099

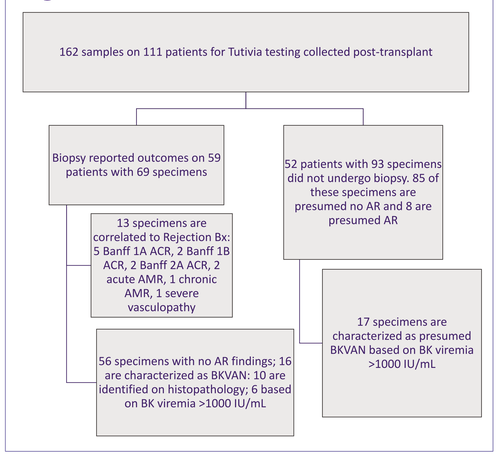
Background

To characterize Tutivia molecular risk-score pattern across BK viral activity (viremia and viruria), biopsy-proven and presumed BK virus nephropathy (BKVAN), and rejection phenotypes including antibody- and cell-mediated rejection in Kidney Transplant Recipients (KTR).

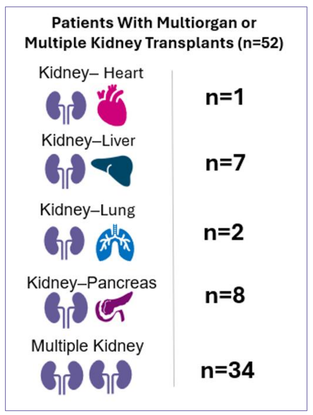
Methods

The Tutivia test for risk of rejection in KTR has been previously described in a validation study[1]. We retrospectively studied all KTR who had Tutivia test done at our center. There were 162 tests from 111 patients, and specimens were characterized as biopsy-proven rejection, BKVAN or no-rejection; or presumed no rejection when no biopsy is available with stable creatinine, or presumed BKVAN with BK viremia > 1,000 IU/mL, Figure 1.

Figure 1: Consort Chart



The cohort included 52 patients who have undergone multiple transplants, including a SPK Transplant with previous failed Kidney and 34 with 1 or more previous failed kidney transplants.



Results

Tutivia performance in 69 samples with biopsy-proven outcomes results in an AUC of 0.82 (Fig. 2, Panels A, B), an accuracy of 85% and hazard ratio for ACR of 12.5 (2.73-57.3) (Table 1). In 162 samples with either biopsy-proven or presumed outcomes, an AUC of 0.76 (Fig. 2, Panels D, E), an accuracy of 83% and a HR of 6.94 (2.57-18.79) (Table 1). The subset of patients with multiple transplants had similar Tutivia test performance (Panels C, F).

Figure 2

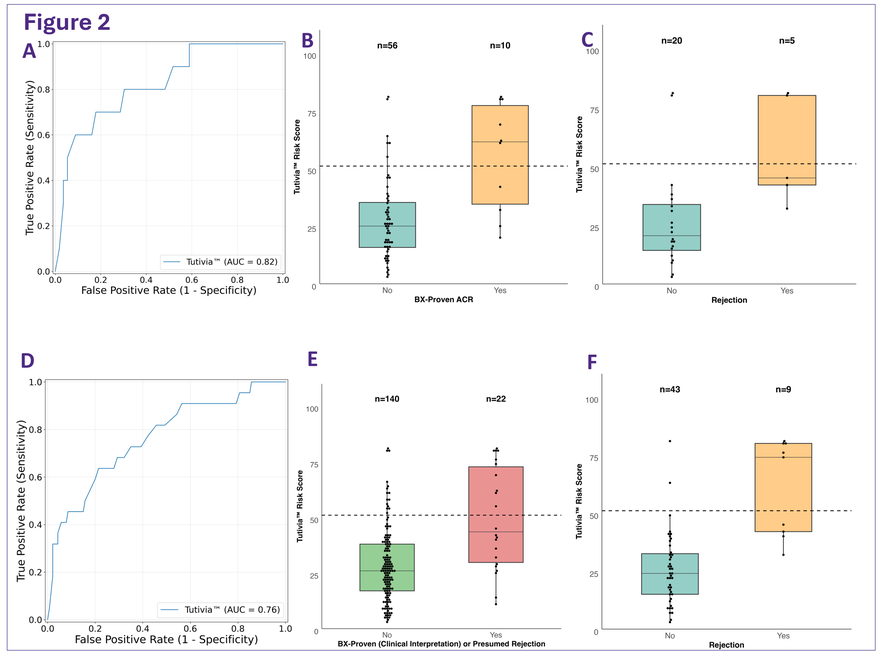


Table 1

Rejection	PPV	NPV	Sensitivity	Specificity	Accuracy	HR
Bx-proven (Pathologist)	0.5	0.877	0.462	0.893	0.812	7.143 (1.8-28.4)
Bx-proven (Clinician)	0.583	0.877	0.5	0.909	0.826	10 (2.5-40.3)
No Bx available (Presumed)	0.231	0.938	0.375	0.882	0.839	4.5 (0.93-21.76)
Bx-proven, otherwise presumed	0.4	0.912	0.455	0.893	0.833	6.944 (2.57-18.79)
Bx-proven ACR only	0.5	0.926	0.6	0.893	0.848	12.5 (2.73-57.3)

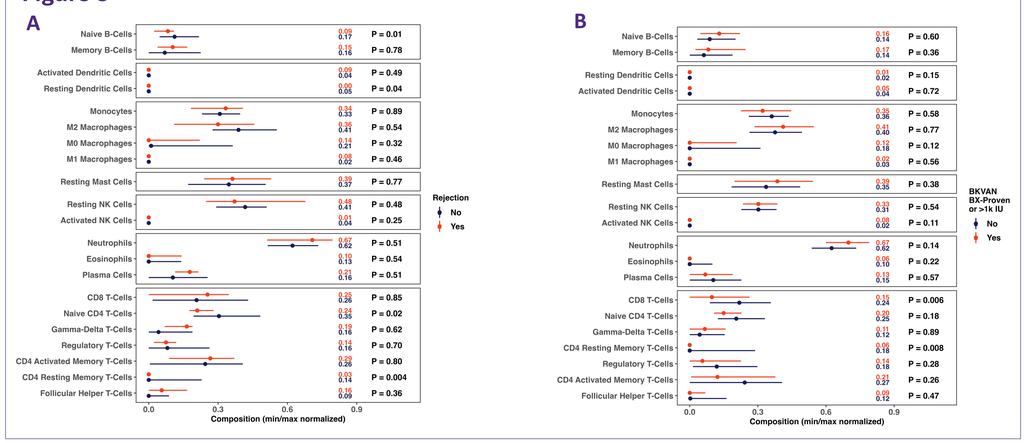
In 32 specimens from 22 patients with Bx-proven or presumed BKVAN and no rejection, 27 had low Tutivia score, resulting in a NPV of 96%. Independent sample t-test of Tutivia score vs BK viruria, BK viremia or BKVAN resulted in non-significant T statistics but significant in the case of any rejection status (Table 2).

Table 2

Category	Total	Yes	No	T statistic	P value
BK viremia any level	162	59	103	1.34584	0.180258
BKVAN Bx-proven or BKVL > 1000 IU/ml	162	33	129	0.388107	0.698453
BKVAN Bx-proven	69	12	57	0.263854	0.792702
BK viruria any level	161	81	80	1.791391	0.075133
Bx-proven (Pathologist: Rejection)	69	13	56	-3.865922	0.000253
No bx; Presumed Rejection	93	8	85	-2.511446	0.013788
Bx-proven (Clinician: Rejection)	69	14	55	-4.523975	0.000025
Bx-proven, otherwise presumed (Clinician: Rejection)	162	22	140	-5.161479	0.000001
Bx-proven (Pathologist: ACR only)	66	10	56	-4.280886	0.000064
Bx-proven (Pathologist: AMR only)	59	3	56	-0.520819	0.60451

Results contd.

Figure 3

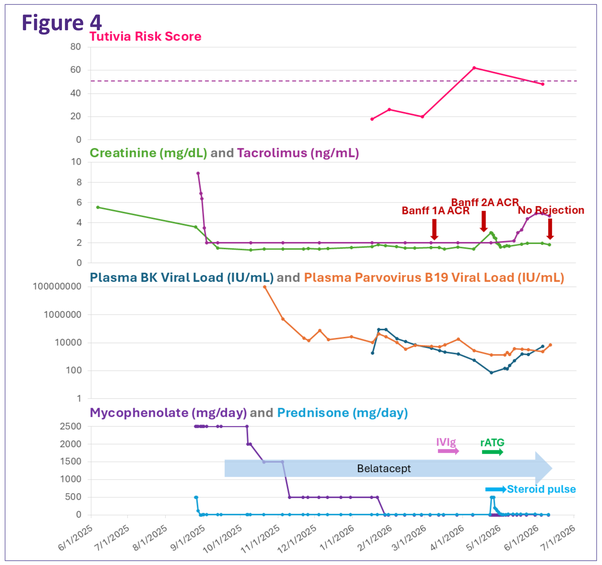


CIBERSORT deconvolution of RNA transcript data showed significantly low expression of naïve B, resting dendritic, naïve CD4 T and CD4 resting memory T cell-types in samples with rejection (Fig 3A), unlike samples with BKVAN, which showed low expression of CD8 T cell and CD4 resting memory T cell types (Fig 3B).

Serial Tutivia Monitoring

Patients with high BK viremia and BKVAN on biopsy had multiple Tutivia measures over the course of IS adjustment for BK. In this illustrated case, patient also had Parvovirus B19 viremia, aplastic anemia and BKVAN (Fig 4). This case demonstrates consistently low-risk Tutivia changing to high-risk with occurrence of ACR and reverting back to low-risk with resolution of ACR.

Figure 4



Conclusions

Tutivia, a novel gene expression-based biomarker test of rejection in kidney transplant recipients performs, in the real-world, similar to that reported in the validation study (1). Tutivia scores were not affected by BK viral replication. Furthermore, recipients with BKVAN or at risk thereof had low-risk Tutivia scores consistently. Tutivia test NPV of 96% for rejection in these patients will aid clinicians in decisions regarding performing a biopsy to rule out underlying rejection and managing BK infection by progressively lowering immunosuppression with confidence, guided by serial Tutivia monitoring.

Reference

(1) Bestard O, et al. Am J Transplant. 2024; 24(3):436-447.