CONVERSION TO EVEROLIMUS IN KIDNEY TRANSPLANT RECIPIENTS: OUR EXPERIENCE IN HOSPITAL KUALA LUMPUR

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Introduction

Standard immunosuppressive therapy post kidney transplantation includes steroids, calcineurin inhibitor (CNI) and mycophenolate acid.[1] Mammalian target of rapamycin (mTOR) inhibitor, Everolimus (EVR) is a viable alternative. This study aims to analyse the baseline characteristic and reason for conversion to EVR in Hospital Kuala Lumpur (HKL).

Methodology

This retrospective registry-based study includes all kidney transplant recipients in HKL who are currently on EVR. Descriptive statistical study was carried out using *SPSS* 28.0 software.

Results

57 recipients are currently on EVR. **Table 1** summarizes our patients' baseline demographics and clinical characteristics. Most are female (n=30, 52.6%) with a mean age of 43.98 ± 12.86 years. Almost all (n=55, 96.5%) were converted from the conventional regime. Most (n=29, 50.8%) had dialysis vintage of less than 5 years. Majority underwent living related transplantation locally (n=37, 64.9%) while 12 (21.1%) had cadaveric transplantation locally and 8 (14.0%) were transplanted overseas. Most did not have diabetes before transplantation (n=52, 91.2%) but 49.1% (n=28) had hypertension. Common aetiology for renal failure includes IgA nephropathy (n=10, 17.5%), hypertension (n=7, 12.3%) and focal segmental glomerulosclerosis (n=7, 12.3%). Definitive diagnosis was not possible in 23 (40.4%) patients.

46 (80.7%) recipients received mycophenolate and tacrolimus combination prior to conversion. Mean duration from transplant to conversion was 48.8 ± 87.6 months. In 28 (49.1%) patients, it occurred in the first 6 months.

Reasons for conversion to EVR regimen included malignancy (n=16, 28.1%), Cytomegalovirus (CMV) infection (n=13, 22.8%) of whom 6 developed CMV disease, BK virus infection (n=12, 21.1%) of whom 7 had biopsy-proven BK nephropathy, and mycophenolate-related complications (n=5, 17.5%). (**Figure 1**)

Reported side effects include proteinuria (n=24, 42.1%) and oral ulcers (n=10, 17.5%). EVR had to be withheld in 2 patients. One had poor surgical wound healing while another had drug-induced pneumonitis.

Figure 1: Reasons for conversion to Everolimus, n (%)

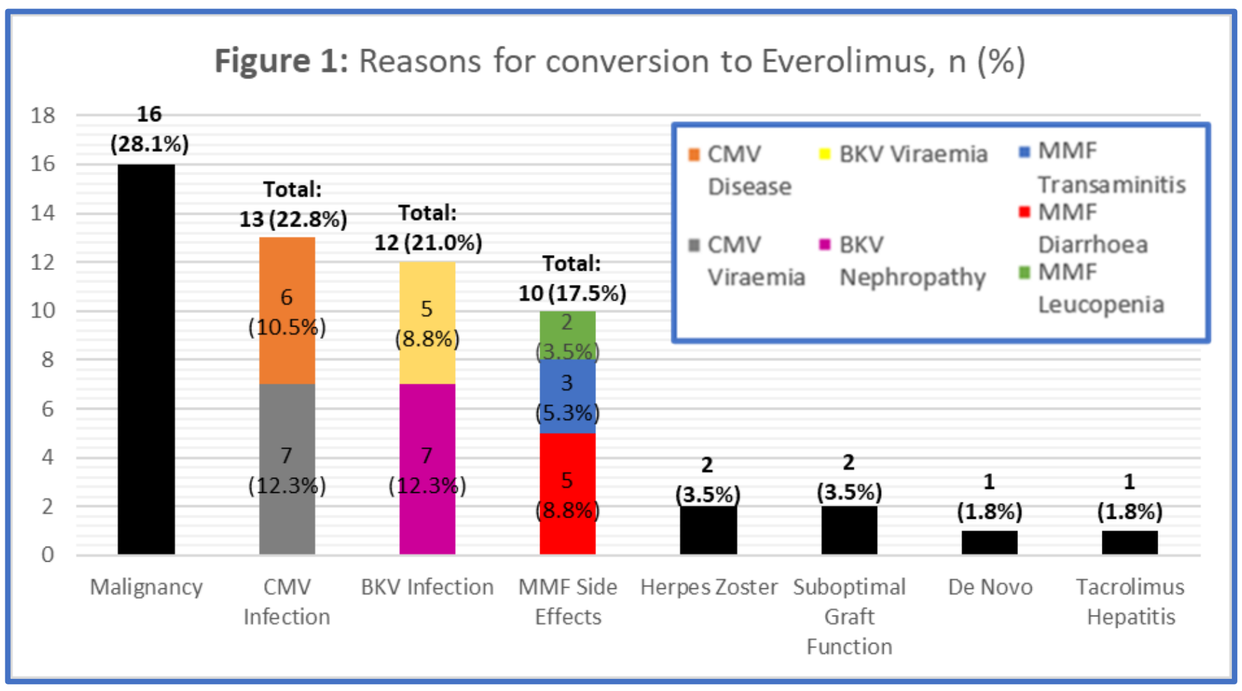

Table 1: Patient Demographics and Baseline Clinical Characteristics

	Parameters	N	%
Gender	Male	27	47.4%
	Female	30	52.6%
Ethnicity	Malay	29	50.9%
	Chinese	27	47.3%
	Indian	1	1.8%
Dialysis Vintage (years)	Pre-emptive	3	5.3%
	0 - < 5	29	50.8%
	5 - 10	3	5.3%
	> 10	10	17.5%
	Missing data	12	21.1%
Type of Transplant	Living-related	37	64.9%
	Local Cadaveric	12	21.1%
	Overseas	8	14.0%
Pre-morbids	Diabetes Mellitus	5	8.8%
	Hypertension	28	49.1%
Primary Disease	IgA Nephropathy	10	17.5%
	Hypertensive Nephrosclerosis	7	12.2%
	Focal Segmental Glomerulosclerosis	7	12.2%
	Polycystic Kidney Disease	2	3.5%
	Alport Syndrome	2	3.5%
	Diabetic Kidney Disease	1	1.8%
	Good Pasture Syndrome	1	1.8%
	Lupus Nephritis	2	3.5%
	Membranoproliferative Glomerulonephritis	1	1.8%
	Obstructive Uropathy	1	1.8%
	Unknown	23	40.4%

Discussion

The immunosuppressive combination most commonly used in *de novo* kidney transplantation includes a CNI (usually tacrolimus), a mycophenolic acid derivative and steroids.[1] Despite their success in preserving function of grafts, a significant number of patients succumb to cardiovascular disease, malignant neoplasms and infections.[2] Hence, mTOR inhibitor has been advocated as a viable alternative. It is a potent immunosuppressive agent which also inhibits vascular endothelial growth factor (VEGF) for anti-neoplastic and cardiovascular protective capabilities.[3] mTOR inhibitor is able to reduce viral infections as well due to an increase in the specificity of CD8+ T cells against viral pathogens such as CMV.[4]

Mouth ulcers result from direct toxicity of mTOR inhibitor on the oral and nasal mucous membranes.[5] The potentially most serious adverse effect associated with mTOR inhibitor is interstitial pneumonitis which is an immune-mediated process. Although clinical presentation varies from minimal symptoms to severe respiratory failure, the reported cases are generally mild to moderate in severity and subside after withdrawal of the drug.[6]

Conclusion

Most conversion to EVR regimen was due to viral infection and malignancy. Although side effects were common, most were mild. Only a small number of cases required cessation of EVR.

References

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