SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Center- and case-level variation in US liver transplant maintenance immunosuppression therapy: A national practice patterns analysis

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Introduction

Background

- Tolerance in liver transplant (LTx) is the most desirable outcome; however, it occurs in only 15% of transplants.
- Immunosuppression (Isx) management in LTx has evolved to include an increasingly diverse choice of medications.
- While informed by patient and donor characteristics, choice of Isx regimen varies widely across transplant programs.

Objectives

- To quantify the impact of program and case base factors in choice of maintenance Isx after LTx in the US.

Methods

Study design and sample

- Retrospective cohort study.
- We used a novel database integrating national registry and pharmacy fill records.
- 24,238 LTx recipients, 2008-2014, were reviewed.

Isx classification

- Group 1: Tac+MPA/AZA+Pred (reference triple therapy)
- Group 2: Tac with MPA/AZA
- Group 3: Tac alone, Tac+Pred
- Group 4: mTOR inhibitor based with or without CNI
- Group 5: Cyclosporine (CsA) based
- Group 6: Other

Statistical analyses

- Bi-level hierarchical models constructed to quantify impacts of program and clinical case factors on Isx choice.
- Compared different Isx regimens pairwise with triple Isx (tacrolimus, antimetabolite, steroids).
- Metrics of heterogeneity included intra-class correlation (ICC), ratio of cluster variance (program impact) to total observed variance, and median odds ratios (MOR).

Results

- In months 0-6, triple Isx was most common (42.9%) (**Fig. 1**) .
- In months 7-12, Isx was most commonly antimetabolite-sparing (35.2%) and steroid-sparing (25.6%), followed by triple Isx (13.5%), mTOR inhibitor- (11.9%), and CsA-based (9.3%) (**Fig. 2**).
- Use of all regimens varied widely across programs, from none to near-universal. (**Figs. 3, 4**).
- After adjustment for case factors, ICCs demonstrated that program effects explain substantial portions of variation, in steroid-sparing (23%), antimetabolite-sparing (26%), mTOR- (28%), and CsA-based (21%) use.
- Case factors explained <10% of variation (**Tables 1, 2**).
- Triple Isx in mo. 7-12 was more common among re-transplant recipients and those with prior acute rejection.
- Hepatocellular carcinoma (aOR 2.2, P<0.001), cancer within 6 mo. (aOR 6.38, P<0.001), and 6-mo eGFR <30 (aOR 2.0, P<0.001) were strongly associated mTOR use compared with triple Isx in months 7-12.
- Acute rejection predicted lower use of mTOR (aOR 0.72, P=0.003).

Fig 1. LTx maintenance Isx regimen distribution, 0-6 mo. posttransplant

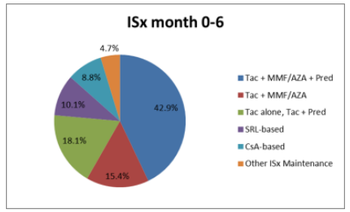

Fig 2. LTx maintenence Isx regimen distribution, 7-12 mo. posttransplant.

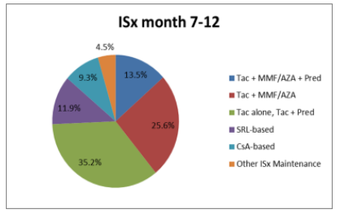

Figure 3. LTx maintenance Isx use across US programs, 0-6 mo. posttransplant

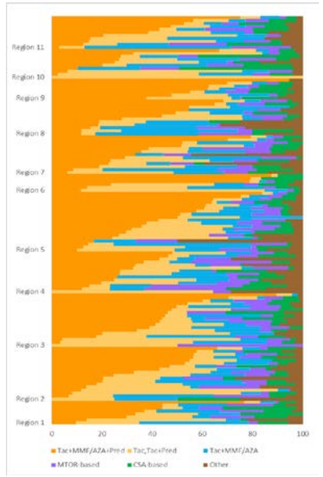

Figure 4. LTx maintenance Isx use across US Centers, 7-12 mo. posttransplant

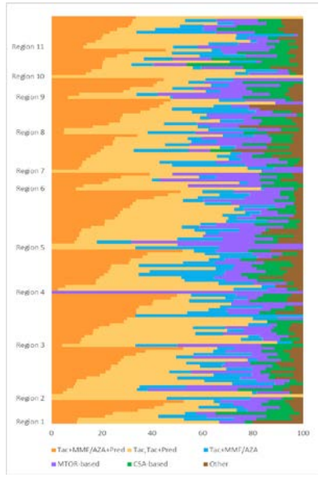

Table 1. Heterogeneity across unadjusted and both adjusted models, 0-6 mos.

ISx regimen 0-6 months (reference: Triple therapy)	Unadjusted ICC	MOR	Adjusted ICC	MOR	Pseudo-R^2
Tac+MMF/AZA	0.39	4.00	0.39	4.02	0.09
Tac alone,TAC+Pred	0.39	3.96	0.39	3.95	0.08
SRL-based	0.32	3.25	0.32	3.28	0.06
CsA-based	0.25	2.75	0.25	2.74	0.06
Other	0.26	2.78	0.27	2.85	0.04

Table 2. Heterogeneity across unadjusted and both adjusted models, 7-12 mos.

ISx regimen 7-12 months (reference: Triple therapy)	Unadjusted ICC	MOR	Adjusted ICC	MOR	Pseudo-R^2
Tac+MMF/AZA	0.19	2.31	0.23	2.56	0.06
Tac alone,TAC+Pred	0.24	2.61	0.26	2.76	0.07
SRL-based	0.27	2.87	0.28	2.98	0.10
CsA-based	0.19	2.28	0.21	2.42	0.09
Other	0.14	2.01	0.16	2.10	0.04

Conclusions

- LTx maintenance regimen varies widely across US transplant centers, and choice largely reflects program biases rather than patient characteristics or evidence of comparative efficacy.

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