Lifetime Cost-Effectiveness of Calcineurin Inhibitor-Free Immunosuppressive Treatment After De Novo Renal Transplantation

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INTRODUCTION

BACKGROUND

Although calcineurin inhibitors (CNIs) have been the mainstay of immunosuppressive regimens, CNIs present a trade off between short- and long-term outcomes.

New CNI-free regimens may maximize the likelihood of long-term graft and patient survival, the ultimate goal of transplantation.

OBJECTIVE

To examine the cost-effectiveness of CNI-free regimens compared to a commonly prescribed CNI-containing immunosuppressive therapy in de novo renal transplant.

METHODS

Time horizon:	Life time
Perspective of analysis:	US payer
Type of model:	Decision-analytic model

Regimens compared:

1. Sirolimus (SRL) + Steroids (ST) + Cyclosporine (CsA) withdrawal = SRL + ST
2. SRL + mycophenolate mofetil (MMF) + ST
3. Tacrolimus (Tac) + MMF + ST

MODEL STRUCTURE

A decision tree was used to model the first year after renal transplantation (Figure 1) followed by annual Markov model cycles to model long-term outcomes (Figure 2).

Figure 1: Decision Tree Structure

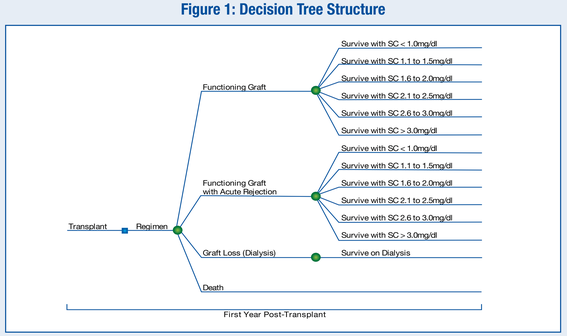
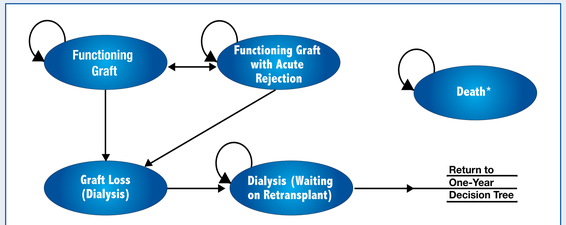


Figure 2: Markov Model Structure

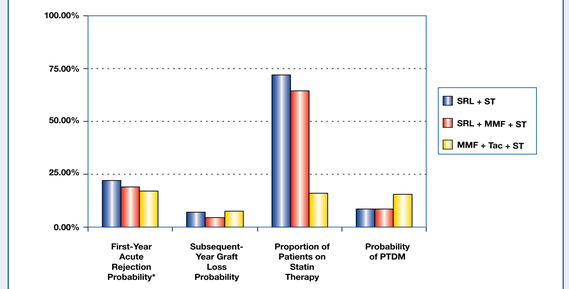


METHODS (CONTINUED)

- Average patient age was assumed to be 46 years of age.[11]
- The percentage of patients receiving transplants from each donor type (living donors, expanded criteria donors [ECD], and deceased non-ECD), the median waiting time for a second transplant, and the annual probability of death by age, donor type, and for patients on dialysis were obtained from published reports[1,21] and literature.[24]
- The probability of acute rejection in the second year post-transplant is assumed to be 2.86%[15] then decline linearly until no acute rejections are experienced after model year 10 for all regimens.
- Mean serum creatinine and standard deviation values were extracted from the literature for each model comparator[5,7,13] and were used to predict graft loss for years 2 onward.[9]
- First year graft loss was assumed to be similar between all regimens at 8.6%.[1] Graft loss for patients having a second transplantation was increased by 9%.[21]
- Post transplant diabetes mellitus (PTDM) is assumed to impact the probability of graft loss,[8,17,22] the probability of death,[6] and average annual medical costs within the model.[23]
- The cost of generic statin therapy is incurred by patients reporting statin use.[5,7,13] Any increase in other medical risks and costs are assumed to be controlled through the use of statin therapy.
- Drug costs were calculated using average daily allowable consumption (DACON) values from secondary market research data and wholesale acquisition costs (WAC).[19]

MODEL INPUTS

Figure 3. First-Year Acute Rejection, Subsequent Year Graft Loss, and Post-Transplant Diabetes Mellitus (PTDM) Probabilities



* Adjusted for induction use and statistical significance using conservative assumptions
Sources: 2, 3, 5, 7, 9, 10, 13, 16, 23

Table 2. Health State Costs and Utility Values

Input Parameter	Health State Costs[12, 14, 18, 20, 25]	Health State Utilities[4]
Functioning Graft	$7,473	0.84
Functioning Graft with Acute Rejection	$36,936	0.84
Graft Loss (Dialysis)	$168,959	0.44
Dialysis (Waiting on Retransplant)	$47,855	0.44
Retransplantation	$75,379	--
Death (with Functioning Graft)	$87,563	0.00
Death (on Dialysis)	$64,634	0.00

Costs and utilities were discounted 3% per annum.

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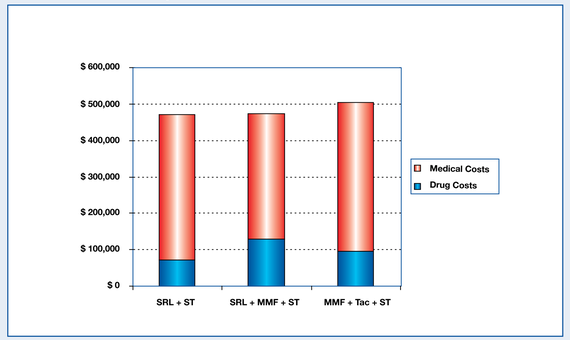
RESULTS

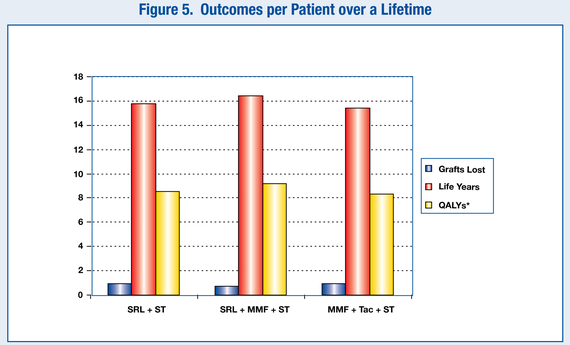
- Patients on SRL+MMF+ST incur higher drug costs than patients on MMF+Tac+ST; however, total costs are lower due to improved other medical costs.
- Patients on SRL+ST incur both lower drug costs and other medical costs than patients on MMF+Tac+ST.
- Patients on SRL+ST and SRL+MMF+ST have fewer grafts lost and greater life years and quality adjusted life-years (QALYs) than patients on MMF+Tac+ST.
- The two CNI free regimens, SRL+MMF+ST and SRL+ST are cost-saving strategies (more effective and less costly) compared with treating with MMF+Tac+ST.

Figure 4. Costs per Patient over a Lifetime



All costs are reported in 2005 US dollars.

Figure 5. Outcomes per Patient over a Lifetime



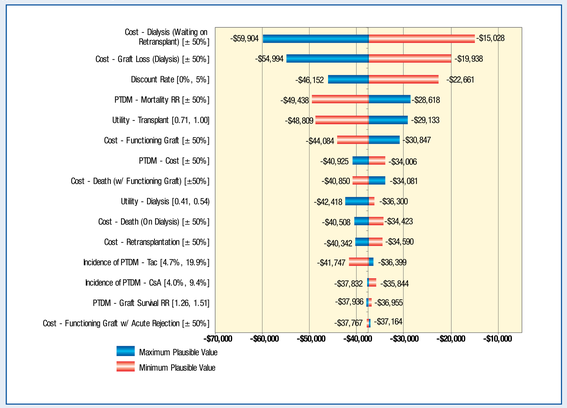
*QALY=Quality adjusted life years

SENSITIVITY ANALYSES

- One-way sensitivity analyses showed that results were sensitive to PTDM probabilities and costs, the discount rate, and health state utilities and costs. One example of a funnel chart is presented in Figure 6.
- Also, sensitivity analyses show that results are very sensitive to the link of serum creatinine to renal function. Debate exists as to whether this predicted renal function is similar for CNI-free regimens.

SENSITIVITY ANALYSES (CONTINUED)

Figure 6. Sensitivity of Model Parameters for SRL+MMF+ST



RR = relative risk; PTDM = post-transplant diabetes mellitus; CsA = cyclosporine; Tac = tacrolimus

CONCLUSIONS

- Using a cost-effectiveness framework to analyze lifetime benefits, treatment with CNI-free immunosuppressive therapies not only show their potential long-term clinical benefits, but are also expected to be cost-saving over the life of the patient compared to the most commonly prescribed therapy using a CNI.
- CNI-free regimens should be considered as options to maximize the lifetime patient benefits of renal transplantation.

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